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GEORGE MORRIS PIERSOL, M.D.

JOHN H. MUSSER, Jr., M.D.

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ORIGINAL ARTICLES

ON ABNORMALITIES OF THE ENDOCRINE FUNCTIONS OF THE GONADS IN THE MALE.

By Lewellys F. Barker, M.D.,
BALTIMORE.

Among the many new facts which have accumulated since the attention of clinicians has been especially directed toward the functions of the glands of internal secretion, none is more worthy of consideration, perhaps, than the evidence first convincingly presented by Bouin and Ancel (1903–1910) pointing to an endocrine function exercised by the interstitial cells of Leydig in the testicles, of fundamental significance for the morphological characters and biological phenomena of the male organism.

Through a long series of investigations (histological, embryological, comparative anatomical, clinical-pathological, and experimental physiological), well summarized in Biedl's treatise[1] and in the monograph of Tandler and Grosz[2] we now appear to be justified in thinking of the male sex-glands or gonads as divisible into at least two parts (1) a generative part proper, producing the sperm-cells, and (2) an internal secretory part (the interstitial cells of Leydig), producing the hormones upon which depend (*a*) the development of the genital tract in the embryo; (*b*) the development of what John Hunter designated the "secondary sexual

[1] Biedl (A), Innere Sekreton, II Aufl., 1913, Bd. ii, 199–343.

[2] Tandler, J. u. S. Grosz, Die biologische Grundlagen der sekundären Geschlechtscharaktere, Berlin, 1913, 1–169.

properties" of the male, namely, changes characteristic of the male, but "which take place only in parts that are neither essential to life nor generation, and which do not take place till toward the age of maturity," and, perhaps, (*c*) in part, the neural states associated with libido sexualis and potentia cœundi.

Time will not permit at this meeting of a full analysis of the evidence for this view, but the most convincing arguments in favor of it are based on:

1. The histological resemblance of the Leydig cells (though mesodermal in origin) to the cells of a secreting gland (*Regaud* and *Policard, Loisel, Bouin* and *Ancel*).

2. The observation that in man and in animals cryptorchid testicles are not only dystopic, but smaller than normal, the small size being due to faulty development of the seminiferous tubules, rather than to absence of the interstitial cells of Leydig. Bilateral cryptorchidism is associated with sterility, but not necessarily with loss of male sexual characters, nor with loss of libido. The masculinity of cryptorchids is in direct proportion to the amount of interstitial gland present and independent of the state of the germinative part. In unilateral cryptorchidism, the individual is not sterile, but if the healthy testicle be removed he becomes so, though the masculine appearance and libido are retained as long as the cryptorchid testicle is not removed; if the latter be taken out also, libido disappears and the "masculinity" of the individual definitely recedes.[3] In a few cryptorchids, the interstitial gland is not well developed and hypogenitalism exists; the individuals then resemble eunuchs and are known as "eunuchoids" (*Griffith, Duckworth*).

3. The observations on human males castrated in early life (eunuchs), especially those of Pelikan and of Tandler and Grosz upon the religious sect known as the Skopsi, who practice the horrible rite of self-mutilation. These observations showed the relations of the gonads (as a whole) to the rest of the body. Eunuchs owing to the lack of the internal secretion of the gonads (agenitalism) grow fat, and the fat exhibits a peculiar regional disposition; the larynx and pelvis remain infantile; there is faulty development of the beard; the extremities grow longer than normal; the muscles are hypotonic; the masculine attributes of the psyche are absent—eunuchs are mentally torpid, lack initiative and aggressiveness; they move more slowly and more clumsily than normal males.

4. The observations on experimental animals in which:

(*a*) The vasa deferentia are ligatured (histologically and symptomatically reproducing conditions like those met with in cryptorchism).

[3] Veterinarians have made a careful study of these conditions in stallions; the experiments on the animal described by Whitehead (1908) are especially illuminating.

(*b*) The spermatic cords are ligatured as a whole on each side symptomatically, reproducing conditions like those met with in total castration.

(*c*) The spermatogenic tissue is electively destroyed by exposure to the *x*-rays, while the interstitial cells of Leydig are uninjured. (Genital organs remain otherwise intact; sexual impulse persists; secondary sexual characters remain unchanged.)

(*d*) Castration is done in different animals at different ages (*Steinach, Foá, Nussbaum, Sellheim, Rörig*) combined, sometimes, with transplantation experiments.

5. The observations on animals which exhibit outspoken rutting periods. The behavior of the testicle of the mole (*Talpa europea*) is especially striking; the germinative part is best developed at the rutting period at which time (March) the interstitial gland is smallest; subsequently, the generative part diminishes in size and the interstitial gland hypertrophies to a maximum in July, August, and September. A month or two before rutting the generative part has again become markedly developed, and the interstitial gland has begun distinctly to diminish in size. Thus it would appear that the great development of the interstitial gland is a necessary preparation for the coming spermatogenesis (*Regaud, Lécaillen, Tandler and Grosz*).

6. The observations on premature sex-development in animals and in man. This is physiological in certain varieties of animals known to breeders; in such races of animals, besides the early sexual maturity, there are a number of associated morphological changes (early closure of epiphyses; short extremities with long trunk; early and complete development of external genitalia).

Pathologically early sexual maturity (*pubertas præcox*) has been repeatedly met with in human beings, both male and female (*Haller, Kussmaul, Neurath*). Girls have been known to menstruate in the first year of life, boys to have seminal emissions in the second year of life. Along with these signs of puberty, the external genitalia enlarge, the axillary hair (*hirci*) and the hair on the mons veneris (*crines pubis*) appeared, the breasts enlarged (in girls) and the voice and psyche changed (in boys). The whole body matured early, but owing to the early closure of the epiphyses (*x*-ray), the individuals had relatively short extremities in proportion to the trunks. It is probable that in such cases a hyperactivity of the internal secretion of the gonads—a so-called "hypergenitalismus"—existed, though this in turn seems to have been stimulated by pathological changes in other endocrine glands (tumors of the epiphysis cerebri; tumors of the inter-renal system or cortex of the adrenal gland).

During the past winter I have had the opportunity of studying a number of patients in whom symptoms existed suggestive of disturbances of the function of the gonads. From the records of these I am selecting two examples: one of them is a eunuchoid

with loss of both the germinative and the internal secretory function (hypogenitalism); the other is a dwarf manifesting partial cryptorchidism with loss of the germinative function and increase of the endocrine function of the gonads (hypergenitalism).

CASE I.—*Eunuchoid, showing signs of hypogenitalism and of dyshypophysism.*

William Z., white, male, aged forty-three years, boiler-maker. Admitted February 7, 1914.

Complaint. General weakness.

Family history. Father died at eighty-six; was 5 feet 10 inches tall, weighed 250 pounds. Mother died at sixty-five, cancer; medium height; never very stout. One brother, forty-four, unmarried; tall and slim. One brother, thirty-five, married; normal; two children. One brother dead, accident; had one child. One brother died at twelve; born an idiot; had a long head which came to a point in the mid-line; had epileptic fits from birth to death; probably hydrocephalic. No history of tuberculosis in family. Father drank moderately of beer and wine, and smoked heavily.

Past History. In childhood had smallpox, followed by "weakness of the eyes." Scurvy at eighteen, when at sea. Typhoid fever at twenty-two. Lobar pneumonia on the left side at twenty-eight. Chills and fever, probably malaria, eight years ago. Seven years ago he had a compound fracture of the left tibia, followed by osteomyelitis, necessitating an operation. One year ago he had another operation for osteomyelitis of the right leg, six months after having been struck on the leg by a heavy wire cable. During the Boer War he was shot in the right leg.

For the past two or three years he has been subject to rather severe frontal and occipital headaches. His eyes have been "weak" since childhood. For several years he has had a chronic infection of the right middle ear, with almost total deafness on this side, and occasional purulent discharge. A polyp was removed from the nose eight years ago. He has had occasional attacks of sore throat. He states that he has had "fainting" and "giddy spells" for the past fifteen or twenty years. Nocturnal epistaxis occurred regularly every six months after the age of twenty-six. During late years these attacks have occurred every three months.

For several years he has had a cough shortly after eating, and this has often been followed by vomiting, a condition which he thinks is due to smoking. Along with this, his fainting spells have become more frequent.

Three years ago the patient had a sudden, stabbing pain in the left lumbar region lasting one-half hour. One week later he had a similar attack. These paroxysms were associated with some chills and fever, but not with hematuria.

For three years, between the ages of twenty-three and twenty-six, the patient, at regular intervals of six weeks, had hematuria.

This flow of blod was painless and lasted about six days. During these six days there was always coincident painful enlargement of the breasts, which was absent during the intervals between the periods of hematuria. After twenty-six the hematuria stopped and the patient had nocturnal epistaxis, occurring regularly every six months. During recent years the nocturnal epistaxis has occurred every three months.

He has never had sexual libido or potentia. He attempted sexual intercourse several times, after the age of nineteen, but the attempts were ineffectual because of inability to obtain an erection.

When cold he has occasional shooting pains in his right thigh, and the leg becomes numb for several days.

The patient is tall and reached his present height at the age of sixteen. In response to criticism by his companions of his feminine characteristics, he has made, he states, many efforts to do "manly work." He has always done hard, muscular work, has been a cowboy, a soldier in the Boer War, and a boiler-maker.

He is a moderate smoker of tobacco and drinks a small amount of beer.

Present Illness. The onset of the present conditions of weakness was insidious, beginning in 1911. He began to be generally weaker, fatiguing very easily. Recently he has gained fifteen pounds in weight, and has become "flabby" in his muscles.

During the past two years his head and feet have grown larger. His memory and his ability to calculate have become poor, and his visual acuity has, he thinks, been progressively lessening.

Physical Examination. The patient is a tall, round-shouldered, slightly kyphotic, rather obese man of forty-three, with rather long extremities. Height, 175 cm. Weight, 190 pounds (calculated normal weight 168 pounds). His skin is smooth and satiny. There is a "freckle-like" pigmentation over the shoulders and arms.

The *facies* and general attitude of the upper part of the body are typical of hyperpituitarism. We note especially (1) the hexagonal shape of the head; (2) the prominence of the lower jaw and chin; (3) the lower teeth over-ride the upper set of teeth—there is prognathism of the lower jaw; (4) wide space between the upper incisors—"hag-teeth"—due to the enlargement of the upper jaw; (5) prominent acra of the face, nose, ears, lips, malar bones, and eye-brows; (6) the hair grows low on the forehead; (7) the skin of the forehead is thick and wrinkled; (8) the characteristic position of the head in relation to the trunk—the head, on a thick neck, sinks down between the shoulders; (9) in the occipital region there is a transverse groove in the skull, and just beneath the groove, an enlarged occipital tubercle.

Hair. The hair on the body and in the face is scanty (for the patient has never shaved). The crines pubis are scanty, and the

upper limit of the pubescence is transverse. The axillary hairs (hirci) are scanty, and the beard and moustache are almost absent.

There is a large amount of subcutaneous fat in general, and the fat over the symphysis pubis is abnormally abundant.

The excess of breast tissue is striking (gynecomastia). The pelvis is broad, the thighs curving.

The arms are long, the hands and feet large; the fingers are not definitely spade-like.

The *penis* is short. The testes are rudimentary, being about as large as a lima bean. The prostate is very small, and on massage of the prostate, numerous lecithin cells were obtained, but no spermatozoa. A few epithelial cells were obtained, but no pus.

Thyroid. There is no palpable thyroid tissue; the thyroid gland must be small.

Thorax. Percussion note slightly impaired over the manubrium. Expiration is prolonged, and there are transient fine moist crackles at the right apex posteriorly.

Bradycardia and *slight hypothermia* have been noticeable in the hospital; pulse 56 to 92; temperature, 97° to 98.6°.

The patient has extreme myopia. Pterygium in the right eye. He has some pyorrhea alveolaris, with some dental caries. There is some nasal obstruction on the right side. There is also slight mastoid tenderness and total deafness on the right.

The right great toe has been amputated. Scars of the old operations are visible over the tibæ.

The patient's memory is poor, and his power of calculation is defective.

Blood Examination. Red blood cells, 5,020,000; white blood cells, 8800; hemoglobin, 80 per cent. (Sahli).

Blood-pressure. 90 to 100 mm. Hg. (Tycos).

Urine. No polyuria. Chemical and microscopic examination negative.

Tuberculin Test (Calmette). 1 per cent.; positive.

Wassermann Reaction (blood). Positive.

Carbohydrate Tolerance. No reducing body was excreted in the urine after the administration of 200 grams of glucose.

Eyes and Eye-grounds. Extreme myopia. Fundic reflex lighter than normal. Optic papillæ oblique. Myopic conus. Both sets of vessels distended. Very slight veiling of the margins of the right disk. Low grade of myopic choroidoretinitis.

Visual Fields. Slight general contraction. No hemianopsia.

X-ray of Head. Normal sella turcica, save for erosion of the posterior clinoid process.

X-ray of Hands. Negative.

X-ray of Feet. Amputation of right great toe. Exostosis on the right astragalus.

X-ray of Thorax. Diffuse infiltration of both lungs (possibly old tuberculous lesions).

Pharmacodynamic Tests. After atropin, gr. $\frac{1}{100}$, the pulse rose from 56 to 64. After adrenalin (15 minims of a 1 to 1000 solution hypodermically) a slight chill, and a rise in blood-pressure from 98 to 118 mm. Hg. (Tycos.)

No reaction noted after pilocarpin, gr. $\frac{1}{8}$.

This patient's condition at once suggests a multiple endocrinopathy. He presents a combination of symptoms, some of which denote over-action, some, on the other hand, under-action of the hypophysis; the size of the testicles calls attention at once to the defective gonads; the azoöspermia indicates a loss of function of the germinative part and the eunuchoidism suggests loss of the internal secretion of the interstitial cells.

In connection with the hypogenitalism it is interesting to note (1) the account of the patient's occupations. He has always striven to overcome the criticism directed against his feminine characteristics by attempting hypermasculine accomplishments. He has been a cow-boy, a sailor, a soldier in war, and a boiler-maker; (2) the periods of hematuria, along with which there was some swelling of the breasts. This is interesting, and makes us ask whether or not the condition could have been an instance of "male menstruation." The nocturnal, periodic epistaxis also suggests an analogy to the vicarious menstruation of the female.

The hips are broad. The crines pubis are transverse, and there is a moderate accumulation of fat on the abdomen. The thighs are of the feminine type, and there is a tendency to genu valgum, which is common in women. The breasts are larger than normal in the male. He is therefore of the *typhus femininus.*

In connection with the dyspituitarism, a possible hypophyseal lesion has to be considered, and a tumor in the region of the sella turcica has been thought of. Of the symptoms which could possibly point to intracranial growth may be mentioned, headaches and slight dizziness, but there has been no projectile vomiting, no choked disk, and no epileptiform seizures. There is also a singular absence of neighborhood symptoms, unless the hypothermia and bradycardia may be so interpreted; there is no hemianopsia and no eye-muscle paralysis, no olfactory disturbances, and no diabetes insipidus. The radiographic formula of the base of the skull, so typical in acromegaly, is not present here. The only *x*-ray anomaly is a flattening of the posterior clinoid process. The symptoms referable to hypopituitarism in the case before us are perhaps just as striking as those of hyperpituitarism, a combination which, as Cushing and others have pointed out, is by no means uncommon. Among such symptoms may be mentioned, the obesity, the genital hypoplasia, and the increased carbohydrate tolerance.

We must conclude that in this case there has been a loss of both

the germinative and the internal secretory functions of the gonads (hypogenitalism), together with a dyshypophysism (mixed signs of hyper- and hypopituitarism).

As has been stated the patient has a positive Wassermann reaction in his blood-serum. How the luetic infection occurred we do not know. Coitus has not been possible, but it is conceivable that in attempts at coitus some trauma has occurred which resulted in infection, or extragenital infection may have existed. The patient denies, however, any memory of symptoms or signs suggestive of a primary sore or of secondary lesions. One must think also of the possibility of a congenital lues, especially as profound endocrinopathies have been known to be associated in some instances with congenital luetic infection.

Case II.— *Dwarfism; unilateral cryptorchism; azoöspermia; hypergenitalism; tuberculous polyserositis; general miliary tuberculosis.*

Robert J., aged twenty-six years, colored, laborer, single; admitted to Ward M of the Johns Hopkins Hospital on December 22, 1913 (No. 35,875), under the care of my colleague, Prof. W. S. Thayer, complaining of "pain in the chest, water on the chest, and shortness of breath."

Family History. Father died of tuberculosis; otherwise negative. Both his parents were "large" people. An older brother is "more developed" than the patient. He had four sisters of normal size.

Past History. Aside from measles in childhood and a mild polyarthritis with night sweats two years ago, the patient says he has had no diseases before the present illness. Denies venereal infections. Habits temperate; alcohol and tobacco used in strict moderation.

Present Illness. Onset gradual two weeks before admission with symptoms of a cold (cough and slight expectoration), and pain in the left side and about the heart. He consulted Dr. Hocking of Govans, Md., who found a pleural effusion and sent him to the Phipps Tuberculosis Dispensary for treatment. He was examined in the Dispensary by Dr. Louis Hamman and sent by him into the stationary clinic.

During his stay in the hospital he was examined by several members of the staff, and on January 9, 1914, I went over him carefully myself. Our records of the case may be summarized as follows:

Colored man; very small stature; height, 151 cm.; upper length, 62 cm.; lower length, 89 cm.; stretch, 151 cm.; fairly nourished but not obese; microcephaly; though small, the head looks mature. Forehead and supra-orbital ridges prominent; nose large; lips not thick, malar bones and zygomata rather strikingly prominent; ears small. Hair high on forehead and recedes at temples; hair on scalp thick; unusually well-developed beard and moustache

for a colored man. Hirci abundant; crines pubis abundant but limited by horizontal line above; perineal hair abundant.

Voice high and infantile. Teeth never developed properly; marked heterodontia; teeth not high above the gums; one peg-tooth near mid line in upper jaw; the two medial incisors are absent.

Tongue long and narrow, coated. Tonsils not visible. Upper arm, 28 cm. long; forearm, 22 cm. Hand relatively large; fingers of normal size. Skin of palm thick; nail-beds long but lunulæ not visible; nails not unusually fragile. Skin over elbows and knees dry, harsh, and thick. Skin of forehead thick and shiny.

Clavicles relatively large. Nipples well-developed and surrounding areolæ of pigmentation large. Breast tissue scanty.

Thorax small. Angulus sterni prominent. No marked retromanubrial dulness. Signs of infiltration of apices of lungs and of pleural effusion on the right side, with Grocco's sign on the left. Pleural tappings (Dr. Smith) yielded turbid fluid; specific gravity, 1012 to 1017; albumin, 30 grams per liter; cell count, 640 to 860 to c.mm., nearly all small mononuclear elements.

Heart displaced to the left by the pleural effusion; pulmonic second sound markedly accentuated; no heart murmurs. Abdomen distended with bulging, dull, flanks; liver large and firm, edge palpable four finger's breadth below the costal margin in the right mammillary line; on December 23 Dr. Futcher heard a leathery friction rub over the liver; spleen also palpable two finger's breadth below the costal margin; paracentesis abdominis (Dr. Levy) yielded 2500 c.c. dark, orange-colored, turbid fluid; specific gravity, 1017; 50 grams of albumin per liter; 800 cells per c.mm., chiefly small mononuclears.

Scrotum small; left testicle in scrotum, but small, size of a large hazel nut; right testis partially undescended, palpable in groin, small. Penis fairly well developed; slight phimosis; patient asserts that he has possessed normal libido and potentia cœundi since fourteenth year. Scapulæ large. Spine normal. Feet small; wears No. 4 shoe. Pelvic measurements: Interspinous distance, 21 cm.; intercrestal distance, 22.5 cm.; intertrochanteric distance, 24.5 cm.; Baudelocque's distance (last lumbar spine to middle of upper margin of symphysis), 16 cm.

No paralyses or anesthesias; reflexes (deep and superficial) normal.

Supraclavicular gland on the right palpable; retrocervical glands and epitrochlears just palpable; other superficial lymph glands not enlarged.

Thyroid isthmus palpable; no struma; no fine tremor of fingers; no eye signs of hyperthyroidism.

Blood Examination. December 22, 1913. Red blood cells, 3,480,000; white blood cells, 2240; hemoglobin, 53 per cent.; no anisocytosis; no parasites.

January 9, 1914. White blood cells, 3400. Differential count

(300 cells): Polymorphonuclear neutrophiles, 76.7 per cent.; polymorphonuclear eosinophiles, 0.3 per cent.; polymorphonuclear basophiles, 1 per cent.; small mononuclears, 20.7 per cent.; large mononuclears, 9.3 per cent.; transitionals, 1 per cent. No myelocytes; no nucleated red cells; no anisocytosis or poikilocytosis of red cells.

Urine Examination. Clear; acid; specific gravity, 1018 to 1025; trace of albumin; no sugar; microscopically a few granular casts and many amorphous urates; tests for blood and bile, negative; no acetone bodies.

Wassermann test of serum (Dr. Bloomfield) made January 2, 1914, was negative.

Ophthalmotuberculin test of Calmette (Dr. Levy) reported December 28, 1913, was negative with both 1 per cent. and 5 per cent. solution.

Feces. Examined January 12, 1914, entirely negative.

X-ray Examinations. January 10, 1914 (Dr. F. H. Baetjer). Sella turcica, normal.

Thorax, slight infiltration of both lungs; shadow at right base (effusion); shadow above heart, possibly enlarged thymus.

Temperature, Pulse, Respiration and Blood-pressure. The patient had continuous fever while in the hospital; from December 22 to December 30 it was high, varying between 100.5° and 104° F.; in the first week of January it averaged about 100° to 101°; later it rose, varying between 100° and 103° until death on January 14, 1914. Shortly before death the sclerae became icteric. The pulse rate varied between 120 and 130; the respirations between 24 and 32 per minute.

The blood-pressure was always low (70 to 90 mm. maximal systolic pressure).

Clinical Diagnosis. Tuberculous polyserositis (pleurae; peritoneum); pulmonary tuberculosis; possibly miliary tuberculosis; cryptorchism; dwarfism; azoöspermia; hypergenitalism.

It was prophesied intra vitam that the autopsy would probably reveal well-preserved interstitial cells of Leydig in the small testicles with loss or diminution of the germinative portions of the sex-glands.

Autopsy No. 4052). (Made in Prof. Welch's laboratory by Dr. Kline, January 14, 1914.)

Anatomical Diagnosis. Bronchial, mesenteric and retroperitoneal tuberculous adenitis; tuberculous peritonitis; subacute pleurisy; atelectasis of right lung; recent tuberculous ulcer of vocal cord; pleural and peritoneal effusions; atelectasis of right lungs; miliary tubercles in lungs, liver, spleen, adrenals and kidneys; fatty liver; anemia; emaciation; jaundice; peptic duodenal ulcers; decubitus ulcers; incompletely descended testis; dwarfism.

Histological Examination of Hormonopoietic Organs (Prof. George H. Whipple).

Testicle. Uniform throughout the histological section which shows the entire gland. Both testicles were examined and were similar. The *tunica* is thickened a little and shows a little evidence of chronic inflammation. The *seminiferous tubules* are uniformly arranged, of small size, with greatly thickened basement membranes. They contain only one type of an undifferentiated cell, in general of spindle or cubical shape, with the long axis pointing toward the lumen. The nuclei are large and vesicular. The protoplasm is filmy. There are no spermatozoa. The basement membrane in places has undergone hyaline degeneration. Again the entire tubule shows a uniform, hyaline metamorphosis. There are some corpora amylacea probably representing deposits in degenerated tubules. Some of these show calcium impregnation.

The *bloodvessels* are not particularly thickened, but in places there is evidence of chronic inflammation, the evidence being nests of mononuclear wandering cells.

The striking thing in the sections is the uniform increase in the interstitial cells of the testicle. They are increased relatively and perhaps even absolutely. Many of them show very distinct, fine, yellow granules of pigment in their protoplasm. The nuclei stain well. Some of these masses of interstitial cells make up strands and columns as large as the shrivelled tubules.

Pancreas. The acini and islands are quite normal. There is a very slight increase in connective tissue and occasionally small inconspicuous scars are visible.

Thyroid. Colloid is quite conspicuous in all the acini, but in some it stains a very much deeper pink than in others. The acini vary greatly in size, but the lining epithelium everywhere is low, cubical in type. No hemorrhage; perhaps a slight increase in stroma. One section shows a discrete tubercle.

Adrenal. Cortex is rather thick and shows perhaps a little increase in the width of the middle zone of the cortex. The inner zone of the cortex shows considerable pigment deposit in its cell column, perhaps slightly more than normal. The medullary tissue is conspicuous and normal in appearance. The bloodvessels are engorged to a considerable extent. There are a few small scars here and there, perhaps dependent upon the general tuberculosis.

It would be interesting, did the occasion permit, to discuss the reciprocal relations of the gonads and the other endocrine glands.

In the first case reported above the inter-relations of the hypophysis cerebri and the gonads are apparent, and clinical experience indicates also a close relationship in some circumstances with the thymus, the epiphysis, the chromaffine system and the inter-renal system.

More and more we are forced to realize that the general form and the external appearance of the human body depend to a large extent upon the functioning, during the early developmental period (and later), of the endocrine glands. Our stature, the kinds

of faces we have, the length of our arms and legs, the shape of the pelvis, the color and consistency of our integument, the quantity and regional location of our subcutaneous fat, the amount and distribution of hair on our bodies, the tonicity of our muscles, the sound of the voice and the size of the larynx, the emotions to which our *exterieur* gives expression—all are to a certain extent conditioned by the productivity of our hormonopoietic glands. We are simultaneously, in a sense, the beneficiaries and the victims of the chemical correlations of our endocrine organs.

The data we are accumulating regarding these chemical correlations are not only theoretically interesting but are practically very important. More than ever before, is the minute examination of the external appearance of the body—the habitus—of significance for the practicing physician who desires to make accurate diagnoses. In this paper I have paid especial attention to the function of the gonads. It is probably no accident that, as one of the best workers in this field has expressed it, the "organs which are for the preservation of the species and the continuity of life (also) possess a modelling influence upon the individual bearer of life."

SYPHILITIC NEPHRITIS.

By Alfred Stengel, M.D.,

professor of medicine in the university of pennsylvania.

and

J. Harold Austin, M.D.,

associate in medicine in the university of pennsylvania.

philadelphia.

In recent years there has been accumulating evidence supporting the view that many cases of nephritis, chronic as well as acute, are caused by the microörganism or the toxemia of the infectious diseases. Thus scarlet fever, diphtheria, tonsillitis, la grippe, pneumonia, and streptococcic infections are reckoned among the causes of nephritis. The lesions of the kidneys differ more or less not only in the different infections but also in cases due to the same infection. There is no distinctive morphological picture by which the antecedent infection in any given case can be identified. The recognition of the etiological relationship is, therefore, based upon the sequence of kidney disease following a well-marked infection. Manifestly such a relationship is more readily established in the case of such acute infections as those named than in a chronic one like syphilis. Moreover, as syphilis in certain locations and in certain of its forms presents a characteristic histological picture, it has been difficult to accept as syphilitic processes certain conditions in which these features were wanting. Thus in the past

what is now clearly recognized as syphilitic aortitis was not differentiated from other kinds of arterial disease, and in some diseases of the central nervous system a long controversy was waged over the question of their syphilitic or non-syphilitic nature. Perhaps the same denial of syphilitic etiology where the expected morphological features of a syphilitic process are wanting may account for the relatively slight role accorded to syphilis in pulmonary pathology, and we venture to suggest that the thought may also be applicable to diseases of the kidneys. Unmistakable syphilitic lesions, such as gummata, are rare in the kidneys, but there are many cases of nephritis of various types in which the etiology is obscure, and in some of these it is not improbable that syphilis is the hidden etiological factor. Besides the instances cited (aortitis, central nervous lesions), in which the ordinary syphilitic features are wanting, we may recall the affections of various mucous membranes and hepatic, splenic, and perhaps pancreatic lesions as further instances of the same sort. It would, therefore, appear quite possible that renal disease might similarly be due to syphilis, though presenting only the features of nephritis as occasioned by other infections.

In the absence of histological evidence, and in view of the difficulty of tracing a nephritis back to such a chronic infection, the proof of the syphilitic nature of certain cases must be indirect. Perhaps in the future, investigations to demonstrate spirochetes in the renal tissue may yield results. Thus far there have been no discoveries in this direction. A few reports have been made of supposed spirochetes in the urine of cases of suspected renal syphilis, but the reliability of these reports may be questioned. Failing such direct proof of syphilis, we must rely upon statistical studies, exclusion of other probable causes, and similar evidence.

A subacute, rapidly developing nephritis has been observed in several individuals with early secondary syphilis where the kidneys had been previously healthy and where as yet no mercury had been given. Karvonen and Erich Hoffman each report a case of this type, and in both cases when, soon after the appearance of the nephritis, mercurial treatment was begun and pushed the evidence of nephritis diminished along with the other manifestations of the syphilis, and, in the course of two or three weeks, the mercury still being used, wholly disappeared. Karvonen[1] from the literature collected 9 cases in which, although the first urinalyses were made only after mercury had been given, yet there was exhibited a rapid diminution or even disappearance of nephritic manifestations under mercury therapy.

In a large number of cases nephritis has been observed in syphilities under mercurial treatment, but this nephritis has been variously interpreted by different observers: by some as a mercurial nephritis; by others as a consequence of the syphilis.

The existence of a syphilitic nephritis was doubted by Hunter

and Wells, and Blackall (1818) attributed the edema and albuminuria complicating some cases of syphilis not to the disease but to mercury. In 1840 Rayer strongly opposed this view and described 3 cases which he considered syphilitic nephritis. Subsequent to these reports many instances of supposed syphilitic nephritis were recorded, and while critically examined, as has been done by Karvonen, more than half fail to be convincing, there yet remains a considerable group of scarcely disputable cases.

Nephritis may be recognized in the secondary stage of syphilis occurring as an acute nephritis remarkably early in the disease, usually in the first two or three months. Fournier describes this form as characterized by an insidious onset, by a great quantity of albumin in the urine, by the rapid development of the condition, and in the severer cases by an early development of uremia; the urine is diminished or there may be anuria. In many respects the condition resembles a postscarlatinal nephritis. Fournier has described such kidneys pathologically as among the large white kidneys with marked tubular degeneration, but frequently also with extensive endothelial hyperplasia and interstitial change, in which respect again they resemble scarlatinal nephritis. In Fournier's experience about one-third of these patients succumb; however, Karvonen found a large proportion of recoveries, while Rose Bradford has noted a tendency to a remittent course with persistence especially of the albuminuria.

In the latter stages of syphilis, amyloid kidney and interstitial nephritis are the most frequent forms of renal disease, but other types of nephritis have been observed. In 186 autopsies on individuals with acquired syphilis, Spier (1877) found 125 with renal lesions, of which 36 were amyloid kidneys. Gummata of the kidney are rare; in Spier's series of autopsies on syphilitics they occurred in 4 per cent., and in Fournier's series in less than 1 per cent. Karvonen described 2 cases of renal gummata and collected 28 cases from the literature. There have been a number of reports of nephritis developing in late syphilis which were apparently cured by antisyphilitic treatment and a large number in which improvement occurred.

In congenital syphilis the renal lesions are more often those of defective development than of nephritis, and rarely give rise to symptoms of urinary change during life. Of late hereditary syphilis the commonest renal manifestation is amyloid disease, and the onset of symptoms is usually insidious, the first being often edema. In addition to amyloid there may develop interstitial or parenchymatous nephritis or rarely gummata.

The latest addition to our conception of syphilitic nephritis has been suggested by Munk.[2] He noted the occasional presence of doubly refractile lipoids in the urine of individuals with severe nephritis of any etiology, but found them so abundant in those cases in which he had grounds for suspecting a syphilitic etiology

as to warrant, he believed, the recognition of a peculiar relation between syphilitic nephritis and the presence of doubly refractile lipoids in the urine. Munk attempted to describe the clinical features of the cases of nephritis of syphilitic origin, and noted particularly the decided albuminuria and abundance of casts of various types as well as a pronounced and persistent edema. These doubly refractile lipoids under the common microscope resemble neutral fat globules, but when examined with polarized light show a dark central cross separating four bright peripheral quadrants. This optical peculiarity was first observed in 1858 by Mettenheimer in the lipoids in certain alcoholic extracts. Müller and Schmidt noted much later doubly refractile globules in certain sputums. The chief impetus, however, to the study of these substances was given by Kaiserling's discovery in 1895, that the fatty globules of the adrenal cortex are doubly refractile. Since that time extensive studies of these bodies have been made by Kaiserling and Orgler, Albrecht, Dietrich, Panzer, Lehmann, Adami and Aschoff, Windaus, Smith, Ciaccio, Fischler, Kawamura, and others, which have led to a considerable knowledge of their chemical and physical nature, their staining reactions, and their normal and pathological distribution. The lipoids, which are known to give rise to doubly refractile globules, include cholesterin esters, mixtures of cholesterin and fatty acids, sphingomyelin, cerebrosides, and certain oleic acid soaps. The physical condition of these doubly refractile globules is one for which Lehmann proposed the name fluid crystals, and appears to be an intermediate state between true fluids and true crystals. Changes in physical conditions, such as drying, heating, freezing, or the action of solvents, cause the disappearance of the peculiar optical properties of these substances; but subsequent manipulation may restore the fluid crystal form and with it the optical properties. Chiefly through a study of the reaction of the various doubly refractile lipoid substances to staining methods it has become possible, in some degree, to distinguish microchemically between the types, and from the studies of Aschoff and his coworkers and of Kawamura,[3] confirmed by the chemical studies of Windaus,[4] it seems probable that the double refractile lipoid globules occurring normally and pathologically in man and mammals are cholesterin esters. Normally these globules have been seen in the adrenal cortex, the thymus, the lutein cells, the puerperal uterus, the mesentery, and the choroid plexus. Pathologically they have been observed in atheromatous areas of the arteries, in amyloid kidney, in chronic nephritis with marked cellular degeneration, in the urine of nephritis, in albuminuric retinitis, in the epithelium of the pulmonary alveoli in pneumonias or tuberculosis and in the neighboring lymphatics and sputum, in the gall-bladder epithelium and that of the hepatic ducts during cholangitis, in pyogenic membranes, in chronic mastitis, mesenteric tabes, actinomycosis, xanthomas, and in certain neoplasms (especially carcinoma, sarcoma

and hypernephroma). The process by which these lipoid globules appear in degenerating cells, whether by infiltration or by decomposition of more complicated lipoid-containing substances already present in the cell, remains unsettled, but their appearance pathologically in a cell is considered evidence of a severe cellular degeneration which is not reversible and of much more serious significance than the common glycerin ester type of fatty degeneration.

With these facts before us we felt that a further study of the clinical significance of the appearance of these doubly refractile lipoids in the urine, and especially of their possible relation to a syphilitic nephritis, was desirable. For this purpose we have examined the urine with a polarizing microscope fifty-eight times from 46 cases. Of these 46 cases, 23 showed nephritis with an abundance of albumin and casts in the urine. Of these 23 cases, 6 had positive Wassermann, 3 had strong presumptive evidence of syphilis but not positive Wassermann, 14 had not the slightest evidence of syphilis. The 6 cases with positive Wassermann all showed lipoids in the urine, whereas of the 14 non-syphilitic cases only 5 showed lipoids in the urine. The rest of the 46 cases studied were made up in part of nephritic cases of the interstitial or arteriosclerotic types, with only traces of albumin in the urine and a few hyaline and granular casts, some with syphilis and some without; in part of syphilitic cases with no nephritis and in part of control cases with neither syphilis nor nephritis. None of these cases showed lipoids in the urine. It is of interest that one of the 6 syphilitic cases with nephritis showing lipoids in the urine, had not received any mercury. (The accompanying table presents the figures more clearly.) There is, we believe, evidence in these figures to suggest that there exists a parenchymatous type of nephritis due to syphilis, characterized by an abundant albuminuria, with many hyaline, granular, and occasionally epithelial casts, with a tendency to produce edema of renal distribution, associated, as a rule, with a moderate reduction of phthalein output and exhibiting an almost constant tendency to the presence of doubly refractile lipoid globules varying in size from that of an erythrocyte to globules three or four times this diameter, seen sometimes floating free in the urine but not rarely as a constituent of a compound granular cell or possibly upon an epithelial cast. On the other hand, similar lipoid globules may be found in severe acute or chronic parenchymatous nephritis of other etiology, but in only a minority of cases. It may be added, however, that with but one exception in our series the cases which showed abundance of these lipoids in the urine were syphilitic.

LIPOIDS IN URINE.

	Total.	Lipoids in urine.
Nephritis with severe albuminuria:		
Nephritis with syphilis . .	6	6
Nephritis, syphilis doubtful	3	2
Nephritis without syphilis .	14	5
Interstitial or arteriosclerotic nephritis (albumin in traces only), some syphilitic, some non-syphilitic .	23	0

In order to determine whether the common experimental degenerative nephritis of animals would be associated with lipoids in the urine, three rabbits were given a uranium nephritis, and one dog a chromate nephritis. The four experiments were negative; no lipoids were found in the urine. Further experiments with mercurial nephritis, phosphorus, and chloroform lesions and syphilitic inoculations are in progress.

We found of further interest the fact that of our last 84 cases of nephritis, for 66 cases there could be recognized from the histories, such possible etiological influence as infections, lead, alcohol, excessive work, exposure, senility, etc; but that for 18 cases no such factors could be determined. Of these 18 cases, there existed in 8 either an unquestionable history of syphilis or a positive Wassermann or both; in 6 more of these cases no Wassermann had been secured; while in 4 syphilis was definitely excluded. It is perhaps significant that syphilis should have been present in so many of the otherwise unexplained cases of nephritis.

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INFECTIOUS DIARRHEA.

By John Lovett Morse, A.M., M.D.,

associate professor of pediatrics, harvard medical school; visiting physician at the children's hospital. consulting physician at the infants' hospital and floating hospital, boston.

Etiology. Infectious diarrhea is more common in hot weather than at other time of the year. The action of heat in the production of the disease is due mainly to the lowering of the general resistance to infection which it produces. It presumably also favors the development outside of the body of the microörganisms which are found in this disease. Microörganisms are, however, the primary cause of infectious diarrhea. The microörganisms which produce this disease are of several different types. They may be divided roughly into three main classes:

(*a*) The dysentery bacillus in all its forms.

(*b*) The gas bacillus and similar organisms.

(*c*) Other organisms, of which the most important are streptococci, the colon bacillus, and the Bacillus pyocyaneus.

The symptoms produced by these different types of organisms are practically identical. It is usually impossible to determine from them which type of organism is causing the disturbance.

Pathology. The pathological lesions of the intestine are very varied. There may be only a catarrhal inflammation. In other cases there are also superficial ulcerations. In others there is hyperplasia of the solitary follicles and Peyer's patches. In many instances ulceration takes the place of the hyperplasia of these structures. In still others a pseudomembrane is formed, which may involve considerable areas. The pathological lesions are usually limited to the large intestine and the last two or three feet of the small intestine. They are ordinarily most marked in the large intestine. The severity of the symptoms does not always coincide with the severity of the intestinal lesions. In general, however, the symptoms are most marked in the cases in which the lesions are the most serious.

There is almost invariably a hyperplasia of the mesenteric lymph nodes. This almost never, however, goes on to suppuration. There are always more or less marked degenerative changes in the parenchymatous organs, especially in the liver and kidneys. True inflammation of the kidneys is, however, uncommon. Secondary infections of other organs, such as the middle ears and lungs, by other organisms as the result of the general weakened resistance are not infrequent.

Symptomatology. The onset of infectious diarrhea is usually acute. It may be preceded for a few days by symptoms of indigestion, but ordinarily there are no premonitory symptoms. The first symptom in most cases is diarrhea. The first stools are made up of fecal matter. Mucus and blood soon appear, however, and after a few hours or a day or two the stools are composed almost entirely of mucus and blood. Pus is seldom visible macroscopically until several days after the onset, and, in many instances, it is never seen. It can, however, almost always be found with the microscope. Membrane is also present in the severest cases. The mucus is often stained green or brown. The odor of the stools, when they are made up chiefly of mucus and blood, is very slight, but sometimes resembles that of wet hay. When the stools contain much pus or membrane, as the result of deep ulcerative or gangrenous processes in the intestine, the odor is putrefactive or gangrenous. The reaction of the stools is variable, but in most instances it is somewhat alkaline. The number of stools is large—twelve, twenty-four, or even more in twenty-four hours. The stools are usually small, being often merely a stain of blood and mucus. In a general way the larger the number of stools the smaller are the individual stools.

Pain in the abdomen and tenesmus are early, marked, and severe symptoms. Tenesmus is especially troublesome and annoying,

and often keeps the baby restless and disturbed, and prevents it from getting the proper amount of sleep. Prolapse of the rectum is not at all infrequent as the result of straining.

Vomiting is a rather infrequent symptom and is seldom troublesome. The appetite is usually much impaired and there is not infrequently the greatest distaste for food of any sort.

The abdomen is sometimes distended, but in the vast majority of instances is much sunken. There is almost never any spasm of the abdominal muscles. There is sometimes tenderness over the course of the colon, but this is unusual. There is usually no enlargement of either the liver or of the spleen. Slight enlargement of the spleen is, however, not very uncommon. In some instances the liver becomes very large, and this enlargement may develop very rapidly. The liver will sometimes enlarge enough in three or four days to reach well below the navel and to the anterior superior spine. The temperature is always elevated in infectious diarrhea. It is usually only moderate, 100° to 102° F., but may be several degrees higher. It is more likely to be high in the beginning than later. The temperature is usually a fairly constant one without marked intermissions or remissions. It lasts throughout the active stage of the disease.

The symptoms are, however, not always so characteristic. The number of stools may be but little increased; mucus and blood may be scanty or even wanting, and tenesmus absent. The symptoms may be, in fact, precisely like those of severe simple indigestion or of indigestion with fermentation. In such instances the continued temperature is the most suggestive symptom. The real condition can only be recognized in such instances, however, by a bacteriological examination of the stools.

The blood almost always shows a moderate polynuclear leukocytosis, usually somewhere in the neighborhood of 20,000. It may, however, be much higher. In the severest cases, in which the toxemia is extreme and the system is unable to react, there may be no leukocytosis or even a leukopenia.

The urine is almost invariably diminished as the result of the loss of fluid through the bowels and the diminution in the intake. It not infrequently shows the evidences of acute degeneration of the kidneys. Acute inflammation of the kidneys is unusual. The urine rarely contains sugar unless the toxemia is extreme or large amounts of sugar are being ingested.

In the most severe and fatal cases, certain symptoms, such as uncontrollable vomiting, marked prostration, and hyperpyrexia, presumably due largely to toxic absorption, develop. These symptoms may also develop in the course of indigestion with fermentaion. They will be discussed more in detail later, and the treatment for them described at the same time.

It is impossible to determine from the symptoms what form of

organism is the cause of the disease in the individual case. There is nothing about the stools which will aid in the differentiation except, in rare instances, the peculiar green color caused by the Bacillus pyocyaneus. If the green color is produced by this organism, it will disappear when nitric acid is added to the stool. If it is due to bile, the characteristic color of Gmelin's test will appear when nitric acid is added. The microscopic examination of the stools is of little assistance in differentiating the various types unless the streptococcus is the cause, in which case it is usually present in large numbers and easily recognized. The presence or absence of the gas bacillus can be determined in from eighteen to twenty-four hours, or even less, by the following method. This method is a simple one, which can be easily carried out by anyone: A small portion of the stool is added to a test-tube of milk. The infected tube is then gradually brought to the boiling point of water in a water-bath and kept there for three minutes. In this way all the bacteria not in the spore state are killed and the development of whatever spores may be present into vegetative cells is unrestrained by the presence of non-spore-forming organisms. The tube is then incubated at body temperature for from eighteen to twenty-four hours. When the gas bacillus is present the casein is largely dissolved (usually at least 80 per cent.); the residual casein is somewhat pinkish in color and filled with holes; the odor of the culture is much like that of rancid butter, as the result of the formation of butyric acid by the gas bacillus. Gram-stained preparations made from the milk show rather thick, short, Gram-positive bacilli, with slightly rounded ends. The fermentation is more easily observed if the milk, after being boiled, is put in a sterile fermentation tube. "Psuedo-reactions" may occur in which there is some liquefaction of the casein, but the shotted appearance of the residual casein is absent and there is no odor of butyric acid.[1] It must be remembered, however, in interpreting the results of this test that the presence of a few gas bacilli does not necessarily prove that they are the cause of the disease. There is, unfortunately, no method for determining the presence or absence of dysentery bacilli which does not require special media and a fairly well-equipped laboratory.

Diagnosis. The only disease with which a typical case of infectious diarrhea is likely to be confused is intussusception. It is, however, usually not difficult to differentiate between these two conditions. Intussusception begins acutely with pain in the abdomen and evidences of shock, the stools of mucus and blood not appearing until later. The onset of infectious diarrhea is less acute, pain is usually not present, or, if so, it is slight, and there are no symptoms of shock, while the stools of mucus and blood appear

[1] See Kendall and Smith, Boston Med. and Surg. Jour., 1910, clxiii, 578.

almost at once. The stools contain no fecal matter in intussusception, while they usually contain some in infectious diarrhea. Fever is common to both diseases, but is usually higher in infectious diarrhea than in intussusception. The abdomen is almost always sunken in infectious diarrhea, but likely to be somewhat distended in intussusception. There is never any muscular spasm in infectious diarrhea, but usually some in intussusception. There may be abdominal tenderness in both conditions. It is seldom marked in either, however, and is not of importance in the differential diagnosis. There is never a tumor in the abdomen or rectum in infectious diarrhea, while there often is one in intussusception. The absence of a tumor does not, however, rule out intussusception. Both conditions are usually, but not always, accompanied by a leukocytosis.

Simple indigestion and indigestion with fermentation are not likely to be mistaken for infectious diarrhea. Mild cases of infectious diarrhea in which the number of stools is not very large and in which there is no blood and relatively little mucus in the stools are very likely, on the other hand, to be mistaken for indigestion with fermentation. Fever, abdominal discomfort, anorexia, wasting, and symptoms of toxic absorption are common to both conditions. These symptoms differ only in degree in the two diseases, and may be more marked in indigestion with fermentation than in mild cases of infectious diarrhea. It is often very difficult to differentiate between them, and it is not infrequently impossible to make a positive diagnosis. The most important single symptom in the diagnosis is probably the temperature curve, the elevation of temperature in indigestion with fermentation being ordinarily either very slight or high and of short duration, while in infectious diarrhea, although usually not very high, it is constant and continuous. In many instances a positive diagnosis can only be made by a bacteriological examination of the stools. An agglutination reaction is usually present in infectious diarrhea by the end of the first week, or a little later, when the disease is caused by the bacillus of dysentery. This reaction is, however, of but little practical importance.

When the temperature is high and the symptoms of cerebral irritation are marked and develop before the appearance of the characteristic stools, as they sometimes do, the disease may be mistaken for some form of meningitis. A careful analysis of the symptoms and physical signs will, however, usually make the diagnosis plain. A lumbar puncture will settle it at once.

Prognosis. Infectious diarrhea in infancy is always a serious disease. The prognosis should always be a guarded one. It is impossible to know in the beginning what the result is to be. Death may occur in three or four days, but most often takes place during the second week of the disease. It may be delayed, however,

for several weeks. Improvement usually begins, in the cases which recover, at the end of the first or during the second week. It may be delayed for several weeks. Recovery is usually slow and likely to be interrupted by relapses. In some instances the disease runs into a chronic form which may last for many weeks. Most of these cases eventually die, but some recover.

Symptoms which render the prognosis more serious are high fever, the presence of much blood in the stools, and the appearance of symptoms of marked toxic absorption, such as persistent vomiting, marked restlessness, and convulsions. The presence of albumin and other evidences of degeneration of the kidney in the urine are not of specially bad prognostic import.

Treatment. The first thing to be done in infectious diarrhea is to thoroughly clean out the intestinal tract. The best drug for this purpose is castor oil. It works quickly, thoroughly, and causes less irritation of the intestines than other cathartics. The dose should not be less than two teaspoonfuls, and may be as much as two tablespoonfuls. It should be given plain. Castor oil should be tried first even if the baby is vomiting, because it is often retained when food and water are vomited. If it is vomited, calomel may be given in its place. The usual dose is 0.1 grain, combined with 1 grain of bicarbonate of soda, every half hour until 1 grain or 1.5 grains have been given. It is wise to follow it with two or three teaspoonfuls of the milk of magnesia in two or three hours after the last dose. The treatment should be repeated if the desired results are not obtained. The lower bowel should also be irrigated at once with physiological salt solution (approximately 1 teaspoonful of salt to 1 pint of water).

All food should be stopped for from twelve to twenty-four hours. It is not desirable, as a rule, to withhold food longer than this time. It is necessary, however, to give water freely during this period, because, although a baby can bear temporary starvation, it cannot get along without water. At least as much water whould be given as the baby would normally take of liquid in the form of food in the given time. The water may be given either warm or cool, and may be sweetened with saccharin if desired. There is no objection to giving it in the form of weak tea sweetened with saccharin if it is taken better in this way. It should be given through a tube if the baby will not take it otherwise.

The most important element in the treatment of infectious diarrhea is the diet. The character of the diet depends on the variety of microörganism which is causing the disease. These microorganisms can be divided, as far as the determination of the diet to be used is concerned, into two groups:

1. The various forms of the dysentery bacillus and the other organisms, except the gas bacillus, which cause the disease.

2. The gas bacillus and allied organisms.

The other organisms, although of many different varieties, are grouped with the dysentery bacilli, because as regards their growth and the production of toxic substances from protein and carbohydrate media they behave in the same way.

The dysentery bacillus, the colon bacillus, and the streptococcus belong to the class of facultative bacteria. This class of organisms can thrive upon either carbohydrate or protein media. They produce harmless products from carbohydrates and toxic substances from protein. They act upon and use up the carbohydrate material before they attack the protein, when both are present in the medium in which they are growing. The products of the breaking down of the carbohydrate material have, moreover, when produced in sufficient amounts, an inhibitory action on the development of dysentery bacilli and, to a less extent, of streptococci.

It is evident, therefore, that when infectious diarrhea is caused by bacteria of this type the food should be largely carbohydrate in character. In this way the organisms are prevented from forming toxic substances, and their growth is, to a certain extent, inhibited. The prolonged withdrawal of food is also contraindicated, because the intestinal contents are then made up entirely of the intestinal secretions, which are protein in character. Some form of carbohydrate should, therefore, be given after a few hours. Sugar is preferable to starch, because it is much more easily utilized by bacteria. Lactose is preferable to the dextrin-maltose preparations, because it is more slowly broken down during the processes of digestion. Being less readily absorbed, it thus provides a carbohydrate medium in the intestine for a longer time than the dextrin-maltose combinations. It is probable, moreover, that a larger proportion of lactic acid is formed from milk-sugar than from the other sugars, and lactic acid has an inhibitory action on the development of the dysentery bacillus. The lactose should be given in the form of a 5 per cent. or 7 per cent. solution in water. It is better to give it frequently in small amounts than in larger amounts at longer intervals, because in this way a continuous supply of lactose is brought to the intestines. The baby should be given at least as much of the sugar solution as it would take of food under normal conditions. Half as much more is usually advisable. There is little or no danger of producing sugar indigestion or glycosuria, if no more than this is given.

After twenty-four, forty-eight, or seventy-two hours, as the case may be, it is wise to give the milk sugar in barley water. The barley water should contain from 0.75 per cent. to 1 per cent. of starch. The starch provides more nourishment and, being still more slowly broken up and absorbed, favors still further the prolonged continuance of a carbohydrate medium in the intestine.

It is necessary to add some protein to the food as soon as pos-

sible in order to neutralize the protein waste of the organism. It should be given as soon as there is evidence of improvement of the condition. Care must be taken not to give so much as to neutralize the action of the carbohydrates. It is usually safe to begin with 0.5 per cent., increasing the amount 0.25 per cent. at a time as fast as possible up to about 1.5 per cent. It may be given either in the form of whey protein or casein. If it is added in the form of casein the mixture should be boiled in order to prevent the formation of casein curds. No fat should be given until convalescence is well established.

Irrigations of the colon with solutions of lactose or dextrose, while theoretically indicated, are of little practical value.

The microörganisms which cause the disease enter the intestinal wall and probably in many instances reach the mesenteric lymph nodes and perhaps the general circulation. The available supply of glycogen is quickly used up or greatly diminished in illness, especially when associated with total or partial starvation, and the conditions favorable for the development of toxic substances by the bacteria which have left the intestines are thus provided. The introduction of dextrose into the circulation would, therefore, furnish a carbohydrate instead of a protein medium for the bacteria to grow in. The dextrose also provides an immediately utilizable supply of energy and spares the body protein. Dextrose infusions are, therefore, indicated in severe cases of infectious diarrhea of this type and in cases which are not yielding readily to treatment. The strength of the infusion should be 2.5 per cent. of dextrose in normal saline solution. Kahlbaum's is the only readily available pure dextrose. Three or four ounces of the solution may be given at a time and repeated every four to six hours. The administration of these infusions should be checked by urinalysis, and must cease if sugar appears in the urine.

The gas bacillus and allied organisms grow rapidly in the intestinal tract when there is an excess of utilizable carbohydrate in the bowel and at the same time an insufficient number of those organisms which form lactic acid from carbohydrates to produce enough lactic acid to inhibit their growth, the gas bacillus being sensitive to lactic acid. The indications to be followed in the treatment of cases of infectious diarrhea caused by the gas bacillus are, therefore, to cut down the carbohydrates in the diet and to introduce acid-producing bacteria into the bowels. These indications can be best met by the use of unheated buttermilk or, better, of mixtures containing no fat, 3 per cent. or 4 per cent. of milk-sugar and from 1.5 per cent. to 2.5 per cent. of protein, ripened with lactic-acid forming organisms. It is not possible to cut out the sugar entirely, because if this is done the lactic-acid forming organisms will have nothing on which to grow. The lactic acid already present in the food exerts an immediately inhibitory action

upon the gas bacillus, while the lactic-acid forming organisms in it, by keeping up their production of lactic acid, continue this action. They also use up the available supply of carbohydrate and thus interfere with the growth of the gas bacillus. Lactic acid given by the mouth is much less effective, because it is rapidly broken down and absorbed and, therefore, does not have a continuous action. Pasteurized buttermilk, in which the lactic-acid forming organisms are destroyed, is less valuable than raw buttermilk for the same reason.

Cutting down the carbohydrates in the diet and increasing the amount of protein in it is sufficient to relieve the condition in mild cases. The percentage of fat should also be kept low. Mixtures containing from 1 per cent. to 1.5 per cent. of fat and from 1.5 per cent. to 3 per cent. of protein, and with no more milk sugar than is necessarily added in the milk and cream to give the desired percentages of fat and protein, are suitable ones. It is well to boil them in order to prevent the formation of casein curds.

It is evident that the line of diet which is suitable for one type of infectious diarrhea is not only not suitable, but absolutely harmful, for the other, and *vice versa*. It is extremely important, therefore, not to make a mistake in the choice. It is unfortunately almost impossible to determine at once what form of microörganism is the cause in the individual case. The various methods to be used to get at the organism at fault have already been detailed. A point which is of some assistance in arriving at a tentative conclusion until these measures have been carried out is that in a given season the vast majority of the cases of infectious diarrhea are due to the same organism. If the prevailing organism is known, the chances are, therefore, that this organism is also the cause in the given case. Another method of determining the cause, a method which is most unscientific but nevertheless often the only practicable one, is to give what seems to be the most rational diet and then observe the results. If the temperature begins to come down and the patient improves, it is almost certain that the organism causing the disease is of the type for which that form of dietetic treatment is indicated. If, on the other hand, the temperature remains elevated or rises and there is no improvement in the other symptoms, it is evident that the causative organism belongs to the other type and that the diet must be changed.

Irrigation of the bowels once or twice in the twenty-four hours is a useful procedure. The object of the irrigation is simply to cleanse the colon. It is impossible to use astringent solutions strong enough to have any appreciable action upon the intestinal wall, even if this were desirable, or antiseptic solutions strong enough to have any effect upon the pathogenic bacteria without running serious risk of poisoning the baby. The irrigating solution should, therefore, be some mild, unirritating solution, such

as physiological salt solution or a 1 per cent. solution of boracic acid. The irrigation should be given with a soft-rubber catheter. No. 25 French, passed as high as possible into the bowel, with the patient lying on the back with the hips elevated. The fluid is then allowed to run in from a bag hung not more than two feet above the level of the patient. It should be permitted to run in until the abdomen is slightly distended, then allowed to run out, and so on until the wash water returns clear. The object of the irrigation being to cleanse the colon, enough liquid should be used to do this, whether it is much or little. Irrigation should seldom be done more than twice in the twenty-four hours. If it depresses or disturbs the patient materially it should be given up, as under these circumstances it does more harm than good.

In subacute or chronic cases in which blood and pus persist in the stools after the temperature has dropped and the evidences of toxemia have disappeared, injections of nitrate of silver are sometimes useful and seem to hasten the healing of the bowel. They may be used in the acute stage, but, as a rule, do but little good at this time. The colon should first be irrigated with sterile water in order to cleanse it. Salt solution should not be used, because the sodium chloride forms with the silver nitrate an insoluble silver salt which is precipitated and the action of the silver solution is consequently diminished. After the bowel has been washed out, from 6 to 16 ounces, according to the age of the baby, of a 2 per cent. or 3 per cent. solution of the nitrate of silver are allowed to run into the colon and the tube then withdrawn. No attempt should be made to have the fluid either retained or expelled. This procedure seldom causes any marked discomfort in babies. If it does, the silver solution may be washed out with salt solution or an opium suppository given. The injections should be repeated every day or every other day. If there is no evident improvement after three or four injections it is useless to continue them. The first stools passed after an injection usually contain more blood and considerable dirty gray material, consisting of slough from the ulcers, intestinal secretions and pus, discolored by the silver nitrate. In favorable cases, however, there is marked improvement in the character of the stools inside of twenty hours.

The various so-called intestinal antiseptics are of little or no value in the treatment of infectious diarrhea. It is impossible to give them in large enough doses to have any effect on the pathogenic bacteria in the intestines without poisoning the baby. If they did have any action it would be exerted on the antagonistic as well as on the pathogenic bacteria. Moreover the bacterial flora can be modified better by regulation of the diet than in any other way. In addition it disturbs the patient to take them and interferes with the administration of food and water. The salts of bismuth

are of little value during the acute stage, whether or not they are combined with sulphur. During the chronic stage they sometimes seem to diminish peristalsis and perhaps promote healing. When used they should be given in doses of from 10 to 20 grains every two hours. It is safer to use the subcarbonate or the milk of bismuth than the subnitrate, because of the danger of nitrite poisoning when the subnitrate is used.

There is no serum which is of any value in the treatment of infectious diarrhea.

Pain and tenesmus are often troublesome symptoms. Injections of 2 ounces of starch solution, of the strength of 1 dram of starch to 1 ounce of water, to which are added from 3 to 5 drops of laudanum, will sometimes control the tenesmus. They are usually expelled, however, before they have had time to do any good. It is generally wiser, therefore, to give the opium by mouth if it is necessary to use it at all. It must be remembered when giving opium that its action is to diminish peristalsis, and that if the peristalsis is diminished enough to interfere with the free emptying of the bowels, serious harm will be done. Only sufficient should be given to allay the tenesmus and prevent the frequent stools due to excessive peristalsis. The safest form of opium to use is paregoric. It may be given in doses of from 5 to 20 drops. Dover's powder, in doses of from 0.125 to 0.5 grain, may also be used. It is better to give small doses at short intervals than larger doses at longer intervals. The use of hot stupes or compresses to the abdomen will, however, often relieve the pain and tenesmus and render the use of opium unnecessary.

In some instances it is impossible to induce the infant to take a sufficient amount of water, or if it does take it, or it is given through a tube, it is vomited. In such cases physiological salt solution should be given subcutaneously to make up the deficit. From 4 to 6 ounces may be given at a time and repeated as often as necessary. It is useless to give a second injection, however, before the first one is absorbed. Salt solution may also be given through the bowel by seepage. Considerable amounts can sometimes be introduced in this way even when the baby is having many stools.

Stimulants are often necessary in infectious diarrhea in infancy, as in other acute diseases. There are no special rules to be followed in infectious diarrhea. Alcohol is of doubtful value. Strychnin is, in general, the most useful, while caffein and camphor are the best quick stimulants. Strychnin may be given in doses of from $\frac{1}{1000}$ to $\frac{1}{200}$ grain. The dose of the citrate of caffein by mouth for a baby is from 0.125 to 0.5 grain and of caffein-sodium benzoate or salicylate subcutaneously about the same. Camphor may be given subcutaneously in oil in doses of 1 or 2 grains.

Special Symptoms. Babies that are seriously ill with either indigestion with fermentation or infectious diarrhea are apt to show one or more rather characteristic symptoms or groups of symptoms. One of these groups of symptoms almost invariably develops toward the end in fatal cases. These symptoms are:

(*a*) Excessive vomiting.
(*b*) Hyperpyrexia.
(*c*) Symptoms of irritation of the central nervous system.
(*d*) Prostration and collapse.

It is probable that these symptoms are chiefly manifestations of toxemia. How much of the intoxication is due to the absorption of bacterial endotoxins and extracellular toxins, how much to the absorption of the products of bacterial fermentation in the intestinal contents, and how much to purely chemical disturbances of metabolism it is impossible to state. It is presumable that the loss of water through the bowels also plays a part in their production.

If when any of these symptoms appear there is any doubt as to whether the bowels have been thoroughly emptied it is advisable to repeat the initial catharsis and irrigation. It is also advisable, if the condition of the nutrition warrants it, to withhold food for about twelve hours. This must be done only after due deliberation, however, if the cause of the infectious diarrhea is any other organism than the gas bacillus. In all of these cases, unless the babies are taking and retaining sufficient liquid by mouth, it is advisable to give salt solution subcutaneously or by seepage.

Little can be done for excessive vomiting beyond the general measures already detailed, except to withdraw all food entirely and wash out the stomach with a solution of bicarbonate of soda of the strength of 1 level teaspoonful to 1 pint of water. In some instances small amounts of this same solution of bicarbonate of soda, of one of the aërated waters, or of ginger ale will be retained when food and water are not. The vomitus not infrequently contains brownish or reddish flecks or streaks as the result of capillary hemorrhages into the stomach. This sign is of serious, but not necessarily of fatal, import.

The hyperpyrexia is best treated by the use of cold externally. It is seldom advisable to give the coal-tar products to infants to reduce the temperature. Sponge baths of equal parts of alcohol and water, at 90° F., are usually effective. If they are not, fan baths may be tried. Fan baths are given in this way: The baby is stripped and wrapped in cheese-cloth. This is then wet with water at 100° F., and the baby is fanned. The temperature is reduced by the evaporation of the water. The cheese-cloth is wet from time to time as the water evaporates. Babies seldom object to this form of bath. If this is ineffectual the cold pack, at from 60° to 70° F., should be tried. Babies seldom bear tub baths well, and it is, as a rule, wiser not to use them.

An ice-bag may also be applied to the head. It must not be forgotten, however, that a baby's skull is very thin and that the effect of the cold is, therefore, greater than in the adult. This is specially true when the fontanelle is open. Great care must, therefore, be exercised in the use of the ice-cap in infancy.

Lowering the temperature of the liquid used in irrigating also aids in reducing the fever. It may be reduced to 100° or 95° F., and in desperate cases to 90° F.

The nervous symptoms are varied. In some instances the babies are stupid, comatose, or relaxed. In others they show the typical picture of coma vigil. Marked restlessness is a very common manifestation. Twitching is not uncommon and convulsions not very infrequent. In many instances there are marked signs of meningeal irritation. The head may be retracted, the pupils unequal, the knee-jerk exaggerated, and so on. In fact the picture may be almost exactly that of meningitis, so much so that a diagnosis can only be made positively by lumbar puncture. The results of this procedure are also sometimes misleading, because the cerebrospinal fluid in this condition sometimes shows a slight globulin test and a moderate excess of mononuclear cells. The pathological condition is presumably one of meningeal irritation or serous meningitis. The treatment of these nervous manifestations is purely symptomatic. Bromide of soda, in doses of from 5 to 10 grains, by mouth may be given for restlessness and excitement. It may be combined with one or two grains of chloral hydrate. It is ordinarily useless to give drugs by enema in these conditions, as they are almost never retained. If the bromide and chloral do not control the symptoms, morphin may be given by mouth or subcutaneously in doses of from $\frac{1}{100}$ grain to $\frac{1}{32}$ grain. It is always advisable in giving morphin to infants to begin with a small dose and then increase it if necessary. An ice-bag on the head sometimes helps. When the fontanelle is full a lumbar puncture will often give relief. Convulsions should be treated in the usual manner.

There is nothing especially characteristic about the manifestations of prostration and collapse in these conditions. They are to be treated in the same way that they are when they occur in other conditions. It is important to remember, however, that all forms of treatment weaken and exhaust the baby. Irrigations must be omitted and the baby disturbed as little as possible. It must be kept warm and protected in every way. They are likely, however, to be associated with a certain amount of vasomotor paralysis and lowering of the blood-pressure. Alcohol is, therefore, contraindicated. Adrenalin is of some value under these circumstances in doses of from 2 to 10 minims of the 1 to 1000 solution, given subcutaneously. Its action is much greater when it is given intravenously. Unfortunately, intravenous injection is not an

easy matter in infancy. It has practically no effect when given by the mouth. Strychnin is, in general, the most useful of the stimulants, while caffein and camphor are the best quick stimulants. Strychnin may be given in doses of from $\frac{1}{1000}$ to $\frac{1}{200}$ grain. The dose of the citrate of caffein by mouth for a baby is from 0.125 to 0.5 grain, and of caffein-sodium benzoate or salicylate subcutaneously about the same. Camphor may be given subcutaneously in oil in doses of from 1 to 2 grains.

THE DAMAGE DONE BY PYELOGRAPHY.[1]

By Edward L. Keyes, Jr., M.D.,

PROFESSOR OF GENITO-URINARY SURGERY IN THE CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK.

AND

Herbert Mohan, M.D.,

NEW YORK.

(From the Pathologic Laboratories of Bellevue Hospital.)

At the present day we are all familiar with the lesions of the renal parenchyma due to injection of collargol, or similar substances, into the pelvis of the kidney for pyelography.

The pathological picture presented by such a kidney may be briefly described as follows: The surface of the organ usually shows black patches of collargol infiltration. These patches are slightly elevated above the surrounding tissue. They consist of a swollen parenchyma, irregularly mottled with black infiltrate. The capsule when stripped back, shows a replica of this staining.

On section we find that these patches, seen on the surface of the kidney, correspond to an underlying infiltrated area. Such an area is a black mottling or striation of the parenchyma, with intervening uninfiltrated spots. It may be irregular in outline, but often it is definitely cone-shaped, with apex at the pelvis and base at the capsule.

The pelvis itself is more or less stained and infiltrated. The cellular tissue about the pelvis may be stained black. The collargol is found within the tubules and the glomeruli. Moreover, masses of collargol, small or large, are found scattered between the tubules. The kidney tissue about such masses is likely to be inflamed or necrotic. The arteries and veins contain collargol.

[1] Read in part before the American Association of Genito-urinary Surgeons, May 16, 1914.

In the two fatal cases of Roessle[2] and von Hoffmann,[3] death was apparently due, in the one to spesis, in the other to rupture of the pelvis of the kidney, with perirenal extravasation of the collargol and urine.

E. O. Smith[4] reports the death of a feeble, aged women five minutes after injection of 20 c.c. of collargol, causing pain. Autopsy showed emphysema, bronchiectasis, aortic sclerosis, arteriosclerosis, empyema of gall-bladder, nephritis, etc. Collargol was found in and between the renal tubules and in the epithelium.

Two explanations have been offered to explain the entrance of collargol into the kidney.

Blum, Ochlecker, and Tennant,[5] experimenting with cadaver kidneys, or kidneys removed from animals, independently reached the same conclusions, viz., that the collargol enters the tubules of the kidney and either passes up these to the glomeruli or breaks from a tubule into the interstitial tissue and so passes along the lymph spaces to the capsule.

Strassman, on the other hand, experimented with living rabbits. He exposed the kidney and ureter, and made his injections very gently, so as not to distend the pelvis unduly. The collargol was retained for varying lengths of time (eight minutes to twenty-four hours). His experiments did not produce infarcts, left no collargol in the kidney tubules, and showed that the collargol reached the kidney capsule *via* the bloodvessels and lymphatics and the connective tissue around the urinary canals. He therefore denies rupture of the tubules or even distention of them.

Strassman's conclusions have been criticised by both Mason and von Hoffmann on the score of neither fulfiling the clinical condition (distention of the renal pelvis to the point of colic) nor exhibiting the pathological lesions resulting therefrom (distention of the tubules).

But sufficient stress has been laid on the importance of not overdistending the renal pelvis. Everyone now realizes that even 10 c.c. is much too large a quantity to inject into some pelves; 5 c.c. is the usual limit; and the safety of gravity injection as compared with syringe injection is accepted. Moreover the lesions resulting from too large an injection have been studied by many, notably by Eisendrath.[6] But we have reason to believe that injection of the renal pelvis *without* distention may damage the parenchyma. The following experiments have been undertaken for the purpose of studying the nature of this damage and of verifying Strassmann's observations:

[2] Münch. med. Woch., 1911, No. 5.

[3] Folia Urologica, February, 1914, viii, 393.

[4] Trans. Amer. Urolog. Assoc., 1913, vii, 36.

[5] Mason, Jour. Amer. Med. Assoc., March 14, 1914, lxii, 839, has brought the bibliography up to date.

[6] Genito-urinary Section, Amer. Med. Assoc., 1914.

Experiment 1. The upper part of the ureter and the kidney of a dog were exposed through an abdominal incision. One c.c. of 10 per cent. collargol solution was then injected into the pelvis. This amount of fluid seemed to distend the pelvis *without putting it under tension*. The needle was *immediately* withdrawn and the kidney removed.

The kidney was hardened and stained in the usual manner. Externally it did not appear congested and no collargol was seen under the capsule or in the cellular tissue about the pelvis.

On section the pelvis was seen to be lightly stained with collargol and a few minute black spots could be seen in the cortex.

Microscopically the pelvis showed a coating of collargol. The parenchyma was almost entirely normal, but traces of collargol were found, apparently in lymph spaces, near the periphery of the cortex. There was no trace of collargol found in the tubules, the glomeruli, or the bloodvessels of the pelvis or parenchyma.

Experiment 2. The opposite kidney of the same dog was simultaneously exposed and injected *in the same manner*, with the exception that the pelvis was kept *distended for fifteen minutes*. The kidney was then removed and the dog killed before he recovered from the anesthetic.

The gross appearance of this kidney was the same as that of the first experiment, with the exception that the pelvis was more deeply stained and the parenchyma showed many black spots, while the veins outside of the kidney were somewhat distended.

Microscopically the pelvic was coated with collargol, which was also found in considerable quantity in the bloodvessels adjacent to the pelvis and to a less degree in the vessels and lymph spaces within the parenchyma. There were distinct but slight traces of collargol in the glomeruli, and either in the epithelia or in the lumina of the tubules.

Experiment 3. The dog used for this and the following experiment was considerably larger than the one previously employed. Accordingly 2 c.c. were injected to produce an approximately corresponding degree of distention of the pelvis. A 2 per cent. solution of collargol was employed. The pressure was *immediately released* and the dog *killed twenty-four hours later*.

The kidney was markedly congested and there was hemorrhage into the cellular tissue about the pelvis within the hilum; but no trace of collargol was found on inspection, either in the pelvis or in parenchyma.

The microscope revealed acute congestion of the kidney, with considerable dilatation of the vessels and parenchymatous hemorrhages; but no collargol in the pelvis, the vessels, or the glomeruli and only a very few faint traces of collargol in the tubules.

Experiment 4. The opposite kidney of the same dog was injected in like manner, but the distention was maintained for

fifteen minutes. This kidney was removed with its fellow twenty-four hours later.

The gross external appearance was similar to that of the preceding experiment, with the exception that the veins running over the kidney were more congested, the kidney rather browner.

Section revealed a black staining of the surface of the pelvis and black infiltration of the cellular tissue about the pelvis. Many small black spots were also visible throughout the parenchyma.

Microscopically the kidney showed a congestion somewhat less intense than that found in Experiment 3 and a collargol distribution similar to, but more marked than, that of Experiment 2.

The collargol in the parenchyma, while still showing marked affiliation for the bloodvessels, was also seen (and in rather greater quantity than in Experiment 2) in the glomeruli, and distinctly both in the epithelia and in the lumina of the tubules.

From these experiments, few though they be, we derive the following conclusions:

1. Momentary gentle distention of the normal pelvis of the kidney doubtless causes no more damage than a congestion of the organ (Experiments 1 and 3), which congestion is doubtless of brief duration.

2. But if the distention persists for a few minutes the injected fluid is absorbed into the bloodvessels and lymph spaces about the kidney pelvis.

3. Although, like Strassmann, we have been unable to detect any collargol forced into the collectiong tubules;

4. Nevertheless, we have found collargol in the glomeruli and in the convoluted tubules.

5. But inasmuch as there was much less collargol within the glomeruli and tubules than in the lymph spaces and vessels.

6. We conclude that the appearance of the collargol within the glomeruli and tubules is a secretory phenomenon.

Secondary or Late Infiltration. Such are the immediate results of slight distention of the normal kidney pelvis. But a case reported by von Hoffmann introduces a new point, for in this case death resulted from rupture of the pelvis, although at the time of collargol injection the patient had not the least pain in the kidney. *The pain came on for the first time twenty minutes after the examination.*

The history of this case is, briefly, as follows: The patient was fifteen years of age, and had had digestive symptoms for five years and colics in the left loin for a year and a half. There was an intermittent tumor in the left loin. Infected intermittent hydronephrosis was diagnosed. Ureter catheterization revealed a marked delay in indigo-carmine secretion from the left kidney and pus from this side. A 5 per cent. solution of collargol was injected slowly through the ureter catheter until it regurgitated into the bladder.

The catheter was left in place for ten minutes after injection, during which time a considerable amount of collargol issued from it, and the patient felt no pain in his side, but complained of a good deal of bladder pain. Half an hour later he had severe left renal colic and vomited. Four days later he died, the pains having continued and grown more severe, the pulse being rapid, the tongue dry, the temperature low. Postmortem examination revealed hydronephrosis of the left kidney, pyelonephritis, abscess in the parenchyma, infiltration of the parenchyma with collargol, and a ruptured pelvis which had caused death.

Since the patient did not have any pain in the kidney at the time of the injection, the infiltration of the kidney parenchyma as well as the death of the patient were due to obstruction of the ureter subsequent to catheterization. The excretion of urine into the hydronephrotic sac was doubtless the cause of pain, infiltration, rupture, and death.

We shall now report a personal observation: The patient, an Italian laborer, aged seventeen years, entered St. Vincent's Hospital in October, 1913. Apart from the common diseases of childhood he gave no history of any significance, excepting that of his present malady. This consisted in attacks of severe pain in the left loin, radiating downward toward the groin. These pains first began in 1910, following a severe lifting strain. They varied in frequency, duration, and severity; but were usually very intense, lasting about two days, and occurring about six times a year. He had never noticed any disturbance of urination or the passage of stone or blood in the urine. The attacks were not accompanied by any recognized fever, but were associated with nausea. He entered the hospital with no definite diagnosis, his physician even asserting that the left kidney could not be felt. But careful examination of the left loin revealed an obscure general thickening of the loin without any definite outline, tenderness, or muscular rigidity. This was assumed to be a large, empty, hydronephrotic sac. Urinalysis revealed an adequate output of urea, a few pus cells, a trace of albumin (and clumps of bacilli that were acid fast when decolorized for a brief period).

October 27. Cystoscopy showed a normal bladder and normal ureter orifices. Ureter catheters passed readily to the kidney pelvis on the right side, but only 10 cm. up the left ureter. From this left side a gush of some 20 to 30 c.c. of urine was immediately obtained, as though from a dilated ureter. The urine obtained from the right side showed 2.8 per cent. urea and no pus. That from the left side showed 1.2 per cent. urea and a few pus cells. Phenolsulphonephthalein came down strongly from the right side and very faintly from the left (but the precise data of this have unfortunately been lost).

Fifteen c.c. of 25 per cent. cargentos were injected into the left

ureter. Radiographs were then taken; those of the left loin failing to show the kidney or any trace of the injected fluid; those of the bony pelvis showing the left ureter filled with cargentos up to the pelvic brim and enormously dilated.

The patient complained of no unusual pain from the cystoscopy and felt *no pain in the loin either during the injection or subsequent to it.*

In the two days that intervened between the injection of the left ureter and the removal of the kidney the temperature rose to 101°, and the left kidney became distinctly distended and notably sensitive; but still the patient had no spontaneous pain whatever in the left side.

October 29. Although there was still grave doubt as to the presence of real tubercle bacilli, it was evident that the kidney would have to be removed, whether tuberculous or not, since the organ itself was evidently almost entirely destroyed and the ureteral obstruction was near the lower end of the ureter. Accordingly nephrectomy was performed.

The kidney was very large and the adhesions about the vessels so dense that it was deemed prudent to leave clamps on them. The operation was concluded in forty-five minutes.

The postoperative history was uneventful. The clamps were removed on the third day. The patient left the hospital on the fifteenth day with his loin healed.

To my great surprise the kidney showed the typical lesions of injection infiltration (Fig. 1). Indeed the capsule was stained with the injected fluid over an unusually large area. Section revealed the familiar gross lesions and a greatly dilated pelvis containing a brownish dilute solution of cargentos.

Microscopic section of the kidney revealed ulceration of the pelvis and extensive areas of suppuration and sclerosis in the parenchyma, while the remaining tubules and glomeruli showed the familiar lesions of suppuration and dilatation. The cargentos were found distributed irregularly throughout the kidney. There were many infiltrated areas containing granular black deposit. Many glomeruli contained back granules in considerable quantity, and here and there the tubules were filled with black deposit. These lesions do not differ from those that have been described in similar specimens.

This case illustrates much more clearly the point suggested by the case of von Hoffmann, for our patient had no pain at any time. Yet the ureter was evidently completely blocked as a result of the injection, the kidney gradually filled, and the patient would have had a renal colic if operation had not been promptly performed. Yet meanwhile, without any colic, and with pressure of urinary secretion only strong enough to distend the kidney moderately, the classical infiltration took place. This is, therefore, an

example of what might be called secondary infiltration of the kidney parenchyma subsequent to injection, in constrast to primary infiltration at the time of injection.

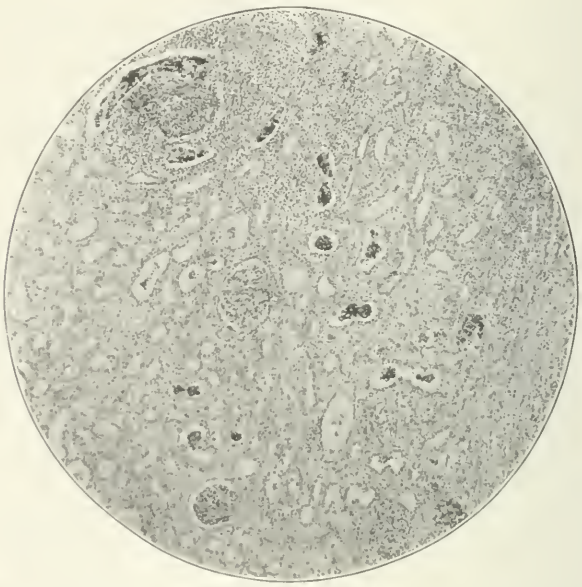

FIG. 1.—Infected hydronephrosis, showing the distribution of collargol in glomeruli and tubules, and the association of collargol with areas of hemorrhage and necrosis (human).

That there is a primary infiltration at the time of the injection, and caused by too forceful dilatation, we cannot doubt. It has been illustrated in many cases, notably by the case of Zachrisson. This patient received an injection of 14 c.c. of collargol into a normal pelvis of the kidney, and the roentgen-ray, taken immediately thereafter, showed a pyramidal shadow of collargol radiating into the parenchyma of the kidney.

After five days of pain and fourteen days of fever he recovered. The *opposite* kidney was subsequently removed and a year thereafter the urine showed nothing abnormal excepting a few casts. Postmortem examination of Smith's patient revealed a similar condition.

These cases illustrate the fact that immediate infiltration can take place. Yet secondary infiltration is perhaps more common than has been supposed. Primary infiltration is certainly painful and must doubtless result in considerable destruction of kidney tissue; but so long as focal suppuration does not follow and the ureter remains open the patient may be expected to recover. Indeed, Smith's is the only recorded immediate death.

Secondary infiltration is obviously a far more serious accident. If the kidney is not promptly drained or removed the ureter may remain closed and the pelvis rupture, as in von Hoffmann's case. Whenever an injection is made into the pelvis in a case of renal retention the patient must, therefore, be kept under close observation and promptly operated upon if symptoms of acute renal retention or infection supervene. Thus will the real danger of pyelography be guarded against.

How does the injected fluid enter the parenchyma in these cases of secondary infiltration? Why does secondary infiltration occur? If the injected collargol may be forced up to the capsule under no other force than that of the urine secretion itself we must conclude that a similar condition of infiltration of the kidney parenchyma with urine must occur in many, if not in all, cases of severe renal colic. Does such an infiltration occur? And if so, is it an element in the etiology of hydronephrosis? Furthermore it is interesting to inquire whether the pathological picture presented by a kidney subjected only to primary renal infiltration differs from that of a kidney subjected only to secondary renal infiltration?

Although we cannot pretend to answer these questions with any degree of thoroughness, we have performed some experiments on dogs which throw an interesting light upon them.

Experiment 5. The whole length of the ureter of a dog was exposed through an abdominal incision and 3 mgs. of 2 per cent. collargol were injected into the lower end of the ureter. The black fluid could be plainly seen ascending the ureter. As soon as it reached the pelvis, and before any dilatation of the pelvis occurred, the injection was stopped and the ureter tightly ligated with silk just above the point of injection. The abdominal wound was then closed and the kidney removed twenty-four hours later. This kidney showed exactly the same changes as that of Experiment 4, with the exception that grossly a considerable amount of collargol showed beneath the capsule. On the other hand, microscopically, this kidney showed rather less collargol in the glomeruli than did kidney 4.

The object of this experiment was to simulate, as closely as possible, a secondary retention. The pelvis of the kidney was certainly not in the least distended at the time of the injection, but the collargol was left in the ureter so as to show the effect of the kidney secretion in producing auto-infiltration. The fact that the pathological changes produced were quite the same as those of experimental primary retention, suggests that in normal kidneys, at least, secondary as well as primary collargol infiltration is a vascular and lymphatic absorption, and that the collargol seen in the glomeruli and tubules is simply being excreted.

In order to confirm this impression the following experiment was performed:

Experiment 6. The whole left ureter of a dog was exposed, as in the preceding experiment, and 0.25 c.c. of a 10 per cent. collargol solution injected into its lower end, while the upper end was compressed in order to make certain that no collargol whatever entered the pelvis of the kidney. Pressure was immediately released from above and the lower end of the ureter ligated. Seventy-two hours later the dog was killed and both kidneys removed.

The injected left kidney was moderately congested and slightly larger than its fellow. Stained areas of parenchyma could be seen through the capsule. On section the pelvis was found dilated and filled with a muddy fluid, while minute black spots were visible throughout the parenchyma.

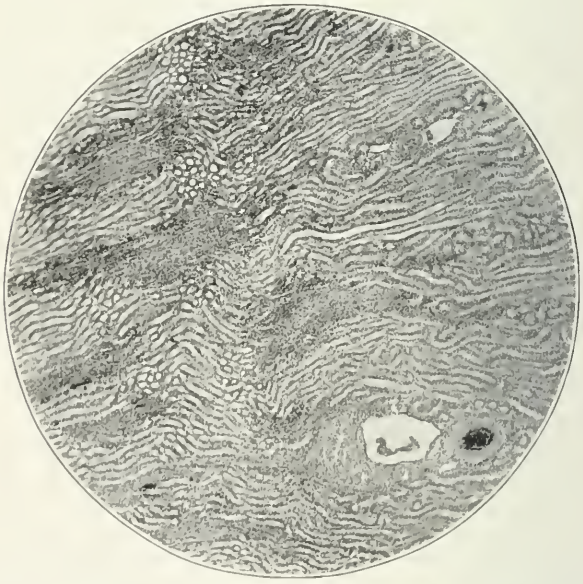

Fig. 2.—Collargol in vessels and in and between tubules, associated with areas of hemorrhage and infiltration (dog).

On microscopic section the most striking characteristic was the association of collargol and blood, both within the vessels and in many small hemorrhages scattered throughout the parenchyma.

Many convoluted tubules of the cortex and many straight tubules of the medulla showed collargol stained epithelia. About such tubules there were hemorrhages containing collargol (Fig. 2). Collargol was found free in the lumina of some straight tubules and also in some of the glomeruli.

The uninjected right kidney showed some congestion, but less than the left. No collargol was visible upon its surface, but section revealed numerous minute black spots in the cortex.

The microscope revealed much less collargol than in the injected kidney. The collargol was found exclusively in the vessels and the glomeruli. The latter contained much more collargol than did the glomeruli of the injected kidney.

This experiment thus afforded ample experimental confirmation of vascular absorption (left kidney) and glomerular excretion (right kidney).

Our next effort was to perform a similar injection upon a hydronephrotic kidney.

Experiment 7. Accordingly the left ureter of a dog was tied off with silk just above the bladder. (The parietal wound became infected, but this did not interfere with the result). One week later the kidney was exposed and found hydronephrotic. The dilated left ureter was punctured, 10 c.c. of urine were permitted to escape, and 3 c.c. of a 10 per cent. collargol solution injected, leaving the kidney distinctly less distended than it had been in the first place. The ureter was again ligatured and the wound closed. Forty-eight hours later the dog was killed and both kidneys removed.

The injected left kidney was markedly dilated and its surface studded with small raised areas of suppuration. The surface of the lower pole, the upper end of the ureter and the fatty tissue about the hilum were stained a deep black; and small black areas were seen beneath the capsule in other parts of the kidney. On section a large quantity of muddy fluid escaped from the distended pelvis, and the parenchyma showed many small black spots.

Microscopically this kidney showed so much suppuration that very little normal kidney tissue remained. But throughout the section the blood, whether extravated or within the vessels, was almost everywhere mingled with collargol. In the medulla streaks of hemorrhage and collargol paralleled each other in the general direction of the collecting tubules (Fig. 3).

The opposite (right) kidney showed no collargol upon its surface, but section revealed many black spots in the cortex. The microscope revealed collargol in the cortical bloodvessels, and in the glomeruli as well (Fig. 4). No collargol was found in the tubules or anywhere in the medulla.

These experiments appear to justify the following additional conclusions:

7. In actual practice we have to consider a secondary infiltration due to renal retention following the examination.

8. This secondary distention is of far greater importance than the primary retention at the time of injection.

9. Secondary retention is the cause of most of the deaths that have been reported from pyelography.

10. The cause of infiltration in these cases is ureteral obstruction. Hence it may occur when there has been no primary distention.

11. Alarming symptoms following pyelography are to be relieved by immediate drainage of the kidney or nephrectomy.

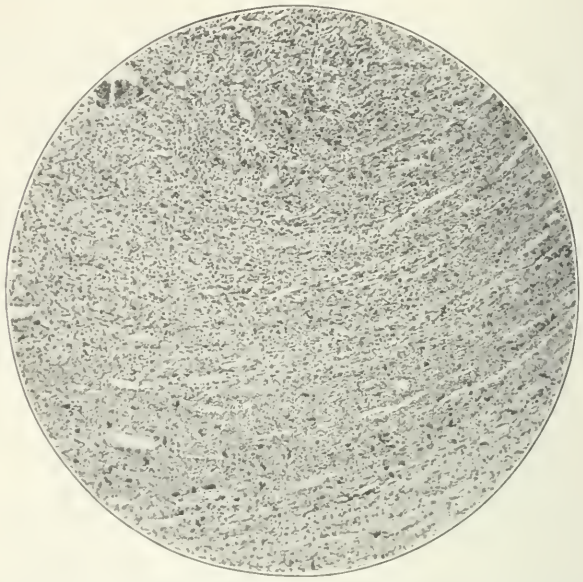

FIG. 3.—Infected hydronephrosis, showing collargol in glomerulus, and associated with an area of hemorrhage and infiltration both inside and outside the straight tubules (dog).

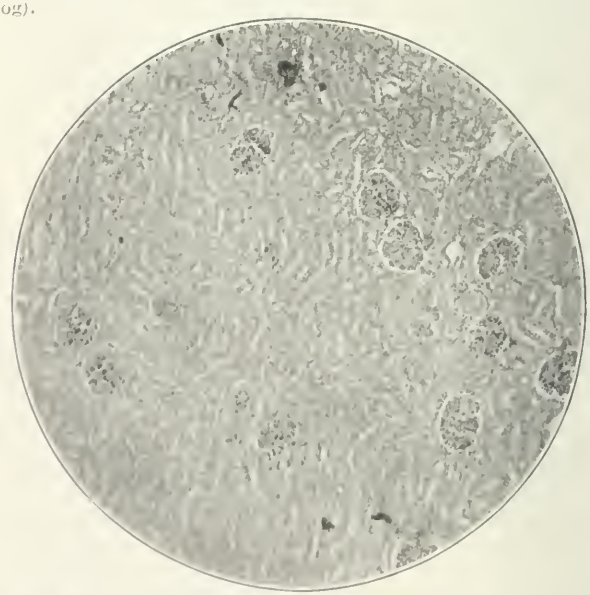

FIG. 4.—Lesions due to excretion of collargol in kidney opposite one injected. Many glomeruli contained collargol (dog).

12. The presence of collargol in the kidney parenchyma, as shown by radiograph or by operation, should not be a cause of apprehension, though it shows that the injection has been made with too much force.

13. The collargol may enter the general circulation and be distributed to the other kidney and elsewhere, in some instances at least, and yet no great harm result.

THE RESULTS AND INTERPRETATION OF THE WASSERMANN TEST.[1]

By Charles F. Craig, M.D.,
captain medical corps, u. s. army.

(From the Department Laboratory, Central Department, U. S. Army, Fort Leavenworth, Kansas).

In the present paper I shall give a summary of the present status of the Wassermann test in the diagnosis and as a control of the treatment of syphilis together with some data of practical value derived from personal experience with the test. The statistical portion of the paper is based upon over 18,000 tests personally performed by me, partly at the laboratory of the Army Medical School, Washington, D. C., and partly at this laboratory during the past five years.

It has now been over eight years since Wassermann, Neisser, and Bruck[2] published their description of what is now generally known as the Wassermann test, and during this time the test has been given a thorough trial in all parts of the world, with the result that the consensus of opinion is that, all in all, it is the most valuable aid that we possess in the diagnosis of syphilis. Certainly, my own experience has convinced me that, when properly performed, this test is of inestimable value not only in the diagnosis of the disease, but as a control of the efficiency of treatment. A positive reaction with the Wassermann test is the most delicate and persistent of all of the symptoms of syphilis, and it is irrational to consider a patient as cured of the disease so long as either the blood or cerebrospinal fluid react positively. The theory, advocated by a few authors, that a positive Wassermann reaction is merely an evidence of past syphilitic infection, has been proved to be erroneous, and it is now generally admitted that a positive reaction, if persistent, means the presence somewhere in the body

[1] Published with permission of the Surgeon-General, U. S. Army.

[2] Wassermann, Neisser and Bruck. Eine serodiagnostische Reaktion bei Syphilis Deut. med. Wochenschr., 1906, xxxii, p. 745.

of living spirochetes. Indeed, one may go still further, as proved by the so-called provocative Wassermann test, and state that even an evanescent positive result, if obtained after the administration of salvarsan or neo-salvarsan, proves the existence of syphilis.

However, valuable as the Wassermann test is in the diagnosis and as a control of the treatment of syphilis, it must be admitted that great harm has been done by the reports of inexperienced workers, and that the results obtained by such workers have made many practitioners skeptical regarding the accuracy of the test. It is most unfortunate that in some laboratories the Wassermann test has been entrusted to poorly trained assistants instead of to a skilled serologist, and this has led to unfortunate mistakes and to the reaction being regarded with suspicion by a not inconsiderable proportion of the medical profession. While this is true, the fact remains that the test, when accurately performed, is hardly equalled in practical value by any other diagnostic method.

As our knowledge of the reaction has increased we have learned that great variations occur in the amount of the substance or substances in the blood that cause a positive result, and that a single negative result is absolutely useless in excluding syphilis in a suspected individual. We have also learned that certain organic and inorganic substances may markedly influence the results obtained, and that, as the test is essentially a quantitative one, certain definite amounts of serum or cerebrospinal fluid must be tested, and the utmost care must be used in titrating each reagent and in performing the test. It is thus evident that the Wassermann reaction is only of value if reported upon by a trained serologist, and only such reports should be considered in estimating its accuracy and value. The test should never be made by one not thoroughly acquainted with all of the factors so far discovered that influence the result, and the profession should frown upon the tendency, which is only too well known, of submitting blood for this very technical test to laboratories of doubtful standing because of financial considerations. In every large city arrangements should be made to have this test performed for those too poor to pay for it by the labortory of the Board of Health, and in such laboratories this work should only be entrusted to those thoroughly trained in the technique of the test.

Technique. I shall not discuss the various modifications of the Wassermann test at present in general use, except to state that I believe that any of the well-recognized methods, if performed by a thoroughly trained serologist who has had a wide experience in the particular method he employs, will give approximately as good results as any other method. I have never seen anything to lead me to believe that the results obtained with

the original Wassermann method are superior to those obtained with other well-recognized methods, as claimed by the most enthusiastic of Wassermann's followers, and I am firmly of the opinion that really positive results are obtained as often with one method as with another, provided those using the various methods are skilled in their use.

The technique that I have employed is essentially that recommended by Wassermann, except that a human hemolytic system is employed instead of the sheep system. An alcoholic extract of fetal syphilitic liver has been used as the antigen, and during the past two years I have also employed a cholesterinized alcohol extract of normal human heart, each specimen being tested, if possible, with both antigens. It may be stated that very little variation has been observed in the results with the two antigens, and I am of the opinion that cholesterinized extracts are just as valuable as antigens as are extracts of fetal syphilitic liver, while the ease with which they may be obtained has removed one of the most serious obstacles to the general use of the Wassermann test.

The Specificity of the Wassermann Test. At the present time it may be stated that there are certain diseases which have been found to give a positive reaction in a certain proportion of cases, with the Wassermann test, and which are not of syphilitic nature. As our knowledge of technique and the factors influencing the result of this test has advanced, the number of positive reactions in disease other than syphilis have steadily decreased, until it is now known that the only diseases that give a positive result with any regularity, other than syphilis, are yaws, relapsing fever, leprosy, and the febrile stage of certain malarial infections. Positive results are rarely observed in other conditions, but only in isolated instances and a syphilitic infection in most instances, can not be excluded. It is certainly true that a large percentage of positive results in non-syphilitic conditions is proof positive of poor technique in the application of the test or of a wrong interpretation of the results obtained.

In my own experience I have obtained 11 positive reactions among 2643 individuals suffering from diseases other than syphilis, or a little over 0.4 per cent. In 4 of these cases the diagnosis was malarial fever and the blood was tested during the febrile stage, when a practically positive result was obtained, becoming negative on the disappearance of the fever. Of the other cases, 3 were diagnosed as tuberculosis, in 1 the diagnosis was undetermined, and in 3 the diagnosis was pityriasis rosea. In the latter cases the reaction obtained was only a plus one (50 per cent. of hemolysis occurred) and in two of the tuberculosis cases a history of syphilitic infection was afterward obtained, while all three recovered under antisyphilitic treatment. When it is remembered that among

the 2643 individuals tested there occurred a large number of both acute and chronic infections, as well as functional and organic diseases of various kinds, the small percentage of positive results in non-syphilitic conditions (0.4 per cent.) speaks eloquently in favor of the specificity of the Wassermann test.

The Percentage of Positive Reactions in the Various Stages of Syphilis. An important question, from the stand-point of the practitioner, is the percentage of positive results that may be expected in the various stages of syphilis. If one studies carefully the results obtained by various observers it will be noted that there is a remarkable agreement between them which speaks well for the accuracy of the test in the hands of different individuals. I have kept a careful record of the positive results obtained by myself in the various stages of the disease, and have found that the percentage of positives has practically remained the same during the past three years, or since enough cases have been tested to allow of reliable conclusions being drawn. It is believed, therefore, that the following table embracing the results obtained in testing 4658 cases of syphilis gives an accurate idea of what may be expected of this test in the various stages of the disease, and it agrees practically with similar tables published by other observers:

Table I.—Result of the Wassermann Test in 4658 Cases of Syphilis.

Stage.	Total cases.	Positive.	Negative.	Per cent. positive.
Primary	908	813	95	89.5
Secondary	1889	1817	72	96.1
Tertiary	638	558	80	87.4
Latent	1173	790	383	67.3
Congenital	28	25	3	82.2
Parasyphilis	22	15	7	68.1
Totals	4658	4018	640	86.2

In considering this table it should be remembered that only one test was made in practically all of the negative cases, and it is undoubtedly true that had repeated tests been made in all, the percentages of positive reactions would have been increased in every stage of the disease. However, it will be noted that if only one test be made in each case we must expect 10 per cent. of negative results in primary cases; about 4 per cent. in secondary cases; 13 per cent. in tertiary cases; and 33 per cent. in latent cases. The figures given for congenital and parasyphilitic infections are valueless, owing to the small number of cases tested. In secondary cases tested more than once I have found that the reaction was eventually positive in 100 per cent. of the cases, but I do not believe that this result is ever obtained if only one test be made, as one would infer from the reports of some authorities.

Date of Appearance of the Wassermann Reaction. It is often stated in the literature that the Wassermann test is of little

value in the primary stage of syphilis, because it becomes positive in so few cases before the onset of secondary symptoms, and this impression has led to the neglect of its use during this stage by numerous practitioners. My experience has been the reverse, for, as will be seen by the table, practically 90 per cent. of the cases tested by me during this stage of the disease gave a positive result. The following table gives the date of the appearance of the reaction in weeks after the appearance of the initial lesion:

TABLE II.—DATE OF APPEARANCE, IN WEEKS, OF THE WASSERMANN REACTION IN 575 CASES OF PRIMARY SYPHILIS.

Week after appearance of chancre.	Total cases.	Positive.	Negative.	Per cent. positive.
First week	76	26	50	34.2
Second week	149	86	63	57.7
Third week	151	102	49	67.5
Fourth week	159	121	38	76.1
Fifth week	40	32	8	80.0

A consideration of the table demonstrates that 34 per cent. of primary cases gave a positive reaction by the end of the first week after the appearance of the chancre; over 57 per cent. by the end of the second week; 67 per cent. by the end of the third week; 76 per cent. by the end of the fourth week, and 80 per cent. by the end of the fifth week. These figures prove conclusively the great value of the Wassermann test during the primary stage of syphilis, and while the demonstration of *Spirocheta pallida* by the dark field microscope is the simplest and quickest way of diagnosing syphilis during this stage of the disease, it is often impossible to make such an examination, and in such instances the Wassermann test should always be performed.

It is important to bear in mind that a negative Wassermann test upon the first, second, or third week after the appearance of a suspicious lesion is no proof that it is not due to syphilis, for the time of the appearance of a positive reaction varies all the way from a few days after the appearance of a lesion to two months, so that the test should be repeated at frequent intervals before regarding the case as non-syphilitic. Here, as in every other stage of the disease, a single negative result is of no value in excluding syphilis.

FACTORS INFLUENCING THE RESULT OF THE TEST. There are several known factors that markedly influence the result of the Wassermann test, the most important being the variation in the amount of complement-inhibiting substances in the patient's blood serum; the ingestion of alcohol; the growth of various bacteria in the blood serum; and the amount of serum tested. These factors will be considered separately.

1. *The Variation in the Amount of Complement Inhibiting Substances.* Until quite recently it has been generally considered that the strength of the Wassermann reaction varied but little,

in the same serum, from day to day, but I have shown that the blood serum of undoubted syphilitics may, in the absence of specific treatment, give a negative reaction during certain intervals, although previous and subsequent tests are positive. My observations regarding this fact were published in 1914,[3] and were stimulated by the fact that in practice I had noted cases in which the blood serum gave contradictory results within a short period of time. Thus I had observed cases in which the reaction varied from a positive one to a plus-minus or negative one within intervals of a few days, the patients in the meantime having received no treatment. While such observations are not numerous in practice, their undoubted occurrence caused an investigation of the phenomenon, and for this purpose I selected ten prisoners at the United States Military Prison at Fort Leavenworth—two in the primary stage of syphilis, four in the secondary stage, and four in the latent stage of the disease. These men were under the most strict discipline, upon a routine diet, and the question of the possible influence of alcohol upon the result of the test could be absolutely excluded. The ordinary technique was used in the performance of the test and samples of blood were collected and tested each day from each of the prisoners. The results demonstrated that the titration of daily specimens of blood serum during each stage of the disease showed great variations in the strength of the reaction, and that these variations occurred without reference to treatment, as none of the prisoners were undergoing treatment. The experiments demonstrated that this normal variation in the strength of the Wassermann reaction must be carefully considered in using the test in the diagnosis or as a control of the treatment of syphilis. The following tables selected from those published in the contribution already referred to will serve to show the variations occurring in the strength of the reaction from day to day. It should be stated that a double-plus (+ +) indicates a positive reaction, there being absolute inhibition of hemolysis; a plus (+) a doubtful reaction; a plus-minus (+−) a doubtful reaction; and a minus sign (−) a negative reaction in the accompanying tables. The amount of serum generally used in the system I employ is 0.08 c.c.

Briefly summarized, this investigation demonstrated that in one case of primary syphilis a plus or doubtful reaction was obtained on three of seven days, the reaction on four days being double plus, or positive; in another primary case a plus or doubtful reaction was obtained on two of seven days, a positive reaction being obtained on five days. In one case of secondary syphilis a negative reaction was obtained on one day, a plus-minus on one day, a plus on three days, and a positive or double-plus reaction on only two days; in another secondary case a plus or doubtful reaction

[3] Craig, Chas. F. Variations in the Strength of the Wassermann Reaction in Untreated Syphilitic Infections. Jour. Amer. Med. Assoc., 1914, lxii, p. 1232.

was obtained on two of seven days. In two secondary cases a positive result was obtained upon every day of the week during which the serum was tested.

TABLE III.—RESULT OF TITRATION OF BLOOD-SERUM IN CASE I (PRIMARY).

Date of test.	Amount of blood-serum, C.C.					Control, C.C.
	0.02	0.04	0.06	0.08	0.1	0.1
November 19	+−	+	+	+	+	−
November 20	+−	+−	+	++	++	−
November 21	+−	+	++	++	++	−
November 22	+−	+−	+	+	+	−
November 23	+	++	++	++	++	−
November 24	+−	+	+	+	+	−
November 25	++	++	++	++	++	−

TABLE IV.—RESULT OF TITRATION OF BLOOD-SERUM IN CASE V (SECONDARY).

Date of test.	Amount of blood-serum, C.C.					Control, C.C.
	0.02	0.04	0.06	0.08	0.1	0.1
December 24	+−	+−	+	++	++	−
December 25	−	−	−	−	+−	−
December 26	−	+−	+−	+	+	−
December 27	−	−	+−	+−	+	−
December 28	+−	+	+	++	++	−
December 29	−	+−	+−	+	++	−
December 30	−	+−	+	+	++	−

TABLE V.—RESULT OF TITRATION OF BLOOD-SERUM IN CASE VII (LATENT).

Date of test.	Amount of blood-serum C.C.					Control, C.C.
	0.02	0.04	0.06	0.08	0.1	0.1
December 19	+−	+	+	++	++	−
December 20	−	+−	+	+	+	−
December 21	−	+	++	++	++	−
December 22	−	+−	+	+	+	−
December 23	++	++	++	++	++	−
December 24	++	++	++	++	++	−
December 25	+−	+	+	+	+	−

Of the latent cases, one gave a plus-minus reaction on two days and a plus reaction on four days of the week, a positive reaction being obtained on only one day; another gave a negative reaction on one day, a plus-minus on another, and a plus reaction on three days; the third latent case gave a plus or doubtful reaction on three of seven days; while the fourth case gave a doubtful reaction on all but one day of the week. All of these cases subsequently gave positive reactions repeatedly, and were treated.

These observations indicate that whatever are the substances

in syphilitic serum that produce complement inhibition they must be present in a certain amount before a positive Wassermann reaction can be obtained, and that the amount varies greatly in such sera from day to day even in untreated infections. From a practical stand-point it is immaterial how these substances are produced, the important fact being that in untreated syphilitic infections the result of the Wassermann test may vary all the way from a positive to a negative within a short period of time, and with the usual amounts of blood serum used in the test. The observations also demonstrate how utterly useless is a single negative reaction in eliminating syphilis in a suspected individual, for in several of the cases tested a negative or a practically negative result was obtained on certain days, although the patients were suffering from undoubted syphilis, and blood serum from the same individuals had previously given a positive result and again became positive within a day or two. It is thus evident that when a negative result is obtained with this test it should be repeated, whenever there is any suspicion of syphilis, for several times before the patient can be considered free from infection.

It is but just to call attention to the significance of these observations in explaining the discrepancies between Wassermann reports from different laboratories where the blood was examined at different times, and where a positive result may have been reported from one laboratory and a doubtful or negative from another. The literature is full of such instances, and they are generally quoted for the purpose of throwing discredit upon the Wassermann test, whereas many of them can undoubtedly be explained by the normal variations in the amount of complement inhibiting substance or substances in the blood serum collected at varying periods of time.

The Influence of the Ingestion of Alcohol. In 1911, Captain Nichols and myself[4] published our observations regarding the effect of the ingestion of considerable quantities of alcohol upon the result of the Wassermann test, and these observations have since been confirmed by numerous observers. We found that the ingestion of alcohol in the form of beer or whisky, as well as alone, and in amounts varying from 180 to 240 c.c. of whisky, 90 c.c. of 95 per cent. alcohol, and 700 c.c. of Munich beer, was capable of rendering a positive Wassermann reaction negative, and that the reaction remained negative for several hours after the last dose of the alcoholic liquor, and, in one case, as long as three days. In 3 of the 9 cases experimented upon the reaction remained negative for twenty-four hours after the last dose of the alcoholic liquor.

In all of the patients tested the Wassermann reaction was double-

[4] Craig, Chas. F. and Nichols, Henry J. The Effect of the Ingestion of Alcohol on the Result of the Complement fixation Test in Syphilis. Jour. Amer. Med. Assoc., 1911, lvii p. 474.

plus before the administration of alcohol, that is, there was absolute inhibition of hemolysis, while a few hours after the administration of the alcohol the reaction became negative. If so marked a change in the reaction occurred in cases giving a double-plus reaction it is evident that in cases giving a plus or doubtful reaction, so often noted in the early primary and in latent syphilitic infections, the same result would be obtained in a far greater proportion of instances.

These observations, therefore, are of great practical importance, as they demonstrate that no dependence can be placed in a negative Wassermann reaction in individuals who have, within twenty-four hours of the collection of the blood, ingested considerable amounts of alcoholic liquors. It is also probable that the ingestion of alcohol in much smaller quantities would so weaken a positive reaction that cases that should react thus will give a doubtful reaction. Therefore a careful inquiry should always be made before the collection of blood for a Wassermann test as to the recent use of alcohol, and if the patients admit its use in any quantity within twenty-four hours they should be instructed to discontinue its use and report at a later date for the test.

The Growth of Various Bacteria in the Blood Serum. In 1911 I called attention[5] to the fact that if certain species of bacteria are allowed to develop in the blood serum to be tested a negative serum may give a positive result, due to the production of a substance or substances in the serum that inhibit the action of complement in the presence of the antigens used in the Wassermann test. While normal sera, when sterile, were never found to give positive reactions even when kept at room temperature for as long as a month, provided they were inactivated by heating at 56° C. for one-half hour before testing, it was found that normal sera contaminated with such common organisms as streptococci and staphylococci might give a positive reaction, provided the sera were kept at a temperature or 37° C. for twenty-four hours or longer. It was also determined that not every strain of a certain bacterial species produced a positive reaction: thus while two strains of *S. aureus* produced a positive reaction a third strain of the same species remained negative in this respect.

The fact that under certain conditions such common bacteria as streptococci and staphylococci when growing in normal human blood serum may give rise to a positive Wassermann reaction, is of great practical importance, and indicates that the blood to be used for this purpose should always be collected with aseptic precautions. Whenever the blood serum is to be kept for more than twenty-four hours before it is tested it is absolutely necessary, if one desires to

[5] Craig, Chas. F. The Relation of Certain Bacteria to Non-specific Reactions with the Complement-fixation Test for Lues. Jour. Exper. Med., 1911, xiii, p. 521.

avoid false reactions, that strict asepsis be used in the collection of the blood, as otherwise bacteria may contaminate it which may give rise to a positive reaction. Fortunately, contaminated sera are usually easily detected, as they appear cloudy and have a disagreeable odor.

The Amount of Blood Serum Tested. From the tables already given, illustrating the variation in the strength of the Wassermann reaction, from day to day, it is obvious that the amount of serum tested is of vital importance if one desires to obtain accurate results with the test. In the experiments demonstrating variations in the strength of the reaction it was found that only those cases presenting the most marked symptoms of syphilis gave a positive reaction with the smallest amount of serum used, *i. e.*, 0.02 c.c., while the percentage of positive results in every case increased with the increase in the amount of serum tested until the best results were obtained when 0.1 c.c. of the serum was used. An amount of serum larger than this could not be used with the methods I employ, because in rare instances a positive result will be obtained with a normal serum. It follows, therefore, that the largest percentage of positive results will be obtained if the maximum amount of blood serum allowable with the particular method employed by the serologist be uniformly used, and reports of doubtful or negative reactions are worthless unless based upon the result obtained with the maximum amount of serum. This fact is also of value in using the test as a control of treatment, as the blood serum may be titrated each time it is tested, and thus the gradual weakening of the reaction noted, or the absence of any effect upon the reaction by the particular therapeutic method employed.

From this brief review of the better-known factors influencing the result of the Wassermann test it is evident that the greatest care must be exercised in making the test, and that all of these factors should be considered in interpreting the results obtained. It is needless to speak here of the grave errors that will always result when every reagent used in making the test is not accurately titrated at frequent intervals, and the supreme importance of titrating the complement before each series of tests is made.

The Wassermann Test with the Cerebrospinal Fluid. It has been shown that while the Wassermann test may be negative with the blood serum it may give a positive reaction with the cerebrospinal fluid. Formerly it was believed that if the test gave a negative reaction in the cerebrospinal fluid and a positive in the blood, and symptoms of disease of the central nervous system were present, the diagnosis should be made of cerebrospinal syphilis, and that this result served to distinguish this condition from paresis, in which both the blood serum and cerebrospinal fluid gave a positive result. It has since been shown, however, that the negative

result with the cerebrospinal fluid depended entirely upon the amount tested, and that if the maximum amount allowable with the particular method in use be tested a positive result was obtained in practically 100 per cent. of cases of cerebrospinal syphilis, and that even when small quantities of the fluid were tested, about 10 per cent. of such cases gave a positive result. Therefore, it follows that the test must be used with caution in differentiating between paresis and cerebrospinal syphilis, although the blood serum is almost invariably positive in paresis and is negative in from 10 to 20 per cent. of the cases of cerebrospinal syphilis.

In paresis the Wassermann test is positive in practically 100 per cent. of the cases in both the blood and cerebrospinal fluid, while in cerebrospinal syphilis, unless the maximum amount of the fluid be tested, at least 50 per cent. of the cases will react negatively with the cerebrospinal fluid and only about 30 per cent. show a positive reaction in the blood. In the method employed at this laboratory, practically 100 per cent. of cases of paresis give a positive reaction when 0.08 c.c. of the cerebrospinal fluid is tested while only about 20 per cent. of the cases of cerebrospinal syphilis react positively when this amount of the serum is tested. With larger amounts the percentage increases, until when 0.15 c.c. of the fluid is tested almost all of the cases give a positive reaction. It will thus be seen that the titration of the cerebrospinal fluid with the Wassermann test is of great importance in differentiating between paresis and cerebrospinal syphilis, and that in most instances a positive reaction with a small amount of the fluid points to paresis.

In tabes the Wassermann reaction in the blood may be said to be positive in from 60 to 70 per cent. of the cases, while in the cerebrospinal fluid, if larger amounts than 0.15 c.c. of the fluid be tested, practically 100 per cent. of the cases result positively (with the system in use in this laboratory). If amounts as small as 0.08 c.c. be tested a positive reaction is obtained in only from 5 to 10 per cent. Even when the smallest amounts of cerebrospinal fluid are tested cases of all three diseases are not so very infrequently met with that give atypical results, so that one should not depend entirely upon the Wassermann test in differentiating paresis, tabes, and cerebrospinal syphilis, but the results of the test must always be taken in conjunction with the clinical symptoms present. While the test is of the greatest value in enabling us in diseases of the central nervous system to distinguish their syphilitic or non-syphilitic origin, it is of far less value when the question of the differentiation of syphilitic conditions of the central nervous system arises. Here the clinical symptoms count for more than the results of the Wassermann test, in many instances, and this fact should always be borne in mind in the interpretation of the test when applied to the cerebrospinal fluid.

Before a patient is declared free from syphilitic infection the

cerebrospinal fluid should be tested, even though the Wassermann test with the blood serum is negative, for it has been repeatedly demonstrated that this fluid is often positive when the blood serum is negative in patients who have been treated and who were presumed to be cured because of the continued presence of a negative Wassermann test in the blood.

The Wassermann Test as a Control of Treatment. In the army laboratories the Wassermann test has been very largely used as a control of treatment in syphilis, and a large proportion of the reëxaminations made in our laboratories have been of this nature. Our results have demonstrated the great value of the test as an index of the efficiency of various modes of treatment, and we have found it of special value in closely following cases treated with salvarsan and neosalvarsan. In a previous publication[6] I have given *in extenso* the results of the use of this test in this manner, and will simply state here that with its aid one is able to trace the gradual disappearance of the reaction after treatment and its gradual reappearance where the method of treatment did not result in a cure. The data derived in this manner have made possible the intelligent use of therapeutic methods in this disease, and have demonstrated that what was once considered heroic treatment does not cure syphilis in the vast majority of instances, but only causes the disappearance of gross symptoms of the disease. Used in this manner the Wassermann test has proved the infinite superiority of salvarsan over mercury in the treatment of this disease, but has also shown us that even salvarsan fails in effecting a cure in a very large number of cases of this most persistent infection.

The greatest value of the Wassermann test, aside from its diagnostic value, is found in the use of it as a control of treatment. Relapses may be diagnosed long before any clinical symptoms of the disease are apparent, thus enabling us to treat the patient before the disease has produced any symptom of relapse beyond a positive reaction, and when it is most amenable to treatment. I believe that it may be stated with truth that, in the vast majority of syphilitic infections, the first symptom of a relapse is the recurrence of a positive Wassermann reaction, and that it may be weeks, months, and perhaps years after the occurrence of a positive reaction before clinical symptoms of the relapse are discernible. For this reason all patients who have been treated for syphilis should have Wassermann tests made at intervals of two or three months for at least one year, at the end of which time, presuming the test to be negative, a provocative Wassermann test should be made, as well as a test upon the cerebrospinal fluid and a luetin test. A single negative reaction after treatment is of no value as a proof

[6] Craig, Chas. F., and Nichols, Henry J., Studies of Syphilis, Bull. No. 3, War Dept., Office of Surg.-General, 1913, p. 16.

of cure unless it is supported by the presence of a negative reaction with the other tests mentioned.

The Provocative Wassermann Test. This method of applying the Wassermann test is of the utmost value in the diagnosis and control of the treatment of syphilis, and while it has been most entensively used in deciding whether a patient is, or is not, cured of the disease, it is also a most valuable diagnostic test, and should be applied in every case where the ordinary Wassermann test is negative but there is good reason to suspect syphilitic disease.

In 1910 Gennerich[7] called attention to the fact that patients previously treated with salvarsan or other drugs and who gave a negative or very weak Wassermann reaction in the blood, became strongly positive after a dose of salvarsan, the blood being tested daily for at least a week after the administration of the drug. His observations were soon confirmed by Milian,[8] and have since been confirmed by every investigator and the provocative Wassermann test, as it is called, is now an accepted method of diagnosing and controlling the treatment of syphilitic infection.

After the administration of a small dose of salvarsan the positive reaction may occur in the blood during the first forty-eight hours, or may be delayed for from three to seven days, and even longer, in rare instances. As the positive reaction may occur within twenty-four hours of the administration of the drug, and as it may be evanescent in character, in properly applying this test it is necessary to make a Wassermann test every day for at least a week, as otherwise the positive reaction may be missed. For this reason the test is not always practicable, but its value is without question, both in diagnosis and as an indicator of the efficiency of treatment.

The following cases, arranged in tabular form, are illustrative of the results obtained with the provocative Wassermann test in some of our cases that had presented a negative reaction with the ordinary Wassermann for many months and were supposed to be cured:

Table VI.—Results of Provocative Wassermann Test in Syphilis.

Case No.	Time since treatment. Months.	Result of Wassermann reaction.	Result of provocative reaction
1	15	−	++
2	16	−	−
3	17	−	++
4	18	−	++
5	19	−	++
6	21	−	−
7	24	−	−
8	24	−	−

The following statement appears to be authorized by the evidence that has accumulated regarding this test: In patients who have

[7] Berl. klin. Wochenschr., September 19, 1910, No. 38.
[8] Paris Dermatol. Gesellschaft., December 1, 1910.

presented a negative Wassermann reaction for a period of over a year, and in whom symptoms have been absent, the provocative Wassermann test often results positively, thus proving that spirochetes are still present and that the disease has not been cured.

Although this test has been but little used in diagnosis it is true that a small dose of salvarsan or neosalvarsan, administered to individuals suspected of being syphilitic but in whom the ordinary Wassermann test is negative, will often produce a positive result and thus establish the diagnosis. For this reason I would urge the more general employment of the test in diagnosis, firmly believing that if it were used generally in early primary cases the diagnosis could be made within a week of the appearance of the initial lesion, and that our percentages of positive results in tertiary and latent cases would be greatly increased. Of course if the dark field microscope is at hand the ideal method of diagnosis in the primary stage of syphilis is the demonstration of *Spirocheta pallida*, but in many instances this cannot be done, and then the provocative test will prove most useful. In applying the test a great advantage is that only a small dose of the drug is necessary, from 0.3 to 0.4 gm. of salvarsan intravenously being sufficient, and we are not only applying a valuable diagnostic test but a therapeutic method at the same time if syphilis be present. In my own experience I have observed several instances in which the diagnosis of the disease was made upon the result of a provocative Wassermann test when the ordinary Wassermann and the luetin tests were negative, and numerous instances in which patients presumed to be cured of syphilis because of the presence of a negative Wassermann reaction in the blood for months reacted positively after a small dose of salvarsan or neosalvarsan. For this reason I believe that the provocative Wassermann test should be used much more frequently than it is in the diagnosis and therapeutics of syphilis.

The Interpretation of the Results of the Wassermann Test. It is still true that a considerable degree of uncertainty exists among the profession regarding the interpretation to be placed upon the results of the Wassermann test. The diagnosis of the disease has been made in some instances upon a plus or plus-minus reaction, while patients have been assured that they were free from infection after one or two negative reactions. Such interpretations of the test are entirely unwarranted and can only be made by those ignorant of the modern developments in the diagnosis and control of the treatment of syphilis with the Wassermann reaction.

The terms that are used in reporting reactions vary in different laboratories, and in the interpretation of the test it is necessary that the terminology employed by the serologist to whom specimens are sent be thoroughly understood. In this laboratory four designations are used for the reaction: double plus (++), indicating complete inhibition of hemolysis, and thus a positive reaction; plus (+),

indicating anything between absolute inhibition and 50 per cent. of inhibition; plus-minus (+−), indicating anything between 50 per cent. of inhibition and complete hemolysis; and minus (−), indicating complete hemolysis, or a negative result. Plus and plus-minus reactions are always doubtful in the absence of a clear history of syphilis or of definite symptoms of the infection.

The significance to be attached to the various degrees of the reaction obviously differs with the stage of syphilis in which they are obtained. A plus reaction within the first two weeks of the appearance of a supposed initial lesion almost invariably indicates syphilitic infection, while such a reaction obtained in what is supposed to be the secondary stage of the disease should not be considered as positive.

As a general rule it may be stated that the diagnosis of syphilis should never be made upon the result of the Wassermann test alone, unless absolute inhibition of hemolysis is obtained. In other words the test to be positive must show no dissolving of the blood corpuscles, and when this is the result I believe that we are justified in making a diagnosis of syphilis, whether symptoms are or are not present, and whether there is or is not a history of infection; provided, of course, that the diseases in which the Wassermann test has sometimes been found positive can be excluded.

The following rules are believed to be reliable in governing the interpretation of the Wassermann test, and have been derived from our experience with this reaction in many thousands of cases:

1. If the diseases other than syphilis, that have occasionally been found to give a positive reaction with the Wassermann test, can be excluded, a double-plus reaction (absolute inhibition of hemolysis) is diagnostic of syphilis. Under such conditions I consider the reaction as absolutely specific, whether symptoms are present or not, and whether there is or is not a history of infection.

2. Under the same conditions a plus reaction (one in which there is at least 50 per cent. of hemolysis) may, in primary, tertiary, and latent infections, be interpreted as diagnostic, provided there is a clear history of infection or clinical symptoms present. In the absence of either history or suspicious symptoms a plus reaction should never be considered as diagnostic.

3. A diagnosis of syphilis should never be made upon a plus-minus reaction (one in which there is less than 50 per cent. of hemolysis). Many normal individuals give such a reaction, and it is of no value whatever as a diagnostic sign of syphilis, and of very little value as a guide to treatment.

4. A single negative reaction is of no value in excluding syphilis. That this is true is clearly demonstrated in the titrations of the blood serum of syphilitic patients already mentioned, where even the most severe secondary cases occasionally gave a negative reaction. Only when a negative reaction is repeatedly obtained, over a

period of at least a year, can it be considered as good evidence of the disappearance of the disease, and in all such cases the result of the test upon the cerebrospinal fluid, a luetin test, and a provocative Wassermann test should be made if one desires to be sure of the absence of syphilis. This may appear to be a very radical stand regarding the value of a negative Wassermann test, but my experience has shown that only by applying all of the tests mentioned can we be sure that a patient is really free from infection.

I have already discussed the interpretation of the results of the Wassermann test with the cerebrospinal fluid.

Conclusion. The advances made during the past few years in the study of the serology of syphilis have resulted in giving to medicine a series of most efficient diagnostic tests, and have thrown a flood of light upon the nature of paresis and tabes. Stimulated by these results, the syphilitic nature of both of these diseases has been demonstrated by the finding of *Spirocheta pallida* in the tissues of the central nervous system of those suffering from them, and there is now no question regarding their syphilitic origin among medical scientists. Serological tests have made possible the diagnosis of syphilis in patients suffering from obscure symptoms or in those who have presented no visible signs of the disease for many years, and have rendered possible the differentiation of syphilitic from other diseases of the central nervous system. The Wassermann reaction, the most important of these tests, has been thoroughly investigated, and the most careful and critical studies have only resulted in demonstrating its great value both as a diagnostic method and as a control of the treatment of syphilis. The wider use of the provocative Wassermann test will still further increase the value of the test in both of these directions, while in diseases of the central nervous system the estimation of the number of cells in the cerebrospinal fluid and the globulin content, when taken in conjunction with the results of the Wassermann test, are invaluable aids in differentiating the nature of syphilitic infections of this system, and in differentiating such infections from other disease processes.

At the present time the physician who neglects the use of the Wassermann test in the diagnosis and treatment of syphilis is doing a great injustice to his patients. This test has conclusively demonstrated that many of our clinical conceptions of syphilis were erroneous; that the disease may be present for years without producing symptoms sufficient to attract the attention of the individual infected; that the ease with which it was supposed to be cured by mercury and other drugs, even including the best of all specifics, salvarsan, is a dangerous fallacy; and that syphilis must be regarded as one of the most insidious and persistent of all infections occurring in man.

ANALGESIA AND ANESTHESIA IN LABOR.[1]

By Edward P. Davis, M.D.,
PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, PENNSYLVANIA.

Before proceeding to consider the management of labor with a view to prevent pain, it may be well to define pain in its clinical aspect. So excitable is a parturient patient, that many complaints of suffering must not be taken as genuine pain. For clinical purposes, to be of importance, pain must be severe enough to disturb the circulation and to cause some degree of shock. Genuine pain from this stand-point is comparatively rare during parturition.

The nervous excitement of labor, especially prominent during the first stage, results from the discomfort of pressure by the presenting part and the irritation of nerve fibres during dilatation of the cervix. In proportion as the patient's tissues are elastic and furnish the normal secretions, the first stage of labor is comparatively painless, and while wearisome, seldom produces shock. Where the cervix is abnormal, and the factors which produce normal dilatation are absent, continuous discomfort may prevent rest and bring about exhaustion.

The management of the first stage of labor demands the use of remedies which allay nervous excitement. In many cases the bromides are sufficient, and a generation ago hydrate of chloral was considered a specific for this purpose. The relaxing effect of a copious hot, high enema, and frequent emptying of the urinary bladder to prevent distention and pressure, are also useful. When exhaustion threatens, our great reliance is opium given hypodermically with atropin, with perfect quiet for the patient, with the hope of inducing sleep.

The use of opium during parturition has been overshadowed by the recent tendency to end labor by surgical operations. In minor degrees of pelvic contraction, the membranes remaining unbroken, it is sometimes possible by keeping the patient under the influence of opium to bring about engagement and descent and to secure spontaneous labor, or make possible the safe use of forceps. So, where the mechanism of labor is at first abnormal, if the membranes can be preserved the use of opium may tide the patient through a long labor and end in successful rotation and expulsion. In my experience, where it is desired to use opium for some time, codein has geen given successfully.

During the second stage of normal labor, Nature's method of lessening pain consists in the deep breathing which the patient

[1] Read before the Lackawanna County Medical Society, Scranton, November 3, 1914.

practises. This brings about a state of mild anesthesia in the intervals of rest between uterine contractions. It is a familiar observation that the healthy woman sleeps between the expulsive pains of the second stage, and her weary attendant often follows her example. If the pulse of a healthy woman in the second stage of labor be observed, it is disturbed but little by uterine contractions when followed by a period of rest. While the patient unquestionably suffers during uterine contractions, the absence of shock in normal cases shows that the pain is not dangerous.

The second stage of labor is painful in proportion to the cerebral disturbance caused by uterine contractions and the delay. A method of treatment to be successful must lessen the sensibility of the cerebrum and facilitate labor.

It is noticeable that all specific attempts to lessen pain during labor call for the isolation of the patient; in many cases the darkening of the room and the maintenance of quiet as absolute as possible.

Krönig and Gauss[2] do not permit the presence of friends or relatives in the room of a patient who is receiving their method of treatment during labor, and Krönig states that relations must be out of the room during the whole time of the birth. This is of no small importance in the success of any method of treatment.

So far as the use of drugs is concerned, we are all familiar with the fact that frequently when the second stage promises to be prolonged a small dose of morphin with atropin, or the inhalation of a small quantity of ether, will not only lessen suffering but stimulate uterine contractions. It is also interesting to observe that stimulants given during the second stage of labor, when the patient seems to be suffering excessively, at first cause the cessation of uterine contractions, followed in a short time by stronger and better pains. The first effect of stimulation seems to be to lessen the irritability of the tired cerebrum and to place the whole nervous system temporarily at rest. In multiparous patients practitioners are familiar with the fact that opium given during the second stage of labor may result in the precipitate expulsion of the fetus, and we are sometimes caught napping under these circumstances.

The attention of the public has been drawn recently, through very questionable journalism, to the method of conducting labor as carried out by Krönig and Gauss in the Freiburg clinic. Krönig's paper[3] may be taken as a reliable statement of this method. It consists in giving scopolamin, a substance allied to hyoscin, with one of the alkaloids of opium, narcophin, or morphin hypodermically, usually in two doses, at intervals of three-quarters of an hour. The first dose contains 0.00045 scopolamin combined with 0.03 of narcophin. The second dose is the first dose of scopolamin alone.

[2] Surg., Gyn., and Obst., May, 1914. [3] Ibid.

The test consists in appealing to the memory of the patient, as it is thought that when she does not remember to have seen an object, or that she was pricked with a needle, that she is in a condition of seminarcosis. This condition is to be maintained by repeating the drugs until labor terminates. While on the average two doses are given as described, others may be used if necessary. Complete isolation, absolute quiet, and constant attention and observation are necessary for this method of treatment. It cannot be used in wards, and hence is not available for charity ward patients. Krönig and Gauss state that they have tried this method in about 3000 cases with satisfaction. They have inquired concerning the subsequent history of 500 children, one year old, and succeeded in tracing 420 of them; 11 per cent. had died in their first year, which is the average death-rate in Baden from all causes.

They state that in some cases pains are less frequent and that the average duration of labor is increased one-half an hour. Some patients not perfectly isolated became excitable. The child often shows the effect of the drug by breathing tardily after birth.

This method has been tried by various American observers, but their experience as yet is not sufficient to warrant a decisive statement. In my observation the use of these drugs has produced severe headache and vomiting in the mother.

Fleurent[4] endeavored to use scopolamin-morphin in conducting forceps operations. In three cases the method was unsuccessful, and he was obliged to have recourse to chloroform. When he gave scopolamin-morphin, an hour after the heart sounds became bad, and it was necessary to deliver the child under chloroform.

Johannsen in Moscow[5] and Hörder[6] have used scopolamin-hydrobromate with pantopon, a preparation of opium, in performing gynecological operations. In prolonged operations they were obliged to resort to ether and chloroform at times. In fourteen cases of labor, pantopon was used hypodermically and produced a better effect than morphin, for uterine contractions were not lessened, but suffering was prevented. Johannsen did not use scopolamin, as he feared its asphyxiating effect upon the child.

Reilander[7] treated 46 primiparæ and 19 multiparæ by the application of cocain, followed by epidural injections of novocain and suprarenal solution, and also by the injection of alypin and suprarenal solution. The cocain was applied to the nasal mucous membrane and did not influence labor pains. The epidural injections were made in the sacral region when labor became active. A small percentage of these patients stated that labor was painless; a considerable number said that pain was less; and a third of the patients could observe no effect whatever.

[4] Zeitsch. f. Geburts. und Gynäk., 1913, Band 74, Heft 1.
[5] Zentralbl. f. Gynäk., 1914, No. 20.
[6] Ibid., 1913, No. 11.
[7] Ibid., 1910, No. 13.

The history of the scopolamin-morphin method is the familiar one of a method tried and discarded, then revived with modifications, and brought into sudden prominence through popular notoriety. Von Steinbuchel, in 1902, was the first to describe it, followed by the investigations of Krönig and Gauss, and Mansfeld. In America, Newell and McPherson gave the method a trial without satisfaction, while Steffans, Leopold, Hocheisen, and Veit were decidedly unfavorable to its use. Krönig and Gauss employed $\frac{1}{150}$ of scopolamin-hydrobromide with $\frac{1}{2}$ grain of narcophin, the latter a proprietary preparation of narcotin-morphin meconate.

Great stress is laid upon the quality of the drugs employed and those manufactured by Straub, chemist of the Freiburg clinic, are supposed to be standard. The most recent American studies on the subject are those of Harrar and McPherson, and that of Rongy.[8] Their results so far do not essentially change the previous verdict of the majority of obstetricians, that in selected cases, with the entire absence of excitement or the presence of relatives, with standard drugs given in moderate doses and with constant skilled attention, that the method often secures temporary oblivion to the pains of labor. Recent experiences by other observers, not yet reported in detail, indicate that great mental excitement and temporary insanity may follow the employment of this method. Unfortunately, unscrupulous popular journalism has given the subject abnormal prominence in the minds of the laity, and furnished abundant material for the practice of quacks. A further and careful trial of the method is necessary, and in comparison with other methods, before its exact value can be determined.

Spinal anesthesia was first tried in labor about twelve years ago, and has received widespread attention from reliable observers. Experience has now limited the method to a small number of cases in which, because of the condition of some vital organ, anesthesia by inhalation cannot be used. Personally the method is too uncertain and was often followed by too much disturbance, and sometimes by dangerous symptoms, to have been adopted as a routine practice in my work, and it is only in occasional and unusual conditions, generally where operation must be done, that I employ the method.

The spinal injection of novocain, although frequently followed by vomiting and sometimes by excitement, seems to be as little objectionable as any of these methods.

My experience in the management of labor has led me to adopt the following, and this statement is made to bring the matter clearly before you.

During the first stage of labor thorough emptying of the bowel

[8] Amer. Jour. Obst., October, 1914.

by hot, high enema, frequent emptying of the urinary bladder, the use of bromides by the mouth, quiet if possible, and comfort for the patient, if it can be secured; and should these measures fail and the patient be threatened with exhaustion from irritation, morphin and atropin should be given hypodermically.

During the second stage of labor, when suffering predominates and uterine contractions are irregular, and evidently lessened by suffering, strychnine $\frac{1}{60}$ to $\frac{1}{30}$, digitalin $\frac{1}{50}$ to $\frac{1}{100}$, codein $\frac{1}{2}$ to $\frac{1}{4}$ grain together are given hypodermically. This dose may be repeated if necessary in an hour. When expulsion is imminent a small quantity of ether is inhaled at the height of a pain. At the moment of expulsion ether is given freely and quickly, producing a temporary anesthesia which soon passes by. When patients so treated are questioned they state that they did not know when the child was born and that its expulsion produced no sensation of suffering whatever. This treatment has not been followed by shock, headache, or nausea, has had no bad effect on the child, and in my experience has given good results. It can be used in general practice, and ether can be entrusted to an intelligent person who will obey the physician's orders implicity at the moment when the child is born.

We are all aware of the fact that chloroform in small quantities is rapid, powerful, and unirritating, but unfortunately it tends to produce uterine relaxation, and hemorrhage is more frequent after its use than when ether is given.

Large doses of opium or prolonged anesthesia undoubtedly affect the fetus, but in my experience no serious result has followed from the ordinary and careful use of these drugs. In cases brought to hospital in impossible labor, where violent contractions threaten rupture of the uterus, we frequently give the patient $\frac{1}{4}$ grain of morphin hypodermatically, and so soon as possible deliver her by abdominal section. In some cases the fetus is slow in breathing after delivery, but we recall no case where fetal death could be ascribed to the use of these drugs.

Those who are interested in the subject of spinal anesthesia will find in Gellhorn's paper,[9] read before the American Gynecological Society last spring, an exceptionally clear and accurate statement concerning this matter. In common with what has been stated, he notes the occurrence of severe headache and irritation in many patients, and states that the indications for spinal anesthesia for gynecological operations are the contra-indications for inhalation anesthesia. As has already been remarked, this agrees with the conditions present in obstetric practice.

[9] Surg., Gyn., and Obstet., October, 1914.

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FUNCTIONAL HEART-BLOCK.[1]

By T. Stuart Hart, A.M., M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY; VISITING PHYSICIAN, PRESBYTERIAN HOSPITAL, NEW YORK.

(From the Presbyterian Hospital in New York City.)

The factors involved in the coördination of the activities of the auricles and the ventricles have for a long time been subjects of investigation by physiologists, clinicians, and pathologists. The many skilfully devised experiments, clinical observations, and autopsy findings have furnished much valuable material upon which our present conceptions are based. That destruction of the A-V bundle results in the complete dissociation of auricular and ventricular activity seems well established. The effect of insults to the A-V bundle of a degree short of complete destruction, the relative importance of the muscle and nerve elements of the A-V junction, the changes in the function of the junctional tissues brought about by factors other than organic lesions, and the influence of the nerves on the independent activities of the ventricles, are some of the questions still open to investigation.

It is with the hope of presenting some clinical facts which have a bearing on the elucidation of these problems that the cases of this paper are reported.

We have applied the term "functional heart-block" to the group of cases here presented not because we believe organic changes are absent, but because these changes are of such a moderate

[1] Read at the meeting of the American Society for the Advancement of Clinical Investigation, Atlantic City, May 11, 1914.

degree or are of such a nature that by the administration of drugs the evidence of functional abnormalities can be considerably modified. The evidence that digitalis and atropin greatly modify the cardiac activity in these cases is quite clear. If we accept the myogenic theory of cardiac activity these cases present a considerable field for interesting speculation. This theory has considerable evidence on which to base its assumption that the property of stimulus conduction is dependent on the formation of definite chemical molecules in the muscle cell, and that with each passage of a stimulus these molecules are disrupted, thus producing a refractory phase which continues until a sufficient time has elapsed to allow these molecules to reform; it is further believed that external nerve influences may have a modifying effect in changing the rapidity of the construction of these molecules. Hence one may ask in such cases as these here presented, Do digitalis and atropin act by a direct influence on the muscle cell or is their effect obtained by producing a change in the activity of the vagus which causes a change in the balance of the influences brought to the muscle cell by the vagi and sympathetics?

It has been our privilege to study more or less completely thirty-four cases of heart-block presenting great diversities in clinical features. The following cases have been selected, since they represent certain types; some of our remarks, however, are based on observations on cases not reported in detail but which present aspects conforming to the types here set forth.

Case I.—*Decompensated mitral insufficiency; digitalis heart-block promptly relieved by atropin.*

L. S., aged sixty-two years, tailor; a native of Russia. Admitted to the Presbyterian Hospital in November, 1913. His chief complaint was dyspnea and swollen legs. The patient had been accustomed to drink six to eight glasses of beer and one whisky a day and smoked six to eight small cigars a day. At nineteen years of age he had gonorrhea and chancre (?), which were treated for two weeks, with complete recovery and no subsequent symptoms. He had never had rheumatism, and had been perfectly free from illness except as above until five years before admission; at this time he felt weak and was examined by a physician, who told him he had "heart disease" and must stop work. Notwithstanding this advice he continued his work until a few days before his admission to the hospital. For three years he has had considerable dyspnea on exertion and swollen legs. For five days preceding his admission he had been taking a half-ounce of infusion of digitalis three times a day.

Physical Examination (November 19). A large man, somewhat obese; propped up in bed; no cyanosis; some dyspnea; respiration 26. There were a few rales at both bases of the lungs. The cardiac dulness was found abnormally increased both to right and left.

The heart sounds were indistinct at the apex and at the base. A loud, blowing, systolic murmur was heard all over the precordium. The pulse was irregular and changed in the course of a few minutes from a rate of 44 to 78; all the heart impulses were transmitted to the wrist; all the radial beats in a short period of time were apparently of equal force. No interpolated heart sounds could be detected during the periods of slow rate; after the exertion of sitting up in bed the pulse rate rose to 86. There was moderate edema of the legs.

Laboratory Findings. The urine output averaged about one liter per twenty-four hours during his stay in the hospital and constantly showed a trace of albumin and a few casts. A functional kidney test with sulphophenolphthalein showed an output of 47 per cent. in two hours; the dye first appeared in the urine ten minutes after its injection.

The blood showed nothing abnormal; the Wassermann reaction was negative.

On the next morning the heart was beating somewhat irregularly at a rate of 40 to 50 a minute and showed no tendency to change to a more rapid rate on exertion. At 10.25 A.M., an electrocardiogram was taken which showed complete block. At 10.30 A.M. $\frac{1}{50}$ grain of atropin was administered hypodermically. Observations of the heart rate showed the following:

November 20, A.M. Pulse somewhat irregular rate 40 to 50.
10.25 A.M. Record taken, As = 86; Vs = 46; complete block.
10.30 A.M. Atropin, grain $\frac{1}{50}$ hypodermically.
10.35 A.M. Vs = 48.
10.40 A.M. Vs = 48.
10.45 A.M. Vs = 48.
10.50 A.M. Vs = 50.
10.51 A.M. Record (Fig. 1) taken, As = 85, Vs = 46, complete block.
10.56 A.M. Record (Fig. 2) taken, As = 85, Vs = 85, P – R = 0.4 seconds.
11.01 A.M. Record (Fig. 3) taken, As = 85, Vs = 85, P – R = 0.22 seconds.
11.06 A.M. Record (Fig. 4) taken, As = 80, Vs = 80, P – R = 0.2 seconds.

The electrocardiographic records of this case here reproduced were all taken by Lead I (right arm and left arm). The record taken at 10.25 A.M. is not shown, since it is identical in form with the record taken at 10.51 A.M. (Fig. 1), which shows a complete block twenty-one minutes after the administration of atropin. The record (Fig. 2) taken at 10.56, twenty-five minutes after the injection of atropin, shows that the block is broken and that the ventricle is responding to each auricular systole, but with a conduction period (P–R interval) of 0.4 second. Five minutes later (Fig. 3) the rate had not changed, but the conduction period was reduced to 0.22 second. The record (Fig. 4) taken thirty-six minutes after the injection of atropin shows that the rate has dropped to 80 and the conduction time to 0.2 second. In none of the subsequent records (the last was taken on December 7, just before the patient

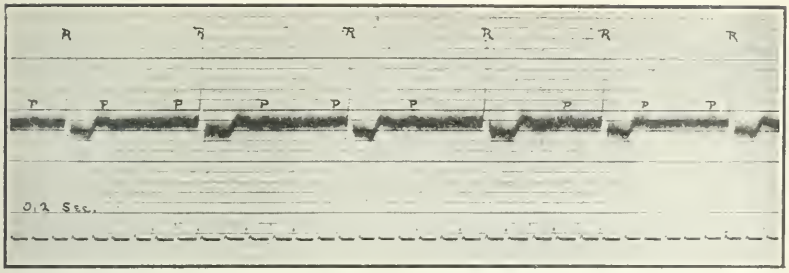


FIG. 1.—Case I. November 20, 10.51 A.M., complete block. As = 85; Vs = 46.

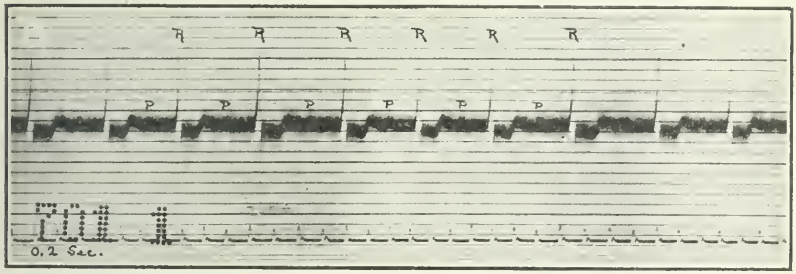


FIG. 2.—Case I. November 20, 10.56 A.M., delayed conduction; twenty-five minutes after atrophine. *P–R* interval = 0.4 second. As = 85; Vs = 85.

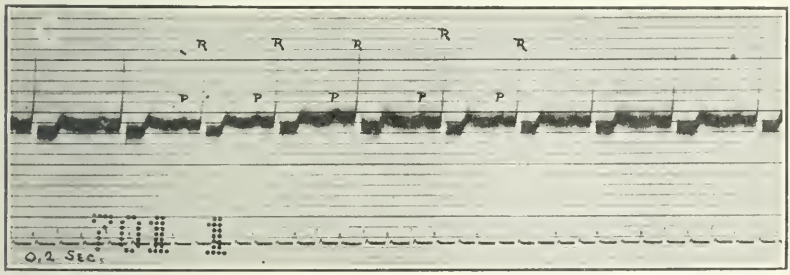


FIG. 3.—Case I. November 20, 11.01 A.M., conduction slow. *P–R* interval = 0.22 second; As = 85; Vs = 85.

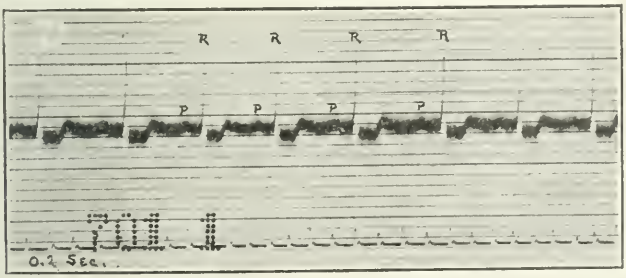


FIG. 4.—Case I. November 20, 11.06 A.M. *P–R* interva = 0.2 second; As = 80; Vs = 80.

left the hospital much improved and with his heart fairly compensated, having been without medication of any kind for two weeks) did the conduction interval measure less than 0.2 second, thus indicating a constant moderate defect in the conducting system aside from any drug influence. During the remainder of this day (November 20) the pulse was counted at half-hour intervals and was always between 85 and 95. Some time early in the morning of November 21 the pulse dropped to 44, and although no graphic records were taken, there is little reason to doubt that the block was reëstablished at this time. At 10.30 A.M. $\frac{1}{100}$ grain of atropin was given subcutaneously and the pulse gradually rose and fluctuated between 60 and 70. On November 22, at 8 A.M., the pulse was 48; atropin, $\frac{1}{150}$ grain, was given subcutaneously every three hours until November 24, when all medication was stopped. During this period and until his discharge from the hospital, on December 7, the pulse was perfectly regular and fluctuated between 75 and 85.

This case represents a type of myocardial defect which is not rare. As MacKenzie[2] pointed out some years ago, these hearts with an abnormally slow conduction are particularly susceptible to the influence of digitalis. Digitalis, according to Cushny,[3] has a two-fold effect: (1) it heightens the tone of the vagus, and (2) it modifies the functional activity of the muscle cells. Atropin apparently acts only by paralyzing the terminal fibers of the vagus.

Since in this case atropin immediately counteracted the effect of the digitalis and brought the heart back to the functional condition in which it was when uninfluenced by drugs of any kind, it is fair to conclude that here the digitalis influence was wholly a vagus effect.

Another point to be observed is that the ventricular activity is alone effected by the atropin administration; there is no evidence of change in the auricular activity. The work of Robinson and Draper[4] and Cohn and Lewis[5] indicates that nervous influences are brought to the junctional tissues more particularly by the left vagus and left sympathetic. Hence it would seem that in this case the left vagus was far more susceptible to drug influences than the right.

The rate of ventricular activity during complete block is also a subject of some interest. It is usually supposed that the ideo-ventricular rate in man is in the neighborhood of 30 per minute. In the case above described the ventricular rate was 46, with complete block. Among our records are eight cases of complete block

[2] British Med. Jour., 1905, pp. 519 and 812, also see Hewlett, Jour. Amer. Med. Assoc., 1907, xlviii, 47; Windle, Heart, 1911–12, iii, 1; Rihl, Zeitschr. f. exp. Path. u. Ther., ii, 74.

[3] Cushny, Morris, and Silberberg, Heart, 1912–13, iv, 33.

[4] Jour. Exp. Med., 1911, xiv, 227.

[5] Ibid., 1913, xviii, 739.

in which the ventricular rate was at times over 45 per minute. May it not be that in such cases the nerve connections of the sympathetic passing to the ventricular tissues may have escaped the damage to other tissues, and so may be free to exert their influence in accelerating the liberation of stimuli produced in or below the junctional tissues.

CASE II.—*Complete heart-block with unknown cause. No valvular defect, rate changed by atropin, but block continues.*

A. S., aged twenty-five years; trained nurse; single; American. Admitted to the Presbyterian Hospital November 10, 1913, for precordial pain. Her mother died at fifty-nine of "Bright's disease and cardiac complications." One brother and one sister died of diphtheria in childhood; otherwise the family history is good.

The patient had always led an active life, with much athletic exercise (tennis, riding, etc.). She had never been short of breath or conscious of her heart in any way. She had measles, chicken-pox, whooping cough, and mumps as a child, and meningitis when five years old. When fifteen she was very sick with an attack of la grippe; at that time her tonsils were much enlarged but not inflamed. Five years ago her appendix was removed. Three years ago she had an attack of catarrhal jaundice. Formerly, but not of late, she had many headaches and occasionally an attack of "sore throat." She has never had scarlet fever, diphtheria, typhoid, malaria, rheumatism, or chorea.

Ten days before her admission she developed a severe pain in the left side of the chest in the precordial region. The pain was at first constant, somewhat relieved by pressure or by taking a deep breath, but she could not lie on the left side with comfort. The pain did not radiate. Later the pain changed to a continuous tenderness, with occasional sharp, sticking pains. For the first two days she had a severe headache. Four days before admission she vomited and had a number of loose bowel movements.

Physical Examination. A healthy, well-nourished appearing young woman with good color. The lungs are normal. There is slight tenderness in the fourth and fifth left intercostal spaces 5 cm. from the sternum. The heart impulse is not visible, but is indistinctly felt in the fifth left space 8 cm. from the midsternal line. The heart action is regular, rate 50. The sounds are of a normal quality; no interpolated sounds are heard. There are no murmurs. The pulsation of the veins of the neck is not visible. Blood-pressure: systolic, 100 mm.; diastolic, 60 mm. of mercury. Urine normal. A thorough physical examination reveals no other abnormality. The Wassermann test is negative. When examined with the fluoroscope an independent rhythm of the auricles and ventricles is distinctly made out.

Numerous electrocardiographic records confirmed the diagnosis of complete heart-block. Neither the auricles nor ventricles con-

tracted in a perfect rhythm, and their activities were entirely independent of one another. On various examinations the rates varied, As = 65 to 75; Vs = 34 to 48.

On November 18 observations were made following the subcutaneous administration of $\frac{1}{50}$ grain of atropin, when the following data were obtained:

3.40 P.M.	As = 75.	Vs = 48, complete block (see Fig. 5).
3.42 P.M.	Atropin $\frac{1}{50}$ grain hypodermically.	
3.47 P.M.		Vs = 48
3.52 P.M.		Vs = 48
3.57 P.M.		Vs = 50
4.02 P.M.		Vs = 54
4.07 P.M.	As = 90.	Vs = 52, complete block (Fig. 6).
4.10 P.M.	As = 100.	Vs = 60, complete block (Fig. 7).
4.12 P.M.	As = 100.	Vs = 60, complete block (Fig. 8).

All the records of this case were taken by Lead II (right arm and left leg). It is evident that the auricles and ventricles are dissociated in all of the records; it is also clear that in any given record neither auricles nor ventricles have a perfectly rhythmic activity of their own, both the auricular cycles and the ventricular cycles varying in length to a considerable degree.

When we come to examine the results of the administration of atropin we find (1) the auricular rate is increased from 75 to 100; (2) the ventricular rate is increased from 48 to 60; (3) the block between the auricle and ventricle is complete and persists in spite of the atropin; (4) the independent arrhythmias of the auricles and of the ventricles disappear after the full effect of the atropin.

The patient's pain gradually wore away after a few days' rest in bed; she left the hospital for a few weeks of vacation and then returned to the strenuous duties of an active hospital nurse, at which she is at present occupied, with no inconvenience or discomfort. Her present pulse is between 40 and 50 and shows the same characters as described before the administration of atropin.

The persistence of the block in this case leads us to conclude that the conduction system is functionally severed. Even on the removal of all nervous influences with atropin the bundle of His is unable to convey impulses from the auricle to the ventricle. Notwithstanding this fact it is quite evident that the activities of the ventricle are modified by vagus influences, for when these were removed the ventricular rate increased from 48 to 60. Furthermore, when the vagus influence is taken away the ventricle becomes rhythmic, it is generally accepted that the so-called *sinus arrhythmias* are due to extrinsic nerve influences; by analogy it seems not improbable that in this case the arrhythmia of the independently acting ventricle is due to a similar cause. On these grounds it would appear that whatever its nature the lesion causing the block has left uninjured structures which still allow the vagus to modify

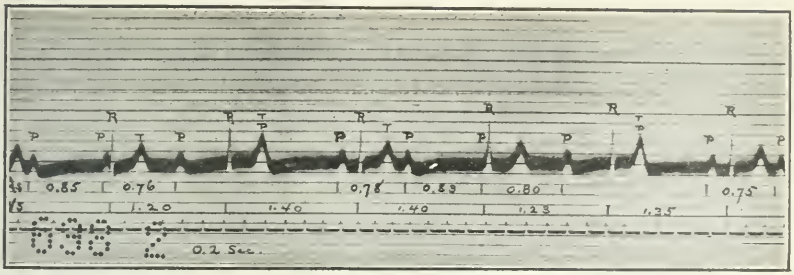


FIG. 5.—Case II. November 18, 3.40 P.M., before atropine; complete block. As = 75 arrhythmic; Vs = 48 arrhythmic.

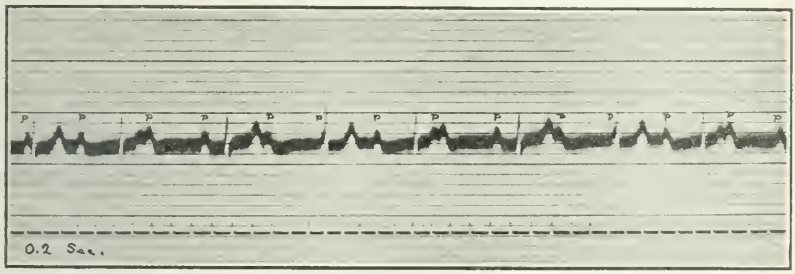


FIG. 6.—Case II. November 18, 4.07 P.M., twenty-five minutes after atropine; complete block. As = 90; Vs = 52.

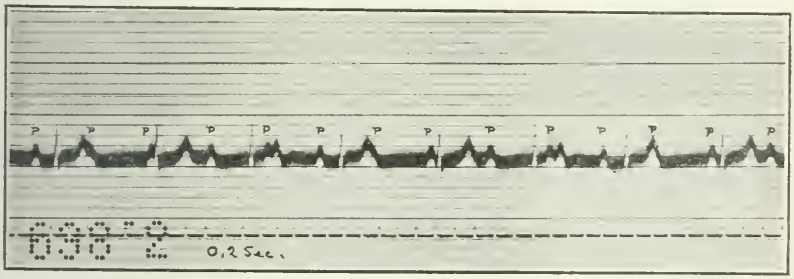


FIG. 7.—Case II. November 18, 4.10 P.M.; complete block. As = 100; Vs = 60.

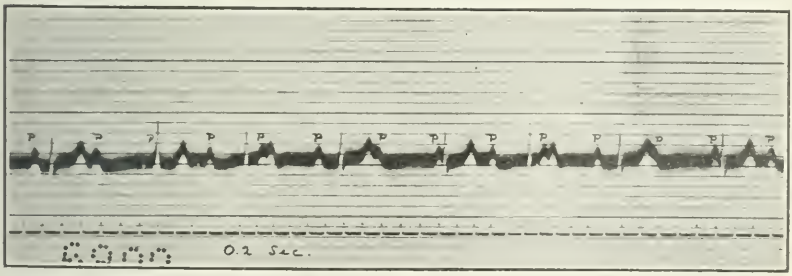


FIG. 8.—Case II. November 18, 4.12 P.M., complete block. As = 100 rhythmic; Vs = 60 rhythmic.

the activities of the ventricle. I have observed two other cases of complete block which responded to atropin in a manner similar to the above; although the block was not broken the ventricular rate was measurably increased.

CASE III.—*Decompensated heart; auricular fibrillation; atropin increases rate without removing block.*

W. H. R., aged forty-eight years, letter-carrier; American. Admitted to the Presbyterian Hospital, September 27, 1913, complaining of dyspnea. His mother died at thirty-nine of "heart disease." He has never had scarlet fever, diphtheria, typhoid, malaria, rheumatism, chorea, or syphilis. He had three attacks of gonorrhea. He had an attack of pneumonia ten years ago. He does not use alcohol or tobacco. Twelve years ago he was told that he had a large heart. Four years ago he "collapsed" while at work; he did not lose consciousness, but following this was confined to the house for two weeks suffering from weakness. For two and a half years he had had gradually increasing dyspnea on exertion. Twenty months before admission he fainted at the end of a day's work and was in the house five weeks from weakness. Nine months ago he stopped work on account of weakness and shortness of breath. He first noticed swelling of the legs four months before admission. For two months he has been obliged to sit up in bed to sleep. The abdomen had become much enlarged and the fluid was drawn off four weeks before admission. Examination on September 27: Cyanotic and dyspneic. There was a right hydrothorax, extensive abdominal ascites, and edema of the legs. The liver extended from the fourth space to 6 cm. below the costal margin in the right midclavicular line; there was no pulsation. The urine averaged a daily output of 600 c.c., with a trace of albumin and a few casts. The sulphophenolphthalein output for two hours was 58 per cent. The blood showed a mild grade of secondary anemia; the Wassermann reaction was negative at this time and on several subsequent examinations.

The apex of the heart was in the seventh space 18 cm. to the left of the midsternal line; no dulness to the right of the sternum. The action was slow and irregular; the rate about 40 per minute. The sounds were somewhat impure and muffled, the aortic second louder than the pulmonic second. No murmurs could be heard. The blood-pressure indicated that the majority of the cardiac contractions were audible below the brachial cuff at 154 mm. of mercury; the diastolic pressure was estimated at 96 mm. All of the cardiac contractions heard at the apex could not be felt in the radial artery. The character of the irregularity as determined by auscultation at the apex was as follows: for short periods the heart beat was slow and perfectly rhythmic, with a pause between the systoles of about one and a half seconds—this rhythm was interrupted at irregular intervals by an extra beat which quickly

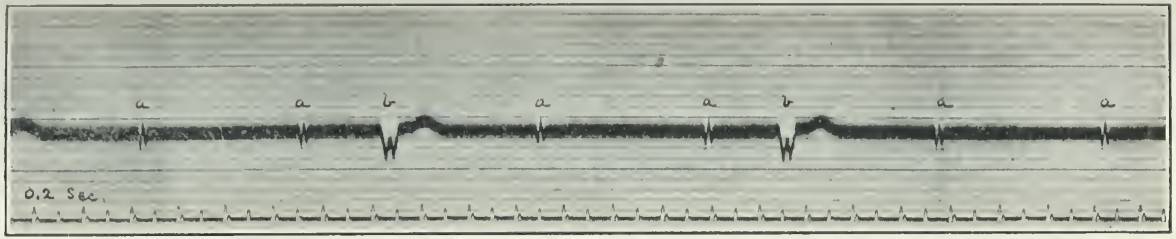


FIG. 9.—Case III. October 11, 1913. Lead I. Ventricular complexes, types *a* and *b*. Vs = 60.

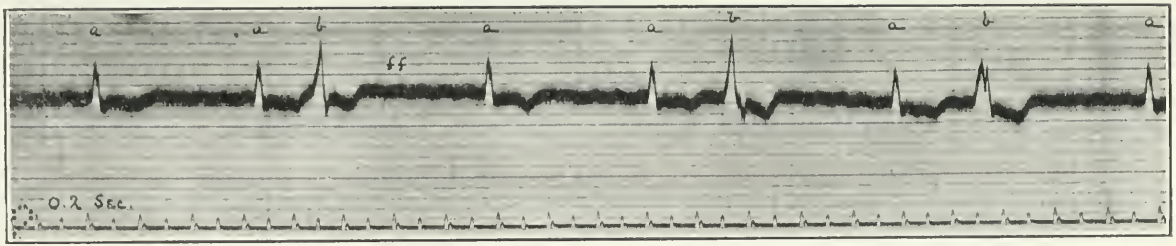


FIG. 10.—Case III. October 11, 1913. Lead II. Ventricular complexes, types *a* and *b*.

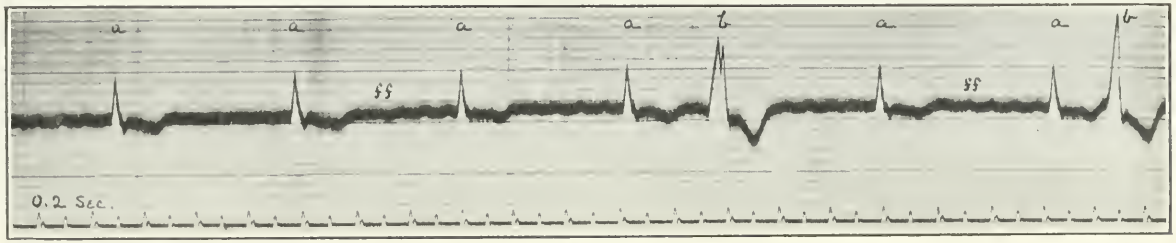


FIG. 11.—Case III. October 11, 1913. Lead III. *ff* = auricular fibrillary waves; ventricular complexes, types *a* and *b*.

succeeded one of the systoles of the slow rhythmic beats and was followed by a pause equal to the intersystolic pauses of the slow rhythm; the sound of the extra beats was less distinct than the others, but both first and second sounds could be heard; the impression was one of a slow rhythmic heart occasionally interrupted by extrasystoles. An electrocardiogram (Figs. 9, 10, 11) taken at this time showed an auricular fibrillation and slow ventricular activity perfectly rhythmic except when the rhythm was interrupted by an extrasystole arising from the left ventricle.[6] The rhythmic beats were separated by an interval of 1.4 seconds and the heart rate, if the rhythm had been undisturbed by the extrasystolic contractions for a period of a minute would have been 36 per minute. The extrasystolic contractions occurred always 0.5 seconds after a beat of the rhythmic series, and each was followed by a pause of 1.4 seconds before the beats of the regular rhythm were resumed.

Briefly the subsequent course was as follows: Removal of the fluid from the chest and abdomen was followed by a period of gradual improvement until October 27, when he suddenly developed a paralysis of the muscles of the right side of the face and a complete motor aphasia, after this he gradually improved and left the hospital the middle of November. He was readmitted December 26 with compensation again broken, ascites, and hydrothorax.

At this time the heart sounds were of poor quality: The pulmonic was louder than the aortic second sound, and there was occasionally heard a short diastolic murmur from the second left space to the apex where it had a musical quality. The pulse rate was between 28 and 32. On auscultation it was evident that the number of extrasystoles had considerably increased over the condition as observed during his former stay in the hospital. In addition to the single extrasystoles following the rhythmic beats as above described a second extrasystole could frequently be detected, of which the second sound was sometimes heard and was at times inaudible. Practically none of the extrasystoles was forcible enough to reach the wrist.

The electrocardiograms on December 29 are shown in Figs. 12, 13, 14; the ventricular rate is 60, the auricle is fibrillating. This shows complexes of the normal ventricular form (type *a*), a second type (*b*) whose form indicates the starting-point to be a portion of the left ventricle near the base, and more rarely a third type (*c*), having its origin in the apical portion of the left ventricle.[7] The time relations of these waves of ventricular activity are quite constant, the ectopic complexes following the preceding complex at an interval of 0.6 second; the normal complex (type *a*) is always preceded by a pause of 1.4 seconds.

[6] Rothberger and Winterberg, Arch. f. des ges. Physiol., 1913, cliv, 571.
[7] Ibid.

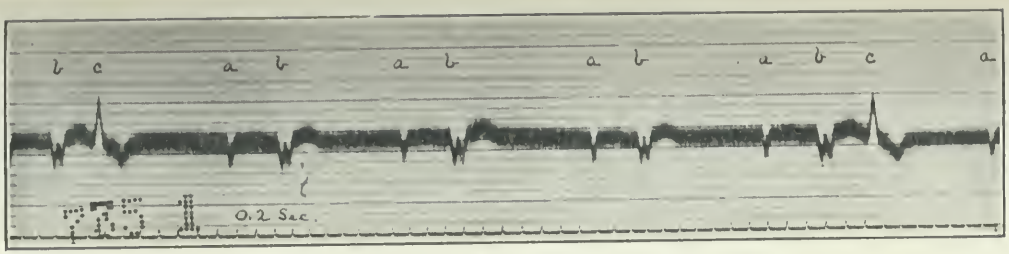


FIG. 12.—Case III. December 29, 1913. Lead I. Ventricular complexes, types *a*, *b* and *c*. Vs = 60.

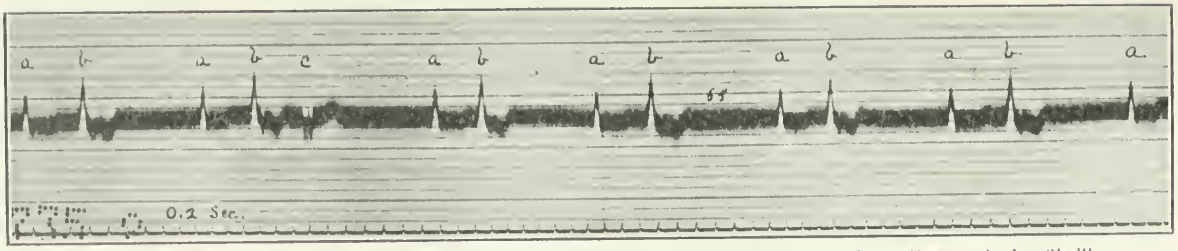


FIG. 13.—Case III. December 29, 1913. Lead II. Ventricular complexes, types *a*, *b* and *c*. *ff* = auricular fibrillary waves.

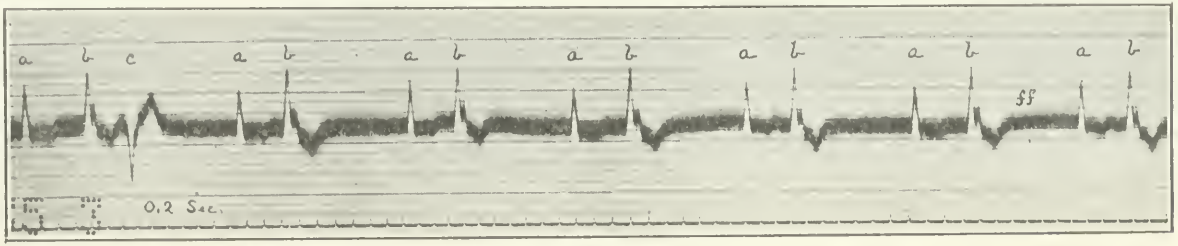


FIG. 14.—Case III. December 29, 1913. 5.35 P.M. Lead III. Ventricular complexes, types *a*, *b* and *c*. *ff* = auricular fibrillary waves.

A few minutes after this record (Figs. 12, 13, 14) was taken $\frac{1}{50}$ grain of atropin was given hypodermically; the effect may be seen in Figs. 15, 16, 17, 18, all taken by Lead III. The changes which occurred may be tabulated as follows:

Time.	Rate. Radial.	Rate. Ventricle.	Ventricular complexes. Type (*a*)	Type (*b*)	Type (*c*)	Figure.
5.35 P.M.	28	60	= 28 +	28 +	4	14
5.41 P.M.	..	(Atropin $\frac{1}{50}$ grain hypodermically)				
5.48 P.M.	32	68	= 32 +	32 +	4	
5.51 P.M.	40	68	= 40 +	27 +	1	
5.54 P.M.	..	60	..	..	..	15
6.00 P.M.	..	75	..	..	..	16
6.01 P.M.	68	76	= 68 +	8		
6.03 P.M.	..	77				
6.05 P.M.	72	76	= 72 +	4		
6.07 P.M.	..	75	..	..	..	17
6.11 P.M.	..	76				
6.15 P.M.	..	76	..	..	..	18

It is to be noted that the auricular fibrillation persists throughout the whole period, the ventricular contractions are increased from 60 to 77 in twenty-two minutes, at the rapid rates nearly all of the ventricular complexes are of the normal form (type *a*), none of type *c* persist, and when type *b* appears it occurs a little earlier than is usual for the normal complexes (type *a*), and is followed by a pause which is completely compensatory (measured by the rhythm of the complexes of type *a*). With the exception of the occasional ectopic beats the ventricle contracts in a perfectly rhythmic manner. The contractions corresponding to the normal complexes (type *a*) all, and these alone, are forcible enough to furnish arterial waves which are palpable in the radial artery.

After the administration of atropin on December 29 the radial pulse remained above 60 for about eight hours and then fell to 35. Subsequently atropin was given regularly ($\frac{1}{100}$ grain t. i. d. hypodermically) for periods of several days; by this means the pulse could be kept between 50 and 60. At these times the patient felt better until dryness of the mouth and paralysis of accommodation caused its discontinuance. At the present time (May, 1914) his general condition has considerably improved, although the rate and rhythm of the heart are much the same as on his admission on December 26.

This case represents a type which was first described by MacKenzie[8] under the term "nodal bradycardia;" at the time of this early description he did not recognize that the auricle was fibrillating, but this was pointed out by Lewis[9] at a later time based on electrocardiographic records of one of the same series of cases which MacKenzie had studied. Similar cases have since been reported by Lewis,[10] Cohn,[11] Draper,[12] and others. The presence

[8] Heart, 1909–10, i, 33.
[9] Ibid., 1909–10, i, 351.
[10] Heart, 1911–12, iv, 15.
[11] Ibid., 1911–12, iii, 23.
[12] Ibid., 1911–12, iii, 13.

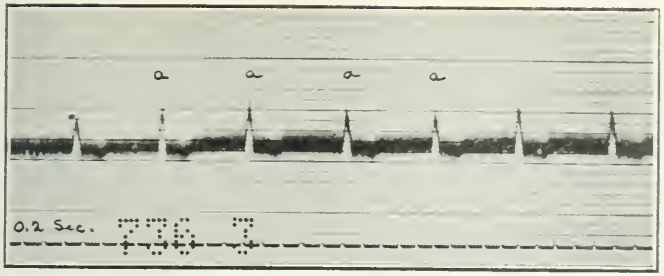


FIG. 15.—Case III. December 29, 1913, 5.54 P.M., thirteen minutes after atropine. Lead III. Vs. = 60.

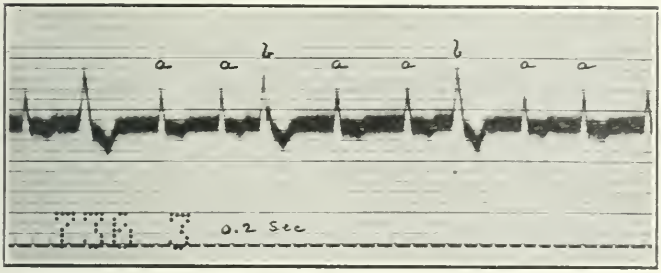


FIG. 16.—Case III. December 29, 6 P.M. Lead III. Vs = 75.

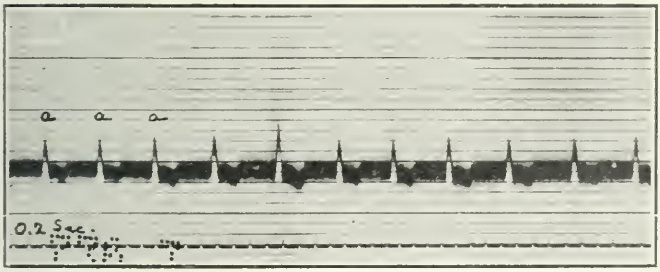


FIG. 17.—Case III. December 29, 6.07 P.M. Lead III. Vs = 75.

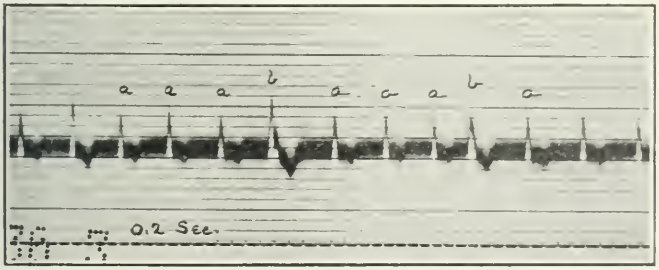


FIG. 18.—Case III. December 29, 6.15 P.M. Lead III. Vs = 76.

of extrasystoles and their increasing frequency indicates the myocardial damage which is progressive; the evidence goes to show that at first one point and later two points in the left ventricle have become excessively irritable. The inefficiency of these beats having an ectopic origin is evidenced by the fact that only a few of these are capable of causing a wave which can be detected in the radial artery, yet it is clear that these same contractions are exhausting to the cardiac tissues, since the pause after the ectopic beat is of the same length as the interval between two beats of the undisturbed ideoventricular rhythm.

We have no reason to suppose in this case that we have removed the block by means of atropin. Except for ventricular extrasystoles the heart is rhythmic. We have simply removed the vagus control of the ventricle. The ventricle is working fairly rapidly (76), but in perfect independence of the irregular fibrillary impulses sent down from the auricles. (This activity reminds one very much of cases of auricular fibrillation which are frequently seen in which after a course of digitalis the pulse becomes comparatively slow—presumably a partial block has been established—and regular at a rate between 70 and 80, although the auricles continue their fibrillary activity. In these cases, however, a dose of atropin not only causes the ventricle to beat much faster, but the artificial digitalis-block being removed the ventricle again beats with complete irregularity.)

In the case here reported the administration of atropin caused an increase in the ventricular rate from 60 to 77 in twenty-two minutes. More impressive than this, however, is the fact that under this influence the number of contractions of type *a* (which are the normal ventricular contractions for this heart) increase from 28 to 72 and the beats of an ectopic origin almost disappear (falling from 32 to 4), this seems to indicate that the removal of vagus influence has permitted the normal pacemaker of this ventricle to increase its rate of production of stimuli over 150 per cent. and thus to supplant almost completely the impulses set free from the ectopic foci.

Here again if we are correct in our interpretation we are forced to the conclusion that in spite of the auriculoventricular block the vagus has no inconsiderable control over independent ventricular activity. We have seen one other case of auricular fibrillation and block with occasional ectopic ventricular contractions which we have studied electrocardiographically with and without atropin; the atropin effect was quite similar to the case here described.

Summary. There are reported in detail three cases of heart-block representing three distinct types:

1. Complete block following digitalis.
2. Complete block with normal auricular activity.
3. Complete block with fibrillating auricles.

Other cases are referred to in support of the evidence presented in detail from these cases.

The effect of atropin administration was studied in each of these cases. In the first case (digitalis-block) the dissociation was removed; the evidence of the modification of ventricular activity was considerable. Evidence of the modification of auricular activity was negligible

In the second case (block with normal auricular activity) the block was not removed but the ventricles were much more affected than the auricles. In the third case (block with fibrillating auricles) atropin did not destroy the block but allowed the ideoventricular rate to be greatly increased.

If we are right in assuming that atropin acts only by paralyzing the terminal filaments of the vagus it is evident that in each of the cases here described the vagus had a very important influence in controlling the ventricle, either through the junctional tissues or directly on the ventricular tissue.[13]

Case I emphasizes the fact that the vagus influence is sufficient to establish a block between the auricle and the ventricle.

Cases II and III indicate that even in the presence of a lesion sufficient to cause complete dissociation between the auricles and ventricles the nervous connections may remain in a condition of functional activity and thus continue to modify the ventricular rate and rhythm.

It is suggested that in certain cases of block the sympathetic nerve connections may escape damage and may thus be capable of exerting a direct accelerator influence on the ventricle.

The disappearance of the extrasystoles associated with an increase in the activity of the predominant pacemaker is illustrated.

For the privelege of studying a number of these cases I am indebted to the courtesy of my colleague, Professor Longcope, whose hearty coöperation while the patients were on his service in the Presbyterian Hospital has made these observations possible.

ACONITE AS A VASODILATOR.

By William Hanna Thomson, M.D.,
NEW YORK.

One of the important questions in modern therapeutics is how to regulate arterial blood-pressure, particularly when it rises above normal. Morbid conditions due to high pressure are very numer-

[13] For further views of the control of the ventricle by the vagus, see Ritchie, Quart. Jour. Med., 1912–13, vi, 62.

ous and equally varied in their causation. We should, therefore, readily recognize it when present, and be fully aware of its special dangers in each case. This paper proposes to discuss only the medicinal agents which may be used to lower blood-pressure, and how they may be administered.

The commonest drugs employed heretofore for this purpose are the various preparations of the nitrites, such as amyl nitrite, nitroglycerin, potassium nitrite, and erythrol tetranitrate, named in the order of the duration of their action. The type of them all is amyl nitrite, whose action is so rapid that it is used only in sudden emergencies, as in attacks of angina pectoris. But the chief objection to amyl nitrite is that its action is not only sudden, but very evanescent, which applies also to all nitrites when the conditions of disease for which vasodilators are indicated is taken into account. These morbid conditions are usually chronic in both their origin and cause, such as the processes ending in arteriosclerosis, chronic interstitial nephritis or in sclerosis of nervous tracts.

These slowly induced textural changes are ordinarily caused by arterial ischemia, and either for their prophylaxis or for their management, all nitrites are of little service, owing to their temporary action. Meantime the organic changes in the walls of the arterioles lead to the obliteration of wide areas of both the arterioles and the capillaries of the affected parts. This alteration is well illustrated in chronic interstitial nephritis, when on baring the unnaturally white skin of the abdomen, it will be found comparatively difficult to produce a reddened mark by drawing the finger nail across it. In phthisis, on the other hand, the same procedure easily causes a scarlet line to follow the finger nail. But that which causes the cutaneous anemia must likewise occur in the capillary circulation of the internal viscera, and thus interfere with their functions. Now as the chief business of the kidneys is to eliminate urea, I have found that in chronic interstitial nephritis there is a characteristic and marked decrease in urea elimination.

My objection to all nitrites, as above stated, is that their vasodilating effects are too transient, the most prolonged of them, that of the erythrol tetranitrite, lasting for less than an hour, which is by no means sufficient for such a permanent morbid condition of general arterial contraction, with heightened blood-pressure, as is present in chronic interstitial nephritis.

After an experience of years in its use for this purpose, I regard aconite as the most efficacious vasodilator which we possess, when given systematically in full doses. Aconite thus administered at once reduces blood-pressure, produces a full and compressible pulse, and greatly increases the percentage of the elimination of urea in interstitial nephritis.

We may here briefly allude to some contrasts between the clinical features of parenchymatous and interstitial nephritis. In parenchy-

matous nephritis the kidneys are large and white in color, while in interstitial nephritis they are shrunken and red. In parenchymatous nephritis, albumin is abundant in the urine, in interstitial nephritis it is either wholly absent or present only in slight amount. In parenchymatous nephritis there is anasarca from beginning to end. In interstitial nephritis every sign of dropsy may be absent. In parenchymatous nephritis the urea elimination may be but slightly below normal, while in interstitial nephritis the urea is diminished from the start, below that of any other form of kidney disease.

The most important action of aconite when administered in interstitial nephritis is to increase the elimination of urea. In a former paper, read before this association, I stated that in a series of cases which I had observed in my wards in the Roosevelt Hospital, the elimination of urea after the administration of aconite, was increased, in a large proportion of these patients to double the amount, previous to the administration of aconite, and in two cases, to three times the amount. In a series of 7 cases of chronic interstitial nephritis observed for two weeks by Prof. J. Edgar Welch, Dean of the Department of Medicine, at Fordham University, the property of aconite to increase the output of urea was not observable until Dr. Welch himself raised the strength of the aconite from that of the present pharmacopeia, which is only 10 per cent., to the pharmacopeia of 1890, which is 35 per cent., and which was the strength of the preparation which I used in my above observations at the Roosevelt Hospital. On doing so, Dr. Welch found that the elimination of urea was immediately increased to the extent that I had observed. I have given as much as 10 drops of this strongest tincture 4 times a day with excellent results in the reduction of pressure.

The symptoms produced by heightened blood-pressure are usually distinct shortness of breath, often with a sense of oppression at the epigastrium, very perceptibly increased by muscular exertion, such as by walking or by ascending stairs, and especially by walking against the wind. Patients in such a condition are frequently obliged to stop, as they express it, "To catch their breath." Not uncommonly actual anginose pains come on, with attacks of dizziness. In one case, a lady now seventy-five years of age, these symptoms were formerly very troublesome, but by perseveringly taking the aconite three or four times a day, she has been free altogether from them for twelve years, provided she does not omit the aconite.

Another case was that of a well-known physician, aged sixty years, a somewhat fleshy man, with a large chest, and a blood-pressure of 185 mm., who had severe attacks of anginose pains, waking him about 2.00 A.M., which passed down the left arm to the wrist. He was treated with the 10 per cent. tincture of aconite, 15 drops, com-

bined with 5 grains of sodium iodide, t. i. d., whereupon all his symptoms improved, and his blood-pressure dropped from 185 to 160 mm. After continuing this line of treatment for two years, he reduced the aconite to only 10 drops, with an entire disappearance of his old symptoms.

The beneficial effects of aconite are particularly pronounced in mental derangements of the nature of melancholia with high blood-pressure. Thus a patient of mine had been gradually passing from a state of melancholia with hallucinations about being financially ruined, until he became maniacally insane, and repeatedly tried to break through the windows. He was then treated by Dr. J. Edgar Welch, who had to employ three men to hold him while he was taking his blood-pressure. Dr. Welch by my directions gave him 15 drops of the 10 per cent. tincture of aconite and 15 drops of the tincture of veratrum veride every half-hour. He took six of these doses before he became quiet, after which he remained permanently better, and in a few weeks was able to resume business, meantime taking 15 drops of the 10 per cent. tincture of aconite, four times a day, to prevent a relapse.

As a veteran teacher of materia medica, I insisted upon the fundamental difference between functional and organic or constitutional medicines. Functional medicines like aconite or opium produce their whole effects in one dose, and however often repeated, the effect of the last dose is no different from that of the first. Organic or constitutional medicines, on the other hand, like iron in chlorosis, and mercury in syphilis, do not produce their effects except by the cumulative action of many doses. Therefore the proper dose of a functional medicine is not reached till it causes its own symptoms. In the above case of maniacal melancholia I was obliged to give 180 drops in the course of three hours, because any less quantity would have produced no effect.

A few years ago I was asked by a gentleman to prescribe for his widowed sister, Mrs. G., without seeing her, because in her then condition she refused to see any physician, or to take any medicine. His story was that she had been subject to severe melancholia until she became maniacal, and had to be committed to an asylum, in which she remained for about six months. She was then allowed to go home where she remained for nearly two years, attended by a trained nurse, but as above mentioned, in strict seclusion. Her high blood-pressure, and this gentleman's description led me to conclude that she was affected by melancholia, and without seeing her, I prescribed aconite, given by her nurse before each meal without the patient's knowledge. She at once began to improve in her mental state. Noticing, however, that she became nervous and excitable toward night, I concluded to add a fourth dose of the tincture of aconite in the evening. After this she wholly recovered, and began to gain flesh, remaining in excellent health and spirits

until her death, which occurred in her sleep, as hereinafter detailed by her brother in a letter to me.

"My sister passed away in her sleep Saturday morning, May 3. She owed to you five years of health and happiness, and I owe you a debt of gratitude which no words can describe. It seems to me in the interest of humanity, your treatment by aconite should be known in the various institutions where circulatory troubles are diagnosed as diseases of the brain."

WHEN AND HOW TO USE TUBERCULIN PREPARATIONS IN PRIVATE PRACTICE.

EFFICACY OF ADMINISTRATION BY MOUTH.

By Solomon Solis Cohen, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JEFFERSON MEDICAL COLLEGE; PHYSICIAN TO THE PHILADELPHIA GENERAL HOSPITAL, PHILADELPHIA.

If tuberculin is to become a useful therapeutic agent, its administration must be made so safe and so simple that it can be employed without fear by the general practitioner. After all, it is but a very small proportion of the tuberculous who come under sanatorium care, or who seek the advice of "tuberculosis specialists;" and any treatment that must needs be restricted closely in its application can do but a minimum of good.

Thanks principally to Arthur Latham and his co-workers, H. D. Spitta, and A. E. Inman, we have now a method of administration of tuberculin and similar bacterial products which meets the necessities of the situation.

The writer of this paper is among those who condemned and opposed the use of the so-called "Koch's lymph" when it was first—and, through the meddling of the German Emperor, prematurely—introduced. Both theory and observation were convincing as to its harmfulness in the overwhelming number of cases; and nothing of what was then said[1] needs be retracted.

But later work, and especially the painstaking studies of Trudeau, have shown not only the cause of the unfortunate results of the first period, but also how they may be avoided.

The early disasters were chiefly owing to two errors: (*a*) *crude dosage;* and (*b*) *unsuitability of cases* treated. With due attention to the selection of cases, and with careful choice and gradation of

[1] S. Solis Cohen, Therapeutics of Tuberculosis, in Hare's "System of Practical Therapeutics," first edition, Philadelphia, 1891, vol. i, pp. 872 to 874.

doses, results are now reached that are well worth while, and that apparently cannot as yet be attained by other means.

It is especially incumbent, therefore, on those of us who combatted the destructive use of tuberculin, to do our part toward the establishment of its constructive use. This paper is so intended. It deals with *pulmonary tuberculosis* only. It will attempt to show *how* and *when* in general private practice, some of the preparations of tubercle bacilli and their derivatives may be employed *as adjuvants to hygienic regime and wise medication,* with distinct benefit to the patient. For sanatorium physicians it might be considered a work of supererogation; but it is addressed to the general practitioner, who can (and should be encouraged to) make use of this additional means of aiding recovery in a frequent and troublesome malady.

Dosage. Although it is necessary—for our purpose, at least—to modify his actual plan of operation, Trudeau[2] established the correct principle of dosage—namely, to begin with a minute dose and to induce tolerance (or immunity) by very gradual increase, with due regard to local, focal and constitutional reactions—including among the latter, such symptoms as headache and malaise, even in the absence of febrile movement. Trudeau followed the common custom of hypodermic injection, and was guided by clinical phenomena in estimating the effect of the remedy.

When Sir Almroth Wright introduced the study of the opsonic index, a further advance was made. Not only did a definite reaction subject to precise means of investigation become the criterion of effect, but also the differentiation between the positive and negative phases of that reaction did away with one source of danger and made possible the choice of the most favorable time for injection. The method, however, was, and is, too troublesome for general application; and it has not found favor, even among sanatorium physicians. It is of advantage in special instances, and particularly in the investigation of novel procedures, as a measure of control; and by it, indeed, the studies of Latham and his colleagues were made demonstrative.

The next great advance came when Latham,[3] studying his cases clinically while Drs. Spitta and Inman verified the results by laboratory methods, demonstrated (1) that the clinical temperature curve furnished an exact and trustworthy method of distinguishing between the positive and negative phases of the tuberculo-opsonic reaction (the negative phase being denoted by a rise of temperature, the positive phase by a decline), and (2) that the administration of tuberculin products (and other bacterins) by the mouth (or rectum) was followed by reactions as definite and

[2] Amer. Jour. Med. Sci., August, 1906, and June, 1907.

[3] Latham, Spitta, Inman, Proc. Royal Society of Medicine, London, 1907–1908, Medical Section, pp. 213 seq.; Latham and Inman, Lancet, London, 1908, ii, p. 1280

as effective, as those resulting from hypodermic injection. These results, the work of competent observers, and of methods of study beyond criticism, have made feasible the general, intelligent use of tuberculin; *i. e.*, its application outside of sanatoriums, hospitals, and the care of specialists with laboratory facilities and training.

Latham was able to show, also, that the therapeutic reactions can be produced by doses of tuberculin even smaller than those employed by Trudeau.

Taking up Latham's methods, I observed[4] (*a*) that by certain modifications of the technic the administration of tuberculin *per os* might be made somewhat simpler, and thus more widely available; and (*b*) that the initial dose might with advantage be still further and very greatly reduced.

I then requested my nephew, Dr. Myer Solis Cohen,[5] to make a further and independent series of observations, using various forms of tuberculin preparations. This study was confirmatory of both Latham's and my own results, and developed a new, and somewhat surprising feature, in the regularity with which in certain subjects definite constitutional reactions (chiefly headache and malaise) followed the administration *per os* of almost infinitesimal doses (*e. g.*, one one-billionth of a milligram) of *tuberculinum purum*—similar reactions having since been observed with other preparations, as well.

As a result of these various lines of observation, the procedure now to be described was adopted, and has for some years been carried out.

I. *Preparation.* Observations were made with "old tuberculin (*O. T.*)," "tuberculinum purum (*T. P.* or *endotin*)," "bacillary emulsion (*B. E.*)," "bouillon filtrate (*B. F.*)" and "tubercule-bacilli residue (*T. R.*)." Latham had used T. R., giving it, by preference, with horse-serum, to promote absorption as well as effect; and this plan was followed at first in the hospital studies necessary to obtain familiarity with the workings of the remedy. When, however, the attempt was made to widen the scope of the work, and especially by entrusting the remedy to intelligent patients for use at home, the procedure was found to be too costly as well as too difficult. Tubercule-bacilli residue was therefore ground up with milk sugar, in such proportion that one gram of the powder contained one ten-thousandth of a milligram of the active substance. Thus a dose of 0.5 gram would contain one twenty-thousandth of a milligram of T. R., and a dose of 0.1 gram would contain one one-hundred-thousandth of a milligram of T. R., etc. This was given in diluted beef juice, whey, albumen water or

[4] S. Solis Cohen, New York Med. Jour., January 20, 1912, p. 132; Critic and Guide, New York, April, 1913, p. 125.

[5] New York Med. Jour., 1913, xcviii, 268; Interstate Med. Jour., 1914, xxi, 297.

skimmed milk (diluted) which answered equally as well as serum. Saline solution was used as the diluent, about half an ounce to an ounce of fluid (15 to 30 c.c.) being given altogether.

When experience had shown that very small doses and extremely minute increments were desirable, the manufacturers who had been kind enough to prepare the experimental powders (Messrs. H. K. Mulford Company) were asked to prepare a series of tablets varying in strength from one one-millionth of a milligram to one one-thousandth of a milligram each. These are now employed, and prove both convenient and efficacious.[6]

Similar tablets of O. T. and B. E. have also been made, and are available for cases in which these preparations are desirable.

When smaller doses than one one-millionth of a milligram are desired, the tablet is dissolved in 1 c.c. or more of sterile water, and the appropriate number of drops added to the diluted beef juice, bouillon, or other vehicle.

When endotin is employed, the ampoules are used, the liquid contents being readily soluble in salt water, beef juice, whey, broth, or horse serum for oral or rectal administration.

Dose. Latham had used one twenty-thousandth of a milligram of T. R. as his initial therapeutic dose in chronic cases, and the same quantity was used in the first observations at Philadelphia. Soon, however, it was found that in some instances febrile reaction occurred, even from so small a dose; or that, although reaction

[6] In order to reduce the number of different strengths of tablets that druggists would have to carry in stock to meet prescriptions, the manufacturers have decided, after consultation with me, to market only two strengths: (*a*) one one-hundred-thousandth of a milligram, and (*b*) one one-thousandth of a milligram, respectively.

To administer a dose of one one-millionth of a milligram, tablet A should be dissolved in ten teaspoonsfuls of water, one teaspoonful of which is to be added to the beef juice and the other nine thrown away. For any number of millionths up to nine, that number of teaspoonsfuls is to be used and the balance thrown away. For doses in the hundred-thousandths up to ten, the tablet itself is available. For doses in the ten-thousandths, tablet B is to be dissolved in ten teaspoonsfuls of water and the required number of ten-thousandths will be represented by the number of teaspoonsfuls used. Since the cost of the tablets is largely in the making and not in the precise amount of tuberculin which they contain, this plan is no more expensive for the patient than the supply of tablets of the exact dose, while much more economical for the manufacturer and the dispensing druggist.

Of course, the powders containing a definite quantity of tuberculin product rubbed up with milk sugar (say one ten-thousandth of a milligram in the gram), such as were used in the earlier observations, could be supplied, and a definite quantity of this dilution (still further diluted if necessary) divided extemporaneously, upon prescription, into any number of powders or triturates desired; but the objection to this method is that the thorough distribution and accurate subdivision necessary for precision in dose is difficult for the ordinary druggist not possessed of special machinery or especially expert in manipulation. I have followed this plan, however, with certain Philadelphian pharmacists willing to take the trouble, and it has been entirely satisfactory. Also a liquid preparation, such as is furnished for "serial dilution" for hypodermatic injection can be used by the physician himself or a trained assistant for oral administration as well; but the dilution of this for a minute dose could not be entrusted to the patient or a member of the patient's household. It is purely a matter of convenience, and ready availability to use the tablets.

might not at first be marked, it became so after slight increase in the quantity administered. Accordingly, the initial dose was reduced to one one-hundred-thousandth of a milligram. In a number of cases this proved to be entirely satisfactory, since it could be increased gradually, without the production of marked reaction, until a dose of one ten-thousandth of a milligram, or even one one-thousandth of a milligram, was reached. The observations already referred to, however, of subjective constitutional reaction from infinitesimal doses of tuberculinum purum, and a few instances of distinct febrile reaction at one one-hundred-thousandth of a milligram of T. R., even when the initial dose was but one-tenth of this, led to still further reduction. I now begin, as a rule, with one one-millionth of a milligram, and aim by gradual increase—not to produce reaction and then induce tolerance, but—if possible, to *avoid toxic reaction, both objective and subjective, entirely.* According to circumstances, the dose is increased by one one-millionth of a milligram or less, at each repetition, until a dose of one one-hundred-thousandth of a milligram is reached—unless meanwhile there should be developed some of the subjective or objective symptoms of toxic reaction—especially fever. In that case, the dose is diminished to the quantity previously tolerated and this is repeated twice before increase is again attempted.

At most two doses of the tuberculin are given weekly, so that it may take four or five weeks or longer to reach the dose of one one-hundred-thousandth of a milligram. If this quantity is absolutely tolerated, the increment added to the successive doses may be augmented.

Here I have no fixed and invariable rule. Attempts have been made to work out an optimum proportional increase in percentages of the preceding dose, for the oral method, as by various observers for other methods; but this is supererogatory and troublesome. According to the time at one's disposal, the apparent severity of the case, and other factors—including tendency to reaction, and progressive improvement—the procedure must be individualized.

When the patient is tolerably robust, and there is no activity or no great activity of local phenomena,—especially if softening and fever be absent, or at most only occasional rise of temperature exceeding 99.5° or 100° F. be manifested—one may justifiably risk increments of one two-hundred-thousandth of a milligram. This will at first be 50 per cent. of the preceding dose, then only 33.3 per cent. of the preceding dose, and so on, in diminishing ratio. If this increment of one two-hundred-thousandth milligram be well tolerated twice weekly, for a week or two, it may be raised to one one-hundred-thousandth. In the course of five to seven weeks a dose of one ten-thousandth of a milligram will thus be reached; at which point a halt may well be made for several weeks. If,

however, the patient is not robust, if there be tendency to fever, or if there be more than a few small or scattered liquid râles, *i. e.*, when tissue changes are, or recently have been, active, it is better to continue with minute increments—say one one-millionth or one five-hundred-thousandth of a milligram (*i. e.*, two one-millionths) even after reaching the one-hundred-thousandth milligram mark; or one may use three one-millionths or four one-millionths, according to circumstances. And the effect, toxic or remedial, of previous doses must always be taken into account. In other words, one must, as in any other medicinal procedure, "mix his (drugs) with brains."

In the manner indicated, avoiding reactive disturbance as much as possible, tolerance to increased quantities of tuberculin is slowly brought about, coincidently with improvement in both subjective and objective clinical phenomena. The dose of one ten-thousandth of a milligram is in some cases never exceeded. Should further increase seem to be necessary, however, the increment usually chosen, other things being equal, is one one-hundred-thousandth of a milligram. The increase is now made very slowly, the same dose being repeated for several weeks to a period of months, before increments as great as one ten-thousandth of a milligram are adopted. The maximum dose reached in nine-tenths of the cases thus far treated has been one one-thousandth of a milligram; but I do not hesitate to go up to one one-hundredth of a milligram, or even to a whole milligram, if in a particular case such advance of dosage should seem to be required. However, the good effects sought for are usually brought about by increases to maximal points between one ten-thousandth and one one-thousandth of a milligram and hence larger doses have not, as a rule, seemed either necessary or desirable. *The effect determines the maximal dose.*

If at any point in the course of treatment toxic reaction occurs, further increase is not attempted until the quantity producing the reaction has been tolerated at least twice; or should the dose which induced the reaction be more than two or three one-hundred-thousandths of a milligram, the usual, and I think the best, plan, is to drop back to the dose previously tolerated, and to continue that quantity for two or three weeks before another attempt is made to secure tolerance of the increment. The more carefully one avoids even the slightest reactive disturbance,[7] the more surely will the agent prove of therapeutic usefulness.

Frequency of Administration. Latham, Spitta and Inman say: "That T. R. is absorbed satisfactorily is shown by the fact that the smallest dose given in this investigation produced an immediate

[7] See paper by Meyer Solis-Cohen, The Subjective and Objective Symptoms of Favorable and Unfavorable Reactions to Tuberculin, Medical Record, New York, October 31, 1914, for description of many signs of reactive disturbance not commonly recognized.

rise in the opsonic content of the blood. This dose was one twenty-thousandth of a milligram, which in reality represents one one-hundred-thousandth of a milligram, or one one-hundred-millionth of a gram. Administered in this way tuberculin stimulates the production of antibodies and so raises the opsonic content of the blood and confers immunity. The negative phase after absorption appears to be shorter and less marked when tuberculin is given in this way than it is when the hypodermic method is employed. Similarly, the positive phase has a shorter duration, and so far as this investigation has gone, seldom lasts more than five days. The positive phase, however, is often succeeded by a short negative phase and then by a more prolonged positive phase.

"Simultaneously with the improvement in the immunity curve produced by tuberculin, occurs the improvement in the patient's condition. The temperature falls, the cough becomes less troublesome, expectoration is greatly diminished and the patient has a feeling of well being."

Myer Solis Cohen and Albert Strickler,[8] studying the leukocytic picture, observed an increase in the lymphocytes and in the polymorphonuclear cells with one and two nuclei (the first two classes of Arneth) after the administration by mouth of old tuberculin (O. T.) and bouillon filtrate (B. F.).

Based upon these various observations, and with the object of avoiding negative phases and prolonging positive phases, I have in most cases adopted the plan of administering the tuberculin twice weekly; that is to say, after intervals of three and four days respectively. Indications in a particular case may, however, point to the desirability of longer intervals, and in cases in which no therapeutic result is manifested, it is sometimes desirable to shorten the intervals in order to determine the degree of immunity, if any, that has been attained. Latham used both horse serum and physiological saline solution to promote absorption of the liquid preparation of T. R. that he employed. As a rule he gave the preference to horse serum, believing that this also possesses some desirable therapeutic property. As already stated, I have used diluted beef juice (pressed from raw meat or meat just "warmed" through), broth, whey, skimmed milk, or albumen water instead. I prefer the beef juice. Latham insists upon an empty stomach as the necessary condition for absorption of all "vaccines," and administers the tuberculin preferably before breakfast, believing the general resistance to be higher in the morning than in the evening. This is an excellent plan with bed patients, especially in febrile cases; and it may also be carried out when the patient, although not in bed, is at home, or at least, not occupied, during the day. Sometimes in the treatment of patients at their own

[8] New York Med. Jour., 1912, xcv, 53.

homes, especially those who are able to work and are employed, it is better to give the tuberculin at night and have the patient remain in bed until noon of the next day—or later, should there be increase of temperature or other definite symptom of reaction. In this way, while observation of the effect of the agent cannot be so close, an undue loss of time from work is avoided. When the time comes that the patient can be allowed to walk about and work, even on the day he takes the tuberculin, either morning or evening may be chosen; or if the dose be given only once a week, as is frequent in such cases, the weekly day of rest offers the best time. It will thus be seen that it is necessary to individualize in each case, and to pay minute attention to all the details of environment, occupation and the like; but it is not necessary here to go into further elaboration on this head.

Duration. The treatment as a whole, is to be continued, with intermissions determined by results, for many months; and resumed from time to time, if necessary, over a period of many years. When resuming treatment after an intermission, the initial dose should be determined by the previous record of the patient. Without attempting to make a fixed mathematical rule, it has been my practice to resume with one-third to one-half of the maximum dose that was previously tolerated, and to increase with relative rapidity, provided the tuberculin continues to be well borne, up to that previous maximum. This quantity is then usually continued for some time without any further attempt to increase; but should progress not be satisfactory, a further slowly progressive increase is undertaken. Should the drug not be well borne, either it must be dropped or the dose reduced to a minimum and gradually increased, as in the first course.

Selection of Cases. Here again we are chiefly indebted to Trudeau[9] for the establishment of correct principles. Without going further into history, or quoting varying opinions, it will suffice, for present purposes to indicate, as a result of personal observations and experience, those cases in which the general practitioner may, without fear, and with considerable benefit to the patient, institute the administration of tuberculin preparations by the mouth.

According to present knowledge, any preparation of the tubercle bacillus or its products is likely to do harm in the majority of what may be termed advanced, active cases. Nevertheless, there are some cases of this general group in which improvement, and even arrest of destructive processes, can be brought about by the cautious administration of one or another form of tuberculin. In my own experience, tuberculinum purum has been, in general, the most efficacious and the least provocative of reactive disturbance.

[9] Loc. cit.

It is in these cases especially that Detre's method of control of tuberculin therapy by the "differential cutaneous reactions" may be of greatest service in selection of the particular agent to be employed.

However, the general practitioner should not attempt—at least for the present—to give tuberculin in these cases at all. In experienced hands, with the patient under continuous, skilled observation and complete control, it may be not only justifiable but desirable, to endeavor to prolong life or increase comfort by the judicious use of bacterial preparations. Under any other circumstances, the risk of doing harm and of hastening death outweighs the problematic chance of doing some good.

It is therefore only in comparatively early cases that I am at present prepared to recommend tuberculin for general use—and not in all of these.

In active—so-called acute—cases, with marked febrile movemovement and energetic tissue changes, I have indeed, seen tuberculin do good; but only in skilled hands, with experienced attendants in charge of the patient, and all the circumstances of the environment under control. Such cases, therefore, are beyond the scope of the present paper.

In quite early cases of a sluggish, or at least inactive type, tuberculin is rarely needed. When suitable environment and proper food can be obtained, and when the physician is not afraid to use drugs judiciously—especially preparations of iodin (including the thyroid gland), of calcium, of arsenic and of iron—recovery will, in the vast preponderance of cases, take place without it.

Sometimes, however, even in the class of cases under consideration, those, namely, in which tissue changes have not progressed beyond the stage of infiltration and in which fever has not developed—improvement may be unduly slow, despite fresh air and good food, judicious regulation of exercise and rest, and the wise choice of medicaments. In another small group of cases, the improvement which sets in during the first few months of good treatment, may come to an abrupt standstill, considerably short of the point at which we can look for permanent recovery. In another, and still smaller, proportion of cases, not only will the improvement come to a standstill, but there may even be retrogression. Some tendency to febrile disturbance may be manifested; there will be loss of appetite, perhaps loss of weight; liquid râles may appear. In each of these three groups of cases—(1) those in which improvement does not begin quickly, or progress with sufficient activity; (2) those in which improvement is prematurely arrested; and (3) those in which retrogression threatens or occurs—tuberculin employed with care and discretion will frequently prove of the utmost advantage.

In the first stages of its use the patient should be kept strictly

at rest; especially so in those cases which show liquefaction or a tendency to elevation of temperature. Afterward it may be necessary to keep the patient at rest only on the day when tuberculin is given, or that and the day following. Still later, when distinct improvement has set in and tolerance to the doses given has been secured, the patient may be allowed to move around as usual, even while taking the remedy.

It is particularly, however, in two other classes of cases that I have seen the best results from the use of tuberculin by the mouth.

Certain patients with chronic pulmonary tuberculosis, go along after the first months or years of improvement, (*a*) without definite recovery, or (*b*) with periods of relapse or recrudescence, in which there may be merely increase of cough, with perhaps slight hemoptysis, a limited area of fine râles, and an insignificant rise of temperature; or there may be days, or weeks, of considerable fever, marked activity in physical signs, and even invasion of new areas. The relapses may thus be very mild or quite severe.

Formerly, in my practice, these latter patients were treated in the following manner. Absolute rest was instituted so soon as symptoms of retrogression appeared, no matter how trifling, apparently, these symptoms might be—perhaps only the headache and malaise that come to be recognized as premonitory indications. Diet was regulated; ice applied over the heart if body temperature exceeded 99.8° F.; perhaps the chest lightly blistered over the area of renewed liquefaction; and appropriate medicaments prescribed—usually creosote carbonate in rather full doses, sometimes digitalis, also in full doses, sometimes quinine hydrobromide, also in full doses. I now find that if, in addition, the administration of tuberculin be instituted and cautiously continued, improvement is more sure and more rapid than when tuberculin is not used. Care and caution are needed, however, in choosing the time, and the dose, and in adjusting the increase of dose; and the maximal quantity reached is rarely so much as one ten-thousanth of a milligram. It is necessary, moreover, to observe the physical signs quite closely in order to make sure that the intensity of focal phenomena is not increased by the tuberculin. Quite often it is best to wait until the relapse begins to show distinct signs of amelioration, or even until after recovery from the relapse—that is to say, until after the subsidence of the most acute symptoms. Tuberculin may then be given with intervals of from three to seven days between doses, and with cautious increase of quantity up to one ten-thousandth of a milligram—rarely beyond this—over a period of some months.

Accumulating experience tends to show that the tendency to relapse is thus greatly diminished, and in some cases apparently abolished; though of course, many years must elapse before a judgment of this kind can be considered final. Thus I well remember such a case, before the days in which I was willing to use tuberculin,

in which eight years passed in apparent health, and then, following an indiscreet change of climate, a very severe and troublesome relapse set in. One should not be over-sanguine, therefore, in his statements or his expectations concerning patients of this group. Still there is sufficient evidence to warrant the opinion that tuberculin helps both to postpone relapses and to diminish their intensity and their duration.

As to those cases which simply "hang fire," as it were—neither recovering entirely nor losing much ground—tuberculin is of distinct service. It should be given say once or twice weekly, for three months or more; then intermitted for a month or two; then resumed; and so on over a period of years. Sometimes it clinches the recovery. Always it brings about marked improvement.

It will be seen, therefore, that tuberculin is advocated neither as a specific nor as a sole curative means, but simply as a slight *additional stimulus* to the natural defensive and recuperative processes of the organism—a little push to start them working in the beginning, or to send them on when they show lack of momentum—a little help to overcome unexpected obstacles or contrary forces that might even turn the wheels backward. And as too strong a push, or a push at the wrong time might upset the machine, one needs always to be careful and conservative in its application.

Case Records. Perhaps brief notes of a few typical cases will bring out more clearly, through concrete illustration, the chief points that have been set forth.

Case I.—*Recurrent tuberculous peribronchitis. Recovery.*

H. D. Jr., now twenty-seven years of age, came under my care at the age of nine years. He was a thin, anemic, ill-developed child, with more or less constant cough and expectoration. Several members of his mother's family had died of tuberculosis, and a previous attendant had told his parents that he "would not live to be twelve years old." Physical examination showed scattered dulness throughout both lungs, especially marked along the borders of the sternum, and both fine and coarse crackling râles. He had fever (102° F.) when first seen, and for fourteen years, despite the marevelous general improvement resulting from hygienic and medicinal treatment, he continued, once or twice yearly, to have brief relapses, attended with fever and with loss of flesh and strength. Profuse, fine râles would be heard, chiefly in the middle areas of the lungs and at the posterior bases—sometimes, however, at the apices. These attacks usually followed a period of prolonged fatigue from overwork or some indiscreet exposure. The young man, however, had grown tall, broad, and robust, weighed about 175 pounds, was a skilled swimmer and tennis player, and kept active in his outdoor occupation as assistant manager of a large estate. About four years ago, during a relapse in the summer time, I added to the usual treatment of rest and creosotal, the use of T. R. tablets

by the mouth; beginning with one one-hundred-thousandth of a milligram and increasing to one twenty-thousandth of a milligram. The recovery was not much quicker than usual (taking about four weeks), but the recuperative tendencies were distinctly stimulated, so that the patient felt better during the attack than was the rule, and was stronger after it. The tuberculin treatment was continued for six months, with gradual increase of dose to one five-thousandth of a milligram; and then (active physical signs having been absent for five months) a somewhat rapid increase to one one-thousandth of a milligram was made for the purpose of provoking and overcoming febrile reaction. During this latter period, rest in bed was enforced on the "tuberculin days," once weekly. After one one-thousandth of a milligram could be borne without rise of temperature, a slightly smaller dose was continued once a week for three months longer. Since then there has been no relapse —this being the fourth year of exemption. However, tuberculin treatment was resumed every year except the present, for a period of two months, beginning, for convenience of notation, with the anniversary of the last attack. The dose used was one ten-thousandth milligram bi-weekly.

Case II.—*Active early tuberculosis of lungs. Recovery.*

S. S., aged twenty-five years, traveling salesman, was first seen in the fall of 1909. He had had a distressing cough for three months or more, was losing flesh and strength rapidly, and had recently developed fever. His evening temperature was 102.2° F., the pulse rate varied around 120. There was scattered dulness, principally at the apices, with fine, dry râles on the left and small moist râles on the right. He was put to bed in the open air (with an ice-bag to the precordium for an hour at a time, several times daily), and fed upon underdone, finely chopped beef, and hot water. Creosotal and tincture of digitalis were administered in ascending doses, for effect. Later, slight blisters (one inch square) were made from time to time (one or two weekly) over the upper anterior chest, being allowed to dry without opening. The patient lost four pounds the first week, two pounds the second week, nothing the third week. In the fourth week he began to gain; and by the end of another month, fever and râles had disappeared, cough was markedly lessened, appetite was good, strength had begun to return, and there had been a net increase of twenty pounds in weight. Digitalis had been withdrawn and capsules of creosote and morrhuol were substituted for the creosotal. Improvement continued, although the patient was now permitted to move around. After some four months longer of treatment, during which "soluble" calcium lactophosphate (given in hot water an hour before meals) had been added to the medication, Mr. S. was allowed to work a few hours daily, calling upon city customers. The total net gain in weight at this time was thirty pounds; and the diet, while still consisting

chiefly of rare broiled or roast beef and hot water, included also milk, eggs, rice, toast, butter, broths, fresh fruit, and green vegetables. In the course of some two months, occasional cough began to return, there was more or less malaise and some tendency to fever, with an impairment of appetite and a loss of five pounds in weight. Some moist sounds were heard at one apex. Rest was reinstituted, and the fever, râles and cough disappeared, but returned when the patient resumed moderate activity. Renewed rest was again followed by improvement, fever subsiding as before. Tuberculin residue was then given, the initial dose being one one-millionth of a milligram and the increase quite gradual. At one one-hundred-thousandth milligram, reaction was manifested by a slight rise of temperature (99.5° F.). Within twenty-four hours, however, the temperature fell to a point slightly subnormal. The same dose was repeated twice weekly for a month, without again causing fever. Cautious increase was now made, pausing or reducing the dose whenever the temperature rose and then attempting to push on again to and beyond the reaction dose, until finally the patient became able to bear one one-thousandth of a milligram without the slightest febrile or other disturbance. During this time (some four months), rest, while not absolute and continuous, was fairly maintained; and complete rest was ordered not only on the day the tuberculin was given, but also on the following day, even when no untoward reaction was observed. If febrile reaction occurred the patient was kept absolutely quiet until it had passed over, and, as a rule, for forty-eight hours longer. After the dose of one one-thousandth of a milligram was tolerated several times in succession, the patient was permitted to move around, except on the day tuberculin was given, and the dose was diminished to one two-thousandth of a milligram. This was kept up for a month longer. Tuberculin was then withdrawn for a month, to be resumed with an initial dose of one ten-thousandth of a milligram. For three years, the plan of taking the T. R. tablets once or twice weekly for a month, and then omitting them—at first for a month, later for two months—was followed pretty regularly. The patient was allowed to pursue his usual occupation all this time, except for absolute rest on the "tuberculin day." The tuberculin was then withdrawn altogether. The patient still remains well, fat, vigorous, and ruddy. I saw him so recently as a week before this acount was written, and could find no evidence of pathological activity in the lungs.

Case III.—*Advanced pulmonary tuberculosis with tendency to alternate quiescence and recrudescence. Prolongation of quiescent periods. Diminished severity of relapses.*

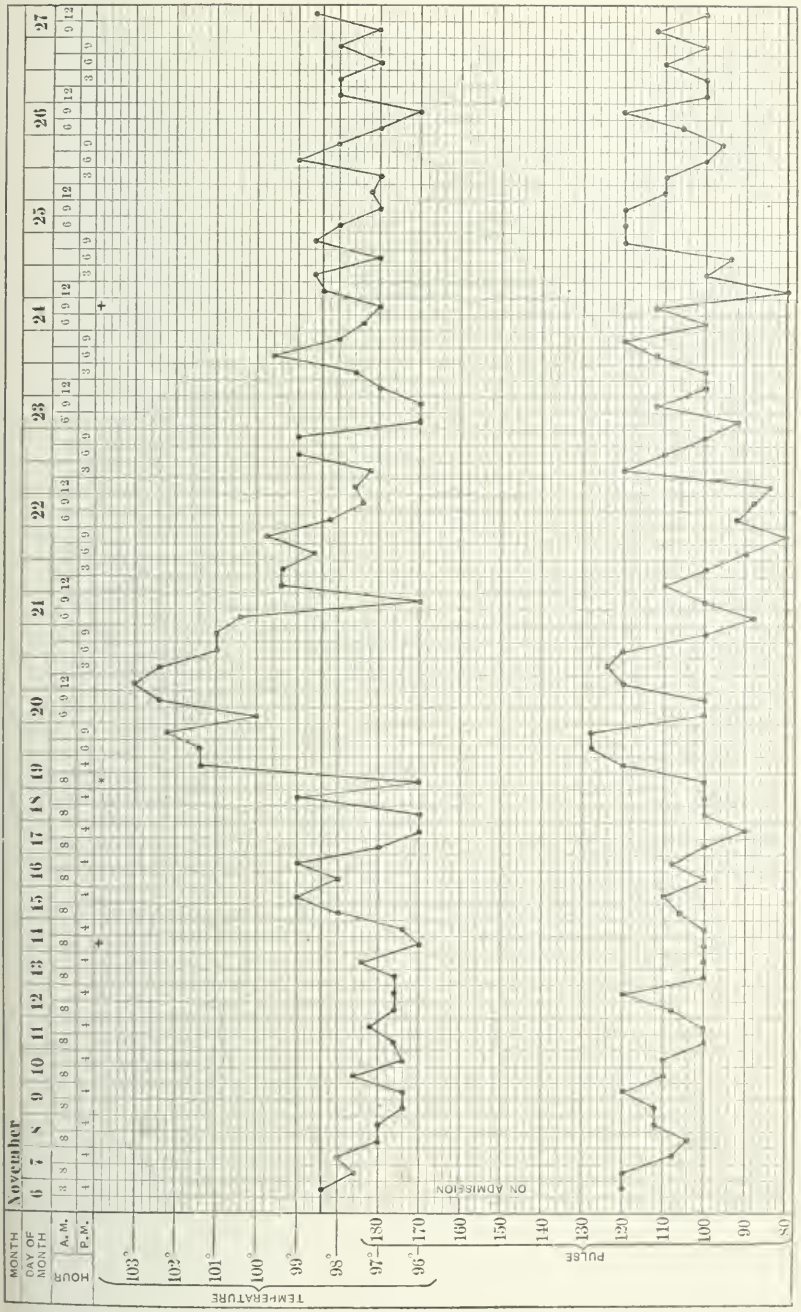
Mrs. S. P., was aged twenty-five years when she came under observation in 1907. Her father and sister had died of pulmonary tuberculosis and a brother of tuberculous meningitis. She had been coughing for some eighteen months, had been losing flesh

during all that time, and had had fever and night sweats for three months. Menses had ceased, and the patient was quite anemic, a condition aggravated by recent hemorrhages. Tubercle bacilli were numerous in the sputum. There was considerable dulness over the lungs, chiefly apical on the left, and middle lobe on the right, but extensively distributed on both sides of the chest, both anteriorly and posteriorly. A fairly large, "active cavity" was evident in the middle portion of the superior lobe of the left. On the right there was a small apical cavity and numerous scattered, high-pitched liquid râles in other parts of the lung. Rest in the open air, and appropriate diet and medication (calcium, creosote, arsenic) were instituted. The patient rapidly improved, gaining considerable in strength, weight, and sense of well-being, and losing fever and sweats. The liquid râles disappeared, the cavities apparently became dry. In some six months there was recrudescence of activity, and after six or eight weeks, renewed improvement. This course continued for some three years, there always being a little further extension of tissue loss as a net result of each relapse. Tuberculin (O. T.) was then cautiously administered by the mouth, the patient being taken into a sanatorium for the purpose of close observation. The initial dose was one one-millionth of a milligram; the maximal dose reached during three months of absolute rest being one twenty-thousandth of a milligram. Improvement was steady and persistent. Calcium was continued, creosote and arsenic alternated, weekly, and tuberculin given once monthly in quantities cautiously increased to one ten-thousandth of a milligram. The patient is kept at complete rest the tuberculin day and the day following; but permitted to move around for half a day on other days. At one time staphylococcic and streptococcic bacterins were used additionally, to combat the mixed infection. Tuberculinum purum and tubercle bacilli residue have been tried in substitution for O. T. the effects appearing to be much the same whatever preparation is used.

The net result has not been to bring about recovery in this rather severe case, but to prolong the periods of quiescence and to lessen both the severity and the duration of the relapses. The comfort of the patient has been markedly increased, and I have no doubt that her life has already been greatly lengthened, and may last for several years more. Tuberculin is resumed and withdrawn, and the dose varied from one twenty-thousandth to one one-thousandth milligram, according to the varying indications; and the same course is pursued in regard to arsenic, iron, and creosote. Calcium is kept up rather continuously. Blisters are applied from time to time.

CASE IV.—*Moderately advanced, active pulmonary tuberculosis. Improvement.*

Miss P. R., aged nineteen years, has come under observation but



Temperature chart showing marked reaction to 1/100,000 mgm. of T.R. administered by the mouth. In this case 1/1,000,000 mgm. had been given with but slight reaction. The next dose was to have been 2/1,000,000, but by mistake 1/100,000 was given. There was no permanent ill result. Later 1/1,000,000 was repeated without febrile reaction.

\+ One one-millionth milligram T. R. *per os*.

* One one-hundred-thousandth milligram T. R. *per os*.

recently, and it is too soon to form any conclusion as to ultimate results. The case is cited merely to permit introduction of a temperature chart showing marked febrile reaction to a dose of one one-hundred-thousandth milligram T. R. *per os*. This was given in error—fortunately without permanent damage. The patient is now afebrile, and not only has the loss of weight, which was rapid prior to coming under treatment, been checked, but a gain of six pounds in five weeks was made. An active cavity in the left upper lobe is becoming quiescent—almost dry. All symptoms have been favorably modified. This improvement is not attributable solely to tubercle bacilli residue, since rest in the open air, appropriate diet, the administration of ichthyol in doses of 5 to 10 minims (encapsulated), and mild blistering over the region of cavitation have done their part. The toxic effectiveness of the oral method of administration of T. R. is, however, strikingly demonstrated, and the lack of permanent ill result is to be noted.

It may be said, in conclusion, that Cases I and II illustrate fairly well the two groups of cases in which tuberculin may best be used by the general practitioner—always, however, with due care and caution. Cases III and IV illustrate a class of cases in which special experience, skilled nursing and favorable environment are necessary. To multiply instances would add nothing to the force of the illustrations, except perhaps to bring out some additional differences of detail in symptoms, progress and treatment, and thus emphasize the necessity for strict individualization in the management of each patient.

ECZEMATOID RINGWORM, PARTICULARLY OF THE HANDS AND FEET.

By M. B. Hartzell, M.D., LL.D.,
PROFESSOR OF DERMATOLOGY IN THE UNIVERSITY OF PENNSYLVANIA.

A little more than half a century ago Hebra described, with his usual astonishing accuracy and clearness, a peculiar form of dermatitis occurring on the inner surface of the upper thigh and on the scrotum, extending occasionally thence up over the pubic region and backward between the buttocks. This dermatitis was accompanied by more or less severe itching, by scaling, and in the severer forms by oozing and some crusting. It presented many of the symptoms of eczema, and he regarded it as a special form of this affection, giving to it, on account of the usually sharply defined border presented by the patches, the name eczema marginatum. A few years later Köbner found mycelial threads in the scales taken

from patches of eczema marginatum, a discovery confirmed later by Pick and Kaposi, which established the parasitic nature of the disease, and removed it permanently from the category of eczema.

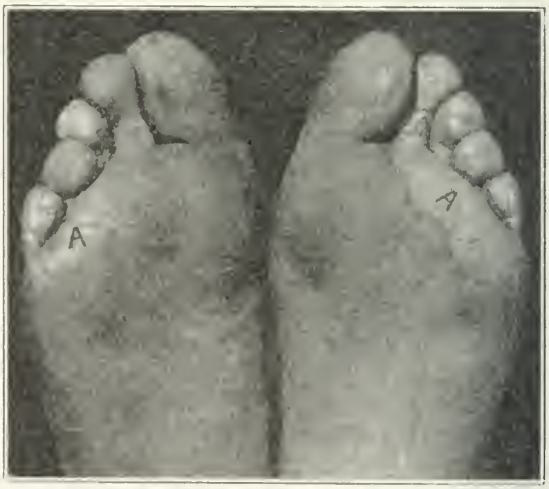
With this eczema-like form of ringworm the profession has long been more or less familiar. Notwithstanding its superficial resemblance to eczema in many of its symptoms, such as marked inflammation of the skin, accompanied by severe and prolonged itching, desquamation, oozing, and crusting, other features, such as the sharp circumscription of the patches, the occasional partial or complete spontaneous involution of the central portion make it evident, even to those with limited experience with cutaneous disease, that it is not a true eczema although resembling it.

Within a few years, indeed so late as 1910, Sabouraud called attention to the frequent occurrence of eczematoid inflammation on the hands and feet, more particularly the fingers and toes, due to the same fungus which causes the eczema marginatum of Hebra, and which resembles vesicular and pustular eczema of these regions so closely as to be practically indistinguishable from them without the aid of the microscope. It is to this parasitic eczema, for it is even more an eczema, so far as its clinical features are concerned, than eczema marginatum, that I especially desire to call attention, more particularly since the profession, with the exception of those specially concerned with cutaneous diseases, is as yet quite unaware of its existence, and failing to recognize its parasitic nature fail completely in its treatment.

Within the past few years four cases of eczematoid ringworm have come under my observation in which the presence of a parasitic fungus was demonstrated without difficulty, and one other case, at present under observation, in which the remarkably prompt disappearance of the disease after the employment of parasiticide remedies left but little doubt of its parasitic nature, although the microscopic demonstration of fungus was not satisfactory.

The first case, which is related from memory, the notes having been lost, occurred in a youth, aged seventeen years, who was sent to me by his father, a physician, for advice concerning an inflammation of the skin occupying the outer side of the left leg, just above the shoe-top. The inflamed area was about the size of the palm, quite ill-defined at its borders, slightly scaly, and accompanied by a moderate amount of itching. The duration of the patch was somewhat indefinite, but it had lasted a month or two. Microscopic examination of scales taken from the inflamed area revealed numerous mycelial threads; and under the use of a parasiticide ointment the disease soon disappeared. It is worth noting that this youth had had formerly an extensive ringworm of the scalp which had persisted in spite of treatment (it was before the discovery of the efficacy of the roentgen rays in this obstinate malady) until he was fifteen or sixteen years of age.

Mrs. S., a woman of wealth and leisure, aged about fifty years, was referred to me by her physician for the treatment of an obstinate affection of the toes of both feet. The disease, which occupied the plantar surface, consisted of an unusual dryness, with slight fissuring, scaling, and some itching. It had lasted a number of years, and although trivial in appearance, had given the patient great annoyance. It had been regarded as an eczema by the many physicians she had consulted; it had been treated by all manner of salves and washes without material improvement, and a course of roentgen-ray treatment had been equally ineffective. The disease resembled a mild squamous eczema, but microscopic examination of scrapings made from the affected surface revealed fragments of mycelium, the scantiness of the fungus elements being due without doubt to the frequent cleansing of the parts which the patient insisted upon. Under the use of parasiticide ointments, especially one containing salicylic and benzoic acids, to which reference will be made again, improvement began at once, and a complete cure after a time followed. This case is specially interesting not only because of its long duration, but because of the failure of a considerable number of physicians, one of them at least a trained dermatologist, to recognize the parasitic nature of the affection.



Ringworm of the toes resembling intertriginous eczema. A, slightly reddened and denuded area. Case III.

Mr. L., a man, aged twenty-four years, a law student, who came to the Skin Dispensary of the University Hospital in March of this year, had suffered for three or four months from an affection of the toes of both feet characterized by redness,

scaling, and fissuring in the flexures and between the toes, accompanied by moderate itching. The disease was slowly spreading backward upon the soles, and a new focus was just beginning some distance away from the original site of the eruption, as a pea-sized red patch with an elevated dry epidermic border. It had first appeared while the patient was in Panama, had continued without interruption up to the time of his visit to the dispensary, and resembled closely an intertriginous eczema, except that the posterior border of the patches where they extended upon the sole were much more sharply defined than is usual in that disease. Microscopic examination of scales from the toes showed an abundance of mycelial threads of unusual length; and treatment by a parasiticide ointment was promptly followed by recovery.

(Since the above was written this patient has returned with a reinfection, probably the result of wearing an old pair of straw bath slippers worn when he had the disease before. After remaining well for four or five months a red and scaling patch appeared in the centre of the anterior part of the right sole, which slowly enlarged until at present it is the size of a silver quarter, and to the outer side of this patch is a smaller oblong one presenting the same features. The under surface of the third toe of the left foot is likewise slightly red and scaly. The epidermophyton was found in scales taken from the larger patch on the right sole.)

In May of this year, Mr. T., a youth, about seventeen years of age, a student in a school for boys in the suburbs of Philadelphia, was sent to me for advice concerning a chronic inflammation of the sides and palmar surface of the right index and middle fingers with a portion of the palm adjacent. It resembled a mild scaly eczema, for which it had been mistaken by his former medical adviser, had lasted for six months, and had been uninfluenced by treatment. An abundance of mycelia was readily demonstrated in scrapings from the diseased area; and recovery took place within an unusually brief time under the use of the salicylic and benzoic acid ointment already referred to. The patient when told that his disease was a variety of ringworm, stated that he had had a ringworm of the axilla and thighs the previous summer.

From the time of Hebra until a very recent period the so-called eczema marginatum was universally regarded as simply an unusually inflammatory form of ringworm due to the same organism which causes the ordinary forms, the greater degree of inflammation being the result of the heat and moisture of the regions affected which greatly favor the growth of the fungus, and the friction to which the parts are subjected. Hebra, however, had early made the observation that "when eczema marginatum attacks hairy parts . . . . no alteration is produced in the state of the hairs—they neither change color, lose their glossy appearance, fall out, nor break off. Nor has anyone ever succeeded in demonstrating the

presence of fungus therein."[1] It remained for Sabouraud, to whom we owe epoch-making discoveries in connection with the trichophyton fungus and related organisms, to correctly interpret the meaning of the immunity of the hair in regions such as the pubis and axilla, attacked by eczema marginatum. He established the fact that these eczema-like forms of ringworm are produced by an organism which differs "botanically . . . from all the ringworm fungi so much that the differentiation may be made by a glance at a preparation through the microscope." This fungus, to which he has given the name epidermophyton inguinale, differs from the ordinary varieties of the trichophyton not only microscopically, but culturally as well; and unlike the trichophyton, does not invade the hair, but the upper layers of epidermis only. Whitfield, who has reported from time to time a considerable number of cases of eczema-like ringworm of the hands and feet, divides them into three varieties. In the first there is a vesicobullous eruption which often appears suddenly and presents the features of an acute eczema; indeed the differential diagnosis is quite impossible without the aid of the microscope. In cases of this type the inflammation is at times quite severe: in one under Whitfield's observation the hands and feet were swollen, covered with vesicles which in the palms had run together to form bullæ. Fungus was found in great abundance in the roof of the vesicles. The author believes some of these cases are the result of infection with an ectothrix instead of the epidermophyton. The second variety resembles an intertriginous eczema, and is found chiefly on the under surface of and between the toes, although the hands may be likewise affected. This form, which commonly follows an acute attack, is very chronic in its course. In the third variety, which was described by Djellaleddin Moukhtar in 1892, the palms and soles are the seat of a more or less marked hyperkeratosis which is usually preceded by a vesicular and pustular eruption. In this last variety, according to Sabouraud, we have to do with a genuine trichophytosis; but Whitfield believes this form may also be produced by the epidermophyton, having obtained cultures of this organism from two cases.

The frequency with which this parasitic eczema occurs is considerable, and it will almost certainly be seen much more frequently than at present when we have learned to suspect the presence of fungus in every case of eczema of the fingers and toes and to examine such cases microscopically. Whitfield saw fifteen cases in a period of three years, and Sabouraud asserts that eight out of every ten cases of so-called intertrigo of the toes are actually parasitic the result of infection with the epidermophyton fungus. Many of these cases have been preceded by eczema marginatum of the groin or

[1] Hebra on Diseases of the Skin, Appendix, vol. v, Sydenham Society's Translation.

axilla; and it has been observed that they are much more common in the well-to-do classes than in those who are seen in the out-patient department of the hospitals.

A final word as to the treatment: In our own limited experience we have found the ointment suggested by Whitfield, which contains 3 per cent. of salicylic acid with 5 per cent. of benzoic acid, most effective; but it cannot be used, as Whitfield has pointed out, without some degree of caution in markedly inflammatory cases, as it occasionally produces considerable irritation.

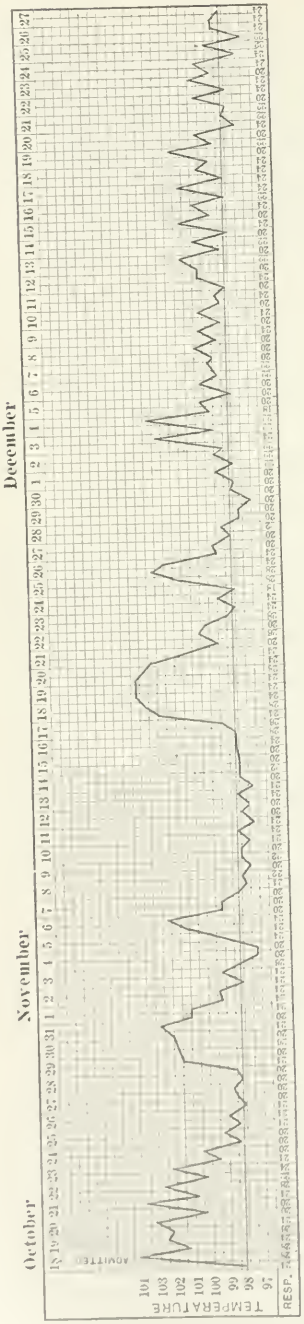
AORTIC ANEURYSM WITH RECURRENT FEVER.

By Alexander McPhedran, M.D.,
TORONTO, CANADA.

Mrs. M., aged thirty-six years, a charwoman, was admitted to the hospital October 18, 1913. She was a vigorous woman, with high color, but she said she was considerably paler than usual. Her father died of aneurysm. She had two living children and one stillbirth, twins. She lived irregularly and drank strong liquors to excess. Five or six weeks before entering the hospital she is said to have been kicked below the right scapula. She complained of pain in this part, and she was troubled with nausea and vomiting. Over the part there was dulness, and the breathing sounds were weak. There were 13,500 leukocytes per centimeter, the increase being in the polymorphonuclear cells. She did not appear seriously ill; with the fall of temperature the leukocytes returned to normal and remained so even in the recurrent attacks of fever. The signs in the chest grew gradually less marked and the pain ceased.

In the general examination of the chest signs of dilated aorta were found. Its pulsation could be easily felt below the episternal notch. Later, by the screen, a pulsating knob on the lower surface of the transverse part of the arch was seen. The Wassermann test gave a marked reaction.

She was kept five weeks under observation in order to note the natural course of the fever—it showed little if any improvement. Then mercurial inunctions were made and potassium iodide given. There was only one sharp rise of temperature after that, but slight, somewhat irregular fever persisted, and six weeks later salvarsan was resorted to. A first intravenous injection of 0.3 gm. was given. There was no reaction. Eight days later 0.6 gm. was given, still without reaction. A similar dose was given eight days later, followed by a slight short reaction, the temperature rising to 100° F., but fell to normal and remained so. A fourth dose was given after



ten days, and the reaction was rather sharp, the temperature reaching 102.5° F., but again fell and remained normal. Thirteen days later the last injection was given; the reaction was less; temperature, 101.5° F. After that the temperature remained normal while in the hospital—six weeks—and her general health improved very much, but there was no change apparent in the state of the aorta or the aneurysm, and the Wassermann reaction was quite as marked.

A month later she returned for examination. She had gained much weight and strength, her color was florid, and she appeared very vigorous. She had married in the meantime.

Discussion. The object of this brief paper is to put on record a detailed statement of one of these rather rare cases of aortic aneurysm accompanied by recurrent fever, doubtless due to syphilis. That the toxemia causing the fever arises from the diseased aorta is most probable, but not certain, as it may originate in foci of disease in other parts. Dilatation and aneurysm of the aorta is due to weakening of the wall caused by the organic changes where the disease is most advanced. At first these "dilatations" will exist during life only, while the aortic wall is under tension, and may not be evident at the autopsy. It is not until they become quite large that such "pouchings" become demonstrable even with the screen or skiagram. Nevertheless they may cause serious pressure results, for example, by occluding a coronary artery with rapidly fatal results, as occurred in a case reported by Winternitz.[1]

[1] Johns Hopkins Hosp. Bull., xxiv, No. 269, 212.

As is usual, once the infection invades the deeper structures, such as the brain and walls of the bloodvessels, it is difficult to eradicate. Even great improvement may follow the use of any of the antisyphilitic remedies, but it is seldom that cure is effected, as shown by the persistence of the Wassermann reaction. Benefit follows even good care and generous diet; greater benefit results from the addition of mercurials, and still greater benefit follows the administration of salvarsan.

This untoward result is probably due to the slight access of the blood-serum to the spirochete, owing to the avascular granulation tissue in which it becomes embedded. Whether resort to repeated courses of salvarsan for a long period may not finally effect a cure by destroying all the spirochetes remains to be proved. There is, however, sufficient evidence to render such a course at least encouraging. The chief difficulty is in getting the patients to submit to the necessarily protracted course of treatment, especially if, as in this woman, they early become restored to a satisfactory feeling of well-being.

THE EARLY DIAGNOSIS OF SPINAL CORD TUMORS.

By Joseph Collins, M.D.,

and

Henry E. Marks, M.D.,

new york.

(From the First Division of the Neurological Institute of New York.)

We report two cases of extra-medullary tumor of the spinal cord, presenting a so-called atypical symptomatology, and with these cases in mind discuss the early diagnosis of the disease.

Case I.—A Russian Jew, eighteen years old, whose heredity and past history are negative, entered the Neurological Institute October 15, 1913, when the following history was obtained: Up to three months ago he was active and strong on the legs. His parents then noticed that his gait was somewhat unsteady, that he was not walking in a straight line. A month later he began to find it difficult to keep his balance, to climb stairs, and to run. He began to trip and tire easily, and on two or three occasions he fell. These infirmities steadily progressed up to three weeks ago. Since then there has been little or no change. The right leg he believes has been weaker from the start than the left. Otherwise he has had no symptoms, and feels quite well. Regarding sensory disturbance, on direct questioning, he recalls that occasionally he has felt slight drawing sensations in the backs of the thighs on

overexertion, but at no time has he had pain, girdle sensation, or other paresthesiae.

He is well developed and nourished. The face has an expression that one associates with existence of adenoids; the tonsils are hypertrophied. The submental and cervical glands are somewhat enlarged, discrete, and hard; the thyroid isthmus is palpable. In the chest and abdomen nothing abnormal can be detected.

His pupils are not quite circular; the left is somewhat greater than the right, but both react well to light and accommodation. The cranial nerves are otherwise quite negative. His upper extremities present no abnormalities. The abdominal muscles function well. He sits up readily from dorsal decubitus without the aid of the arms. The epigastric and abdominal reflexes are lively and about equal. His spinal column shows no deformity, no tenderness and range of movement is quite free in all directions.

Examination of the lower extremities reveals definite alterations. Over both hips there is laterally a little flattening, especially on the right. The buttock and thigh muscles as a whole have a somewhat flabby consistence. A low grade of hypotonia is present in the hamstring groups, particularly the left. Range of motion is normal in all the joints except for dorsiflexion of the right ankle, which is moved upward in moderate valgus position. Despite normal range, however, there is considerable loss of power. Flexion at the thighs is poorly sustained, and only with great effort; adductor power is feeble, abductor power almost nil, the left thigh is weaker than the right. At the knees, both flexors and extensors are somewhat weak, especially the flexor groups. At the ankles, dorsiflexion on the right is feeble, on the left only slightly affected. The plantar flexors are apparently unimpaired. There is some secondary static swaying of the upraised legs, but no dynamic tremor, ataxia, or asynergia. The knee- and ankle-jerks are somewhat exaggerated but equal. On the left there exists typical Babinski and Oppenheim phenomena, and marked ankle-clonus. On the right a rapid extensor response, inconstant Oppenheim, and exhaustible clonus. On standing certain instabilities appear: the trunk twists on the pelvis, the pelvis sways laterally, the legs flex and extend irregularly at the knees. All these movements are of small range, however, and do not materially disturb equilibrium even with feet together. Well-marked Rombergism exists with a predominant tendency to fall to the right. His gait shows no gross impairment; at most it is mildly spastic ataxic. He is able to climb stairs, to run, and to perform other movements calling for strength and coördination.

Sensation. No zone of hypersensibility can be determined. Over each thigh anteriorly is a small indefinite patch of combined hypesthesia and anesthesia, otherwise touch is everywhere intact. A slight grade of hypalgesia starts just beneath the groin, somewhat

abruptly on the right, more gradually on the left, and continues (though relatively greater on the right than on the left) without definite alteration anteriorly to the toes. Posteriorly no disturbance can be detected on the right; on the left there is a vague relative hypalgesia from the knee hollow downward. The level and character of thermoesthesia is approximately the same as for pain, namely, the level of the groin or slightly below. On the right extremity anteriorly cold is not perceived and heat is either diminished or not felt. On the left extremity anteriorly the same disturbances are apparent but are less marked. Posteriorly a mild therm-hypesthesia exists right and left from the knee hollows down. There is considerable impairment of postural and passive movement in the toes. Vibration sense is abolished and the Weber circles appear abnormally widened.

The electrical reactions of accessible muscles are normal. The blood and spinal fluid show no abnormality.

The patient remained in the hospital two weeks. During this time a slight improvement was noted. His condition after that, however, grew steadily worse. At first he was able to walk to the dispensary unaided. Soon he had to use a stick, later he could only come when someone supported him; finally he was unable to come at all. By February, 1914, the spasticity of his legs had progressed to such an extent that he could not stand unaided. He described now a feeling of strain on the right side below his umbilicus, a slight drawing sensation about the waist line after sitting for any length of time, and on defecation a sense of internal tenesmus, as if the intestine had not emptied itself. Still there was no actual pain.

Physical examination, February 11, 1914, four months after he was first seen, revealed a marked spastic paraplegia, double Babinski phenomenon, and double clonus. The sensory disturbances had greatly advanced. From the groin downward the whole right leg except for a small patch here and there was anesthetic. Over the left leg, especially along its internal surface, were irregular bands of diminished touch perception. Pain and temperature sensibilities had suffered practically an obsolute loss from just above the knees to the ankles anteriorly; and elsewhere from the level of the groin downward, especially on the right, they were gravely disturbed. Sense of posture and of passive movement was completely abolished in the toes. No areas of hyperesthesia could be determined and the changes from normal to diminished sensation remained much as first described.

The diagnosis of tumor, which had previously been made, was now considered possible, and the patient was urged to submit to operation. On February 14, 1914, laminectomy was performed by Dr. Elsberg. Removal of the spines and laminæ of the ninth, tenth, and eleventh dorsal vertebræ. To the right of the tenth dorsal lamina, dorsolateral to the cord, was seen a bluish mass,

over the lower part of which a nerve root was stretched. After considerable bone had been rongeured away a soft extradural bluish tumor, about 4 cm. in length, was exposed. The nerve root, posterior dorsal eleventh, which ran over the tumor, was divided. The tumor was freed and removed. It was 4 cm. long, about 1 cm. thick, and on section was fibrous, containing spicules of bone. On microscopic examination it proved to be a fibroma with calcareous degeneration.

Almost at once the patient began to improve. A month after the operation, though still weak, he was walking short distances without assistance. On April 17, 1914, he showed the following condition: the right epigastric reflex is lively, the left present, the abdominals are feeble right and left; range of movement at all the joints is normal. At the hips flexor power is excellent; adductor fair; abductor still rather feeble. At the knees and ankles no definite impairment can be detected. There is possibly still a slight increase of tone on the right, but this is all that remains of his marked spasticity. The knee- and ankle-jerks are on the lively side and equal. Double Babinski and clonus still persist. His gait is somewhat shambling and slightly spastic, but he can walk a mile or more without fatigue. He mounts stairs and stands on one leg without difficulty. The superficial sensory disturbances of the legs have totally disappeared. There is still some loss of posture sensibility and of passive movement sensibility in the toes, however, and Rombergism still persists.

Case II.—A Russian girl, aged fifteen years. Heredity and past history negative. At the age of eleven she began to feel sharp twinges of pain over the precordia, at first daily, then at gradually lengthening intervals up to six or seven months apart. The pain was never severe or radiating, but was localized beneath the breast. A so-called attack would consist of but a single twinge or catch and no more, of a moment's duration. She was believed to have heart disease. At the age of fourteen years she went to work as an errand girl. After about nine months she began to feel tired in her legs at night. Three months later she began to drag her right foot. She was told at a hospital that she was suffering from flat-foot. About six weeks later she was dragging her left foot. At the same time she began to complain of a slight sense of heaviness beneath the left costal margin, relieved by pressure, and of hurried action of the bladder with occasional incontinence. At this time she entered the Neurological Institute July 20, 1911, when the following note was made: The patient is well developed and nourished. The cranial nerves and upper extremities are quite negative. The epigastric reflexes are present equal but sluggish, the abdominal not obtainable. In the lower extremities no atrophy can be determined. Both legs are somewhat hypertonic, amounting to slight spasticity on the right. The knee- and ankle-jerks are equal and greatly exaggerated. Double

Babinski and ankle clonus exist, the latter exhaustible on the left. She stands insecurely with feet together, the right leg being very weak. Her gait is that of double foot-drop with spasticity. The right leg, which is much more profoundly affected than the left, she swings outward very much as does a hemiplegic. Over both legs, especially along the outer surfaces, are patches of hypesthesia and anesthesia for all sensory qualities. There is some blunting of posture and passive movement of the toes. No zone of hyperesthesia can be determined. Electrical examination is negative.

The patient's condition went steadily from bad to worse. The following is extracted from a note made six weeks after her admission: She is now wholly unable to stand or walk. Marked spasticity appears in the legs on attempts at active and passive motion. In dorsal decubitus the feet are in typical pes cavus posture. The peroneal muscles are wholly inactive, producing double foot-drop with inward inclination. Active movement at the ankles is totally abolished. The thighs are thin and the muscles of the right side have the appearance of being slightly atrophic. The lower legs are so thin that they can be spanned with the hand. All the tendon jerks are exaggerated, and there is continuous patella and ankle clonus. Double Babinski is likewise present. Deep sensibility of the lower extremities is profoundly impaired. She has no idea of the position of her feet and legs. Loss of tactile sensibility is very indefinite both in quality and distribution. Over certain portions of the lower extremities she feels the cotton wool with some distinctness; over other areas she does not recognize it. Tactile sensibility becomes acute on the left side posteriorly after the iliac crest is passed. On the right side it does not become acute until the border of the ribs is reached. Anteriorly right and left it first becomes normal at the level of the umbilicus. Pain sensibility does not seem to be particularly obtunded. Temperature disturbance has much the same disturbance as tactile, and consists of reduction, confusion, and absolute loss. Above the umbilicus mistakes are few.

The patient remained at the Neurological Institute seven weeks, then entered the Hospital for Ruptured and Crippled. Here she gradually improved. At the end of seven months, with the aid of braces and crutches, she could walk about a block. A month later approximately she threw one crutch aside. Four weeks later the braces were removed from the left leg and she discovered she could bend the knee almost normally. Soon afterward she was able to walk one or two steps without crutches. After about a month of steady improvement her legs began to gradually weaken, until in May, 1913, a condition of complete paraplegia had been reached again.

Physical examination revealed a condition somewhat similar to that noted when she left the Neurological Institute, except that it was more pronounced. In contrast to the marked objective dis-

turbance, especially on the motor side, her only subjective sensory complaint has been and was the mild feeling of heaviness beneath the left costal border. The slight twinges of precordial pain had ceased eighteen months before.

Operation, May 22, 1913, at the Hospital for Ruptured and Crippled, by Dr. Alfred S. Taylor, Associate Surgeon to the Neurological Institute. Right unilateral laminectomy, from dorsal third to dorsal seventh inclusive disclosed an extradural cyst lying under the dorsal third, fourth, fifth, and sixth laminæ, mostly to the right of the median line and dorsally. Two projections from the main cyst reached over to the left of the median line dorsally. The cyst was loosely adherent to the dura and was attached to the bone by thin fibrous tissue, above and below. The cord beneath showed no other change than that due to prolonged pressure. Wound closed without drainage by layer sutures. Primary union.

Two weeks after the operation she began to move her toes. A week later she could flex and extend her knees. Seven weeks after the operation, with the aid of crutches, she was walking from one end of the ward to the other. At the end of July, 1913, she discontinued using crutches. For the past eight months she has felt no functional disability whatever.

At present the patient goes to school. She walks a mile or so a day and never has felt stronger or healthier. Physical examinarion shows a slight general atrophy of the right thigh. The epigastric and abdominal reflexes are active and equal. Range of motion is normal at all the joints, muscular power excellent, tone without defect. The knee, patella, and ankle-jerks are active but not exaggerated, and are equal right and left. Plantar stimulation gives a normal response. Clonus is absent. She walks and runs, stands on one leg, and can mount two stairs at a time in perfect fashion. Superficial sensibility shows no defect except possibly a slight tactile blunting over the dorsum of the right foot. Deep for sensibility is quite intact.

The Early Diagnosis of Tumors within the Spine. A consideration of these cases naturally raises the question of the early diagnosis of cord tumors. Up to comparatively recently a classical unfolding of symptoms was generally demanded before a diagnosis was ventured. In particular great stress was placed upon the sensory irritative phenomena of the so-called initial or radicular stage. Above all the cardinal significance of pain as an early symptom was strongly emphasized (Bruns, Oppenheim, Flatau, and others). Gradually, however, reports began to creep into the literature of extra-medullary spinal growths running their course with minor sensory phenomena, with slight pain or absent throughout. In other words it was shown that the preliminary or root stage might be insignificant or totally wanting.

The two cases here reported belong to this group. In Case I pain was absent; in Case II it was slight and atypical. Other

subjective sensory disturbances played an extremely minor role. In both cases the onset and march of symptoms were essentially motor. The symptoms commonly regarded as cardinal for the early recognition of spinal cord tumors were lacking.

It is upon this point that we wish to lay particular emphasis. The absence of pain and paresthesias is not a rare or exceptional phenomenon in extramedullary tumors. Nothing is more fallacious than the belief that pain is a necessary symptom. The steadily growing literature of so-called atypical cases convinces us that classical criteria for early diagnosis must fall away and new ones must be established.

In 1902 Oppenheim[1] wrote: The absence of pain in spinal cord tumors is extremely rare, and he mentioned the observations of Clark, Bailey[2] and Sibelius.[3] In 1906 Flatau and Sterling[4] reported a case, with slight abdominal pain, and referred to a case of Jaffe and two of Schultze, the only additional ones they were able to collect. Since then, thanks to our keener conception of the disease, the literature has been growing rapidly. With no attempt to exhaust the list we may mention the names of Nonne,[5] Oppenheim,[6] Oppenheim-Cassirer, Bing and Bircher,[7] Flatau,[8] Stursberg,[9] Panski,[10] Sanger,[11] Thomayer,[12] Trömmer,[13] Schultze,[14] Bregman, Sailer,[15] Joachim,[16] Boettiger,[17] E. Müller and Heilbronner,[18] all of whom have contributed one or more cases. And if our diagnoses past and present were put to the crucial test, how few of us would not be involuntary contributors? Not many of us probably would escape the experience of Nonne,[19] who diagnosed a myelitis because of the complete absence of pain, and found at autopsy a cyst reaching from the seventh to the tenth dorsal roots. Pain is a valuable symptom when present, but it is frequently absent, and, as Stursberg,[20] insists, should never weaken the suspicion of tumor, provided other diagnostic conditions are fulfilled.

Just as the complete absence of pain must be recognized if an early diagnosis is to be reached, so it must also be recognized that

[1] Lehrbuch der Nervenkrankheiten, 1902, 3d edit.
[2] Jour. Nervous and Ment. Dis., 1896, xxii, p. 171.
[3] Jahresbericht auf dem gebiete der Neurologie und Psychiatrie, 1899, p. 686.
[4] Deutsche Zeitschrift Nervenheilk., 1906, xxxi, p. 199–223.
[5] Neurologisches Centralblatt, 1908, p. 749.
[6] Münch. med. Woch., 1906, No. 46, p. 2272.
[7] Deutsch. Zeitschr. f. Chirugie, 1909, xcviii, p. 258–76.
[8] Lewandowsky Handbuch der Nuerologie.
[9] Deutsch. Zeitschr. f. Nervenheilk., 1906–07, xxxii, p. 113.
[10] Neurologisches Centralb., 1912, xxxi.
[11] Ibid., 1908, p. 795.
[12] Ibid., (Ref.), 1908, No. 2, p. 80.
[13] Ibid., 1908.
[14] Mitteil. aus dem Grenzgeb. der Med. und Chir., 1903, xii, p. 153.
[15] Centralb. f. Nervenheilk., 1901, p. 111.
[16] Deutsch. Archiv. f. klin. Med., 1905–6, No. 86.
[17] Archiv. f. Psychiatrie, 1901, xxxv, 83–108.
[18] Deutsch. Zeitschr. f. Nervenheilk., 1908, xxxiv, p. 289–303.
[19] Loc. cit.
[20] Centralbl. f. das Grenzgeb. der Med. und Chir., 1908, xi, p. 91.

pain when present may present little or nothing characteristic. The neuralgic character may be entirely lacking. The pain instead of being radicular may be of a centrifugal type, appearing in parts of the body far removed from the segmental localization of the tumor. In one of Flatau's,[21] cases (tumor in the eighth cervical, first dorsal region) pain first appeared in the left foot. In a case reported by Ramson-Thompson[22] (extradural sarcoma in the region of the eighth cervical to twelfth dorsal roots), pain not only appeared in the epigastrium but in the lower dorsal vertebra and legs as well. Abrahamson reports a case of tumor at the eighth cervical level in which the first sensory symptoms consisted of paresthesias of the legs; Oppenheim and Heilbronner, tumors in the mid-dorsal region, likewise with pain confined chiefly to the lower extremities; Henschen a case of tumor at the level of the cervical segments with girdle sensation in the lower abdomen. In one of our own cases (H. A., 3181), after a progressive spastic paraplegia of three years' duration, the patient developed a girdle sensation in the lower abdomen. This disappeared and was followed a year later by girdle sensation in the upper abdomen. Approximately five years after the onset of symptoms the patient began to experience his first real pains, boring pains which started in the dorsum of the feet and thence shot upward to the thighs and hip-joints. Laminectomy revealed an extradural tumor at the level of the sixth dorsal vertebra. Not only do pains radiate downward, they may also radiate upward above the tumor, as is shown by observations of Oppenheim and Flatau,[23] tumors in the dorsal and lower cervical cord respectively, in which pain was felt in the neck and occiput. We also have a case to add to this group.

Pains may be referred to various viscera and lead to mistaken diagnoses. In Collins[24] and Quante's cases the patients were believed to have appendicitis; Fränkel's patient had his appendix removed; Schultze's case was treated for gall-stone colic and Starr's for angina pectoris; Case II, above reported, was believed to have had heart disease; one of Putnam's cases was treated for indigestion. Abdominal pain is not at all infrequent, as Oppenheim's[25] series teaches, and as one of us has pointed out, is all the more readily mistaken for some visceral disease because of its apparent relationship to eating, flatulency, and constipation.

Pain is not only inconstant and frequently atypical, confusing or masking the picture in its referred form, without segmental localizing significance in its centrifugal form, but it loses further in value as a differential diagnostic symptom between extra- and intramedullary growths. Not a few cases of intramedullary tumor have already been reported running a course with more or less

[21] Loc. cit.
[22] British Med. Jour., 1894.
[23] Loc. cit.
[24] Medical Record, 1902, lxii, pp. 882–91.
[25] Deutsch. Zeitschr. f. Nervenheilk., 1903, xxiv.

marked pain. A striking contrast is offered by Thomayer[26] in two cases—one of an extradural tumor producing a syringomyelic dissociation with complete absence of pain, the other an intramedullary tumor accompanied by pain and complete anesthesia. Other characteristic qualities also fall away. In both intra- and extramedullary tumors as well as verterbral, variations in pain may occur with different body postures (Bregman,[27] Michaels). Sensitiveness to pressure may be present in extramedullary growths as well as vertebral (Schultze,[28] 4 cases), and in both pain may be aggravated by coughing, sneezing, laughing, etc.

Inconstant are also the hyperesthesias, the paresthesias, and the subjective and objective radicular zones. The first manifestations of tumor may be and are frequently medullary. Far from being an early symptom the constrictive hand may first be felt months after the motor display is well advanced: in 1 of our cases two years from onset and in another three years later. In 9 cases of dorsal tumor in our series, verified by operation, the constrictive band was typical in only 2 cases, in a third vague, in the remaining 6 cases entirely absent. In 2 cases of cervical tumor it was likewise lacking. The duration of these cases up to time of operation varied roughly between one and eight years. In 15 cases of verified tumor, hyperesthesia was present in only 6 cases, in 2 of these appearing as ill-defined areas, namely, in the foot and over the sacrum; in the remaining 4 as the typical zonal bands. Furthermore, we have been unable to establish any constant relationship between girdle sensation and objective findings. In only 1 of our 15 cases in fact, were both simultaneously and typically present.

What has just been said for irritative root phenomena applies also to paralytic root signs, which when present appear, as a rule, much later. Pure root anesthesias are uncommon. When present they usually soon merge into medullary sensory disturbance. For a radicular anesthesia to be well defined at least three roots must suffer considerable damage. The uncertainty of this sign for early diagnosis is therefore apparent. It has been conclusively shown that a single sensory root or even a motor root may be completely destroyed by an extramedullary tumor without the slightest radicular sensory defect on the one hand or definite paralysis on the other (Bruns[29]).

A word concerning medullary sensory disturbance: It may mask or precede the radicular phenomena; it may be dissociated as in syringomyelia (Thomayer, Devic-Tulot,[30] Putnam-Warren[31]); it may be slight or patchy with irregular distribution, it may vary from day to day or may appear in regions far removed from the site of the tumor, as in the case of Roux Paviot, where a tumor in the

[26] Neurologisches Centralbl., 1908.
[27] Zeitschr. f. Nervenheilk., 1906, xxxi, p. 68.
[28] Loc. cit.
[29] Geschwülste des Nervensystems, p. 347.
[30] Revue de Med., 1906, No. 3.
[31] Amer. Jour. Med. Sci., 1899, p. 377.

cervical dorsal region produced anesthesia of the soles of the feet. Finally, as one of our own cases illustrates, bony exostosis of the three upper dorsal vertebræ with pressure on the cord and thickening of the membranes—despite complete paraplegia of seven years' duration—sensation may remain quite intact.

The Criteria for Early Diagnosis. What then should be our basis for the early recognition of cord tumors? First of all we must realize that pain and other classical data are valuable but not essential phenomena, but that the essential element in the diagnosis (first emphasized by Schultze[32]) is the determination of a gradually progressive motor and sensory spinal paralysis, the upper pole of which, despite increase in cross-section intensity, varies slightly if at all. In every case of so-called transverse myelitis, therefore, the possibility of cord tumor should be considered. This applies to acute forms of myelitis of obscure origin as well. Flatau,[33] for example, reports a case in which after a short illness sudden paralysis of the legs appeared; Bregman and Steinhaus,[34] the sudden development of a complete paraplegia within forty-eight hours. Not only this, but the acute cross-section paralysis may be ushered in and accompanied by fever, making the resemblance to an acute infectious myelitis even more disconcerting. Cases of this sort have been studied by Panski and Bregman.[35]

There is only one moral to be drawn. The diagnosis of myelitis of unknown origin is made far too often; exploratory leminectomy is not done often enough. In all doubtful cases we are not only justified, but, it seems to us, in duty bound to the patient to give him this chance. The danger of the operation stands in no relationship to the certainty with which he will otherwise succumb.

The force of these statements is emphasized by the two cases reported above. Case II may be regarded as completely cured; Case I is rapidly improving and will probably terminate in complete or nearly complete functional recovery. Both, from a diagnosis point of view, are so-called atypical cases.

We urge that the term atypical be discarded from the symptomatology of cord tumors. Painlessly advancing tumors are not atypical. They form a definite and important group more significant because less tangible than the classical series. Unless this is generally recognized, unfortunately it must usually be brought home by bitter experience—we shall continue to make serious errors in diagnosis. It is to be hoped that the day is not far distant when exploratory laminectomy will be undertaken with the same freedom as exploratory laparotomy. The risk under proper conditions is not great and the results are among the few happy ones in organic diseases of the cord.

[32] Loc. cit.
[33] Cited by Panski.
[34] Medycyna, 1902, 25 28.
[35] Ibid., 1905, 23-27.

REVIEWS

Practical Therapeutics: With Especial Reference to the Application of Remedial Measures to Disease and their Employment Upon a Rational Basis. By Hobart Amory Hare, M.D., B.Sc., Professor of Therapeutics, Materia Medica and Diagnosis in the Jefferson Medical College of Philadelphia. Fifteenth edition; pp. 998; 144 engravings, 7 plates. Philadelphia and New York: Lea & Febiger, 1914.

It is a fine tribute to the worth of any work to have experienced fifteen editions during its lifetime; few medical books can boast of such a record. Twenty-four years have witnessed a remarkable shift in the therapeutic emphasis, and this excellent volume has been kept abreast of each advance.

The same satisfactory arrangement of former editions has been retained. Some important additions have been made in the chapters dealing with salvarsan, neosalvarsan, tuberculin, anesthetics, digitalis, and other cardiac drugs. The text on vaccine therapy seems judicial and unbiased; it gives the reader the last word on this mode of treatment. Some of the illustrations might have been omitted, or at least changed. The book treats its subject in an easily referable manner, avoiding many of the technical and nicer points of discussion which might appeal to some minds of scientific bent.

After all, the book is not intended for such as these, but to serve students and busy practitioners needing quick, tangible directions on therapeutic methods. For them it remains by far one of the best exponents of therapeutics in the English language.

As in the first and each succeeding edition, so in this latest one, three distinguished authorities have again contributed to certain chapters. The articles dealing with the treatment of diseases of the eye have been revised by Dr. George E. de Schweinitz, those dealing with gonorrhea and syphilis, by Dr. Edward Martin, and those upon diseases of the puerperal state, by Dr. Barton C. Hirst.

Its publishers tell us that, excepting only Gray's *Anatomy*, this book has been more widely used than any other work in any department of medicine. Undoubtedly this new edition will make many new converts to the use of a book representing views of eminent clinicians, backed up by more than thirty years of constant experience as medical teachers and active practitioners. T. G. S.

A Treatise on Diseases of the Nose, Throat and Ear. By William Lincoln Ballenger, M.D., Professor of Laryngology, Rhinology, and Otology in the College of Physicians and Surgeons, Chicago. Fourth Edition; Pp. 1080; 536 engravings, and 33 plates. Philadelphia and New York: Lea & Febiger, 1914.

The appearance of the fourth edition of this text-book on the nose, throat, and ear within six years from the time of its first publication is an evidence, at least, of its popularity. Among specialists this book is so well known that it would seem superfluous to describe in detail its arrangement or contents; suffice it to say that this edition covers in a very complete manner the entire field of the nose, throat, and ear. While anatomy, physiology, pathology, symptomatology, and the general and medicinal treatment receive a certain amount of space, the best and larger portion of the book is devoted to the operative side. Among the new subject matter which has been added to this edition is an excellent article on the labyrinth, well illustrated and sufficiently detailed to give a careful reader a complete understanding of the mechanism of the static labyrinth, also Newmann's and Hinsberg's labyrinth operation is described, while other additions are Mosher's operation on the ethmoidal sinuses, the use of autogenuous vaccine in hay fever and His leukocyte-extract therapy and its value in infectious diseases when complicated by inflammation of the nasal sinuses and meninges.

We are disappointed in the omission of suspension laryngoscopy, and also, it would seem, that laryngoscopy and bronchoscopy are insufficiently treated.

The amount of material in this book is remarkable, covering almost every conceivable branch of nose, throat, and ear lore, and for this reason is valuable as a book of reference. It is impossible for the author to treat all of the various operations on the nose, throat, and ear with sufficient detail to enable one who has never heard of these operations to proceed at once to their performance, and for this reason we regret that the author has not inserted references to the literature where complete descriptions may be found.

The literary style of the book is really the only feature open to serious criticism. The greater part is sufficiently clear, and in its conception almost brilliant; but at times one runs across statements either so poorly expressed as to veil the meaning or expressing ideas so vague that one feels as though the author was lost in a maze of conflicting literature. As a practical work, however, for the use of students and general practitioners as well as for the specialist, the book is of undoubted value, and for the greater part absolutely trustworthy.

G. B. W.

A Manual of Diseases of the Nose and Throat. By Cornelius G. Coakley, M.D., Clinical Professor of Laryngology in the College of Physicians and Surgeons, Columbia University, New York. Fifth Edition; pp. 615; 139 engravings, and 7 colored plates. Philadelphia and New York: Lea & Febiger, 1914.

The mere fact that this book appears in its fifth edition speaks most deservedly for its popularity. It is, as its title indicates, a manual, useful for undergraduates and those taking elementary post-graduate studies in laryngology, and as a reference book for the busy general practitioner without leisure or inclination for deeper study.

The general construction of the work is the same as in previous editions, extensions having been added to keep it abreast of the recent advances made in the subjects treated. The chapter on diseases of the accessory sinuses, for instance, has been enlarged, and is well illustrated with drawings from specimens in the author's own collection, and fulfils its purpose for the class of readers mentioned above, although it would prove of less value to the more advanced specialist. It would seem that the subjects of direct laryngoscopy, bronchoscopy, and esophagoscopy might have received some consideration, not only from the stand-point of the removal of foreign bodies, but also in allusion to the usefulness of these procedures for diagnosis and treatment. However, it is manifestly impossible in a work of this character to cover all phases of a subject that has grown so enormously in the last decade or two; and for teaching the fundamentals of examination, diagnosis, and treatment there are few that equal this manual. The chapter on therapeutics, giving many well-known and well-tried formulas, is most useful, and the book is well indexed. G. M. C.

Dietetics: or Food in Health and Disease. By William Tibbles, LL.D., M.D., L.R.C.P., M.R.C.S., L.S.A., Medical Officer of Health, Fellow of the Royal Instiute of Public Health, etc. Pp. 627. Philadelphia and New York: Lea & Febiger, 1914.

This comprehensive work supplements the author's former book on *Foods: their Origin, Composition, and Manufacture*, and with it forms a complete system of dietetics. In this volume Tibbles does not limit himself to a discussion of diet in its relation to disease, but considers it from the point of view of preventive medicine as well. Furthermore, he has kept abreast of the times in that he has not spoken merely of the primary elements of diet, but has included in his discussions the results of recent studies

on the lipoids, on the salts, on the insufficiencies of certain proteins and on the vitamines.

The book is divided into two parts: In Part I including eight chapters, the following subjects are taken up: the digestion and absorption of foods; the heat value and digestibility of foods; metabolism; the amount of food required in many circumstances; the feeding of infants and children; the food in old age; special diets; and stimulants, spices, and condiments. In Part II, covering fourteen chapters, the author discusses the various diseases, taking up first those facts in the physiology, pathology, etiology, symptomalogy, and clinical classifications which have a bearing on rational theories of treatment. Chapters are devoted to diseases of the stomach; diseases of the intestines; diseases of the liver, etc.; the metabolic diseases; diseases of the skin; diseases of the nervous system; the fevers and the fever diet; the vitamines and the deficiency diseases.

Throughout the work, Tibbles has quoted quite freely from the original workers, tables summarizing their results being frequent, and often extended quotations are inserted. Where questions of doubt have arisen he has given the various views and, as a rule, had appended his own opinion.

It is a conveniently arranged book, the index is fairly complete, and there is sufficient heavy typing throughout the text to add materially to its value as a ready reference book.

The thoroughness and detail with which each subject is considered indicate such a grasp of the subject as can come only from a wealth of information and a large experience. T. G. M.

A Manual of Practical Hygiene. For Students, Physicians, and Health Officers. By Charles Harrington, M.D., late Professor of Hygiene in the Medical School of Harvard University. Fifth edition, revised and enlarged by Mark W. Richardson, M.D., in collaboration with W. H. Clark, X. H. Goodnough, William C. Hanson, M.D., Hermann C. Lythgoe, and George H. Martin. Pp. 933; 125 engravings and 24 plates. Philadelphia and New York; Lea & Febiger, 1914.

Prevention is without doubt the spirit of modern medicine, and no volume within recent years covers this branch with as much completeness of detail as does this new edition of one of the best-known hygienes published in this country. Appreciating the rapid strides made in this vast field as well as the inability of one man alone to cover it thoroughly, the editor has secured the expert collaboration of his colleagues on the Massachusettes State Board

of Health, the first board of this kind to be established in America, and one noted for the high character of its laboratory investigations and its public health administration.

The chapters on medical inspection of schools, food, air, soil, water, military, tropical, naval, and marine hygiene are specially enlightening and well done. Much of the book has been rewritten, and in each part this has been done by one who has made a specialty of the topic under discussion. The chapters contain many recent and important statistics; this edition contains one hundred more pages than the well-known previous one, and twelve additional plates are included. Many of the illustrations are splendid half-tones pertaining to the hygiene of the occupations.

If this book has a few shortcomings they are of little moment. It should meet the most critical demands of every one interested in public health and hygiene. T. G. S.

THE CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Vol. III, No. 4, August, 1914. Pp. 253; 66 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THE clinical talk on surgical and general diagnosis, which opens this number of *Murphy's Clinics*, is devoted to ileus, including its varieties, symptoms, management, and illustrative cases. This is well worth reading, even though some portions smell suspiciously of the lamp. In other parts of the volume there is enough of the direct, incisive, didacticism of Dr. Murphy to compensate for this fault, which after all is a very rare one in these volumes.

Then there is an interesting discussion of arthroplastics, with special reference to the operation at the hip; several interesting cases of nerve anastomosis for facial paralysis; and a report of a further operation on the patient, with ascending root neuritis, whose case was first reported in the April number of the *Clinics*. In regard to the latter case, Dr. Murphy comes to the conclusion, after the second operation, that the patient's pain was really central and not peripheral in origin.

There are also a number of cases of bone surgery, such as malunion of a Colles' fracture, cases of congenital and of recurrent dislocation of the patella, and a case of sarcoma of the humerus.

Though the publishers of *Murphy's Clinics* have recently publicly apologized, at Dr. Murphy's request, for the objectionable manner ("too boastful and not in good taste") in which they had advertised this periodical, no apology is needed for the seemingly endless supply of valuable clinical material brought before the profession

at such frequent intervals. Dr. Murphy sifts the wheat from the chaff, and with tireless enthusiasm inculcates principles of diagnosis and treatment of proved and lasting value. A. P. C. A.

Local Anesthesia: its Scientific Basis and Practical Use. By Professor Dr. Heinrich Braun, Obermedizinalrat and Director of the Kgl. Hospital at Zwickau, Germany. Translated and edited by Percy Shields, M.D., A.C.S., Cincinnati, Ohio, from the third revised German edition. Pp. 399; 215 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

In Braun's *Local Anesthesia* we have the standard German text-book upon the subject under consideration.

The subject is covered in great detail, and but few omissions of any importance are to be noted. On page 162 the author mentions the work of Crile, Matas, and Corning, but does not give the emphasis to Crile's work on anociassociation that its value deserves.

The initial chapter is an interesting *resume* of the earlier history of local anesthesia. Of special interest are the author's remarks upon sensation, pain, and the psychology of pain. It would appear that the material under the author's observation consists largely of individuals less susceptible to pain and other mental effects of operative procedures than those with whom American surgeons have to deal.

Certain of the earlier chapters are of a highly technical character, and while enhancing the value of the work as a book of reference, add nothing of value to the treatise as a practical hand-book.

Among the drugs in actual use as local anesthetics the author strongly favors novocain combined with suprarenin. Indeed, this is referred to almost entirely in the practical directions for local anesthesia. The warning against the use of strong solutions of cocain is well stated. Stovain is entirely condemned for anything but spinal anesthesia. The method of anesthesia by layers of tissue planes is adequately described. In the description of the technique we find a number of unnecessary illustrations, for instance, Figs. 21, 22, and 27.

It is, however, in the actual description of local anesthesia of the various regions of the body that the author gives us that which is of most value, and also that most open to question. There is no doubt that major cranial operations can be done under local anesthesia, but why, except in rare instances, should they be done thus? The methods also, while theoretically perfect, are by no means easy of application. The reviewer can see no possible reason why a radical breast operation need ever be done under local anesthesia.

The discussion of the local anesthesia of the floor of the mouth and tongue is excellent. Local anesthesia of an inflamed tympanic membrane would seem to involve as much pain as a rapid puncture. It is not to be considered, and is impossible in children. We heartily agree with the use of local anesthesia as described in certain instances of empyema, strangulated hernia, and intestinal obstruction. But there is no reason why operations of election upon the female pelvic outlet should be done except under general anesthesia.

The reviewer does not believe that injection anesthesia of the brachial plexus is harmless or that it has any real value.

In general it may be stated that the book is an excellent presentation of the theory and possibilities of local anesthesia, but an unsafe guide as to its real uses. For the use of the practising surgeon an omission of repetitions and a general condensation would improve the volume. The book is well made and illustrated, and is a valuable and attractive addition to anyone's book shelf. G. R.

MALARIA. By WILLIAM B. HERMS, M.A., Assistant Professor of Parasitology, University of California. Pp. 163; 39 illustrations. New York: MacMillan Company.

IN his monograph on Malaria, Professor Herms has made a very considerable contribution to the subject. He approaches it almost entirely from the standpoint of causation of the disease and discusses its control by eradicating the mosquito. He does not enter into the treatment of the disease *per se*.

In the early chapters emphasis is laid on the economic loss caused by malaria through sickness, deaths, loss by wages and depreciation in land values. Three chapters are devoted to an excellent discussion of the various types of malaria and the life history of the various mosquitoes. Over half the book deals with the prophylactic control of malaria and to measures which may be successfully carried out for its complete eradication, giving practical measures for the extermination of the mosquito.

These methods, based on eleven years of practical experience, embrace both the temporary ones such as oiling the breeding grounds of mosquitoes, the use of other larvicides, etc., and the more permanent corrections by proper irrigation of the land.

This book which is entertainingly written should prove of interest not only to physicians in general, but to the country practitioner, and to the practical farmer it should prove well worth having.

B. B. V. L.

A Laboratory Handbook for Dietetics. By Mary Swartz Rose, Ph.D., Assistant Professor, Department of Nutrition, Teachers College, Columbia University. Pp. 127. New York: The Macmillan Co.

This little manual consists of three parts: a concise resume of the subject of food values and food requirements; a series of problems in dietary calculation; a collection of tables for reference. The author states the average protein requirement for an adult as one gram per kilogram. She does not refer to the older, more liberal standard to which many authorities still cling. In the tables Fisher's 100 calorie unit, is wisely adopted as the most convenient for comparison, but the caloric values, etc., per pound, per ounce, and per gram, the units of the market, the home and the laboratory are also given. The problems are intended to familiarize the student with the calculations required in estimating individual and collective dietaries. Special attention is given to the economic factor, cost, and caloric efficiency being constantly contrasted.

This little book, intended primarily no doubt for normal and high schools, is an indication of the wide interest taken in nutrition in strictly lay circles and calls attention to the scant familiarity with the subject, particulaly in its practical aspects, displayed by most physicians, medical students and nurses. C. B. F.

Dysenteries, Their Differentiation and Treatment. By Leonard Rogers, M.D., F.R.C.P., B.S., F.R.C.S., C.I.E., I.M.S., Physician to the Isolation Ward (Cholera and Dysentary), Medical College Hospital, and Professor of Pathology, Medical College, Calcutta. Pp. 336; 10 illustrations; 2 temperature charts, and 3 diagrams. London: Henry Frowde, Hodder & Stoughton.

This book more or less summarizes its author's investigations and findings in the field of the dysenteries during a twelve-year experience in Calcutta. In the major portion of the work, two hundred and forty-two pages, he discusses the amebiases from every possible standpoint.

This portion of the volume merits especial attention in as much as Rogers calls attention for the first time to the rapid specific action of the soluble salts of emetin when used hypodermatically in amebic dysentery, together with the treatment of hepatic amebic abscesses by aspiration and injection of quinine without drainage. His results are vastly better than the best previous figures attributed to other methods of treatment as well as his

own cases handled comparatively successfully by means of ipecacuanha.

His chapters on bacillary dysentery, other forms of dysentery, hill dysentery and sprue present nothing new of especial interest and are in no sense comparable to his lines on the amebic variety.

The work must be commended in most respects; principally as a well-presented epitome of an observing man's labors in a fertile field and as the initial report on pioneer therapeusis in amebic dysentery and its complications. The subsequent confirmation of the author's results should prove this volume an epoch-making work. T. G. S.

Radium Therapeutics. By N. S. Finzi, M.B. (Lond.), M.R.C.S., L.R.C.P., L.S.A., Chief Assistant in the X-ray Department of St. Bartholomew's Hospital. Cloth. Pp. 112; 25 illustrations. London: Oxford University Press.

The author, who is well known as a radium therapist and roentgenologist, has covered the subject in an admirable and concise manner in this little book. The various methods of application of radium are dealt with briefly. Each condition in which it has been used is mentioned, although but little is said unless the treatment is regarded as of some definite service, in which case a brief description is given of the best method of application. A short chapter is devoted to the physics of radium and another to the physics and general applications of other radio-active substances. The book makes a handy reference work for beginners, especially. H. K. P.

Tropical Medicine and Hygiene. Part I. Diseases Due to Protozoa. By C. W. Daniels, M.B. Cantab., F.R.C.P. Lond.; Lecturer on Tropical Diseases, London Hospital; formerly Director London School of Tropical Medicine, etc. Second edition. Pp. 277; 73 illustrations. New York: William Wood & Company.

This first volume, as its title indicates, deals only with diseases due to, or probably due to, protozoa. Considerable stress is laid upon their prophylaxis, a feature which should make it a valuable guide for practical sanitarians.

This second edition has as a new feature an alteration in its arrangement which has diminished much of the repetition found in the earlier work. A more uniform method of dealing with the

various headings might have added still more to the strength of the chapters. The author gives no references, and his index is somewhat meager. The book must, however, be passed upon as an excellent handy treatise; presenting in an interesting manner the main facts of the subject under consideration, and dealing with a wonderful phase of general and more especially tropical medicine. T. G. S.

Gunshot Injuries. By Col. Louis A. Lagarde, United States Army Medical Corps (retired); late Commandant and Professor of Military Surgery, U. S. Army Medical School; Professor of Military Surgery, Medical Department, N. Y. U., etc. Pp. 398; 160 illustrations. New York: William Wood & Company, 1914.

Due to the marked change in the type of armament of the present day, our idea of bullet wounds and their treatment have of a necessity been changed. This change demanded a new text-book on the subject, which is admirably met by the work under discussion. The author has endeavored to present a thorough and complete treatise of the subject. The first chapter treats of ballastic explosives, firearms and projectiles, in a detailed and instructive manner. Chapters II to XII inclusive, handle the surgical side of the entire subject. The bulk of the matter in the text has been taken from lectures, which for more than twelve years have been the basis of our civil and military medical schools. A wealth of statistics have been massed from the records in the Spanish-American, Anglo-Boer, Russo-Japanese and Turko-Balkan Wars, supplemented by material obtained in civil life, in the hunt, and experimentally. In an additional chapter, exceedingly interesting, novel, and instructive information is obtained in the medicolegal aspect of gunshot wounds.

Throughout the work one is impressed with the exhaustive thoroughness with which the subject is treated from the reception of the wound to the ultimate result of the case. E. L. E.

Appendicitis. By Edmund Owen, F.R.C.S., D.Sc. (Hon), Surgeon to the French Hospital; Consulting Surgeon to St. Mary's Hospital, etc., London. Pp. 214. New York: William Wood & Co, 1914.

This little book has been written not as an essay on appendicitis, but as an argument for early surgical treatment of the diseased

appendix. At the present day there is by no means a uniform opinion as to the treatment of cases of appendicitis. The author cites numerous instances of cases which have been disappointments because of delayed surgical intervention. He states that waiting or "the interval," "waiting for localization," "waiting for walling off," "waiting for nature's reaction" are all criminal. Even in the recurrent types he advises operation early, even in the presence of the history of former recoveries.

Early intervention, the earlier the better after diagnosis is assured, is the cry. You can not operate too early, and many operate too late. Special emphasis is made that the medical attendant be not misled by subsidence of pain and temporary improvement in pulse and temperature, as frequently this is merely indication of a perforation or of a ruptured abscess; that cases must not be considered lightly because of apparent absence of clinical signs or of their short duration. Ulceration may be present within a few hours, and show little or no symptoms.

Watch carefully in children and in those cases of stealthy appendicitis.

The writer does not favor small incisions in any case, and advises against a "gridiron" in pus cases, advising here an oblique incision through the oblique muscles in line of the external fibers.

Finally he quotes many tables of statistics, all of which prove his point, namely, early (first twenty-four hours) operation gives infinitely the lowest mortality.

The work makes very pleasant, interesting, and instructive reading. E. L. E.

Ursachen und Wesen Angeborener Diathesen. Eine Experimentelle Studie von Stabsarzt, Dr. Hans Eckert, Assistant der Königs, Universitäts Kinderklinik der Charité; Private dozent an der Universität Berlin. Pp. 68. Berlin: S. Karger.

This study was designed to throw light upon Czerny's hypothesis that the newborn contains depots of the chemical substances necessary for growth derived *in utero* from the mother and needing only the addition of water for elaboration in tissues. He studied the increase in weight of six puppies from one litter, killing them at periods varying from five to sixty-seven days after birth, and analyzing the bodies for content of water, total dried substance, nitrogen, calcium, magnesium, phosphorus, iron, potassium and sodium, and total ash. He finds a relatively constant percentage of these substances within the age limit named, thus failing to support Czerny's views. In one weak, poorly developed animal, he noted a conspicuous diminution in the phosphorus content, and he discusses the possible significance of this. J. K. A.

Review of Military Hygiene. By Colonel Valony Harvard, M.D., U. S. A. Second Edition. New York: William Wood & Co., 1914.

It is difficult to express adequately the benefit that may be derived from the study of this book, which covers the subject so thoroughly. "The medical officers were primarily surgeons, and so designated, now they are chiefly sanitarians." This manual must be invaluable to the officers of the Medical Reserve Corps, National Guard, and Contract Surgeons. To cover so important a subject the essentials must be clear, accurate and comprehensive and this work fulfils the demand. The statistics throughout are most interesting and instructive. Typhoid fever and antityphoid vaccination are exhaustively taken up, as is the chapter on venereal diseases. The chapter on recruiting is excellent. "Exercise" is intensely interesting and instructive. It is well divided into exercises of strength, speed, endurance and skill with statistics to show that "competitive and spectacular athletics are undesirable." Parasitic diseases have been gone into in great detail. The subject of water is considered as to "quantity required, water in nature, examinations of, and purifications of," in a most scientific manner. The discussion of food, animal and vegetable, their nutritive value and amount necessary are considered in several chapters in a most pleasing and complete way and concludes that protein 60 grams, fat 60 grams, carbohydrates 500—total 2854 calories would be the correct amount for soldiers. The "rules to be observed in eating and drinking" are excellent, as is the chapter on beverages, which gives latest facts about alcohol. The suggestion that the usual 20-ounce protein ration be cut to 6 ounces seems to be well grounded. The recommendation that a wheeled kitchen, such as is used by the Russian Army, be adopted, is very good. The construction, furnishing, care, and sanitation of posts, barracks, and quarters are minutely taken up. Ventilation, heating, and lighting are thoroughly discussed. The disposal of excreta, garbage, and waste matter is treated according to the latest scientific methods. Several chapters are devoted to soil, and camps, expounding the subject most clearly. All types of batteries are considered. The types used at San Antonio, Texas is preferred. The chapter on general sanitary rules for the field is very instructive, as are the chapters on service in warm climates and in cold climates. The subject of disinfection and disinfectants is masterfully handled. Naval and marine hygiene and quarantine are considered thoroughly. The plates throughout are excellent, and the book can be highly recommended to the Medical Profession.

T. G. A.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLINTON SPRINGS SANATORIUM AND HOSPITAL, CLINTON SPRINGS, NEW YORK.

A Contribution to the Functional Diagnosis of Renal Disease.—B. Griessmann (*Deutsch. Arch. f. klin. Med.*, 1914, cxiv, 32) has made exact studies of the excretion of water, sodium chloride and nitrogen in a small series (five) of nephritics. The patients were placed on a diet of rice, condensed milk, and raspberry juice. The diet was analyzed for its content in the above mentioned constituents and the patients were kept on it until they had reached a state of equilibrium. Each experiment was divided into four periods: (1) The preliminary period in which the patient was kept on a milk or milk-rice diet until there was equilibrium in nitrogen, sodium chloride, and water. (2) During the second period, the patient received the standard diet plus 20 grms. of sodium chloride. The additional salt dissolved in 400 c.c. of water was given only on the first day of this period. (3) In the third period, one or two liters of water were added to the standard diet. The extra water was also given only on the first day of the period. (4) In the fourth period, the patient received the standard diet plus 20 grms. of urea dissolved in 250 c.c. of water given on the first day. Two of the patients had markedly contracted sclerotic kidneys, as autopsy proved. Two suffered from arteriosclerotic renal changes, while the fifth had chronic glomerulo-nephritis. The changes in water excretion were the least noticeable. Defect in the excretion of sodium chloride was found in all of the cases, being especially marked in one of the cases of interstitial nephritis. In the other cases there was a moderate delay in excretion. The urea excretion was studied in only three cases. A marked delay was noted in one of these also, a patient with contracted kidney. The experiments show, Griessmann says, that as a rule disturbances in excretion of sodium chloride and nitrogen are combined.

Nevertheless, there are cases in which the disturbance of function chiefly affects only the salt or the urea. Thus the classification of renal diseases on the basis of excretion of salt and urea (Widal, Müller) seems justifiable.

Factors Concerning the Coagulation of Blood.—Cannon, Mendenhall and Gray (*Amer. Jour. Physiol.*, 1914, xxxiv, 225) have devised a graphic method for the study of blood coagulation. The instrument consists of a light aluminum lever with a long arm, on the end of which is a writing pen which moves over a smoked drum. On the shorter arm there is placed a piece of fine copper wire 8 cm. in length. This wire extends into a cannula. In all the experiments a constant temperature of 25° C. was maintained, and cannulæ of the same size were always used. This insured the taking of the same amounts of blood. They were able to show that the intravenous injections of small doses of adrenalin, or subcutaneous doses of larger size, given to cats, shortened the coagulation time from one-third to one-half the normal. Larger doses (0.3 mg. per kilo) given intravenously, first slowed and then hastened blood coagulation. The effect upon coagulation is not dependent upon synchronous changes in the arterial blood-pressure. After the removal of the liver or intestines, adrenalin in small doses causes no hastening of coagulation, even when added to the withdrawn blood. These experiments were made in an attempt to explain the hypothesis that the liver or intestines, or both, are aroused by adrenalin to greater activity, as a result of which one or more of the factors concerned in coagulation are released. Stimulation of the splanchnics in anesthetized cats accelerates the coagulation time very promptly. The effect wears off in from ten to thirty minutes, and is less marked when the experiment is repeated. If the adrenal gland on the side of stimulation is first removed, no acceleration of coagulation was observed. Hence the assumption that the hastening is due to the release of some component of the adrenal gland. In a similar way, the irritation of large nerve trunks, or a large operation performed under light anesthesia, gives a marked increase in the rapidity of coagulation. States of emotion cause the same in less than one-half minute. Cannon, Mendenhall and Gray, assume that in states of pain or emotion the increased rapidity of the coagulation time is the result of an increased output of adrenalin.

Blood Findings in Some Psychoses.—Itten (*Zeit. f. d. ges. Neurol. u. Psychiatr.*, 1914, xxiv, 341) has made careful blood studies in 140 cases of schizophrenia, 20 epilepties, 10 idiots, and 5 cases of chorea. The studies included morphological examinations; estimation of the coagulation time according to Burker's method; the resistance of the red-blood cells, and the determination of the specific gravity according to Hammerschlag's technique. The results of his findings are as follows: In schizophrenia the red-blood cells are found much increased, especially in states of catatonia and stupor, probably due to vasomotor disturbances. The white cells show slight increases, particularly in acute cases and chronic hebephrenics. Neutrophile leukocytes are the ones increased, but with the subsidence of acute symptoms there is a tendency for the development of a lymphocytosis. This continues

in cases with an unfavorable prognosis; while in cases showing improvement it tends to diminish in favor of a neutrophilic, and, frequently, eosinophilic increase. During states of excitement the blood picture is as in the acute cases. In most cases the coagulation time is slightly hastened. Itten thinks that the lymphocytosis, and frequent eosinophilia, are perhaps due to some perversion of the internal secretions, especially since it is not infrequent to see symptoms suggestive of a status thymico-lymphaticus. In cases of epilepsy the white blood count is low in the intervals, and tends to increase shortly before and after the attacks. Before, and during the attack, there is a lymphocytosis followed by a leukocytosis of the neutrophile type, a point of considerable diagnostic value since hysterical and paralytic seizures are not associated with a primary lymphocytosis. The coagulation time was always shortened, particularly before and immediately after the attacks.

The Cerebrospinal Pressure.—The present study was undertaken by Dixon and Halliburton (*Jour. Physiol.*, 1914, xlviii, 128), with the object of examining the pressure of the cerebrospinal fluid under various experimental conditions. Tests were made of the validity of the Monro-Kellie doctrine which assumes that since the brain, its vessels and lymphatics are enclosed in a bony case, and that the brain occupies the whole skull and is incompressible, that therefore the total blood content is almost constant. On this assumption the brain can increase its blood content only by turning out the cerebrospinal fluid, and when this fluid has gone the brain comes in contact with the skull so that no further expansion of the vessels can occur. Using suitable manometers Dixon and Halliburton noted the affect of the various changes in the arterial and venous blood-pressure upon that of the spinal fluid. After hemorrhage a fall in the spinal pressure was noted, which they regard as a passive result of the altered vesicular conditions. Following the compression of the bloodvessels, particularly of the aorta, a rise in pressure was noted, which was also thought to be due to altered vesicular conditions which prevent the free absorption or facilitate the secretion of fluid. This fact may be brought into connection with the rise in spinal pressure which is observed clinically under conditions of sudden rise in blood-pressure such as may occur during an acute nephritis. After stimulation of the vagus and sympathetic nerves, various results were noted depending probably upon the affect of stimulation upon blood pressure itself. By experiment Dixon and Halliburton could show that alterations in the cerebrospinal pressure exert a marked passive action on the cerebrovenous pressure. Dixon and Halliburton studied the affect on the cerebrospinal pressure of substances which increase the cerebrospinal fluid secretion, namely: choroid extract which produces an increase in pressure due to a specific increased secretion of fluid; anesthetics and hypnotics; and finally carbon dioxid. Other drugs were used by reason of their ability to produce vesicular changes which would manifest themselves upon the cerebrospinal pressure, namely, adrenalin, a vasoconstrictor; amyl nitrite, a vasodilator; and pilocarpin. Adrenalin appears to affect the cerebrospinal fluid only indirectly through the vesicular system. The increased cerebrospinal pressure tends to fall more rapidly than

the blood-pressure. Following the administration of amyl nitrite a rise in spinal pressure is noted. As the result of investigation Dixon and Halliburton conclude that the cranial contents cannot any longer be regarded as a fixed quantity without the power of expanding or contracting in volume. The cerebrospinal pressure is influenced passively to a small extent by changes in the arterial and venous pressures, but these are insignificant compared with the independent changes in pressure which occur as the result of secretory activity. Of all the conditions which influence the secretion of the spinal fluid Dixon and Halliburton are inclined to attach the most importance to a deficiency of oxygen or an excess of carbon dioxid in the blood.

Blood Findings in Epilepsy.—Fackenheim (*Congress for Internal Medicine at Wiesbaden*, 1914) has made systematic blood examinations over a period of two years upon 100 epileptics of the chronic progressive type, and has found these results: 67 per cent. showed a reduction of hemoglobin to between 50 and 60 per cent.; 31 per cent. showed an anemia of 60 to 70 per cent., and only two cases had a hemoglobin of over 85. Apparently the reduction in hemaglobin stands in direct relation to the epileptic attacks, that is, shortly before the attacks the reduction of the hemoglobin was greatest, while in the intervals the hemoglobin tends to approach a constant level in the separate cases. The number of white-blood cells was considerably increased shortly before an attack and markedly increased afterward in 78 per cent., the mononuclear cells of the large type showing an especial increase. In every case there was an increase in the rapidity of the coagulation time averaging between two and three minutes. The coagulation time was most rapid in the period of about ten hours preceding an attack. In the beginning of a status epilepticus, blood coagulation may take place in fifteen seconds, in another case it occurred in twenty-four seconds, and then become decreased over a period of about two days following the attack. Fackenheim discourses somewhat upon the varying relationship of the reflexes to the attacks as well as disturbances in metabolism and believes that the cause of the phenomena of epilepsy is to be found in disorders of the internal secretions.

Lipemia.—Sakai (*Biochem Zeitschr.*, 1914, lxii, 387) was able to show that lipemia cannot be produced by feeding fats to normal dogs, because they leave the blood as rapidly as they enter it from the intestines. It can be induced, however, in dogs which have been made anemic by venesection, or poisoned by phenylhydrazin hydrochloride. It occurs when the hemoglobin reaches between 20 and 30 per cent., and is most pronounced in animals which were in a good state of nourishment when the experiments were commenced. Lipemia, caused by giving a diet poor in fats, and associated with a rapid loss in weight, is increased by the administration of milk. Since in some anemic animals a strong lipemia occurs after the use of palmin, whereas this does not occur in the normal, one must assume that in the former case fats leave the blood more slowly than normal. Suitable chemical analyses gave fat values up to 5 per cent. in the blood serum, and the cholesterin content was likewise increased, though to a less degree. This increase is probably explained on the basis of its ready solubility in fats. One

would expect that this increased transportation of fats with a cachexia would result in a corresponding loss of body protein, but such is by no means the case, nor is every cachexia associated with a lipemia. Surface tension tests show that for each individual of a species there exists a fairly constant normal lipase value for the blood serum. This falls rapidly after the production of anemia, and seems to return to normal in a manner inversely proportionally to the grade of lipemia induced. It is the same way in cases made anemic by poison, but in animals poisoned by phloridzin practically no fall in the lipase content occurs. It would, therefore, appear that the lipemia in these experiments, at least, was due to an inability to rid the blood of fats by reason of a blood serum deficient in lipase.

The Clotting of Blood as Seen with the Ultramicroscope.—Using the slit ultramicroscope of Seidentopf, the oxalated plasma of various animals and suitable amounts of an aqueous solution of thrombin, Howell (*Jour. of Physiol.*, 1914, xxv, 143) has studied the process of coagulation, which in accord with the results of Stuebel, proceeds after the manner of crystal formation. The process is most beautifully seen when solutions of thrombin and fibrinogen are used. Aqueous solutions of thrombin exhibit a few particles showing Browman movement, but the field is practically dark; fibrinogen solutions, however, show numerous active particles and a strongly luminous light-cone in which individual particles can not be seen. Howell inclines toward the view that under the influence of thrombin there occurs an aggregation of the invisible particles (amicrons) of this light-cone with further consolidation into the needle-like crystals of fibrin, beautifully shown in the article by photomicrographs. Howell finds no evidence of the fibrin network so often described, except when the conditions are such as give rise to incomplete clotting.

On the Effect of Extirpation of the Spleen on the Course of Pernicious Anemia.—A. v. Decastello (*Deutsch. med. Woch.*, 1914, xl, 639, 692) reports in detail observations in 5 cases of pernicious anemia subjected to splenectomy. Frequent examinations were made over a period of months. From his small series of cases Decastello feels that improvement in the blood-picture and in the general condition of the patient can be anticipated with considerable confidence; indeed, the patient may return practically to normal. This improvement, however, in the light of our present knowledge, is more probably to be interpreted as a remission than a cure. Therefore, it is not yet justifiable to assume that removal of the spleen eradicates the cause of the disease, or that the disease is due to a previously increased hemolytic activity on the part of the spleen. Decastello thinks that it is much more likely that the operation produces nutritive stimuli to the bone marrow through some change in metabolism as a result of the loss of the spleen.

Studies of the Uric Acid of the Blood.—E. Steinitz (*Deutsch. med. Woch.*, 1914, xl, 953) has made a study of the uric acid of the blood quantitatively by the method of Folin and Denis. He finds that the normal blood of a patient on a purin-free diet always contains uric acid in amounts sufficient for quantitative determination. The value of this endogenous

uric acid of the blood amounts to 0.002 to 0.004 per cent., the average being 0.003 per cent. In true gout this is increased to 0.004 to 0.008 per cent., the average being 0.0055 per cent. In atypical gout the amount of uric acid is less, as a rule. It varies between 0.004 and 0.006 per cent., the average being 0.0045 per cent.; rarely it is normal. It was found that purin-free diet had relatively little effect within a short period of time; any continuation of the diet, however, often caused a marked reduction in the endogenous uric acid of the blood. Atophan produces a marked decrease of the uric acid of the blood. This diminution begins soon after the absorption of the drug. The well-known increase in excretion of uric acid in the urine is, therefore, probably due to action on the kidneys. The diminution of uric acid in the blood is more rapid after large doses given over a short period of time. Repetition of such atophan cures appears to be most effective as the uric acid rises quickly after discontinuing the drug. On the other hand, small doses of atophan are capable of neutralizing the effect of a diet rich in purins. The therapeutic inference is that short atophan cures with large doses should alternate with small doses and a more liberal diet. The diagnostic value of a quantitative determination of uric acid is great, Steinitz believes. From an increase of endogenous blood uric acid alone, however, it would be unwise to diagnose gout or gouty diathesis.

The Functions of the Interrenal Portions of the Suprarenal Glands.—Crowe and Wislocki (*Johns Hopkins Hosp. Bull.*, Balt., 1914, xxv, 287) have made a study of the following points: (1) the effects of complete removal of both suprarenal bodies; (2) the effects of removal of either the right or left gland alone; (3) the relative importance of the cortex and medulla of the adrenal; (4) the relation of the adrenal to carbohydrate metabolism; (5) the results of adrenal transplantation; and finally what relation may exist between the adrenals, the thymus, and the lymphatic system. On the basis of many operative and histological observations the following conclusions were drawn, subject to further confirmation. The experiments were performed on dogs. The suprarenal glands are vital organs in which the cortex is more essential to life than are the medullary portions. Their removal is followed by convulsive seizures, a subnormal temperature, and other signs of acute adrenal insufficiency; when recovery occurs normal growth and sexual functions ensue, with no marked change in disposition, increase in weight, or polyuria. Following partial removal of the gland the remaining portion undergoes hypertrophy, chiefly in the fascicular zone of the cortex, while the medullary portion remains unchanged. Though a transient glycosuria follows the operative procedure, there is no permanent alteration of the carbohydrate tolerance resulting from adrenal insufficiency. Autoplastic transplants may "take" but do not function; in such "takes" the cells of the cortex may survive while those of the medulla are absorbed. That there is a definite relationship between the adrenals and lymphatic system seems certain; for after long standing adrenal insufficiency the animals at autopsy show enlarged mesenteric and retroperitoneal lymph glands, enlarged intestinal lymph follicles, and not infrequently thymus hyperplasia.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL

Post-traumatic Ossification of the Region of the Elbow-joint.—Lehmann (*Deut. Zeitschr. f. Chir.*, 1914, cxxvi, 213) made a study of this condition on the basis of thirty-seven cases. He says that the elbow more than other joints shows a predilection for post-traumatic ossification. This is in part explained by its anatomical formation. These ossifications were found after traumas of all kinds, but especially after luxations. The trauma is the primary cause, but an individual predisposition must be assumed. The view of Machol that only reduced dislocations are followed by ossification is not borne out, although an injudicious method of reduction increases the tendency considerably. The bone formation can develop from the intramuscular connective tissue as well as from the periosteum. Practically there is no difference between the ossification of myogenous and that of periosteal origin, since both occur alongside of each other. The neighboring soft tissues participate in the structure of the callus. A proper treatment of the recent injury is the best prophylaxis against the ossification. It should aim at the most complete rest and preservation of the injured soft tissues, and should favor absorption. Vigorous massage and passive movements should be avoided. A fibrolysin cure is to be recommended for the persistent thick induration. The complete ossification can undergo spontaneous absorption, so that conservative treatment should receive much consideration. An operation is indicated only when there are long continued and severe disturbances of function and when there are complications from pressure on nerves and bloodvessels. In general, operations should not be done before the termination of the process of ossification.

The Function of the Periosteum in Bone Transplants, Based on Four Human Transplantations without Periosteum and Some Animal Experiments.—McWilliams (*Surg., Gyn., and Obst.*, 1914, xviii, 159), on the basis of his clinical and experimental work, reached the following conclusions: If the periosteum be excised from an area of bone and a section of bone within this area, going into the medullary cavity, be removed (not, however, involving the whole diameter of the bone) and the endosteum scraped away as well, then it is found that the cavity fills in perfectly with new bone, which of necessity must come from the

old bone alone. This is probably due to the fact that the nutrient artery is intact. If a section of the whole diameter of a bone be removed then the bone will regenerate between the ends of the fragments if the whole or a part of the periosteum be preserved bridging the defect. If a section of the whole diameter of a bone be removed, very little subsequent filling of this defect by bone will take place if the entire periosteum has been removed from between the ends of the fragments. Provided a graft be living and taken from the same patient its future life depends on an efficient blood-supply, irrespective of the periosteum or whether it is in contact with living bone or not. If minute fragments of a living graft be transplanted then the periosteum may be disregarded because the osteoclasts in the fragments may not die because of an easy access of blood into them, and the pieces may grow and coalesce and not become absorbed. His statistics show that 50 per cent. of such transplantations will be successful. If a larger piece of living bone be transplanted then it is safer to leave the periosteum attached to the graft to assure its future reformation, since otherwise the osteoclasts in the bone of the graft may die because cut off from the nutrient artery. The periosteum survives because of its sufficient blood-supply from the surrounding tissues, its inner surface forms osteoblasts which themselves proceed to reform the bone of the graft, in the event that the osteoblasts within this have died from a deficient blood-supply. His statistics show that 41 per cent. of transplantations are successful in which large grafts without periosteum are grafted. A graft on a graft, neither having a covering periosteum, will not live even though one graft be in contact with living bone. Periosteum when transplanted alone into the soft parts may produce living bone. The splitting of the periosteum of a graft, even though the transplant is entirely surrounded on all sides by periosteum, seems to be unnecessary and accomplishes nothing. Altogether sixteen transplantations with periosteum were performed, and of these all but one (93 per cent.) were successful. Altogether twenty-five transplantations without periosteum were performed. Of these 48 per cent. were successful (all in animals) while 52 per cent. were unsuccessful The influence of the blood-supply is demonstrated by the fact that 50 per cent. of the transplantations without periosteum, made with minute fragments, were successful, while 41 per cent. of those without periosteum made with large, single fragments were successful. From a consideration of all the foregoing facts the conclusion seems irresistable that bone-grafts of whatever size, in order that one should be positively assured of their subsequent living, should be transplanted with as much periosteum covering their surfaces as possible.

Bullet Wounds in War.—Posnett (*Lancet*, 1914, ii, 642) says that he attended close on 1000 rifle bullet wounds, in a large general hospital, during the Boer war, and offers for present use his conclusions drawn from this experience A clean cut wound of the abdominal viscera will in most cases heal very rapidly and require very little treatment. Multiple abdominal wounds may require operation but are best treated expectantly for a few days until symptoms of some local trouble arise. Bullets may pass through the most vital tissues without doing any permanent injury. There is often great initial shock from bullet wounds,

especially, if when shot the soldier was hungry, and tired by marching. The impact of the bullet against the body is very severe. One patient felt as if he "had been hit by a crow bar wielded by a giant," and had been thrown three or four yards out of the saddle. With an empty stomach, a wound of the stomach or intestines seems to close rapidly without any trouble, and so long as there has been no leakage of gastric or intestinal contents the patient will probably recover in a short time, but if leakage takes place symptoms of localized peritonitis may be expected which will require a laparotomy. Wounds of the bladder usually require a suprapubic cystotomy as they do not heal readily and generally leak into the surrounding tissues. A clean wound of the kidney seldom requires any interference, but a wound cutting the ureter across about two inches below the renal pelvis called for a nephrectomy. What may be called local shock is a condition sometimes encountered in wounds of the soft parts, probably, due to the shaking up of the tissues by the great velocity of the bullet. There is a feeling of considerable stiffness in the part for several days and the nerves in the immediate neighborhood although not touched by the bullet, may be more or less neuralgic. It is better, if possible, to wait a few days for this local shock to subside before proceeding to any operation.

A Common Mechanism for Most Injuries of the Shoulder Region.—Thomas (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1018) believes that most fractures of the skeleton in the shoulder region, in which he includes dislocations and sprains, are due to hyperabduction. Dislocations and sprains tear the ligaments which are to the skeleton at the joints what the bones are between the joints, and sustain indirect violence as much as the bones. When the normal limit of abduction is passed the whole skeleton in the shoulder region, ligaments and bones, takes the strain, and any break will take place where for the moment the skeleton is weakest or the strain is greatest. It occurs most frequently in the shoulder joint, with or without a dislocation, a tearing of the ligaments without a dislocation constituting a sprain. The degree of force applied determines the extent of the lesion common to both, the tear of the axillary portion of the capsule, which includes all of the ligaments of the joint. With the arm in the sling position the result of healing is the same after a sprain as after the reduction of a dislocation, *i. e.*, a typical stiff and painful shoulder, the etiology of which has been so obscure and the subject of so much discussion. More or less palsy of the upper extremity follows in the great majority of cases, in some being very severe but in most only transitory. If instead of keeping the arm at the side during the healing process the patient, as an athlete, soon carries the arm vigorously into abduction the humeral head is easily pried out of the socket again by the leverage effect of hyperabduction in the absence of the resistance of the normal ligaments. Repetition of this accident occurs more easily, cicatricial contraction in the axilla is prevented, and the capsule heals across the gap between the torn margins necessary to permit the dislocation, and is, therefore, abnormally long. Exercise to stretch the contracted axillary portion of capsule is indicated in stiff and painful shoulders and contraction of the abnormally lengthened capsule, by operation, in recurrent dislocations. Any palsy in the former disappears with the return of normal motion.

It is due to inclusion of some or all the branches of the brachial plexus in the axillary inflammation consequent upon the joint lesion. Most obstetrical palsies of the upper extremity are, probably, due to the same cause, following an injury to the shoulder-joint of the child at birth from the pressure of its shoulder against the maternal pelvis. This resulted in a mild grade of posterior subluxation in nine cases and in an injury of the joint without dislocation in four cases. The latter recovered full motion and power later, and the former recovered power in proportion to the motion obtained at the shoulder. Künster, in 1889, maintained that these obstetrical palsies were due to injuries to the skeleton in the shoulder region and not to injuries of the brachial plexus. The resistance to reduction in old dislocations of the shoulder is due, chiefly, to the cicatricial changes in the torn and now abnormally arranged capsule. Traumatic brachial paralysis with flail-shoulder, in many cases, is due to a tearing of the ligamentous and muscle supports of the humerus at the shoulder-joint and a consequent slight falling of the humerus from the socket. This is, usually, not recognized until later and is then ascribed to paralytic relaxation from injury to the brachial plexus. In 6 cases in which the humerus was restored to its normal level by operation within eight weeks after the accident, the power of the paralyzed muscles returned. They are the first cases of the kind in which such recovery has been reported, because they are the first in which such treatment has been followed.

Typhoid Perforation.—Armstrong (*Surg., Gynec., Obstet.*, 1914, 342) says that recent figures embracing 9713 cases of typhoid collected in England, Canada, and the United States, show that more than one-third of all deaths are due to perforation. In 15,224 collected cases there were 544 deaths, or about 1 in 31½. The size of the perforation varies from that of a small pin to that of a lead pencil. Only rarely is it larger. It is always situated almost directly opposite the mesenteric attachment. It is found somewhere in the terminal two feet of the ileum, in the overwhelming majority of cases. The first indication of perforation is pain. It is usually a sudden crampy pain or is sudden and persistent. The next important symptom, because of its constancy and significance, is change of expression, showing pain, pallor, distress, etc. Tenderness was present in 88 per cent. of the 83 cases and absent in 12 per cent., and is generalized or local. In 85 per cent. there was distinct rigidity and in 15 per cent. there was not. Little or no value can be attached to absence of liver dulness, especially, in a distended abdomen. The fall of temperature, so often spoken of, rarely occurred. In 95 per cent. of the cases the pulse quickened. Fitz's statement is emphasized that perforation may take place without suggestive symptoms and suggestive—so-called characteristic—symptoms may occur without any perforation having taken place. The symptoms calling for immediate incision are summarized as follows: pain, persistent; definite change for the worse in the expression of the patient; tenderness either abdominal or rectal; rounding up of the abdomen; and increased resistance to pressure. Local anesthesia is sufficient for the operation. One should always look for a second and a possible third perforation, though seldom found. The hospital house-staff should be made to feel that it is a reflection on their professional attainments to overlook a perforation. This will lead to early operation.

Seminal Vesiculitis.—Thomas (*Annals of Surgery*, 1914, lx, 313) says that seminal vesiculitis is a far more prevalent disease than the average physician surmises and masquerades under a manifold symptomatology finding its expression oft times remote from the urinary tract; the inflammation is invariably due to a mixed infection, from which in its chronic state it is commonly impossible to isolate the gonococcus. The disease, analogous to pus tubes in the female in many respects, presents serious and similar problems from the standpoint of treatment, and is not accorded the consideration that its medical importance demands. The particular treatment in any given case should depend upon the anatomico-pathological state of the vesicles, ejaculatory duct, and vas deferens. This can be determined by proper vesicular palpation, massage and microscopical examination, supplemented when necessary by vasopuncture and collargol radiography. Experienced massage will in the majority of patients suffice to effect a cure in due time; in many, however, massage having proved ineffectual, convalescence may be accelerated by vasopuncture, vasotomy and direct medication of the seminal vesicles; in certain cases, not so few as may be imagined, seminal vesiculotomy or vesiculectomy should and must be performed if we are to cure or relieve these patients of their annoying symptoms. Bilateral vasopuncture and collargol medication has resulted at least in the temporary cure of a number of cases of persistent chronic vesiculitis. Collargol radiograms in a series of normal and pathological cases have demonstrated: (1) by comparison *in vivo* and *in vitro*, the graphic portrayal of an ejaculatory duct sphincter; (2) the intimate relationship between the ureter and seminal vesicle, whereby ureteral irritation and urinary obstruction may occur in the event of an enlarged and inflamed vesicle; (3) the presence of stricture or obstruction of the vas; (4) congenital anomalies of the vesiculæ seminales; (5) inflammatory enlargements of the vesicles, especially loculated collections of pus or seminal pyovesiculosis.

Diabetes and Surgery.—Fischer (*Deut. Zschr. f. Chir.*, 1914, cxxxi, 404) gives his experience of forty-five years with this condition. He says that while the older writers were much opposed to operation in diabetics, under the protection of asepsis we have become more daring. Hutchinson, frequently, operated on diabetics without finding the danger much greater than usual, while Umber thought that it was not necessary to limit operations in diabetics more than in non-diabetics. Most surgeons, however, are still cautious and restrict themselves to operations of necessity on these patients. In other cases they delay the operation until the sugar has been removed. Tuffier counsels not to operate when the reflexes have been abolished. But this happens early and Fischer does not agree with this opinion since wounds in diabetics usually heal well with care. He cites, particularly, 13 large operations on diabetics, after as much diminution of the sugar as possible, or without it (in incarcerated herniæ). They included two mammary amputations for cancer (women of forty-five and forty-eight years, one died), operation for incarcerated hernia in two women and two men (two with narcosis, one died, two without narcosis), one cancer of lip (without narcosis, man aged sixty-two years), one exarticulation of the big toe (man aged seventy-two years), and one exarticula-

tion of the hand (woman aged seventy-three years), both for tuberculous caries, an amputation of the middle of the thigh (woman aged fifty-seven years, for sarcoma), the removal of a large ulcerated lipoma (woman aged forty-three years), a resection of the upper jaw for sarcoma (man aged forty-six years), and a fistula in ano (woman aged thirty-three years). He lost one of these cases, with mammary cancer from diabetic coma, in which the coma came on after the narcosis, and the patient on whom he amputated in the thigh, the coma coming on the day after operation. He refused to operate on one patient with an incarcerated hernia because she was in deep coma. Five of the operations were done in the preantiseptic days and two of these died of sepsis. The mortality for all his cases was 48.8 per cent., for those operated on for diabetic surgical conditions 54.5 per cent., for those on whom amputations were done for diabetic gangrene 72.7 per cent., and for major operations performed on diabetic patients 36 per cent. Other operators have been more fortunate, especially Karewski with his mortality of 14.7 per cent., and Küster in his amputations. But they had much more favorable material and better operative conditions.

Statistics and Operation for Obturator Hernia.—Wagner (*Deutsch. Zschr. f. Chir.*, 1914, cxxxi, 223) says that little more than 200 cases of obturator hernia have been reported. According to Rose, the mortality of these cases is 78.7 per cent, according to Grazer 79 per cent. Wagner reports a case in a woman, aged seventy-two years, who had gastric disturbances for twenty years and for ten years could take little more than liquid food on account of which she was much emaciated. Two days before operation, she was seized with severe abdominal pain, continuous vomiting finally becoming fecal, and voided no urine. First under local anesthesia, a herniotomy was performed, but a median laparotomy under general anesthesia was added. A strangulated loop of small intestine, about 10 cm. long, had escaped through the obturator foramen and could be reduced only by manipulation and enlargement of the canal through the abdomen. A cord of omentum was adherent to the intestine near the obturator foramen and was detached from it. After release of the strangulation the affected portion of intestine recovered its circulation, but at the site of the adhesion to it of the omental cord it was almost completely occluded by a chronic induration. An entero-anastomosis was performed. The greater part of the sac was removed, the remainder was ligated with silk and the stump passed internally by a forceps and sutured level with the peritoneum. Eight days after the operation the laparotomy scar was ruptured by coughing and had to be sutured again. Notwithstanding this accident, the patient improved and ate meat, bread, eggs, etc., things she had not been able to eat for years. Obturator hernia is almost always found in old women who have borne children. Earlier diagnosis and operation are necessary to improve the mortality. Taxis should be avoided as too dangerous. The operations to be considered are herniotomy, laparotomy, and a combination of the two. No one operation will suffice for all cases. Laparotomy should be done in all doubtful cases in which there is no visible external tumor. In all other cases one should begin with a herniotomy under local anesthesia. If this shows the necessity of it, a median laparotomy should be done.

A radical operation is to be preferred. This may be an osteoperiosteal operation through the abdomen, according to Bardenheuer, or a muscle flap operation, according to Straeter. A hasty operation can be done by suturing the canal through the abdomen with silk. By the combined route the obturator canal can be closed with the use of the hernial sac.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Treatment of Tuberculous Peritonitis by Injection of Nitrogen into the Peritoneal Cavity.—Brückner (*Berlin. klin. Woch.*, 1914, li, 103) reports a case of tuberculous peritonitis apparently cured by repeated injections of nitrogen into the peritoneal cavity. This patient had received no benefit from two laparotomies nor from roentgen ray therapy. After withdrawing 2.5 liters of fluid, 500 c.c. of nitrogen were injected into the peritoneal cavity with the same technic as is employed for the induction of an artificial penumothorax. Three more injections were given in the course of two months, during which time the patient rapidly improved and the fluid in the abdomen that remained after the tapping, gradually disappeared. Eight months after the first nitrogen injection the patient seemed perfectly well. The abdomen was soft and no trace of the disease remained except some thickening of the omentum on the right side. The injection of air or oxygen has been recommended for the treatment of tuberculous peritonitis and favorable results have been reported from their use but Brückner thinks that nitrogen is better adapted for this purpose.

The Use of Atropin in Stomach Disease.—Pletnew (*Therap. Monatsheft.*, 1914, xxviii, 30) speaks highly of atropin as a symptomatic remedy in gastric distubrances. He states that atropin checks secretion, reduces acidity, diminishes pyloric spasm and, probably by a combination of the actions, relieves gastric pain and distress. He believes that the action of atropin is not curative in these conditions but that atropin deserves a wider use as a symptomatic remedy. Atropin is superior to morphin as a gastric sedative for the reason that a period of increased secretion follows the primary sedative action of morphin.

Clinical Observations on the Influence of the Inhalation of Strophanthus Tincture in Cardiac Insufficiency.—Moczulski (*Wien. klin. Woch.*, 1914, xxvii, 31) says that tincture of strophanthus has a distinct effect upon cardiac action when administered by inhalation. He noted that a single inhalation of strophanthus tincture was often able to considerably improve cardiac efficiency. He believes that the action

of strophanthus in many cases is even quicker when given by inhalation than when given by intravenous injection. The fact that one can influence the action of the heart by inhalations of relatively small doses of strophanthus tincture (10 drops) certainly speaks for the use of strophanthus inhalations for therapeutic purposes. The method is easy of application, and there are no untoward symptoms on the part of the gastro-intestinal tract such as are obtained when the remedy is given by mouth.

Vaccine Therapy with Sensitized Vaccine.—Besredka (*Berlin. klin. Woch.*, 1914, li, 97) believes that, of all varieties of vaccines, sensitized living vaccine, both from theoretical reasons and in actual practice, is able to develop the maximum amount of protective substances He quotes experimental and clinical work of a great number of observers to support this view. In general, experimental work has shown that animals immunized with living sensitized organisms develop a weak agglutinating fever but, on the other hand, their serum has a high bactericidal power and is rich in antibodies. Animals immunized with heat-killed organisms develop a high agglutinating power but their serum has a weak bactericidal effect and is only moderatly rich in antibodies. Animals, immunized with ether-killed organsims, have a marked agglutinating power, but their serum is weak in its bactericidal properties and the amount of antibodies is negligible. Experimental work is also quoted that indicates that the protective substances persist for a longer time when animals are immunized with sensitized vaccine. That the use of a living sensitized vaccine is without danger, Besredka points out that 15,000 persons have been inoculated in a vaccine prepared from living typhoid bacilli without local or general reactions resulting. Furthermore, hundreds have been treated with living sensitized staphylococci, streptococci, gonococci, etc. Besredka is also convinced of the greater therapeutic value of the sensitized vaccine.

Experiments on the Curative Value of the Intraspinal Administration of Tetanus Antitoxin.—Park and Nicoll (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 235) make the following recommendations for the treatment of tetanus with antitoxin, basing them upon experimental and clinical evidence. In every case strongly suspected of being tetanus, they advise that from three to five thousand units of tetanus antitoxin should be given as early as possible intraspinally, slowly by gravity, and always, if possible, under an anesthetic. In order to insure its thorough dissemination throughout the spinal meninges the antitoxin should be diluted to a volume of from 3 to 10 c.c. or more, according to the patient's age. Unlike experimental tetanus in the human type of the disease, there is frequently a focus constantly pouring out more and more toxin, for which reason the authors believe it advisable to repeat the intraspinal injection in twenty-four hours. At the same time it is advisable to give a dose of 10,000 or 15,000 units of antitoxin intravenously in order to insure the quickest possible neutralization of all toxins in the tissue fluids. A similar dose given subcutaneously three or four days later will insure a continuance of the highly antitoxic condition during the next five days. They do not believe that there is any advantage in giving larger amounts of antitoxin than those indi-

cated. The proper and thorough surgical treatment of the wound and the use of sedatives, stimulants, etc., are very essential factors in the treatment of the disease. The authors are of the opinion that intraneural injections of antitoxin are an uncertain and round-about way of reaching the diseased nerve-centres, which may be much more simply and thoroughly accomplished by intraspinal injections.

The Value of Hexamethylenamin as an Internal Antiseptic in Other Fluids of the Body than Urine.—Hinman (*Arch. Int. Med.*, 1914, xiii, 841) says that hexamethylenamin is dependent on the liberation of formaldehyd for its antiseptic value. Hexamethylenamin is not converted into formaldehyd in any of the normal alkaline fluids of the body; therefore, it can be of no prophylactic value in any of these fluids. After some infections of these fluids there may be under certain conditions a change in reaction sufficient to produce slight liberation of formaldehyd, but it was not possible to show that there would be enough to give antisepsis. In localized infections of pronounced acidity, hexamethylenamin is not taken into them from the circulation in amounts sufficient to form formaldehyd in antiseptic strength (the gall-bladder, possibly, excepted). The therapeutic use of hexamethylenamin as an internal antiseptic is justified, experimentally, for urinary conditions alone, and then only when it is excreted into an acid urine.

The Treatment of Chronic Gout with Acitrinum Compositum.—Lampe (*Berlin. klin. Woch.*, 1914, li, 933) reports very favorable results with the use of acitrinum compositum in the treatment of 30 cases of chronic gout. This remedy is a combination of colchicin with acitrin, a derivative of atophan. This preparation seems not only to cause an increased excretion of uric acid and nitrogen by the kidneys but also has a marked analgesic action due to its colchicin content. Lampe observed no untoward effects from its use.

The Treatment of Syphilis of the Nervous System.—Fordyce (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 552) believes that in estimating the results obtained by the intensive treatment of syphilis of the nervous system one must not forget the influence of the psychologic effect of a new method of treatment and the fact that in many cases of tabes and paresis there are periods of remission covering months or years. Observations of this kind, however, were made before we employed the more precise methods of diagnosis and controlled our treatment by means of the examination of the spinal fluid. Furthermore, many of our most striking results have been obtained in patients who had long-continued and marked symptoms such as girdle sensation, pains, and impairment of locomotion. The change in the clinical symptoms as well as the serologic findings would certainly give strong presumptive evidence that the results were due to an actual improvement in the condition and not a normal remission. Each case is a problem in itself and must be approached in an individual manner. Different pathologic conditions are present, so that while on the one hand we have an active process, on the other there is a degenerative one. Complicated, perhaps, with an endarteritis, softening, or scar

formation. Symptoms which are due to interference with nutrition or pressure we cannot expect to influence. When salvarsan is employed it should be done so intensively and combined with mercury. The criticism of certain writers against the employment of salvarsan in the secondary stage of syphilis is entirely fallacious, for we know that when it is given in the proper manner combined with mercury, the so-called neurorecidives do not occur. In an experience of over two years, during which this method of treatment has been followed, not a single case of nerve recurrence has been observed. The cases submitted show that it is possible in some instances by intravenous medication alone to influence the clinical and serologic findings, and when this does not take place the only alternative may be intraspinal medication. Until we are more familiar with the effects of serum fortified, *in vitro*, the Swift and Ellis method of salvarsanizing serum, *in vitro*, should be the one of choice. In certain cases the serum from a patient so treated may be reinforced with from 0.25 to 0.5 mg. of salvarsan. It must always be borne in mind that the spinal cord reacts intensively to irritants even of a mild grade. When a degenerative process is present the resistance of the cord is much below that of a normal one and the brunt of the irritation falls on the degenerated areas. Fordyce is convinced that the intelligent and energetic treatment of the infection in the early stages properly controlled by the serum reaction would do much to prevent the subsequent development of nerve syphilis. It must, however, be thorough to eliminate the possibility of residual foci, which experience has taught have a predilection for the meninges. The early history of salvarsan shows that these accidents occur more precipitately after its use than under the older and milder methods of treatment.

The Use of Salvarsan in Non-syphilitic Diseases.—Best (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 375) reviews the literature regarding non-syphilitic diseases treated with salvarsan. The list of diseases is a long and varied one, even though apparently incomplete. The diseases treated by the author include cases of anemia, chancroid, chyluria, elephantiasis, epithelioma, erythema multiforme, leprosy, lupus vulgaris, pityriasis rubra, psoriasis, tuberculosis, and trichinosis. The author states that it is justifiable to formulate the following rules for the use of salvarsan in non-syphilitic diseases from the study of the reported cases including those personally observed by him. Salvarsan is specific in diseases caused by any variety of spirillum. Salvarsan has curative properties in those diseases in which the infecting organisms are found in the blood or lymph, or in other locations where they can be easily reached. Salvarsan has great therapeutic value in those diseases in which arsenic has been successfully used. Salvarsan, if used with caution in repeated doses over a long period, has a therapeutic value in those diseases in which previously arsenic gave indifferent results. Salvarsan, used as an adjuvant to some other drug or drugs, is useful in those diseases in which a decided and quick tonic, stimulating and alterative effect is desired, depending on the other drug or drugs for the ultimate result. The mode of administration is important and should be as follows: intravenous in those diseases in which a specific action is desired; full dose intramuscular injections repeated

once or twice at long intervals (eight weeks), in those cases in which the tonic, stimulating and alterative effect is desired, as well as a certain specific action; small, oft-repeated (week or ten days) doses, intramuscularly, over a long period of time, in those chronic diseases in which a purely tonic, stimulating, and alterative effect is desired.

The Use of Small Doses of Salvarsan in the Treatment of Secondary Anemia and Nutritional Disturbances.—Kall (*Münch. med. Woch.*, 1914, lxi, 1506) has had good results with the injection of very small doses of salvarsan in cases of secondary anemia and malnutrition. He gives the salvarsan in doses never more than 0.05 or 0.075 gm. and believes it is a very simple and effectual method of giving arsenic. His usual practice is to give from ten to fifteen injections and to repeat the course after an interval of several weeks.

The Roentgen-ray Treatment of Tuberculous Glands.—Mowat (*Brit. Med. Jour.*, 1914, 2792, 10) says that the great advantage of roentgen-ray treatment of tuberculous glands is that it saves the patient the unpleasantness of undergoing in many instances a severe operation. The results are equally satisfactory whether the glands are large or small, numerous or scanty, superficial or deep, because by means of filters the penetrating power of the roentgen rays can be controlled and by using hard tubes those glands deeply situated can be reached. Even when the glands have broken down, marked improvement has resulted in some of the author's cases. The details of the technique used in applying the roentgen rays are noted in the article. The cases may be treated as often as twice a week. Many of the cases treated by the author were only seen once a week or even less frequently, and Mowat believes that even more rapid cures would have resulted with more intensive treatment.

Clinical Observations on Strophanthin.—Johannessohn and Schaechtt (*Deutsch. med. Woch.*, 1914, xl, 1412) in view of the excellent results obtained by the use of strophanthin intravenously, have endeavored to find a preparation of strophanthin that is active when given by mouth. The uncertainty of action of most preparations of strophanthin when given by mouth has been explained by possible injury produced by the digestive fluids. It was found experimentally that the enzymes, pepsin and pancreatin did not inhibit the action of strophanthin but that the acidity and alkalinity of the juices were alike able to weaken its action. The authors experimented with the so-called g-strophanthin of Thom that may be given in larger doses than other varieties of strophanthin. The intravenous dose is double that of other preparations and the dose by mouth is three or four times greater. They found that, *in vitro*, this strophanthin was not inhibited by any of the digestive fluids, either acid or alkaline. They concluded from their clinical observations that this preparation was very rapid in its action when given by mouth. Its diuretic action was marked and in consequence striking results were obtained in cases of edema and ascites, in very short periods of time. The cardiac stimulent action was similar to that of digitalis. No cumulation was observed and is less to be feared than with digitalis, for strophanthin is excreted more rapidly.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M.D.,

OF PHILADELPHIA.

The Significance of Doehle's Inclusion Bodies in the Diagnosis of Scarlet Fever.—R. Isenshmid and W. Schemensky (*Münch. Med. Wchnschr.*, 1914, lxi, 1997), in reviewing the work done by various investigators on the inclusion bodies of Doehle, states that in general most authors incline to impart more or less of a diagnostic value to these bodies. Only a very few regard them as the specific cause of scarlet fever. While found within the polynuclear leukocytes in the early days of practically every case of scarlet fever, yet authorities are unanimous in stating that they also occur in other diseases, namely the infectious type. In the authors' investigation two stains were used, the carbol methyl-green of Pappenheim, and the borax methylene-blue of Mason. Eighty cases of typical scarlet fever were investigated, the inclusion bodies being found in every one. While the bodies occur in many different forms, the authors found the long, triangular form with the long tail-like end to be more characteristic of scarlet fever than the other forms. So also are the bodies arranged like diplococci. The authors admit that these bodies are of diagnostic importance when they are not to be found in the blood but that during the early hours or days of the illness Doehle's bodies are often missing. The characteristic bodies were found in four out of five cases of croupous pneumonia. In diphtheria diagnosis Doehle's bodies are of value only when absent, showing that scarlet fever is not developing, or when found in great numbers when the case is more probably scarlet fever than diphtheric. The bodies were not found in cases of rötlen, measles, and pertussis. The absence of Doehle's bodies in a febrile attack, rules out fresh scarlet fever. The presence of Doehle's bodies excludes rötlen and makes measles an unlikely possibility.

Remarks on Methods of Diphtheria Prophylaxis.—Karl Kassowitz (*Münch. med. Wchnschr.*, 1914, lxi, 1935) gives his conclusions as to diphtheria prophylaxis based on methods used used by him in an epidemic of this disease in a settlement kindergarden. The principle of his method consists of a combined bacteriologic and serologic testing of each individual associated in the institution with subsequent effective isolation and serum prophylaxis. The method of some boards of health in school epidemics, of suspending classes for two weeks and a general disinfection, while apparently rigorous is ineffective in many instances because unknown or undiscovered carriers can become the foci of a fresh infection even after two weeks. The elimination of the diphtheria carrier is the first principle of an effective diphtheria prophylaxis. The indication for serum prophylaxis should be based only on the proof of diphtheria bacilli on the mucous membranes of the suspected individual. The substitution of optional serum prophylaxis

for general bacteriological investigation of possibly infected cases is no protection against the development of further infections. By means of Schick's intracutaneous diphtheria reaction the field for prophylactic immunization can be still further narrowed. In the epidemic reported by Kassowitz, a bacteriological examination was made by cultures of all exposed children. This was repeated within one week. All suspicious cases, bacteriologically, were isolated. The school was closed, but only until a thorough disinfection was accomplished. These three procedures stopped the epidemic. The bacilli-carriers were given Schick's intracutaneous toxin injection and only those showing a positive reaction were given antitoxic serum. The cases were kept under constant observation with repeated bacteriologic and serologic control. The school was opened after its disinfection and no further cases developed although all but two of the eight proven carriers had returned to school after they had been proven negative by treatment. The original case, causing the epidemic had been returned to school one month after developing the disease and within ten days following his return five new cases appeared. He was included among the subsequent list of carriers.

Salvarsan in Scarlet Fever.—F. Glaser (*Deutsch. med. Wchnschr.* 1914, xl, 1760) reports the results of salvarsan used in the treatment of 42 cases of scarlet fever. The use of salvarsan is justified in this disease by three factors: The positive Wassermann reaction occurring at the height of the disease in many cases, the beneficient effects of the drug on severe necrotic inflammations of the throat, and lastly the therapeutic effect of salvarsan on a large number of protozoal diseases, such as malaria, frambesia, etc., to which class scarlet fever may possibly belong. Lenzmann and Klemperer have claimed excellent results from this treatment and note reduction in temperature from 1° to 2° C. with marked general improvement and local improvement of the throat and lymphatics. Torey warns against large doses which cause diarrhea, collapse, and nephritis, but admits the temperature is reduced and that general improvement is marked by this treatment. Jochmann, in 117 cases, claims the same good results, especially the necrotic sore throat, but claims the subsequent complications of the disease are not prevented by the salvarsan. Chill, vomiting, and diarrhea are mentioned by all these observers as occurring in over half of the cases. The methods used were intravenous and subcutaneous as in Glaser's 42 cases. In the latter 0.1 gram salvarsan was used for every 10kg. of body weight. Three septic cases practically moribund, were not affected by the salvarsan. Out of 15 cases with doubtful prognosis two died. In half these cases the effect on the temperature was marked, and the membrane in the throat was influenced favorably. The good effect on the ulcerative processes was unmistakable but chills, vomiting, and diarrhea were frequent and tended to lower the patient's strength. Complications, such as otitis media, glandular enlargement, and nephritis were not warded off in this group, by the treatment. In the last group of 24 cases, with an absolutely good prognosis, the injection of salvarsan caused a critical fall of temperature in over half of the cases. The chill, vomiting, and diarrhea accompanying many of the injections passed off in a few hours. The treatment apparently had no effect on

the eruption, the desquamation process or the complications. The conclusions reached from this series of cases were that salvarsan, in many cases, clears up the diphtheroid sore throat in scarlet fever, and affects favorably the general condition, especially reducing the temperature. It has no effect in the toxic cases nor in complications. In over half the cases, one injection caused chills, vomiting, and diarrhea.

Severe, Non-diphtheretic Laryngeal Stenosis in Children.—Ernst Köck (*Münch. med Wchnschr.*, 1914, lxi, 1805) describes a type of laryngeal stenosis in young children which is characterized by rather acute onset with coryza, croupy cough, increasing dyspnea, and laryngeal stenosis with moderate fever. Some of the cases cleared up after four or five days under the treatment for croup and bronchitis. A number of cases required intubation, and some tracheotomy. In all the cases the cultures taken from the larynx were negative for diphtheria but showed streptococcal and staphylococcal infection. The diagnosis of atypical pseudocroup was finally made in these cases. Attention is especially called to the inflammatory changes caused by irritation of the intubation tube and the cannula on the mucous membrane of the larynx. In one case which died a post-mortem examination showed a high grade inflammation with abscess formation. The same condition existed in the other cases which recovered. A pyogenic infection of the laryngeal mucous membrane plays a particularly harmful role, and from the experiences with the above cases Köck claims that the laryngeal mucous membrane breaks down more quickly from pressure of the tube in pyogenic infections than in pure diphtheria infection. Where diphtheria is excluded primarily by culture and a pyogenic infection proven, a primary tracheotomy should be done. Where the pyogenic infection is proven after intubation has been performed, a secondary tracheotomy is indicated.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

The Relation between the Bodily Development of the Fetus and the Development of the Parents.—Goldfeld (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1912, Band. xxii, Heft 2), finds that injurious occupations on the part of the mother, and the abuse of alcohol, naturally lessen the development of the child, and he quotes Letourneur's thesis, who found that in pregnant women having little rest, and following a difficult trade, that the weight of the newborn averaged 3081 grams. Pregnant women whose occupations were much easier, but who had little rest during pregnancy, gave birth to children averaging 3130 grams. Women having laborious occupations, but able to take rest

during pregnancy, had children weighing 3319 grams; and where the mother had no hard work and abundant rest the weight of the child rose to 3318 grams, if the rest taken was less than the average. Goldfeld publishes tables of the different trades, with the average weight of the infant born of mothers working in these trades. His results agree with those already quoted, that difficult work and lack of rest very much diminish the weight and size of the fetus. He also gives a tabulated statement of the increase in weight in the second, as compared with the first child. So far as the age of the mother is concerned, the largest children were born of mothers between twenty and thirty years of age, and over forty years. So far as the occupation of the mother is concerned, women working during the day seemed to give birth to large children, although the weight of the fetus in these cases was sometimes exceeded by those of more sedentary occupation.

Suprarenal Insufficiency Complicating Pregnancy.—Zuloaga (*Arch. men. d'Obs.*, May, 1914) finds that this condition sometimes produces considerable disturbance during pregnancy, labor and the puerperal state. It is often present before pregnancy and is made very serious by the advent of gestation. Where the toxemia of pregnancy results from chorionic villi, this in turn may affect the suprarenal capsules, and in some cases it seems probable that pernicious nausea is caused by these lesions. Sudden death complicating pregnancy, labor, and the puerperal state, may be sometimes referred to this condition. A diagnosis of suprarenal insufficiency becomes, in view of these facts, important. Persistent vomiting, altered arterial tension, and general evidences of toxemia indicate this condition. The use of suprarenal extract, either from the fresh gland or dry material, or the administration of adrenalin is indicated. Pregnancy should not be terminated for toxemia until this treatment has first been tried. Where there is distinct tendency to this condition the occurrence of pregnancy should be avoided.

The Importance of the Retention of the Membranes.—Guildal (*Arch. men. d'Obs.*, May, 1914) gives the results of his observations in Meyer's Clinic in Copenhagen. He finds that the management of natural delivery plays an important part in the retention of the membranes, that this complication arises in direct proportion with active interference during labor. Abnormalities of the placenta, and especially marginal placenta, predisposes to this occurrence. It cannot be demonstrated that the retention of the membranes has any important influence in causing hemorrhage. Puerperal morbidity is somewhat increased by this accident, but the removal of the membranes artificially does not seem to lessen the morbidity. Membranes that are practically adherent are usually discharged spontaneously from the fourth to the ninth day. It is quite possible that some of the chronic forms of endometritic have their origin in the retention of fetal membranes.

An Epidemic of Contagious Pemphigus in the Newborn.—Reinhardt (*Ztschrft. f. Geb. u. Gyn.*, Band 76, Heft 1, 1914) reports an epidemic of contagious pemphigus in infants under the care of the

Dresden Clinic. The first case appeared on the seventh day after the birth of the child, with small blebs in the hands and feet, after the stump of umbilical cord had separated. It seems probable that the mother of this child brought the contagion into the Hospital, as in the portion of the city from which she came there had been a widespread epidemic. The mother would not leave the child in the Hospital, but had no pemphigus herself. The second case occurred in an infant born eight days after the first, the blebs appearing first in the face and about the eyes. Mother and child left the Clinic and the mother bathed the child at her home, which resulted in spreading the infection and producing a universal eruption. Although the child was very ill it recovered, and the mother showed no signs of the infection. A short time after the third case occurred. The mother of the child died of puerperal sepsis. The child recovered from its pemphigus and was discharged from the Clinic in eight days. Although every effort had been made to end the infection, within a short time five other children were attacked, and later on additional. One child died, the infection penetrating the superficial layers of the skin and causing deep phelgmon. After it was supposed that the first epidemic had ceased, a second group of four children were attacked, three of whom were born in the Clinic. A period of four weeks then passed during which no new case developed, when another appeared, and two of the later cases died.

Two months then elapsed without pemphigus, while the Clinic had undergone the most vigorous disinfection, then suddenly three children were attacked, two severely, both dying with symptoms of general septic infection. Salvarsan was tried in these cases without evident result. Eight days after the last epidemic mentioned, a group of three cases developed, which were severe. One child died about six months after the first beginning of the epidemic. At the time of writing four months had elapsed, during which no case had developed. In diagnosis the question of syphilis is always an interesting one, but at present this can be settled by microscopic examination for Spirochæta pallida. As regards the germs causing the condition, staphylococci in all three varieties, streptococci, diplococci, gonococci and the pyocyaneus have all been isolated. Experimentally the disease has been inoculated from the human subject in monkeys, the infective bacteria being found in the chorium. So far as treatment is concerned, the persistent use of antisepsis which will not poison the infant, such as boracic acid by powder or bath, is indicated.

The Mechanism of the Passage of Carbonic Oxide from Mother to the Fetus, and the Part Played by the Placenta.—Nicloux (*Archiv. mensuelles l'Obstétrique*, January, 1913), has studied the mechanism of the transmission of carbonic oxide from mother to child, and the part played by the placenta. His experiments indicate that the blood plasma alone is the vehicle of conveyance, and that the phenomenon of respiration is essentially conducted by both the placenta and the individual tissues. Where the fetus is poisoned by carbonic oxide the result follows the action of this substance upon the maternal blood, while in the respiratory phenomenon oxygen is the essential agent. Before the maternal and fetal circulations are absolutely independent, soluble substances pass from mother to child through the epithelia

of the placenta and chorionic villi. The placenta may be considered as a dialyzing membrane on one side of which is the maternal blood and its corpuscles charged with carbonic oxide, and on the other the fetal blood with its blood cells as yet immune. That the carbonic oxide in the blood of the mother will pass to that of the fetus is evident, but the mechanism of its passage has not heretofore been clearly made out. Nicloux considers the placenta as analogous to the gills of the fish. He placed in a glass vessel containing distilled water and oxycarbonated blood several fish, and after some hours he found that the blood of the fish contained considerable quantities of carbonic oxide. A considerable proportion of the hemoglobin had been transformed into the oxycarbonated hemoglobin. It is significant that the water acted as a dissolving medium, and when the fish were placed in the salt solution isotonic to the blood globules there was no change in the carbonic oxide. Reasoning from this and similar experiments, his conclusion that blood plasma is an essential substance in the conveyance of material from mother to fetus, seems a rational one.

The Closure of the Ductus Arteriosus after the Birth of the Child.—Linzenmeir (*Zeitschrift f. Geb. u. Gyn.*, Band 76, Heft 1, 1914) finds that the important element in producing closure of the ductus arteriosus after childbirth, is the kinking of the duct following the alteration in the position of the fetal heart. Unquestionably the occurrence of respiration and the filling of the lungs have much to do with this. The movement of the pericardium is also an element. The muscular fibers of the duct make tension in two directions in a spiral longitudinal way, and also by lessening the lumen through contraction.

Teratoma of the Thyroid in the Fetus.—Russell and Kennedy (*Journal of Obstetrics and Gynecology of the British Empire*, February, 1913), report the case of a multipara who during pregnancy thought that her size was unusual as she had rapid increase during the last three weeks. It was thought that brow-presentation was present with hydramnios. The membranes were pierced and 14 pints of fluid drawn off, when a tight binder was applied. Labor did not progress, the head remaining in the transverse diameter, with defective flexion. On examination under an anesthetic an abnormal swelling in the neck of the fetus was discovered, and the child was delivered by forceps. It was fully developed, but dead. The weight was $6\frac{3}{4}$ pounds, the length 20 inches. The mother's recovery was uncomplicated. It is interesting to note that polyhydramnios which often accompanies abnormal conditions of the fetus, was present. The brow-presentation naturally resulted from the fetal abnormality. The fetus was fully developed, mature, and a female. The literature shows that such deformities have occurred more frequently in the male and that birth has usually been premature. There was no hereditary history of malformation. On examining the fetus a cervical tumor formed a lobulated swelling in front of the neck as large as a large orange. This was situated beneath the deep cervical fascia and in the middle line extending from the chin to the suprasternal notch. The mass protruded more to the right than to the left. The sternomastoid muscle on the left side was flattened against the left lateral aspect of the tumor, while

on the right the tumor overlapped the right sternomastoid muscle. About two-thirds of the bulk of the tumor was on the right side of the median line, while the lower margin of the right lobe overlapped the clavicle. The tumor had a distinct fibrous covering and could be separated from all the structures of the neck except the larynx, trachea, and esophagus. It was composed of three lobes, the smallest in the middle, occupying the upper third of the mass. The trachea and esophagus were upon the posterior surface of the tumor, where it could be plainly seen to have its origin in the thyroid gland and that portion corresponding to the thyroid was cystic, containing colloid and mucoid material. The tumor surrounded the trachea in front and on either side, and was attached to it, this attachment extending from the root of the tongue downward to a short distance below the thyroid cartilage. The tumor was attached to the trachea. The esophagus was not compressed by it. The carotid arteries, jugular veins, and vagus nerves were behind the tumor. On section, the tumor was irregularly cystic with a large cyst in front of the trachea corresponding to the thyroid gland. The other organs of the body were normal, the lungs unexpanded, and no air whatever had entered them. On examining the tumor minutely very little thyroid tissue was present. It was adenomatous in many places with cystic and colloid degeneration. In others there were papillomatous growths, the whole having a fibrinous tissue stroma. All three layers of the embryo were represented in the tumor, which was undoubtedly a teratoma. Hair follicles and fibrinous tissue representing the embryonic scalp were present. Gland tubules and sweat glands could be distinguished, and embryonic retinal tissue was found. In one portion bone was developing from cartilage. Embryonic nerve tissue was present in abundance.

Obstetrics in Primitive People.—In the *British Med. Jour.*, June 13, 1914, Cook contributes a paper on obstetric medicine in Uganda, His experience is interesting as showing what happens in parturition among practically primitive people. Women confined at home are usually delivered in a kneeling posture, the child being received in a bark cloth. The cord is cut with a sharp reed and is not tied. His statistics embrace 2232 cases, and it was supposed that the average native confinement would turn out to be easy. Such, however, was not the case, although the head of the native infant is usually small, the women well formed and apparently normal in development. On investigation, contracted pelves are common, although rickets is unknown. This seems to be caused by making little children carry heavy burdens upon the head. This results in forcing the sacrum down and lessening the anteroposterior diameter of the pelvis. Twin pregnancies are common, syphilis is common, and miscarriages frequent. As regards obstetric operations, the use of forceps was indicated in 14.5 per cent., which is more frequent than in many European clinics. The perineum was repaired in 9 per cent. and probably owing to the prevalence of syphilis, the placenta was removed by hand in 4 per cent. It is interesting to observe that syphilis is present in one or both parents in 13 per cent. The results are seen in the large percentage of abortion and stillbirths. Infection with parasites is a frequent cause of abortion, and many native women take native drugs, which cause uterine con-

tractions, sometimes with fatal result. These drugs contain alkaloids not yet accurately isolated. Rupture of the uterus following their use is not uncommon. As regards malaria complicating pregnancy, 5 grains of quinine hydrobromate may be given twice daily without fear of abortion, if potassium bromide and opium are given to allay irritability of the uterine muscle. It is interesting to observe that among Cook's cases were 11 craniotomies, 5 cephalotripsies, 4 decapitations, 1 embryotomy and 6 Cesarean sections. There was also an unusual frequency in posterior rotations and abdomnal presentations of the occiput.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Nervous Phenomena following Bilateral Oöphorectomy.—A paper expressing very decided views, from the standpoint of the neurologist, upon this much disputed question was presented last spring before the Neurological Section of the American Medical Association by Gordon (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1345). He has studied over a number of years the postoperative histories of 112 cases, in 89 of which the ovaries alone, in the remaining 23 ovaries and uterus were removed. In 34 instances young women suffering from various manifestations of neurasthenia, hysteria, or psychasthenia complained of vague disturbances in the abdomen, and consulted surgeons, who at once incriminated the ovaries and removed them. The results in 9 were an apparent temporary improvement, to be shortly followed, however, by a return of the former conditions, while in the remaining 25 cases there was no improvement whatever, the former nervous and psychic phenomena on the other hand becoming aggravated following the operation, in several instances temporary confinement to institutions becoming necessary. In all these cases the removed organs were found anatomically normal, and the results of the operation were little less than disastrous. In the remaining cases the reproductive organs were found to be diseased on one or both sides, and radical operations were performed. In most of these patients, local symptoms, such as pain in the abdomen and back, etc., were relieved, but subsequently nervous phenomena of various types appeared—insomnia, obsessions of various characters, restlessness and incapacity for mental work or for concentration, and in some cases complete loss of desire for enjoyment, loss of all interest in home and children, and other morbid manifestations that eventually necessitated institutional care. Since in the removed organs portions of healthy tissue were invariably found, the author concludes that the removal of the latter is in some relation to the morbid phenomena observed, and that all surgery on the female

reproductive organs should, therefore, be as conservative as possible, no operation being performed under any circumstances on healthy organs on account of vague nervous disturbances.

Spinal Anesthesia in Gynecology.—An extremely enthusiastic report on his experiences in the application of spinal anesthesia to gynecological work was presented by Gellhorn (*Surg. Gyn. and Obst.*, 1914, xix, 492) to the American Gynecological Society at its last meeting. Although able to report but a comparatively small series of cases in which he has used it (127 abdominal and 42 vaginal operations), Gellhorn emphasizes the fact that these include practically all types of gynecological procedures, including the most extensive, thereby showing its wide range of applicability. He says that the abdominal walls are more fully relaxed than with any other method of surgical anesthesia; moreover, in his experience the postoperative course is easier than after inhalation narcosis in the majority of cases. In 6 instances he was unable for various reasons to give the spinal injection; in 3 in which it was given the effect was entirely insufficient, and a general anesthetic had to be used throughout, while in a considerable number of additional cases a few whiffs of ether were necessary. Death occurred in four of his patients, this in no instance, however, being in any way associated with the anesthetic. In regard to disagreeable sequelæ, Gellhorn reports one instance of persistent, severe headache, lasting for over a week, a number of milder cases yielding easily to bromides. Backache lasting one or two days was noted in 10 cases, numbness or pain in the feet and legs in 3, a gradually subsiding partial paralysis of one leg in 1, and a slight, transient psychic disturbance in 1. There were no late complications. In a very large proportion of cases examined, acetonuria followed the spinal anesthesia, but disappeared spontaneously after about five days, and was apparently without pathological significance. In conclusion, Gellhorn expresses the opinion that the large amount of skepticism with which this method of anesthesia has been received by the majority of American surgeons is the result purely of prejudice, which is bound gradually to give way before its demonstrable value, and although he does not make the statement in so many words, it is evident from his article that he has adopted spinal anesthesia as his method of choice in a large portion of his operative work.

Lithotrity in the Female.—The great rarity of this operation in women as compared with men is commented upon by Grandjean (*Rev. prat. d. Maladies d. Org. Genitourinaires*, 1914, xi, 30), who attributes this to three chief causes, (1) the relative infrequency of vesical calculi in women, (2) the facility of access to the female bladder through the vagina or by dilatation of the urethra, (3) the difficulty of lithotrity in women. Notwithstanding the easy ways of approach, by which many stones occurring in the urinary bladder of the female may be removed entire, the author thinks the operation of lithotrity has numerous advantages over the other methods. It is much less of a procedure than either forcible dilatation of the urethra or vaginal cystotomy, and is not associated with the danger of subsequent incontinence, as is the former, or of a vesico-vaginal fistula, as is the latter.

Moreover, when properly performed, traumatism is negligible, the patient has to stay in bed only a day or two, and convalescence is nothing. The difficulties of lithotrity in women are purely of a technical nature, he thinks, and may easily be overcome with practice. They depend upon several factors, such as the absence of the fixed point of resistance, furnished in the male by the prostate, the easy dilatability of the urethra, permitting at times the fluid to run off, and thus necessitating instrumentation in an empty bladder, and the various more or less inaccessible pouches that may result from the presence of a cystocele or of uterine displacements, and into which the stone may drop.

Ether Poultices in the Treatment of Pelvic Inflammation.—Condamin (*Rev. prat. d'Obst. et de Gyn.*, 1914, xxii, 173) advocated the use of ether dressings for the treatment of the acute or subacute stages of pelvic inflammation. He has found this treatment to give marked relief from pain, to diminish tympany, and to reduce temperature. He says it is usually most agreeable to the patients, many of whom will ask for a new application as soon as the dressing is dried out. No mention is made of objections to the odor, either on the part of the patients being treated, or of others in the ward. The technique is as follows: In mild cases, an application for two hours morning and evening is usually sufficient. A piece of absorbent cotton covering 15 to 20 square centimeters is well soaked with ether and laid over the lower abdomen; it is covered by a larger layer of dry cotton, and then by a sheet of oiled silk extending well over the edges, the whole being held in place by an abdominal binder which makes moderate pressure. If at the end of an hour the patient no longer feels a comfortable sensation of warmth, the binder may be loosened, and the cotton remoistened. In more severe cases, a continuous application of ether is necessary; for this purpose one or two small rubber tubes are laid over the first layer of cotton, their outer ends projecting through the binder, and being clamped with hemostats. From time to time small quantities of ether may be injected through these tubes by means of a syringe, thus keeping the cotton constantly moist without disturbing the patient. In some cases, the author has tried the application of ether to the vaginal vault by means of tampons, either with or without the tube, but has found this method less efficacious than the abdominal, and at times associated with some discomfort to the patient.

Malakoplakia Vesicæ.—A interesting case of the unusual condition of fungoid growth affecting the urinary tract, known as "malakoplakia," is reported by Ferrari and Nicolich (*Folia urologica*, 1914, viii, 644). The patient was a much emaciated woman, thirty years of age, who was admitted to the hospital complaining of pain in the right flank, with frequent and painful micturition. The urine contained quantities of pus, but no tubercle bacilli could be demonstrated, and guinea-pig inoculation was negative. On cystoscopic examination, the entire internal surface of the bladder was found covered with pale yellow patches, resembling nothing so much as drops of wax. The left ureteral orifice could not be located, but a catheter was inserted into the right and purulent urine obtained. The patient gradually lost weight, and

died after about two months. At autopsy careful search for tuberculosis revealed nothing but a small caseous nodule the size of a pea, evidently an old, completely healed lesion, in one lung. Both kidneys were enlarged, and contained small, scattered abscesses. Each kidney pelvis and the ureters were much dilated; the inner surface of the renal pelves were covered with roughly circular, elevated plaques, 0.5 to 1 cm. in diameter, with well-defined boundaries, and in some instances a slightly depressed center. Similar, but less numerous plaques were found in the ureters, and large numbers of them were distributed all over the bladder, as had been determined by the cystoscope. Microscopically these plaques consisted of large, pale epithelial cells, with somewhat vacuolated protoplasm, and a minimum amount of intercellular connective tissue. In the deeper portions were a few capillary vessels, and there was much inflammatory infiltration throughout. Scattered between the large cells, and inside of some of them, were numerous peculiar bodies, or "inclusions" as the authors term them, consisting of round or polygonal structures, having a more or less concentric arrangement, staining deeply with hematoxylon, and giving the reactions for iron and lime. There were also numerous short, thick, gram negative bacilli, probably Bacillus coli. No tubercle bacilli could be demonstrated, and there was nothing in the histologic picture to suggest tuberculosis. Nothing definite could be determined as to the origin of the process, and the authors are inclined to agree with the views of previous writers that it is not of a tuberculous or neoplastic nature, but is a granuloma, arising as a result of urinary infiltration of the mucosa, this being rendered possible by lesions, or a diminished resistance, of that tissue the result of cachectic conditions.

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

MARK W. RICHARDSON, M.D.,

SECRETARY OF THE MASSACHUSETTS STATE BOARD OF HEALTH.

The Quincy (Illinois) Typhoid Epidemic.—Edwin O. Jordon and Ernest E. Irons (*Journal of Infectious Diseases*, July, 1913, p. 16) report that this epidemic of typhoid fever was water-borne, due in the first place to the fact that the water supply was taken from the Mississippi River at a point in close proximity to a sewer outlet; and in the second place to the fact that the mechanical filters used for purifying the water supply were not uniformly efficient but became occasionally very inefficient. This epidemic, furthermore, was similar to others due

to a similar cause in that it was preceded at an interval of ten days or two weeks by a very much more widespread epidemic of gastro-enteritis. About 1 in 187 of the population was attacked with typhoid fever. The addition of bleaching powder to the water in the mains reduced to a remarkable extent the number of typhoid cases occurring in the city of Quincy during the latter part of 1912. In December, however, the amount of bleaching powder was reduced to such an extent that sewage bacteria passed through unharmed and this was the period during which the typhoid epidemic occurred. The resumption, early in January, 1913, of adequate hypochlorite treatment was followed by immediate subsidence of the epidemic.

The Propagation of Amebic Dysentery in Animals.—A. W. Sellards and W. A. Baetjer (*Amer. Jour. Trop. Dis. and Prev. Med.*, 1914, ii, 231) suggest a modification of the usual methods for the inoculation of animals with amebæ and discuss the results obtained by this modification, more particularly with reference to the continuous propagation of typical strains in animals, with a comparison of the symptoms to those seen in man, and the etiology of some obscure diarrheas in man. The animals were inoculated by direct injection into the cecum, the exposure of the cecum being made by an exploratory laparotomy. Amebic infection followed this procedure with marked regularity even when the material was obtained from mild cases and was poor in amebæ. In contrast with this, the feeding experiments or the inoculation per rectum of typical material under favorable conditions usually gives only about 50 per cent. of positive results. It is usually stated that a strain of dysentery dies out upon subinoculation after a few passages in animals, degenerative changes appearing in the amebæ. By a combination of methods using intracecal inoculations and injections per rectum the authors carried a strain of dysentery through eleven successive passages, the virulence increasing definitely and the morphology remaining typical. The strain was then allowed to die out. The symptoms in animals corresponded closely with those seen in man. Acute and chronic infections were produced as well as the development of the carrier state and of a liver abscess. A fatal septicemia occurred with great regularity in the acute cases. No evidence was obtained to support the view that extensive amebic lesions of the intestine can develop without dysenteric symptoms. Pathologically the lesions in man and animals were similar in their essential features. Some obscure diarrheas were studied in which amebæ were found more or less constantly. The symptoms in these did not suggest the diagnosis of amebic dysentery from a clinical stand-point and the amebæ present did not correspond to either *A. coli* or *A. histolytica* in their morphology. The inoculation of animals with these amebæ produced symptoms like those occurring in the patient. The morphology of the amebæ in the infected animals changed somewhat tending to approach *A. histolytica*. Sellards and Baetjer do not consider that these atypical amebæ necessarily constitute a species distinct from *A. histolytica*.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL,

AND

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

Spontaneous Cirrhosis of Liver in Rabbits.—From time to time, interest has been displayed in the problem of the experimental production of cirrhosis of the liver. Beitzke (*Centralbl. f. Allge. Path.*, xxv, 625) issues a word of warning upon the use of rabbits and the conclusions of experiments performed upon these animals. He found a definite cirrhosis of the liver in two old rabbits with an accompanying enlarged spleen. There was no ascites in either instance. The microscopic findings showed a well advanced cirrhosis of the portal type in which a slight inflammatory process was also evident. He could offer no explanation for the development of the cirrhosis. One of the animals was more than three years old. Such observations are valuable in checking hasty conclusions made upon a small series of experiments.

Studies on Icterus.—Hymans, Bergh, and Snapper (*Berlin klin. Woch.*, 1914, Nos. 24 and 25) have brought forward some interesting observations upon the general subject of icterus. Although icterus is the condition in which bile pigment is present in the circulating blood, it must be remembered that there is also a certain amount of it present under normal conditions. This normal amount of bile in the blood varies within certain limits and it is only when quantities of 1 in 60,000 occur in the serum that it is excreted by the kidneys. Moreover, the bile pigment may increase considerably in the blood serum in pneumonia, heart disease and pernicious anemia without there being any definite organ lesion associated with an increased production of bile. A diminution of bile in the serum occurs in phthisis, contracted kidney, and malignant tumors. Within a certain range of concentration the bile pigment in the serum will not lead to a coloration of the tissues. Normally bile pigment does not appear in the serum of dogs, while in horses a great amount is commonly present. This evidence of a physiological bile content in the serum is against the theory that icterus always results from hepatic bile stasis (see also Whipple, *Jour. Expl. Med.*, 1913). Whether a different origin may be suggested for the physiological bile pigment of the blood from that of the pathological is not determined in this work. The authors have, however, determined an extrahepatic origin of bilirubin under pathological conditions.

Transudates contain little bile pigment, while exudates contain much. In the latter the bilirubin is proportional to the albumen content. In hemorrhagic effusions bile pigment may be demonstrated in large quantities. They have demonstrated the local development of these pigments in experimental hemorrhagic lesions. The locally produced bile is absorbed by the blood and when it reaches a certain concentration in the serum it is excreted by the liver cells or, if these cells are injured, the blood concentration of pigment increases. It is only when the amount of bile pigment in the blood have increased to a certain degree and in part is being secreted by the kidney that an absorption of it takes place in the tissues with the development of icterus.

Tuberculosis in Childhood.—Harbitz (*Internat. Cent. f. Tuberculose Forschung*, 1914, viii, 598) of Christiana, examined at autopsy 484 children from one to sixteen years of age. Of these he found 198 or 41 per cent. with tuberculosis and the majority of these (119) were acute. In the first year of life there were 201 cases examined of which 40 or 20 per cent. were tuberculous. The most frequent type of the disease was that of the thoracic lymph glands and the lungs. All stages of the tuberculous process were found, although evidence of connective tissue encapsulation was not frequent. Caseous destruction of tuberculous areas with cavities were also met with. In one instance the author believed that he was dealing with an intrauterine infection. The mother was tuberculous and the child was removed from her immediately after birth but died twenty-five days later, while the mother died on the twenty-eighth day. The frequency of tuberculosis in children is rather remarkable in these findings. Of 40 children at the age of fifteen, there were 32 with tuberculous lesions. Szontagh in a similar study found that the tuberculous process in children was in 95 per cent. of cases in the peribronchial lymph glands. Hamburger (*Wiener. Med. Wchnschr.*, 1914, No. 15) found that the incidence of tuberculosis rises rapidly from 1 per cent. in the first year to 95 per cent. in the eleventh to the fourteenth year. Children are very readily infected by the tubercle bacillus and only a short period of contact with tuberculous objects is necessary to acquire the disease. In the first year of life all cases are fatal. In the second year 50 per cent., and from eleven to fourteen years only about 2 per cent.

Congenital Anomalies of the Kidney.—In a series of 4500 autopsies, Motzfeld (*Ziegler's Beitrage*, 1914, lix, p. 539) has collected an interesting series of kidney anomalies. The importance of recognizing the frequency with which various anomalies occur has become more impressed upon us with the development of renal surgery. The absence of one kidney, the presence of two ureters on one side, and an abnormal position of the kidney, all have a bearing in the diagnosis and surgical treatment of this organ. In this series of cases the absence of one kidney was observed in thirteen individuals, while the absence of both kidneys occurred in two. Thirteen of these were in males, and two in females. True hypoplasia was found in twelve cases of which the majority were females and on the left side. This condition had no effect on the general health. The author refers to a second group in which a difference in the size of the kidneys is an acquired condition.

He has observed 11 cases of unilateral atrophy of the kidney, the majority of which were associated with chronic interstitial nephritis, or severe arteriosclerosis of one renal artery. All of these occurred after middle age. Horse-shoe kidney was seen in twelve instances, while an abnormal position of one kidney, usually the left, was observed in six. Hydronephrosis was present in twenty-one instances, many of them being associated with congenital or acquired strictures or thickenings of the ureter. He furthermore points out that anomalies of the ureter are not uncommonly associated with other anomalies, particularly those of the central nervous system.

Juvenile Gangrene.—The many studies that have been made upon juvenile gangrene have gradually thrown light upon the etiology of the process so that the determining factors are quite readily classified. Amongst these hues, trauma, embolism, infective thrombosis and intoxications are the important predisposing factors. There still remains, however, a group of cases in which the exciting cause is not evident. Gerlach (*Frank. Zeit. f. Path.*, 1914, xv, 243) reports such a case at some length, as well as the pathological study of the tissues. The condition arose in a young man of nineteen years, without evidence of a definite preceding injury. The right foot and leg became gangrenous, requiring amputation. The arteries and some of the veins were completely occluded. There was a great proliferation of the intima, which, in places, obliterated the lumen, while in others, the final occlusion was brought about by thrombosis. The author speaks of the condition as an endarteritis obliterans and objects to the term arteriosclerosis, although he does admit the designation of angiosclerosis. The characteristic of an inflammatory thickening of the intima with a splitting of the internal elastic lamina was the chief alteration in the arteries. The only suggestion which he could offer for the progressive arterial disease, was the excessive use of tobacco. Periarterial inflammation was wanting. He brings forward the feature that not a few of the cases of the presenile gangrene occur in the third decade of life in Jews.

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ORIGINAL ARTICLES

NEW USES OF SPECIFIC SKIN TESTS IN CERTAIN OF THE INFECTIOUS DISEASES.[1]

By Frederick P. Gay, M.D.,

UNIVERSITY OF CALIFORNIA, BERKELEY, CALIFORNIA.

The expression "tuberculin reaction" suggests at once to our minds a current test of corroborative and marked value in clinical diagnosis. Whether the reaction elicited be general or local, we know that its appearance indicates that the individual has suffered or is suffering from a tuberculous lesion. We now understand that a positive tuberculin reaction in man probably indicates an active tuberculous process only when it is taken in conjunction with other clinical signs. In a similar way a positive tuberculin reaction in a cow does not of necessity mean that the animal is a menace to the milk supply, and it is only in the production of experimental herds that it is usually possible or necessary to kill off all reactors. At all events up to the present the tuberculin reaction has been used and can be interpreted only in respect to its diagnostic significance. We purpose discussing (1) the extension of local specific reactions like the tuberculin reaction to the diagnosis of other infectious diseases, and (2) certain other novel uses of these reactions which are of distinctly prognostic significance.

Koch's original interest in the administration of tuberculin in the tuberculous individual lay in its possible therapeutic value. This possibility has been realized, but only in a limited sense;

[1] The Samuel D. Gross Lecture of the Pathological Society of Philadelphia, October 22, 1914.

tuberculin is generally admitted to have a distinct but restricted usefulness in the cure of tuberculosis. But at the same time Koch saw and described the diagnostic uses of tuberculin. He noted the characteristic rise in temperature that follows the subcutaneous injection of tuberculin in a tuberculous animal or individual, and also the local reaction at the point of inoculation and about the tuberculous foci. But although he noted the localized reaction its diagnostic possibilities were not understood until some seventeen years later. In 1907 v. Pirquet described the simple and accurate test for tuberculosis carried out by applying tuberculin to an abrased surface of the skin (cutaneous reaction), and in the same year Calmette described an equally simple but more dangerous reaction that may be evoked in the tuberculous individual by instilling a diluted tuberculin in the conjunctival sac. These two types of localized reaction have to a large extent supplanted the generalized tuberculin test suggested by Koch.

The priority of describing a localized specific reaction in the infectious diseases of diagnostic or prognostic significance belongs, however, not to Kock or to v. Pirquet but to Edward Jenner in connection with his study of smallpox. I prefer, however, to discuss the significance of his observations in another connection.

Following the descriptions of v. Pirquet, of Calmette, and of Wolff-Eisner on the diagnostic value of localized tuberculin reactions, similar reactions have been employed in other infectious diseases. It may be mentioned categorically that the local application of the respective etiological agent has been used with more or less diagnostic success in at least hay fever, glanders, gonorrhea, leprosy, trichophytosis, sporotrichosis, and the infectious abortion of cattle. Without further discussion of these interesting results we will consider in more detail certain even more recent applications of specific localized reactions which seem to me not only of interest in themselves but indicative of a new field of usefulness.

Let us consider first the method of diagnosis proposed by Edith Claypole[2] for infections due to members of the streptothrix group of microörganisms. Dr. Claypole has found that skin tests may be employed not only to diagnose streptotrichosis differentially from tuberculosis, with which it is clinically frequently confounded, but even between members of the streptothrix group. Dr. Claypole began her work in my laboratory some three years ago with an ambitious, and I believe rather successful, attempt at a classification of the much confused group of microörganisms that may be referred to as streptotrices.[3] This group is confused not only in respect to the individuals to be included, but also in respect to

[2] Human Streptotrichosis and its Differentiation from Tuberculosis, Arch. Int. Med., 1914 xiv, 104.

[3] Claypole, On the Classification of the Streptotrices, Particularly on Their Relation to Bacteria, Jour. Exper. Med., 1913, xvii, 99.

priority of nomenclature. For reasons that are given in Claypole's paper it has seemed better to refer to them as streptotrices and the diseases they produce as streptotrichosis. Among the disease entities in man and animals that are produced by this group of organisms may be mentioned madura foot, actinomycosis, nocardiosis, and pseudo-tuberculosis. These diseases are, as a rule, characterized as slow, progressive, localized processes which are, however, capable of an acute general pyemic or pneumonic course. In her general comparison of the type organisms of this group, Claypole has shown that they run from mycelial, non-acid-fast forms through non-acid-fast or partially acid-fast bacillary forms to strongly acid-fast forms that are closely allied to the tubercle bacillus. Not only are these gradual transitions in type demonstrable from one species to another, but they may actually occur in the cultivation of a given species. A given organism may from time to time be more or less acid-fast and bacillary, or again at one time almost wholly mycelial and later bacillary. By means of antisera to the mycelial, to the partly acid-fast bacillary, and to the acid-fast bacillary types it was possible to show that neither extreme organism reacted with the antisera to the other extreme species, but that the intermediate partly acid-fast organism reacted with its own antiserum and with the antiserum to either extreme type. The acid-fast streptotrices, moreover, reacted with an antiserum to B. tuberculosis.

In a considerable number of human cases of cervical adenitis and pulmonary disease that clinically are indistinguishable from tuberculosis some form of streptothrix has been found in pure culture. I may simply mention the names of Flexner,[4] Lubarsch,[5] Ophüls,[6] Burnet,[7] and Foulerton[8] in this connection. That a distinct though unknown percentage of glandular, pulmonary, and bone tuberculosis, so-called, is due to infection with a streptothrix is becoming evident from the work of Bridge,[9] Foulerton,[10] and Claypole. Even with the examination of discharges and sputum the diagnosis is overlooked. In the presence of a non-acid-fast streptothrix the carbolfuchsin stain results in the report of "no tubercle bacilli found." On the other hand an acid-fast streptothrix, particularly if non-mycelial, is passed as B. tuberculosis. By means of Dr. Claypole's differential skin test, streptothrix infections

[4] Pseudo-tuberculosis Hominis Streptothrica, Jour. Exper. Med., 1898, iii, 435.

[5] Zur Kentniss der Strahlenpilz, Ztschr. f. Hyg., 1899, xxxi, 185.

[6] Acid-proof Bacilli in Five Cases of Pulmonary Gangrene, Jour. Med. Research, 1902, viii, 242.

[7] Streptothricee dans une adénopathie cervicale, Compt. Rend. Soc. de biol., 1913, lxxiv, 674.

[8] Streptothrix Infections, Lancet, London, 1899, ii, 779; Some Observations on a Series of Seventy-eight Cases of Streptothrix Infections, Ibid., 1913, i, 381

[9] Streptothrichosis (Actinomycosis) of the Lungs, Jour. Amer. Med. Assoc., 1911, lvii, 1501.

[10] Loc. cit.

may be readily diagnosed, and it is barely possible that when recognized they may respond to a specific treatment.

Claypole prepared solutions from two types of streptothrix, in all respects similar to old tuberculin (concentrated glycerin-bouillon growths). Her cases were all tested by the skin test of v. Pirquet with old tuberculin, with Streptotricin H. (Streptotricin Hominis, mycelial, non-acid-fast), and with Streptotricin E. (S. eppingeri bacillary, partly acid fast).

In 45 control cases which gave no clinical evidence of tuberculosis 22 reacted to old tuberculin, but none to either of the streptotricins. In 55 cases of suspected tuberculosis, comprising 42 lung, 11 gland, and 5 bone involvements, 37 reacted to tuberculin (67 per cent.); 13 of these cases reacted to Streptotricin H.; 8 to Streptotricin E., and 6 gave reactions to two of the test solutions.

Of the 13 Streptotricin H. reactions 11 were lung cases. In 9 of these no tubercle bacilli were found, but in all of them thread-like, Gram-positive organisms resembling Streptothrix H., in the 2 others, acid-fast bacilli were found as well as the mycelial organisms, and one reacted to tuberculin and one to Streptotricin E. (acid-fast), as well as to Streptotricin H. The other two positive Streptotricin H. cases were glandular; both were negative to tuberculin. In one of these cases Gram-positive segments and rods were found histologically.

Eight cases reacted to Streptotricin E., 6 with lung involvements and 2 with bone lesions; 3 of the lung cases were negative to tuberculin and had no tubercle bacilli in the sputum, without doubt infections with a less acid-fast organism than B. tuberculosis. Two of the 3 remaining cases reacted to tuberculin and to Streptotricin E. In one of these tubercle bacilli were found in the sputum. The sixth case reacted to both streptotricins and had a mycelial Gram organism and an acid-fast organism in the sputum. The bone cases did not react to tuberculin and the infections were by inference due to the Streptothrix eppingeri group of organisms.

The data from these cases should convince us that we now have a means of differential diagnosis between mycelial streptothrix infection, partly acid-fast streptothrix infections and tuberculosis. Dr. Claypole is now engaged in studying the possibilities of specific treatment in this recognizable group of streptothrix infections, in some of which vaccine treatment has already been successfully employed.

Let us next consider a form of the cutaneous reaction which is of distinct prognostic significance. Although this reaction was recognized by Edward Jenner[11] and carefully worked out by v. Pirquet[12] its significance in public health administration has,

[11] An Inquiry into the Causes and Effects of the Variolæ Vaccinæ, London, 1798.
[12] Allergy, Arch. Int. Med., 1911, vii, 259.

I believe, only recently been brought into prominence by Dr. Force,[13] of the Department of Hygiene in the University of California. We have already referred to Jenner as the discoverer of the skin reaction. We can do no better than quote the words he used in reporting his failure to inoculate fourteen persons who had previously been infected with cowpox with smallpox.

"It is remarkable," writes Jenner, "that variolous matter, when the system is disposed to reject it, should excite inflammation on the part to which it is applied more speedily than when it produces smallpox. Indeed it becomes almost a criterion by which we can determine whether the infection will be received or not. It seems as if a change which endures through life has been produced in the action or disposition to action in the vessels of the skin; and it is remarkable, too, that whether this change has been effected by smallpox or the cowpox that the disposition to sudden cuticular inflammation is the same on the application of variolous matter."

This "sudden cuticular inflammation" of Jenner is recognized by v. Pirquet as "the immediate reaction" which follows attempts to vaccinate those who have recovered from smallpox or have been recently vaccinated. It indicates, in other words, that protection already exists in that individual, that antibodies are present which destroy the vaccine colony and prevent the evolution of the classical vaccine pustule. Force suggests simply that this immediate reaction be looked for in twenty-four hours and that its presence is as indicative of proper vaccination as the usual pustule which appears only at the end of several days. The presence of this immunity reaction would obviate the repeated and vain attempts to produce true vaccinia in such an already protected person.

Force and Beckwith[14] have further ingenuously employed a localized reaction of this type in the differential diagnosis of smallpox. They find that rabbits may be immunized against vaccinia or variola by subcutaneous injections of vaccine virus. Such animals show a specific local reaction on the intradermal injection of vaccine virus or of pus from a smallpox vesicle. They do not, however, react to varicella material. Force has recently been able to obtain an early diagnosis in two cases of suspected smallpox by this method.

Another skin test which may come to assume prognostic value is the luetin reaction for syphilis described by Noguchi. This reaction is produced by the local application of a preparation from a pure culture of Tr. pallidum to the abrased skin. It occurs only in cases of syphilis, and particularly in those cases in which the Wassermann reaction is negative. It occurs most frequently in late tertiary cases (80 per cent.), and becomes more intense after energetic

[13] Investigation of the Causes of Failure in Cow-Pox Vaccination, Jour. Amer. Med. Assoc., 1914, lxii, 1466.

[14] Unpublished Communication through the courtesy of Dr. Force.

antisyphilitic treatment. According to Noguchi[15] it indicates allergy, whereas the Wassermann reaction indicates an active syphilitic process. Its author further suggests that it may well be of value in indicating those cases that will derive benefit from treatment.

The Shick[16] intradermal test with diphtheria toxin, described in 1912, is of important prognostic significance. It indicates not only whether an individual has or has not diphtheria antitoxin in his blood, but very accurately whether or not he is protected from diphtheria. One-fiftieth of the minimal lethal dose of diphtheria toxin for a guinea-pig is injected intradermally in the individual to be tested. If antitoxin is present in the blood no reaction follows; if there is no antitoxin the bleb is surrounded in twenty-four to forty-eight hours by an area of redness and infiltration measuring from 1 to 2 cms., which slowly fades. It seems absolutely proved from the work of Schick and of Park and Zingher[17] that individuals who react to the irritation of the toxin have less than $\frac{1}{30}$ of a unit of antitoxin per c.c. of blood, and are not protected against diphtheria. Those who do not react are protected. The active immunity of such protected people may readily be raised by giving Behring's toxin-antitoxin vaccine. Those that give a positive reaction, the unprotected, do not respond well to active immunization and should be given antitoxin.

One of the recent interesting uses of a specific skin test is as an indication of protection against typhoid fever. The local application of extracts of the typhoid bacillus has already been tried as a diagnostic test for typhoid fever, but with indifferent success. In connection with experimental studies on methods of immunization against typhoid fever, in which my associates and I have been engaged for the past two years, many interesting questions have arisen. Dr. Claypole and I[18] have found a typhoid vaccine that produces practically no symptoms even in large doses in man, and at the same time, to judge from animal experiments, protects better than any other form of typhoid vaccine that has been described. It may simply be referred to here as the sediment of the bodies of alcohol killed, ground, sensitized typhoid bacilli from several strains. In common with many others we have found that the estimation of antibodies, particularly of the agglutinins is no measure of the degree of resistance against typhoid infection. In animals the real test of immunity is infection with the typhoid bacillus.

[15] Practical Application of the Luetin Test, New York Med. Jour., August 22, 1914.

[16] Die Diphtherietoxin-Hautreaktion des Menschens als Vorprobe der prophylaktischen Diphtherieheilserum injektion, Münch. med. Wchnschr., 1913, lx, 2608.

[17] Active Immunization in Diphtheria Treatment by Toxin-antitoxin, Jour. Amer. Med., Assoc., 1914, lxiii, 859.

[18] An Experimental Study of Methods of Prophylactic Immunization against Typhoid Fever, Arch. Int. Med., Nov., 1914.

In the case of human beings that have been vaccinated against typhoid fever we have had no assurance that they are really protected, and still less the assurance as to how long the protection lasts. By careful tabulation of morbidity statistics we may eventually learn how long a given type of immunization protects on the average. There is no assurance, however, for the individual who may be among the unfortunate ones who have failed to respond to the treatment. Dr. Force and I[19] believe that in our typhoidin test we have found a means of indicating individual resistance to typhoid fever. We found that 41 out of 42 cases (97 per cent.), that gave a history of typhoid fever gave a positive skin reaction to a concentrated bouillon culture of B. typhosus. It may be noted that two of these positive cases had typhoid fever, forty-one and thirty-three years previously. Typhoid recoveries, it may be recalled, are to all intents thereafter protected against the disease. Repeated attacks are probably paratyphoid infections. 86 per cent. of an equal number of those that gave no history of typhoid fever gave a negative reaction. It was difficult at first to explain the 14 per cent. remaining that gave a positive test with no history of previous typhoid. We believed, as our confidence in the accuracy of the reaction grew, that these positively reacting cases may have had aborted or undiagnosed typhoid fever. This explanation is rendered probable by an observation brought to our attention by Dr. Edward von Adelung. Dr. v. Adelung was a member of a family party that visited Germany nineteen years ago. Some two weeks after they had all drunk at a suspected water source, two of the members of the party came down with a fever that ran the typical course of typhoid, and was so diagnosed. The other two had at the same time mild symptoms lasting one and three days respectively, and consisting of headache, fever, malaise and flushing, which they regarded as abortive typhoid. Neither of these latter individuals give any other history of typhoid fever. All four members give a positive typhoidin reaction.

We find that individuals that have been artificially vaccinated against typhoid give, in the majority of cases, a positive skin reaction for from one and a half to two years. It may be positive for even longer periods. There are, however, a few individuals that fail to react a few months after vaccination. This experience agrees with what we know clinically about the duration and occasional failure of typhoid immunization. We feel justified in recommending to our students that they return for a skin test a few months after vaccination and at intervals thereafter. When they fail to react they are advised to be re-vaccinated.

Our suggestion and growing belief that this skin reaction with

[19] A Skin Reaction Indicative of Immunity against Typhoid Fever, Arch. Int. Med., 1914, xiii, 471.

thyphoidin is a real measure of the protection that the individual enjoys against typhoid fever is strengthened by observations on immunized rabbits. We have already shown that the agglutinin titer is no indication of the resistance of a given animal to infection, and observations on the Widal reaction in man tend to the same belief. The typhoidin reaction, on the other hand, is positive in that category of individuals that are known to be protected against typhoid fever, namely, typhoid recoveries; it does not occur in people who give no history of the disease except in a small percentage that may reasonably be suspected of having had an abortive attack. The reaction further occurs in the majority of those that have been vaccinated against typhoid within the last two years, and then gradually disappears. We had scarcely hoped to show differences in typhoidin reaction between incompletely and perfectly immunized rabbits as tested by our method of infection, which in incompletely protected animals produces carriers, but our results in this respect have exceeded our anticipations. Normal rabbits invariably give a negative intradermal typhoidin reaction. When series of rabbits are immunized, each with a different vaccine preparation, it is found that the better protected series gives a higher percentage of positive typhoidin reactions and a correspondingly smaller number of them become infected on injection of B. typhosus.

We have taken some interest in attempting to determine the mechanism of this typhoidin reaction. The problem was inviting since so many explanations as to the cause of the tuberculin reaction have been offered. It is perhaps most generally accepted as being due to some reaction that takes place between an antigen (tuberculin) and antibodies that have been formed in the tuberculous animal. One of the disputes is as to whether the antibodies that react are concentrated in cells or circulate in the body. It has been very difficult to prove the circulating hypothesis, as the susceptibility to tuberculin has been successfully transferred by the blood to another animal in very few instances. This passive transfer has been easy to demonstrate in rabbits immunized against the typhoid bacillus. When such an animal's serum is transfused into a normal rabbit the latter becomes susceptible to the typhoidin reaction, whereas the immunized animal when transfused with normal blood loses its susceptibility. Another interesting proof of the antigen-antibody nature of the typhoidin reaction has been by the intradermal injections of sensitized (treated with immune serum) and of unsensitized typhoid vaccines in human beings. The sensitized vaccine, although it gives no untoward symptoms when used for immunization, does produce an intradermal induration and areola, the untreated vaccine does not.

In running thus hurriedly over recent applications of specific local tests I have endeavored to show that in streptotrichosis the

method serves to differentiate closely related infections, and in the case of rabbits immunized against vaccine virus it may be used indirectly to diagnose human smallpox. In the case of the Schick reaction with diphtheria toxin and the typhoidin reaction of Gay and Force, local tests indicate protection or lack of protection against the disease in question, and therefore indicate when immunization is necessary. The accelerated vaccine reaction of Jenner and v. Pirquet becomes of value as indicating protection against smallpox and the fruitlessness of further attempts at producing vaccinia.

These latter prognostic applications of localized specific reactions open up, I believe, a new field of usefulness for tests of this sort.

ON THE INDICATIONS FOR ARTIFICIAL NUTRITION.

By Max Einhorn, M.D.,

PROFESSOR OF MEDICINE AT THE NEW YORK POST-GRADUATE MEDICAL SCHOOL.

Artificial or extrabuccal nutrition is frequently resorted to in our medical practice. As is well known, we possess four different methods of artificial nutrition, namely: (1) subcutaneous alimentation; (2) esophagogastral alimentation; (3) duodenal alimentation; (4) rectal alimentation.

It appears of interest to broach the subject of artificial nutrition with regard to its indications and also the special methods best suited.

With this object in view, cases in which artificial nutrition may be required can be divided into three groups:

1. Cases of subnutrition in which the digestive canal presents no obstacles to the passage of food.

2. Cases of difficult or impossible nutrition caused by obstacles to the passage of food along the digestive tube.

3. Cases in which absolute rest of certain portions of the digestive tract is imperative in order to effect a cure.

It will be best to discuss the above subject in each group separately.

Group I. *Subnutrition with a Free Food Passage Along the Digestive Canal.* Subnutrition or insufficient nutrition can be observed in almost all acute and most chronic diseases. Ordinarily, however, the physician, by rational instructions and an appropriate selection of foods, succeeds in introducing by the usual way (per os) an amount of aliment sufficient for the special case.

In rare cases the introduction of an adequate amount of food becomes difficult—if not entirely impossible—by a pronounced lack of appetite or marked aversion for food. But even then the usual mode of nutrition is persisted in, provided the difficulty

of food ingestion is merely temporary, *i. e.*, lasts a few days. So soon, however, as the insufficient nutrition is protracted, and attempts to overcome it by the diverse means at our disposal fail, the necessity of artificial nutrition makes itself felt. In complete abstinence from food artificial nutrition will be the more demanded.

As a whole, total food abstinence is met with principally in the insane and melancholics, also in several severe affections of the central nervous system, while insufficient nutrition is found in chronic diseases of the most various types.

With regard to the selection of the special kind of artificial nutrition in this group, the esophagogastral method will be selected. For the aliment is undoubtedly best utilized when subjected to the work of the entire digestive apparatus.

In case the repeated insertion of the stomach-tube is especially annoying to the patient, the duodenal tube may be used instead, provided the patient is not rebellious to treatment. In this instance the capsule at the end of the tube should best be made of gold, platinum, or hard rubber. The same method as that of duodenal feeding is applied with the difference that here the end of the tube with the capsule may remain in the stomach. The length of the tube in the digestive canal from the lips should be about 54 cm. The duodenal tube is, therefore, fastened in such a manner that mark II is situated outside the mouth. The thin tube does not molest the patient and is left in the digestive tract for about two weeks.

The food substances here used are, likewise, identical with those in duodenal alimentation, with the difference that larger quantities may be injected at each feeding.

Whereas in absolute food abstinence the total quantity of aliment is given through the tube, in insufficient nutrition one proceeds somewhat differently. As much food as possible is administered by the mouth, and what is still lacking is given by the tube. As soon as the patient ingests a sufficient amount of aliment by the mouth, artificial nutrition is stopped.

Group II. *Difficult or Impossible Nutrition Caused by Obstacles to the Passage of Food along the Digestive Tube.* This group represents the largest number of cases in which artificial nutrition is employed. It may be advantageously split into two subdivisions: (*a*) Organic stenosis of a high degree (including malignant stricture even of a minor degree); (*b*) medium-sized benign organic stenoses and spastic strictures.

(*a*) Difficulty in the passage of food caused by marked stenoses of the esophagus, cardia, pylorus, duodenum, or small intestine demands *rectal alimentation*. The same obtains if the difficult passage along the above localities is caused by pronounced obstacles compressing the digestive tube from without or by malignant stenoses of any degree.

Similar stenoses along the colon require *subcutaneous alimentation.*

In all these cases artificial nutrition is but a temporary adjuvant, and the stricture requires separate treatment, whenever possible. Thus in benign stenoses, when feasible, stretching should be performed; in malignant strictures, or in benign stenoses either not yielding or not accessible to stretching, likewise in tumors pressing from without an operation for the radical removal of the trouble should be undertaken.

In case the latter is impossible one must be satisfied with the surgical reëstablishment of a food passage, making nutrition possible. Thus in obstacles along the esophagus and cardia a gastric fistula, in those of the pylorus and duodenum a gastro-enterostomy, in those of the small intestine and colon—according to the location of the obstacle—an entero-enterostomy or enterocolostomy, or colocolostomy, or ultimately an *anus preter-naturalis* should be established.

In case an operation for some reason or other is unfeasible, artificial nutrition will naturally have to be carried on as long as life persists.

In these instances subcutaneous and rectal alimentation can be to advantage conjointly employed, or, if necessary, used alternately.

(*b*) *Medium-sized Benign Organic Stenoses and Spastic Strictures of the Digestive Tract.* In obstacles to the food passage due either to benign organic stenoses of a moderate degree or to spastic conditions—the selection of the special mode of nutrition will depend upon the location of the difficulty.

In spastic states of the esophagus and cardia—provided they are of such a high degree that the usual mode of nutrition be entirely impossible—and in moderate-sized stenoses of the same regions, gastral nutrition by means of a somewhat thin stomach-tube will be employed. In moderate benign strictures of the pylorus, or duodenum or in spasm of the pylorus, duodenal alimentation will be resorted to. If the latter for some reason or other fails, rectal alimentation will be used instead.

Stenoses of the small intestine—interfering with the prochoresis to such a degree that complications endangering life begin to appear—require rectal alimentation. If the affected area is situated in the colon, subcutaneous alimentation should be instituted.

In the whole subdivision (*b*) the separate treatment of the principal lesion should, likewise, never be lost sight of. The artificial nutrition is but a temporary adjuvant, and should be employed until the obstacles—if this be possible—have been removed or the natural mode of nutrition reëstablished.

Group III. *Absolute Rest of Certain Portions of the Digestive Tract is Imperative in Order to Effect a Cure.* In this entire group the ordinary way of nutrition, while at times somewhat impaired, is, however, always possible. The extrabuccal alimentation is here employed as a means of curing or ameliorating diseased states.

This group may be suitably divided into two parts: (*a*) diseased states of the digestive tract proper (exclusive of stenoses); (*b*) diseased states of other organs situated without the digestive canal.

(*a*) *Diseased States of the Digestive Tract Proper* (*Exclusive* of *Stenoses*). Severe inflammatory processes, injuries, and ulcerations of the digestive apparatus often demand perfect rest of the affected part in order to achieve complete recovery. This, however, is possible only then when the food contact is entirely removed from the diseased area.

If the lesions just named involve the mouth, pharynx, or esophagus, gastral alimentation by means of a stomach-tube or a thin tube *à demeure* will be resorted to.

In case the seat of the lesion is located in the stomach or duodenum, duodenal alimentation will be employed. It is self-understood that in affections of the duodenum the capsule end of the tube will have to lodge about 5 to 10 cm. or still more below the diseased part. In fresh hemorrhages of the esophagus, stomach, or duodenum rectal alimentation is best administered during the first two or three days, and then duodenal alimentation instituted. Ulcers of the stomach and duodenum have been particularly benefited by this mode of treatment. Besides in the affections just mentioned duodenal alimentation can be employed to great advantage in the following conditions: dilatation of the stomach (due to weakened musculature) and severe neuroses accompanied by persistent vomiting.

In case the above lesions (described at the beginning of this group) are situated in the small intestine, rectal alimentation is employed, if needed—and if located in the colon—subcutaneous alimentation. It is self-understood, however, that in the last-named instances artificial nutrition will be resorted to merely as an extreme measure, for neither rectal nor subcutaneous alimentation, nor the two combined, are able to supply adequate nutrition to the organism.

(*b*) *Diseased States of Other Organs Situated Without the Digestive Canal.* At first sight it appears rather strange that artificial nutrition should be indicated in diseases of organs not participating directly in the act of digestion. If we consider, however, what intimate relations exist between the digestive apparatus and the organs of circulation as well as of elimination—with each ingestion of food there is an overflooding of the circulation with new material and as a consequence an augmented activity in the circulatory and eliminative systems—it is plausible that leniency toward the digestive tract will exert a beneficial influence on other remote organs.

In fact it has been long known that a scanty insufficient nutrition, as, for instance, "Karell's diet," applied for a short period, is of distinct benefit in disturbed compensation of the heart.

Occasionally the ingestion of the smallest amount of food into the stomach produces an irritative state of the neighboring organ, the heart, especially if the latter is badly diseased. In such instances artificial nutrition (rectal or duodenal alimentation) may be indicated.

In two cases of severe myocarditis causing stenocardia in a high degree—and in which the minutest quantity of food given by mouth brought on attacks of severest dyspnea greatly endangering life—I have seen duodenal alimentation applied without the slightest inconvenience to the patient. This mode of nutrition greatly alleviated the condition of the two patients and prolonged their life.

. There is, therefore, an indication for artificial nutrition in severe affections of the heart in which the ordinary mode of alimentation is accompanied by severe dangerous symptoms. Rectal or, still better, duodenal feeding will then be used.

Diseases of the liver occasionally require a course of artificial nutrition (rectal or, still better, duodenal alimentation), in order to relieve somewhat the functions of this important organ. In several cases of cirrhosis of the liver[1] I have observed the greatly beneficial influence of duodenal alimentation on this disease.

CONTINUOUS CLONIC SPASM OF THE LEFT ARM (EPILEPSIA CONTINUA) CAUSED BY A TUMOR OF THE BRAIN.

By Charles W. Burr, M.D.,

PROFESSOR OF MENTAL DISEASES, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

The title describes the symptom of greatest interest, others, less important but still noteworthy, are brought out in the history.

The patient, an American housemaid, aged fifty-six years, unmarried, was admitted to the Philadelphia Home for Incurables in 1902. In 1897 she had noticed a swelling in the right breast which proved, a year later, to be a carcinoma. The breast was then amputated, but the growth recurred in the scar, and in consequence she was admitted to the Home and for several months nothing unusual happened. Then the patient noticed slight muscular twitchings in the left arm, recurring ten to twenty times daily and continuing from a few minutes to half an hour. In addition she complained not only during the attacks but also in the intervals between of a weakness in the left arm unaccompanied by pain. A week after the onset of the twitching she had an attack of Jacksonian

[1] Max Einhorn, On the Beneficial Effect of Duodenal Alimentation in Cirrhosis of the Liver, Medical Record, July 26, 1913.

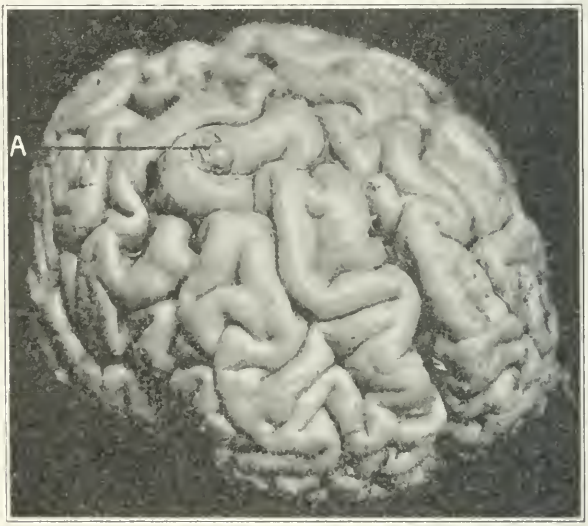
epilepsy. It began on attempting to pick up something from the floor with the left hand. The arm was involuntarily jerked upward above the head while the forearm was flexed to a right angle. An attendant, who was standing by, tried to lower the arm, but was unable to do so on account of its rigidity. Violent clonic convulsive movements instantly began in the arm and continued for about ten minutes without involvement of any other part of the body, except that both eyes rolled and the eyelids on both sides quivered. The patient was greatly frightened by the attack, and while it lasted screamed, paid no attention to commands, would not listen to questions, or make any attempt to explain how she suffered. Her excited state was evidently caused by loss of emotional control, mere fright, but after a short time she certainly became dazed, if not indeed absolutely unconscious, for a minute or two. After the attack was over she had only a vague recollection of what had happened (not entirely because of amnesia but partly from lack of attention caused by fear), and for about a quarter of an hour complained of complete loss of power and sensibility in the arm. She rubbed and pinched the arm vigorously, saying, "My arm is dead. I have got no feeling in it." For the following three or four hours there was nystagmus in both eyeballs and palsy of voluntary movement of both internal recti muscles. During the following two weeks she had five similar atacks of Jacksonian epilepsy, all of them immediately following voluntary movement of the arm, but many times she used the arm without any convulsion occurring. In other words, while voluntary muscular effort was a factor in precipitating an attack it was not the only factor, because most of the time she could use the arm perfectly well without any consequent convulsive effect. She never had any more attacks like these six, but the twitching of the arm became more and more frequent until, after a few weeks, it was practically never still during waking hours, but was constantly twitching and jerking, not severely, but enough to make it useless. She would sit all day with the arm flexed at the elbow and fastened to the arm of a chair by wrapping both in a shawl, claiming that the warmth and fixation relieved somewhat the constant twitching. Toward the end the twitching did not cease even during sleep, and if, while asleep, she made any large unconscious movement of the arm the twitching became so severe as to waken her. This was seen many times by her attendant, who watched her closely. In addition to the muscular contractions, causing movements of the arm, there were frequent, slight, spontaneous contractions of individual muscles not strong enough to move it. Contractions of single muscle bundles never occurred; either many, several, or only one muscle might contract at any one moment, but never a part of one muscle. There was never any fibrillary twitching. Tapping any muscle in the arm caused local "humping" and increased the already present twitching

or brought it on if absent. There was no muscular wasting, but distinct loss of voluntary power seemed to be present for some weeks before death, though it was difficult to demonstrate, because by that time any attempt on the patient's part to use the arm brought on extremely severe spasmodic movements, and it was almost impossible to distinguish voluntary from convulsive movements. The biceps and triceps jerks in the left arm were very marked, but it was impossible to obtain them on the right side, owing probably to the extreme edema resulting from the carcinoma. Sensibility to pain, touch, and temperature were normal over the whole body, except that the swollen right arm was slightly less sensitive to touch than the left. A painful stimulus on the left arm increased the twitching, but mere touch did not. Though the patient never complained of any trouble in the left leg, never even mentioned it, occasional slight spasmodic twitchings were visible in it. They were not severe enough to interfere with walking, and there was no loss of power in either leg. The left knee-jerk was larger than the right, but there was no Babinski jerk, indeed no plantar jerk of any kind, and no ankle-clonus. The patient did not complain of any of the characteristic general symptoms of brain tumor—neither headache, vertigo, nor vomiting—and optic neuritis was absent. She rapidly failed on account of the progress of the carcinoma, and in about twelve weeks after the first appearance of the twitching in the arm died.

The diagnosis was metastatic carcinoma of the brain, and the necropsy revealed the following condition: The right ascending frontal convolution was quite a little larger than the left and on its surface, about 4 cm. from the longitudinal fissure, projecting a little from the surface, was a tumor about the size of a large pea, growing from the pia-arachnoid and pressing into but not destroying the cortex. The tumor was shelled out with ease. There was another similar mass about the same size on the inferior surface of the left lobe of the cerebellum. Microscopic examination showed the two tumors to be carcinomatous. The illustration shows well the size and location of the first-mentioned growth. Though the right ascending frontal convolution was larger than the corresponding ascending parietal, caused apparently by local edema (no overgrowth of connective tissue or any foreign cells being present in it), the difference is unduly great in the picture because of fore-shortening.

It is not unusual to find at necropsy in cases of carcinoma more or fewer secondary growths scattered over the brain. As a rule they are so small or so situated as to cause no cerebral symptoms. Less frequently the tumor is so large as to produce all the general symptoms, or so situated as to cause definite symptoms of focal disease. We have no accurate statistics in this country concerning the frequency of secondary cerebral involvement in cancer, because it is not customary to examine the brain in such cases, unless there

are cerebral symptoms, and not always then. We have no knowledge as to how often there are small cerebral metastatic growths without cerebral symptoms, but judging from European statistics the association is very frequent.



Small pial metastatic carcinoma in the right ascending frontal convolution. *A*, indicates tumor.

It is unusual for a tumor to be situated just where it will produce the symptoms occurring in this case, and for death to ensue, from carcinomatous intoxication, before the tumor has grown enough to cause destruction of tissue. There are several interesting problems involved in explaining the case. Though the tumor was the cause of the cerebral symptoms, other factors than mere mechanical pressure must have acted, because it was constant, or rather slowly increased over a period of months, while for a long time the twitching movements were intermittent, *i. e.*, there were times when the twitching ceased entirely. At the end, when the twitching in the arm was constant, it is to be presumed that the motor cortical cells were continuously irritated by the tumor itself and by the slight localized pia-arachnoiditis around it. (There was a small area about as large as a dime around the tumor the seat of meningitis.) It is probable that the Jacksonian fits which occurred early in the course of the illness were precipitated by sudden alterations in blood-pressure acting on cells just ready to explode. The fact that voluntary movement of the arm produced, or if they were already present, increased the twitchings is probably to be explained in the same way—the cells were so irritated mechanically by the tumor that the slightest increase in excitation set them off.

The total absence of sensory disturbance, except for a short time after the Jacksonian fits, is interesting, and is of some value in deciding the exact boundaries of the cortical sensory centre. It would seem that in this patient the part of the anterior ascending frontal convolution invaded by the tumor, and presumably the entire convolution, had no sensory function. The transitory anesthesia after a Jacksonian fit is of no value in localizing sensibility. The common view today is that the ascending frontal convolution is entirely motor, but it may be that there are individual differences in the boundaries of sensory representation. This would explain the differences in the findings of different observers.

Several cases of continuous twitching of an arm or a leg or both have been reported. So far as I know Kojwenikoff was the first, in 1894, to give the condition a name, epilepsia continua. He reported four cases, none of which came to autopsy, and drew the following conclusions. In all his cases, he writes, the duration of the phenomena and their unilateral distribution indicate a lesion of the cortical cells, and since brain abscess, syphilis, edema, embolism, and brain tumor were excluded, he concludes that the cause was encephalitis with sclerosis. Kojwenikoff's conclusions were based entirely on his own four cases, and he does not speak of cases like mine in which a small tumor was the irritant. Oppenheim, in his text-book, refers to a case of tumor of the leg centre he had seen in which ryhthmical twitching of the toes continued for four days. He also speaks of clonic facial spasm occurring in a case of tumor near the facial centre. A few other authors refer to the matter.

Epilepsia continua is not a thing in itself, not a disease, but a mere symptom, and occurs as a result of many conditions; indeed, anything continuously irritating the motor cortex may cause it. If the irritation be local the twitching will, as a rule, affect only one part of the body, though sometimes a localized lesion may cause a widespread explosion: if the irritating lesion be very diffuse, then the twitching may be universal. Thus it is not unusual in well-developed cases of paresis to see twitching confined to one leg or arm, or involving all the extremities and even the face, depending upon how widespread the cortical disease is. Much more rarely the twitching may appear at the onset of the disease and precede marked mental symptoms. The tremor of the tongue on extension and of the corners of the mouth on talking, which often appears in the early stage of paresis, is really similar to epilepsia continua, and is caused by superirritability of the motor cells. Later the tremor becomes a continuous twitching. In so-called myoclonus epilepsy the movements occurring between the convulsions are, as a rule, very coarse, but even in it there may be only twitching. Indeed, many types of movement disorder may occur in epileptics. In one case, for example, for about six weeks before death in status epilepticus, there were periods between the convulsions when the

patient had the movements of St. Vitus' dance, and at other times showed athetosis in both arms and legs, and at still others merely the twitching of epilepsia continua. The explanation of this variability in type of motor disorder probably is that the character of the movements depends largely on the intensity of the irritation as well as on the area covered by the lesion.

The important thing in diagnosing the condition is to find the underlying cause. The diagnosis of brain tumor in my case was based entirely on the occurrence of the symptoms of a focal brain lesion in a person suffering from carcinoma. It is always safe to diagnose cerebral metastasis in any case of carcinoma in which cerebral symptoms occur if hemorrhage and thromosis can be excluded. The absence of choked disk, cerebral vomiting, vertigo, and headache do not exclude tumor, carcinoma, or any other malignant growth being present elsewhere in the body, and the presence of focal symptoms points strongly toward it because the classical symptoms of tumor occur only when the growth has attained some size, but a very small tumor may cause focal symptoms if situated in any part of the cortex having specialized functions.

PULSUS ALTERNANS.

By Hermon C. Gordinier, A.M., M.D.,
physician to the samaritan hospital, troy, new york.

In 1872 Traube, in an admirable article, directed attention to a hitherto undescribed condition of the pulse, with rhythmical irregularity in volume, which he called pulsus alternans, the sphygmogram showing waves of large and small amplitude, following each other in regular succession. He also noticed in the case which he described that while large and small beats were placed alternately throughout, the interval which separated the large from the small beats exceeded that which separated the small from the large beats. He further observed that the rhythm of the heart's action was perfectly normal.

Despite this early publication of Traube no other case of a similar character was recorded until 1892, when Sansom, in his book on the *Heart and Aorta*, refers to a case of cerebral hemorrhage, Cheyne-Stokes respiration, and general arteriosclerosis, with radiograms showing typical pulsus alternans. He states that the peculiar derangement of the rhythm of the pulse as seen in the sphygmogram was not at any time detectable by the finger. It is an example of alternating pulse, a more ample one being always succeeded by a less ample tracing, each beat being perfect in all

its elements, the irregularity being in volume only, and the cyclic sequence being invariable. Sansom says, to explain the large followed by the small pulse, we must assume that the ventricle delivers a full content in the large beat and an imperfect content in the small beat. The nervous mechanism which regulates this occurrence is the vagus. The lesion affecting its origin in the floor of the fourth ventricle is one which, calling into play its function of inhibiting the heart's movements in slight degree, is insufficient to elongate the diastolic pause, but antagonizes the sympathetic incompletely, so that this influence of the latter comes into play too soon in every alternate cycle. He also refers to another case of clinical alternation occurring with the onset of Cheyne-Stokes breathing. Hering believes that both the experimental and clinical alternation is to be explained on the hypothesis of a hyposystole or partial asystole. He has observed in the exposed hearts of lower animals that under pathological conditions all the heart muscle fibers are not in the same degree of contraction; that during the smaller beat of alternans, different degrees of contraction of the ventricle occurred. In this study Hering also showed that when tracings were taken from the clinical apex, or apex of the left ventricle in animals, the larger wave of the cardiogram corresponded to the smaller wave of the radiogram, thus producing a distinct incongruity between the apex beat and the pulse curve. On the other hand, when the cardiogram was taken from the third left intercostal space, or over the body of the right ventricle, the highest upstroke of the cardiogram corresponded to the strong beat of the radial. These results were constant and repeatedly observed. After the death of the animals needles were inserted through the intercostal spaces at the points where the cardiograms were taken, and on opening the thorax it was found that the needle in the fifth intercostal space was lodged in the left ventricle just above the apex. The needle in the third intercostal space was found in the conus of the right ventricle.

Hering believes that this incongruity between the cardiograms from the apex and those from the conus region, and the radiograph curves in alternans shows that the musculature which causes the apex beat has little or no propelling effect on the contents of the left ventricle. He further states that alternation is due to a disturbance of contractility without disturbance of rhythm, rapidity of rate, or lack of stimulus production, but is dependent on pathological changes in certain areas of the myocardium, the smaller beat being an evidence of the fact that the diseased areas of the myocardium react to stimulus production but slightly or not at all.

These observations of Hering were verified and somewhat elaborated by Rihl, who in 1906 reported 4 cases of clinical alternation, with two autopsies. All 4 cases were accompanied by general arteriosclerosis, chronic myocarditis, and hypertension. In the

3 cases that came to autopsy marked myocardial changes were found associated with general arteriosclerosis and chronic interstitial nephitis. In one case the coronary arteries were greatly sclerosed and the seat of aneurysmal dilatation. Rihl found the cardiac rhythm perfectly normal. He found that the height of the apex differed, a large and small beat following each other in regular succession. This shows alternation in the left ventricle. None of his cases showed evidence of alternation of the auricles. In all his cases an occasional extrasystole was observed, after which in each instance the alternation was more pronounced. He also found that anything that caused the heart to beat more rapidly, such as walking or other exercise would make the alternations more marked.

In 1905 Volhard discussed clinical alternation, and published 2 cases of true pulsus alternans and 2 cases of pseudopulsus alternans or continuous bigemina. The cases of true alternans were in young men, one a case of mitral stenosis with decompensation, aged twenty-seven years, and the other a case of chronic Bright's disease with albuminuric retinitis, aged twenty-five years. Both died within a few weeks after entering the hospital. His conclusions were that in man cardiac alternation is due to variation in strength of the contraction of the auricles as well as the ventricles; that the change in the pulse is due to difference in volume and that the cardiac rhythm is absolutely normal; that the smaller wave of alternans is due to the weakened contraction of the small systole plus the high aortic pressure; that with extrasystoles the alternation is very much pronounced; that continuous bigemina, or pseudopulsus alternans, resembles closely true alternans, but may be distinguished by the long compensatory pause following the small wave, and the small wave occurring at its normal time period.

Engleman has shown from experiments on lower animals that alternation is due to disturbances of contractility and not conductivity. Wenckebach is of the same belief and divides pulsus alternans into two forms: In one the time of the small wave exceeds that of the large, and the other in which the time interval of the small wave is the shorter. The first form he explains by the fact that the small wave is transmitted more rapidly into the aorta than is the larger; and the second form, with the large time interval of the small wave, by the hypothesis that alternation is due to weakened or exhausted contractility.

Hoffman believes that, owing to the disturbed function of contractility existing in alternation, contraction occurs more quickly than normal, and hence the periods of time of the systole and diastole are necessarily both shortened. In other words the heart muscle reaches the point of maximum contraction and relaxation much more quickly than in health.

Mackenzie, in his book on *Diseases of the Heart*, second edition,

states that a striking and characteristic sign of exhausted contractility is sometimes seen in the size of the pulse beat. He further states that "I have repeatedly dwelt upon the fact that the deviation and force of contraction depend in a measure on the length of the preceding period of rest. In hearts with good contractility, recovery after a contraction is so rapid that little or no difference can be detected in the size of the beat after pauses of varying duration. In cases of exhausted contractility, on the other hand, recovery is slow, so that the size of the beat has a distinct relation to the length of the preceding diastolic pause. This is exemplified in cases of extrasystoles. In those with good contractility the succeeding beat following the compensating pause may not be much increased, or may be very large, and the succeeding beats may be almost uniform in size. Whereas the same phenomenon occurring in hearts with exhausted contractility, the large beat following the diastolic pause, may be followed by several smaller beats of varying size in regular alternation. This difference in the size of the beats is an important one, as it indicates a grave exhaustion of contractility. Not infrequently the difference in the size of the beats persists for a shorter or longer period in such manner that the large beat alternates with the small beat, the pulsus alternans.

Mackenzie explains the pulsus alternans as follows: When contractility is depressed, if time be allowed for a full and strong contraction, the longer duration of contraction encroaches upon the period of rest, so that by the time the next stimulus arrives the contractility has not sufficiently recovered and a smaller and shorter contraction occurs. As this contraction is shorter in duration the period of rest is thereby lengthened before the next stimulus arrives, so that the contraction would be stronger and larger; being larger it will again encroach upon the period of rest and the process of alternation goes on.

Of the more recent studies on this complex cardiac mechanism those of Davenport, Windle and Thomas Lewis are instructive and interesting. Windle states that pulsus alternans is properly given only to that form of pulse in which a strong beat is regularly followed by a weaker one, the duration of the pulse periods being generally equal, although at times there may be slight alternation in the rhythm of the beats as well as in the force; but the difference in duration from one pulse to the next is small, and invariably the larger period belonging to the stronger beat, the weaker beat being therefore slightly delayed. From the polygraphic curves taken from his twelve cases, Windle states that he observed but one example of alternation of the clinical apex, while in all disparity in force of alternate radial pulses was decided and at times extreme. In the exceptional case the stronger beat of the heart curve coincided with the weaker one of the pulse. Thus this example confirms

Hering's observations. He also offers in explanation of this apparently incongruous phenomenon, Hering's theory that the musculature which forms the apex is not concerned in propelling the ventricular contents into the aorta. In this latter case alternation was often pronounced in records of the jugular pulsation; invariably the large *a* wave corresponded to the higher of the radial pulse beat. He observed no variation in intensity of the pitch or duration of the heart sounds or murmurs coincident with alternation of the pulse. His observations lend support to the view of Hering that alternation of the heart beat may be due to a partial systole of the ventricle. Lewis states that heart alternation occurs under two circumstances: (1) when the cardiac muscle is not altered structurally, as an accompaniment of great rapidity of rate; (2) when the pulse is of normal rate and under such circumstances the muscle is markedly degenerated.

Lewis' experiments were upon rabbits with ligature of the coronary arteries. He found that obstruction of one or other coronary artery was followed by rapid and new rhythms arising in the ventricle, the ventricular rhythm dominating that of the cardiac chambers, and that if the heart rate is greatly increased, alternation frequently appears both of the ventricles and auricles independently. As a result of these experiments, Lewis observed a divergence between the alternation in the ventricle and carotid, and explains this phenomenon on the coexistence of alternation in the force of the auricular contractions, thus supporting the view of Volhard, whose tracings showed that the large apical curve corresponded to the smaller radial beat alternation occurring in the amplitude of the *a* waves in the jugular, the small radial beat being preceded by the small *a* wave.

Lewis further states that the electrocardiographic curves obtained in clinical alternation are similar to those obtained experimentally, there being a divergence between the heights of *R* and *T* waves and the amplitude of the radial upstrokes. These facts demonstrate the identity of clinical and experimental alternation.

From a careful survey of the above-mentioned observations one is led to the opinion that both clinical and experimental alternations is the result of varying degrees of impairment from exhaustion of that most important function of the myocardium, contractility, which may be due to temporary exhaustion from the overwork of great rapidity of action or to permanent exhaustion and early cardiac failure, the result of grave pathological changes in the myocardium. The sequence of events of contraction of the cardiac chamber in alternation is normal. There is no defect of conductivity and the myocardium responds to stimulus production. The only abnormal rhythm is the variation in volume of the pulse beats and ventricular output, each large beat being succeeded by a smaller one, and so on indefinitely. This variation in amplitude

of the pulse beat, which is an evidence of exhausted contractility is of itself, owing to the lack of time interval between the small and large beat and the greater interval between the large and small beat, a menace to the further restoration of this function, because of the marked shortening of the preceding diastolic pause, which is so essential to a full restoration of the function of contractility. It is this shortening of the diastolic pause in all cases of long-continued tachycardia that results in early cardiac exhaustion.

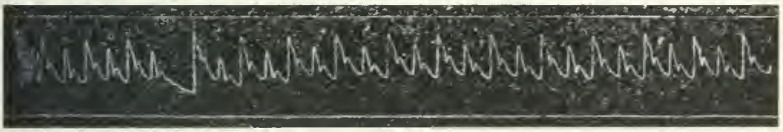


FIG. 1.—Pulsus alternans, with an occasional extrasystole. S. B. P., 230; D. B. P., 170. Chronic interstitial nephritis, chronic myocarditis, and general arteriosclerosis. Note the time interval of the small wave is the same as that of the large wave, $\frac{3}{5}''$.

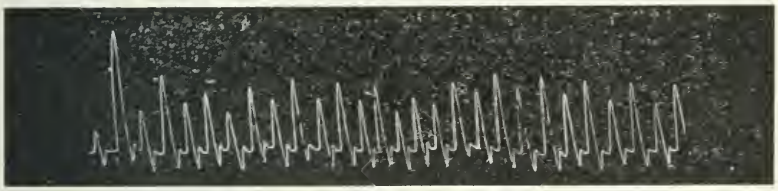


FIG. 2.—Paroxysmal tachycardia which continued six days, showing the alternation of acute myocardial exhaustion.

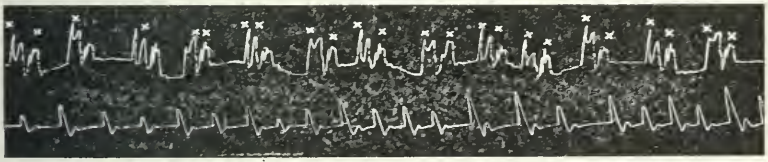


FIG. 3.—Pseudopulsus alternans, or continuous bigeminy due to extrasystoles. Mitral stenosis and regurgitation.

FIG. 4.—Dicrotism resembling clinical alternation, second week of typhoid.

Temporary exhaustion of contractility often occurs with the production of a typical pulsus alternans from an overtaxation of the cardiac musculature, the result of a too rapid rate, such as may occur in paroxysmal tachycardia, auricular flutter, auricular

fibrillation, or the long-continued tachycardia which accompanies Graves' disease. Experimentally it may be produced in healthy hearts by electrical stimulation, the injection into the bloodstream of digitalis, antiarin, aconitin, glyoxylsäure, and hemolytic serum. It is most frequently encountered, however, when the heart is beating within its normal rate, and when it denotes a grave pathological condition of the myocardium, with failing contractility. Most of the observed cases of this type of pulsus alternans have occurred in patients with general arteriosclerosis and hypertension, associated with chronic myocarditis and chronic nephritis. It frequently comes on during a period of Cheyne-Stokes respiration and continues to the fatal issue. It is usually not observed, however, until compensation is failing and the heart chambers are suffering from dilatation, the heart fibers having undergone both fibroid and fatty changes. It is not at all uncommon in the greatly dilated hearts of mitral stenosis or insufficiency where decompensation has occurred. It also occurs during and directly after recurring attacks of angina pectoris. Mackenzie has reported a notable example of this sort, and one of the five cases of clinical alternation which have recently been under my observation occurred after a repetition of attacks of angina pectoris, and lasted but a week, when the myocardium gradually failed and the patient succumbed. In this case the systolic blood-pressure was always under 140 mm. Hg. Alternation frequently comes on during a period of Cheyne-Stokes respiration and then continues to the fatal issue.

The relation of extrasystoles to alternation is most interesting and of great practical importance; in fact, many cases of regular bigemina have been confused or mistaken for and described as true cases of pulsus alternans. This so-called pseudopulsus alternans, or continuous bigeminia, may be distinguished from true alternans by the long-time interval, diastolic or long compensatory pause following each small or extrasystolic beat, and this in turn being followed by a larger beat, while the small beat has its normal time interval; whereas in true pulsus alternans the longer period follows the large beat or the large and small beat are equidistant from each other.

In a large number of my tracings showing extrasystoles, alternation has frequently succeeded for a single or a number of beats, the large wave following the long compensatory pause after the extrasystolic contractions, thus showing a decided impairment of the function of contractility. In many of the recorded cases of true alternation an occasional extrasystole is interpolated, and following such extra beats the alternation immediately becomes more in evidence. Not only may alternation follow extrasystoles, but, as shown by Windle, it often precedes the extrasystolic contractions. Several such examples have come under my observation. While I do not ordinarily regard the appearance of extrasystoles as of evil prognostic import, I do so regard those extrasystoles

which by repeated observation are found to be invariably followed by alternation extending over a considerable period of time. In two such examples of my own, death has occurred from decompensation and failing myocardium within two years.

Of the 5 cases of clinical alternation which have been under my care for the past two years, 3 have died—one at the age of seventy-eight years, of failing heart, following a series of attacks of angina pectoris, resembling a true anginoid status, with the clinical evidences of general arteriosclerosis and chronic nephritis, without hypertension. One died suddenly, when aged sixty-eight years, of general arteriosclerosis, high blood-pressure, chronic nephritis, and chronic myocarditis. A third, a man, aged forty years, died with all the evidence of decompensation, Cheyne-Stokes breathing, and uremia, the blood-pressure remaining high until near the end. The alternation in this case was first observed at the onset of the altered respiratory rhythm. The 2 cases now living are clinically typical examples of interstitial nephritis, general arteriosclerosis, hypertension, and chronic myocarditis. The older patient is aged seventy-two years and the other fifty-two years.

In 4 of these cases it was impossible to detect by palpation of the radial pulse the slightest evidence of alternation nor could one perceive by palpation of the clinical apex the slightest evidence of such a condition. In one case, however, the variation in volume between the large and small beat was so great that palpation of the radial was highly suggestive, although not positive, of alternation. The small beat resembled so closely the secondary wave in dicrotism that I was unable to distinguish between it and alternation until radiograms were taken. I therefore believe that palpation alone of any artery, radial or carotid, is a poor index of the presence of alternation or of the condition of the true action of the heart or of the height of the blood-pressure. I do believe, however, that defects of contractility from myocardial degeneration in the permanent irregularity of auricular fibrillation, or continuous bigemina, may be detected by comparing the rate of the radial pulse with that of the apex beat, determining the latter either by palpation or ausculation, and noting the deficit between the rate of the apex and that of radial. It is no uncommon observation to find that a third or half of the systoles of the left ventricle fail to be registered at the wrist. Many of the systolic contractions are so feeble that the intraventricular pressure does not overcome that of the aorta, and therefore the aortic valve is not lifted. If, however, the aortic pressure is overcome the pulse fails to reach the wrist because of the high blood-pressure plus the peripheral resistance.

In my cases of alternation no change in the intensity, pitch, or quality of the heart sounds were detectable. An extra or interpolated third sound was never heard. In one case, with a relatively loud systolic apex murmur, no change in its timbre occurred. In 3 cases no marked alternation was observed in cardiograms taken

from the clinical apex. In 2 cases, however, such alternation was very distinct. The respiratory excursions, because of the dyspnea in individuals with myocardial insufficiency, is so great that it is often difficult without temporary cessation of the respiratory act to get satisfactory cardiograms. In all cases the rhythm of the heart's action was normal. In three of the cases where satisfactory phlebograms were obtained the *a–c* interval was not increased, showing that conductivity was normal.

From this study the following conclusions may be drawn:

1. That pulsus alternans, while not common, is not very rare. I agree with Mackenzie and Windle in giving it the third place among pulse irregularities, extrasystoles being placed first and the persistent irregularity of auricular fibrillation the second.

2. Clinical alternation is frequently overlooked because it cannot be recognized without the graphic registration of the pulse.

3. Its presence is positive evidence of defects of the function of contractility, this in turn being due to temporary or permanent myocardial changes.

4. From a prognostic stand-point the presence of pulsus alternans, save the temporary form, due to great rapidity of rate, is grave, as it indicates extensive myocardial degeneration, most patients dying from cardiac insufficiency within three years of its onset.

5. Extrasystoles, invariably followed by alternation, also indicate exhaustion of contractility and carry with them a grave prognosis.

6. Persistent false bradycardia, due to feeble systoles, where the deficit between the apex beat and the pulse rate is but little altered by the exhibition of cardiac tonics, such as digitalis or strophanthus, also indicate grave defects of contractility, with extensive myocardial degeneration and unfavorable prognosis.

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WHAT FACTS OF DIAGNOSTIC OR PROGNOSTIC VALUE CAN BE DETERMINED FROM TEST-MEAL EXAMINATION OF PATIENTS WITH GASTRIC SYMPTOMS?

A CLINICAL ANALYSIS OF 7041 CONSECUTIVE CASES EXAMINED BY A UNIFORM METHOD.[1]

By Frank Smithies, M.D.,

GASTRO-ENTEROLOGIST TO AUGUSTANA HOSPITAL, CHICAGO, ILLINOIS.

The work forming the basis of this report was personally performed in my services at the Mayo Clinic and at Augustana Hospital. A close association of clinical, laboratory, and operative observations was possible in 7041 consecutive patients. Independent records were kept of histories, analytical data, and pathological findings. When the individual case had been finally disposed of the facts determined independently were grouped. In this way, unbiased, non-subjective information was assured.

The patients of this series came on account of self-styled "dyspepsia" or "indigestion," or, in the routine history taking, symptoms were elicited which pointed to some primary or secondary gastric disturbance. Their ages ranged from fifteen to seventy-eight years; there were two males to each female; while all occupations were represented, yet it is interesting to note that 32 per cent. of the patients were from farms or rural communities. The average length of time of the period of gastric disturbance was 6.4 years. The shortest time was two weeks (a case of inoperable cancer) and the longest period was more than forty years.

Methods. The emptying power of the stomach was estimated by the administration of a physiological meal of mixed food after the patient had been taken off "diet" and his stomach was, as far as possible empty. Experience taught us that a twelve-hour time interval was of greater diagnostic worth than the four- to six-hour interval as recommended by Riegel and others. The secretory factor was determined by means of the Ewald breakfast of second day bread. This was selected on account of its ease of administration, its lack of disagreeable features, its constancy, and its facility of removal. In the ordinary case the time limit was fifty minutes after administration. Where clinical symptomatology indicated abnormally rapid emptying power the stomach was examined from twenty-five to forty minutes after the test-meal had been given. The size and position of the stomach were determined by inflation through the stomach tube, with the patient recumbent. We used

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an inflation bulb, expelling one and a half ounces of air at each compression. The boundaries of the stomach were determined by the auscultatory method while the inflation was in progress.

In the space allotted for this paper only a brief summary of the work can be attempted. A detailed report is in preparation. It is difficult to present the work without its being merely statistical. A attempt has, however, been made to emphasize the clinical pointings.

Size of Stomach. The average capacity of the stomach was twenty-seven ounces in females and thirty-three ounces in males where dilatation did not exist. In instances revealing dilatation the average capacity in females was forty-one ounces and fifty-two ounces in males. The greatest gastric capacity was associated with non-malignant, pyloric stenosis.

The Macroscopic Appearance of Removed Gastric Extracts. In addition to evidences of gastric retention this observation was not infrequently of significance.

Color. Traumatic blood was noted in 6.4 per cent. of all cases. Its presence was quite as constant when simple spasm existed at the cardia as when ulceration was present with or without spasm. Its appearance upon lavage had *no consistent relation to any form of gastric disease other than cancer.* Forty-four cases of gastric ulcer had lavage less than forty-eight hours following hemorrhage, and in these cases there was no recurrence of either gross or microscopic bleeding from the maneuver. In the cancer cases (96 per cent. being of the medullary type) traumatic blood on lavage was observed in more than half of the 218 consecutive cases.

Bile Coloring. Various shades of green or yellow were observed in 11 per cent. of the cases in the series. The yellowish shades were the results of straining as a consequence of tubing or occurred in 74 per cent. of the patients who had had a previous gastro-enterostomy (seventy-six). The green coloration from bile was noted quite constantly in cases of gastric atony, ptosis with relaxed pylorus, dilatation with or without ptosis, intermittent pyloric spasm, induration about the pylorus due to ulcer or cancer, and from obstruction below the papilla of Vater. The green shades usually indicated that bile had been present in the stomach for some hours and had become oxidized. In two instances the growth of a chlorophylaceous mould was mistaken for bile before chemical tests or microscopic examination had been made. In 196 instances the presence of much traumatic blood rapidly hid evidences of bile coloring.

Of the cancer cases it is interesting to observe that coffee-colored or dark-brown extracts were noted in but 19 per cent. When such were observed the cases were inoperable. The color of gastric contents was quite as apt to be tan or brownish in partial stenosis with dilatation or atony from non-malignant causes as from cancer.

As will be shown below, however, the odor was a fairly reliable differentiating point between the two conditions. There were 314 cases of achylia gastrica. In 96 per cent. of this group the *dead-white* color of the gastric extract, associated with markedly absent chymification, was a characteristic finding.

Odor. Extracts from normal stomachs have a peculiarly, bland and somewhat sweetish odor. Modifications—quantitative and qualitative—in acidity cause variations. In non-retention cases the sharpness of the sour odor is usually a reliable gauge of the free hydrochloric acid content. In retention cases, high or low free hydrochloric acidity may be masked by the odor from fermentative or putrefactive processes. In 84 per cent. of the cancer group of this series, acrid, rancid odors due to volatile, organic acids were almost pathognomonic. In 76 per cent. of the non-malignant retention class (ulcers, gall-bladder disease, or ptosis with or without atony) the yeasty aroma was almost similarly characteristic. This simply elicited sign proved in our experience to be extremely useful in differential diagnosis. Putrefactive odors are generally due to sloughing of cancer tissue, deterioration of a quantity of blood in the presence of low hydrochloric acidity, fecal contents from obstruction below the duodenum or from perforation of ulcer or cancer into an adjacent viscus.

Amount of Gastric Extract. The average quantity of test-meal removed in the entire series was 108 c.c. The average quantity in the non-retention group was 76 c.c. The average quantity in the retention class was 350 c.c. So-called "hypersecretion" was as frequently observed in pyloric spasm from appendix or gall-bladder disease as from duodenal or gastric ulcer. It is not difficult to mistake partial pyloric stenosis for irritative hypersecretion. But 21 per cent. of the non-stenosing ulcers (duodenal or gastric) exhibited what might be termed hypersecretion. In young adults of both sexes the most common association of hypersecretion was pyloric spasm with diseased appendix or gall-bladder. Some degree of such was constantly present if the symptoms had persisted longer than an average time of 2.8 years.

Mucus. Mucus is a sign of doubtful diagnostic worth. It is more commonly in excess in stenosing cancers or ulcers than when the pyloric channel is free. While 1 per cent. of hyperacidity and hypersecretion cases were associated with pathological increase in mucus, 46 per cent. of the malignant retention group and 29 per cent. of the non-malignant retention class revealed such increase.

Chymification is an index of masticatory thoroughness, of the character of food ingested, of the combining power of hydrochloric acid, of the presence of normal gastric ferments, and of variations in gastric peristalsis and empyting power. The last factor appears to carry the greatest weight in all cases except those of primary or secondary achylia While high hydrochloric acid content gener-

ally assures good chymification, the presence of organic acids and foreign microörganisms (as in gastric cancer) frequently accomplishes similar ends.

The Incidence of Retarded Gastric Emptying Power. This term "emptying power," is especially chosen. "Hypermotility" should be largely limited to what is indicated by "hyperperistalsis." It does not necessarily follow that hyperperistalsis is associated with increased or even normal rate of the stomach's emptying. In fact, our records demonstrate that hyperperistalsis is most commonly found in instances of pyloric spasm or pyloric stenosis that have gastric or extragastric foundation.

Of our entire series, 12 per cent. of the cases showed some grade of retarded gastric emptying power macroscopically. In 8 per cent. of the series this was a *constant* finding. In 4 per cent. it was an intermittant manifestation. In 87 per cent. of the group when gastric retention was a persistant observation, some degree of gastric dilatation was an associated complication. In two out of every three cases where this occurred there was clinical history of delayed vomiting. Some of our most marked instances of gastric dilatation proved to have almost perfect emptying power. Persistent demonstration of gastric retention is an indication for surgical intervention. It denotes mechanical abnormalities or obstruction. In these instances, dilatation of the stomach is a symptom and not the disease. In a given case the degree of gastric retention may vary markedly accordingly as the stenosis is or is not associated with gastric or pyloric spasm. Dilatation of the stomach may likewise vary greatly in degree.

In our series the causes of persistent gastric retention were, in the order of the frequency of their demonstration, gastric cancer, duodenal ulcer, gastric ulcer, cholecystitis with adhesions, gastric atony, tumor of the pancreas, tumor of the liver, hypernephroma, tuberculous peritonitis, and retroperitoneal sarcoma. The causes of intermittent gastric retention were pyloric spasm associated with appendicitis or cholecystitis, gall-stones, duodenitis or gastritis in the presence of increased free hydrochloric acid, and gastroptosis.

In gastric cancer, emptying power was retarded in more than 70 per cent. of instances, irrespective of the location of the growth. In surgical duodenal ulcer, approximately two out of three cases revealed gastric stagnation. In surgical gastric ulcer in rather more than 50 per cent. of instances some grade of retention was proved. Of the pyloric spasms, associated with appendicitis, cholecystitis, gall-stones, or duodenitis, in rather more than 3 per cent. of instances retention was demonstrated. The sign of differential worth in this class of case is that of the variability of the exhibition of retention at different examinations. This sign is of special value to the surgeon who contemplates gastro-enterostomy in such instances. Unless definite obstruction exists at or

near the pylorus the best operative results are only to be expected when artificial stricture is surgically produced. We have the records of the examination of 482 cases of pyloric spasm with intermittent gastric retention, when later the appendix had been removed or operations upon the gall-tract had been performed. In but twenty-one instances was any form of gastric stagnation subsequently demonstrated.

These observations of the incidence of gastric retention, cannot in any way be compared with such information returned from examination by means of the Roentgen ray. It should be urged that, in the method outlined, we are dealing with physiological problems as they occur in a given individual. No one has yet shown that the examinations of gastric function by means of bismuth or barium compounds with the aid of the Roentgen ray is physiological. Consequently, only a long series of observations that have been checked up by surgical procedure or by the subsequent history in medical cases, extending over several years' time, will enable actinologists to formulate statements that will indicate what meaning we can attribute to retention of bismuth or barium in the stomach at the end of, say, a six-hour interval.

The most common causes of increased rate of emptying of the stomach in our series occurred in conjunction with achylia gastrica (primary or associated with severe anemia), vagus hypotonia, temporary or permanent atony without marked gastric dilatation, non-obstructing gastric cancer, colitis, and in numerous nervous states of the young adult.

Gastric Acidity. During the past five years, attempts have been made to belittle the significance of estimations of gastric acidity. This attitude has been brought about largely because of the persistence of surgical teachings. It is expected that those who anticipated that a simple color test would serve in place of clinical cerebration would be doomed to disappointment. While we have been compelled to revise some of our previously held opinions regarding the diagnostic worth of acid estimations of gastric extracts, yet when considered as a part of evidence making for proper conception of disease it would seem that such information can in no wise be neglected. The confusion has arisen chiefly because it was not until recently shown, just what effect upon gastric physiology had extragastric disease. Consequently, the findings in disease extrinsic to the stomach were interpreted, clinically, in the light of known primary gastric ailments.

For the purpose of brevity we would classify our acidity findings under three groups; (1) that comprising recognized disease of the stomach itself; (2) that including lesions of the duodenum, gall-bladder, appendix, and the large bowel; (3) that comprising so-called functional or central disturbances.

Acidities were all estimated by the Toepfer method.

GROUP 1.—ACIDITY IN INTRINSIC GASTRIC DISEASE.

(*a*) Acute gastritis:	
Average—Free HCl	32.0
Total acidity	50.0
Combined acidity	18.0
(*b*) Chronic gastritis:	
Average—Free HCl	42.0
Total acidity	62.0
Combined acidity	14.0
(*c*) Chronic atrophic gastritis:	
Average—Free HCl	12.0
Total acidity	21.0
Combined acidity	9.0
(*d*) Achylia gastrica:	
Average—No free HCl	
Total acidity	8.0
Combined acidity	6.0
(*e*) Gastric ulcer—acute:	
Average—Free HCl	64.0
Total acidity	78.0
Combined acidity	12.0
(*f*) Gastric ulcer with recent hemorrhage:	
Average—Free HCl	35.0
Total acidity	48.0
Combined acidity	13.0
(*g*) Chronic non-retention gastric ulcer:	
Average—Free HCl	42.5
Total acidity	55.0
Combined acidity	13.5
(*h*) Chronic gastric ulcer with retention:	
Average—Free HCl	56.4
Total acidity	74.2
Combined acidity	17.8
(*i*) Chronic perforating ulcer:	
Average—Free HCl	64.1
Total acidity	76.2
Combined acidity	12.0
(*j*) Ulcus carcinomatosum—(64 cases):	
Average—Free HCl	33.4
Total acidity	51.0
Combined acidity	16.0
(*k*) Primary gastric cancer—(122 cases):	
Average—Free HCl	7.46
Total acidity	28.3
Combined acidity	21.0
(*l*) Ulcerating primary gastric cancer (14 cases):	
Average—Free HCl	2.0
Total acidity	34.0
Combined acidity	30.0

SUMMARY. *Group* 1. It is shown that the highest gastric acidities are uniformally determined in acute and subacute perforating ulcer of the stomach; that in simple, chronic gastritis the picture from the stand-point of acidity closely resembles that of ulcus carcinomatosum or of simple gastric ulcer when recent bleeding has occurred, that only 54 per cent. of cases of gastric cancer reveal absent free hydrochloric acid; that in 45 per cent. of instances of gastric cancer the acidity returns may be readily confused with those of simple gastric ulcer, chronic gastritis, or achylia gastrica

unless the figures are rigidly interpreted in the light of clinical history, etc.; that in gastric ulcer with retention there is an increase in both free hydrochloric and total acidity, which fact is in sharp contrast to instances of retention developing in gastric cancer, in which event, as retention comes on, free hydrochloric is progressively lowered, while total acidity simultaneously increases. Other things being equal, in a given case, the diminution of free hydrochloric associated with an increase in total acidity, with the development of obstruction and the demonstration of organic acids, speaks for malignancy.

GROUP 2.—ACIDITY WHERE THE LESIONS ARE MAINLY OUTSIDE THE STOMACH.

(*a*) Duodenitis with pyloric spasm:	
Average—Free HCl	68.0
Total acidity	74.0
Combined acidity	6.0
(*b*) Duodenal ulcer without stenosis:	
Average—Free HCl	59.2
Total acidity	73.0
Combined acidity	14.0
(*c*) Duodenal ulcer with stenosis:	
Average—Free HCl	46.0
Total acidity	84.0
Combined acidity	28.0
(*d*) Cholecystitis, subacute:	
Average—Free HCl	66.0
Total acidity	71.0
Combined acidity	5.0
(*e*) Cholecystitis, chronic:	
Average—Free HCl	32.0
Total acidity	46.0
Combined acidity	14.0
(*f*) Appendicitis, subacute or chronic (usually in young adults both sexes):	
Average—Free HCl	64.0
Total acidity	73.0
Combined acidity	8.0
(*g*) Colitis, subacute or chronic:	
Average—Free HCl	35.0
Total acidity	42.0
Combined acidity	7.0
(*h*) Following gastro-enterostomy for gastric or duodenal ulcer:	
Average reduction in free hydrochlic acid	17.0
Total acidity	32.0
Combined acidity	12.0

SUMMARY. *Group* 2. Of this division the highest free hydrochloric acidities are present in cases of pyloric spasm associated with subacute cholecystitis, appendicitis, and duodenitis. The figures closely resemble those returned in gastric ulcer, as does also the clinical history with the exception of the incidence hemorrhage or chemical proof of bleeding and the time factor. The onset of stenosis in duodenal ulcer increases combined acidity at the expense of the free hydrochloric acidity. After gastro-enterostomy for non-malignant stenosis there is a consistent and noticeable lowering of free hydrochloric and also total acidity, which cannot,

apparently, be wholly explained on the basis of regurgitation of *succus entericus*. In more than three out of four such instances, proof of this having occurred, can, however, be demonstrated by ferment tests or microscopic examination of stained smears.

GROUP 3.—FUNCTIONAL AND CENTRAL DISTURBANCES.

(*a*)	In epilepsy of the young adult:	
	Average—Free HCl	56.0
	Total acidity	62.0
	Combined acidity	5.0
(*b*)	In neurasthenia, with or without moderate gastroptosis:	
	Average—Free HCl	34.0
	Total acidity	46.0
	Combined acidity	9.0
(*c*)	In marked gastroptosis:	
	Average—Free HCl	37.0
	Total acidity	52.0
	Combined acidity	14.0

These figures interpret themselves and require no special comment.

The demonstration of altered or occult blood in gastric extracts by the benzidin or the guaiac tests was possible in 25 per cent. of the cases in the entire series. It was present in 42 per cent. of all retention cases irrespective of the causative lesion. It was demonstrated in 75 per cent. of the 712 cases of gastric cancer. It was almost as frequently shown in duodenal as in gastric ulcer. It would seem that apart from the association of occult blood with malignant processes, its demonstration in gastric extracts has very slight clinical worth.

The Incidence and Significance of Organic Acids in Gastric Extracts. These are rarely demonstrated in non-retention cases, either malignant or non-malignant. In malignant disease, associated with partial stenosis and gastric dilatation, lactic acid was present in 53 per cent. of 712 operatively demonstrated instances. It was rarely demonstrated when free hydrochloric acid rose as high as 10, and in 92 per cent. of cases where lactic acid was found, extensive growths, generally inoperable, were present. Only 3 per cent. of the non-malignant achylias were associated with lactic acid. In but 7 per cent. of the non-malignant retention cases was lactic acid present. It was found in less than 0.5 per cent. of instances of ptosis with atony.

Volatile fatty acids were present in 61 per cent. of the malignant cases and in but 3.2 per cent. of the instances of benign retention or atony. In no instance of non-retention or of simple achylia or hypoacidity were volatile fatty acids demonstrated.

The Significance of the Demonstration of Specific Ferments in Gastric Contents. Space does not permit our going into detail respecting the incidence and diagnostic worth of proving the absence or presence of pepsin and rennin in gastric extracts. It

would seem that proteolysis is closely associated with the presence of free hydrochloric acid, so long as the acid concentration is below 0.4 per cent. and that milk-curdling ferment follows similar laws. In malignancy peptolysis appears to be increased at the expense of proteolysis.

We have made observations upon 827 instances of gastric disease for the detection of specific ereptases in gastric juices,[2] in the hope of recognizing early gastric cancer or malignant ulcer. We have used the formaldehyde titration method as suggested by Sorenson and Schiff. In our experience the average formol titration index in 87 instances of proved gastric cancer was 22.3; the average index in 22 cases of ulcus carcinomatosum was 19.8; the average in 99 cases of duodenal ulcer was 12.4; of 57 cases of simple gastric ulcer 11.6; of 32 cases of benign achylia, 14.1; of 16 instances of pernicious anemia, 14.5; and of 5 cases of cancer of the liver, 4.25. It would appear that in certain instances the estimation of the ereptic power of gastric juice toward peptone solutions is of considerable value when interpreted in the light of clinical history and symptomatology.

We have examined 108 cases for proteolytic ferments by the edestin method, suggested by Fuld and Levison.[3] The results thus far would appear to indicate that early cases of cancer of the stomach, where the free hydrochloric acid is shown to be low show high peptolysis and low proteolysis. In the simple ulcers both peptolysis and proteolysis are low.

We have already mentioned elsewhere our expereince with the demonstration of peptid-splitting ferments in gastric juice, using solutions of glycyltryptophan as the test dipeptid.[4] We made more than 1600 observations. In rather more than 40 per cent. of our proved cases of cancer (186) the reaction was positive. In about 7 per cent. the tryptophan test was positive. Diagnosis of malignant disease of the stomach was in each case quite possible, independent of the chemical test. While gastric abnormalities other than cancer exhibited positive glycyltryptophan reactions, in no class of the disease of the stomach was the test so frequently obtained as in cancer. Low free hydrochloric acid was frequently associated with positive glycyltryptophan tests, and in more than 50 per cent. of these reactions the gastric extracts contained bile or blood or both.

Wolff-Junghans' Test for Soluble Albumin in Gastric Extracts. We have tested 747 gastric extracts where there was low or absent free hydrochloric acid, quantitatively for soluble albumin,[5] according to the method suggested by Wolff of Ewald's clinic. Our work appears to indicate that in cancer this test was a more constant

[2] To be reported shortly.
[3] Biochem. Zeitsch., Bd. vi, Heft 5 u. 6, S. 473.
[4] Smithies, Arch. Int. Med., September, 1912, p. 672.
[5] Smithies, Amer. Jour. Med. Sci., May, 1914, p. 713

finding than when estimations for presence or absence of hydrochloric acid, of lactic or fatty acids, or of positive glycyltryptophan tests. It was approximately as constant a finding as tests for altered blood and the demonstration of motor inefficiency. It was not so constantly positive as the demonstration of organisms of the Boas-Oppler type or increase in the formol index. In extragastric malignancy and in gastric syphilis the manifestations of the test were inconstant. In the differentiation between malignant and non-malignant achylias the Wolff test, when interpreted in connection with other clinical and laboratory data, proved of considerable value. Positive manifestations were rarely obtained in the achylias of pernicious anemia, simple achylia gastrica and simple achlorhydrias not associated with gastric retention. Simple gastric and duodenal ulcers when accompanied by pyloric stenosis or marked gastric dilatation give confusing responses to the Wolff technique.

Significance of the Microscopic Examination of Gastric Extracts. We have made 6283 microscopic examinations (using the high power) of unfiltered gastric extracts that have been stained by the agar differential staining technique which we devised about three years ago.[6] In brief the summary of our work is as follows:

Starch digestion is not a constant index of the acidity of the stomach juice. Diastatic action of saliva often depends more on motor conditions than upon secretory. The character of the ingested food is a modifying factor. In some instances of low gastric acidity, with normal motility, it would seem that an anti-diastase were present in gastric extracts.

Microscopic remnants of the motor meal have no diagnostic significance other than that indicated when found in association with food macroscopically.

The Diagnostic Significance of the Microörganisms in Gastric Extracts. From our studies we have developed four microscopic pictures which seem almost pathognomonic for certain types of disease. Apart from these we can see nothing very significant. Certainly high gastric acidity by no means insures bacteriologic cleanliness.

Complex 1. *That of benign gastric retention (usually ulcer).* In 89 per cent. of our cases of this type the presence of large numbers of actively budding yeasts, associated with large and small sarcinæ and bacilli, apparently of the colon group, and food bits were demonstrated. The gastric acidity was generally above 50.

Complex 2. *That of gastric cancer.* In 93.8 per cent. of all our proved, late, malignant cases, organisms of the Boas-Oppler group, associated with food retention and acid averaging below 10, was a characteristic picture. In but 30 per cent. of instances were budding

[6] Smithies, Arch. Int. Med., June, 1912, p. 736.

yeasts concomitant. In but 10 per cent. were sarcinæ associated. Threads of streptococci were found in 6.2 per cent. (more commonly in the non-retention group). There is no characteristic microscopic picture of early gastric cancer other than that associated with gastric ulcer of the retention type. In less than 1 per cent. of our cases of gastric cancer were we able to demonstrate so-called "cancer cells" with active mitoses. These were all late cases or cases where the cardiac orifice was involved with a sloughing growth.

Complex 3. *Achylia Gastrica. Primary or Secondary.* In gastric extracts of low or absent hydrochloric acid, when there is atrophy of the mucosa and where motility is not interfered with, there are found long chains of streptococci (resembling beads of a rosary); groups of large, deep-staining cocci, and a peculiar, short, fat, acid-fast rod or cocco-bacillus that grows in short chains or pairs, or alone.

Complex 4. When perforation into an adjacent viscus has taken place in malignant ulcer or primary cancer, or where obstruction has occurred below the duodenum, the picture of immense numbers of thick cocco-bacilli, with or without spirillæ or streptococci, in association with low acidity, retarded food progress and putrefaction, as evidenced by the odor, is shown in more than 94 per cent. of instances.

THE PRESENCE OF CONTINUED HIGH TEMPERATURE IN MALIGNANT TUMORS.

By John Phillips, M.B.,

ASSISTANT PROFESSOR OF MEDICINE IN THE WESTERN RESERVE UNIVERSITY, CLEVELAND, OHIO.

The presence of continued high fever in malignant tumors is a symptom that has not been sufficiently emphasized by the majority of clinicians. That it does occur in a considerable number of such cases is undoubtedly true, as the study of large series of cases by various authors shows. The purpose of the writer is to report a typical example of continued high temperature in adenocarcinoma of the kidney, with a review of the literature.

The case I wish to report was that of a man, aged forty-four years, who was admitted to Lakeside Hospital, April 19, 1911, complaining of pain in the left side of the abdomen during the preceding four months. The family history was of no importance, except that one sister had died of cancer, and another sister had been operated on several years ago for a fibroid tumor of the uterus which had undergone sarcomatous degeneration. There had been

no recurrence of the sarcoma. The patient had always led a very active life and been in unusually good health.

The present illness dates back about four months, when he began to have a feeling of discomfort in the upper part of the left side of the abdomen. At no time had he suffered from severe pain, but at intervals of a week or ten days he would have a few sharp twinges of pain, which would quickly disappear. Two days before his admission to the hospital he noticed in his left side just below the ribs a prominent mass. His bowels, though always regular, had been constipated during the preceding two weeks and there had been no movement for forty-two hours before coming to the hospital. At no time had there been any jaundice, and the tumor mass must have enlarged rapidly, because he had been examined by several physicians during the two months previously, without anything abnormal being palpated.

Physical Examination. The patient is a large, robust man, showing no cachexia and no apparent loss of weight. Nothing abnormal was found except a prominent bulging in the upper part of the left side of the abdomen. Here, emerging from under the left costal border and extending downward 10 cm., is an elastic smooth swelling, freely movable and descending on respiration. This swelling is not tender to the touch, and gurgling of gas in the colon can be felt between the tumor and the palpating hand. Anteriorly it extends forward almost to the median line and posteriorly well toward the flank. The catheterization of the ureter showed nothing abnormal.

A carbohydrate test meal was given and removed one hour later. The amount obtained was 180 c.c., and consisted of clear fluid with a moderate amount of mucus and food particles. Analysis showed free hydrochloric acid 30, and total acidity 50. There was no lactic acid and the benzidene reaction was negative.

The blood examination showed: red blood corpuscles, 4,964,000; leukocytes, 8800; hemoglobin, 100 per cent. The differential count gave the following result: polymorphonuclears, 74.5 per cent.; small mononuclears, 14.5 per cent.; large mononuclears, 8 per cent.; eosinophiles, 2 per cent.; basophiles, 1 per cent. The red corpuscles stained normally and showed no unusual variation in size and shape. No malarial parasites were found.

On May 5, 1911, the patient was operated by Dr. Crile, an incision to the outer border of the left rectus muscle being made, extending at its upper part to the costal border. On opening the peritoneum the colon presented itself in the wound. This was retracted and a large cyst was found posterior to the mesocolon. The latter was split and the cyst brought into view and aspirated, about six liters of a thin dark liquid being removed. The exact origin of the cyst could not be determined. The walls were sutured to the peritoneum and fascia and drained. Microscopic

examination of sections obtained from the cyst wall showed no evidence of malignancy. The patient made an uneventful recovery from the operation. The urine examination both before and after the operation showed nothing abnormal. Chemical examination of the fluid showed no evidence of pancreatic ferments.

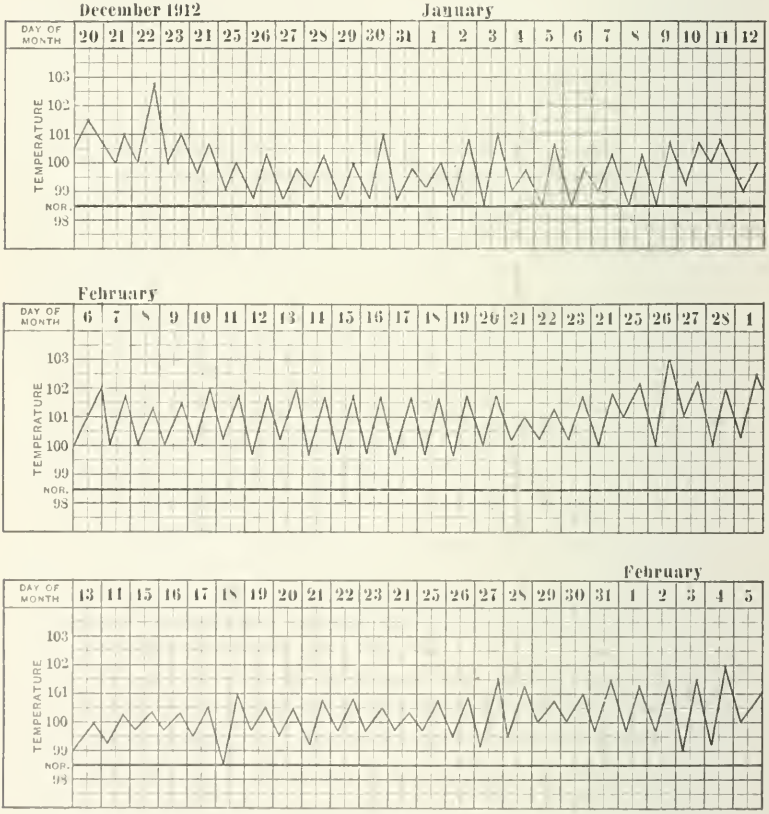
In the succeeding eighteen months the patient remained in very good health. During the first three months he led a very quiet life, but after that he actively engaged in business. He did not have his usual vigor, but his weight remained about the same, 220 pounds. On October 10, 1912, while playing golf he began to feel feverish and dull. His bowels were constipated, but there was no nausea, indigestion, or jaundice. He was relieved somewhat by a cathartic, but for two or three days each week he felt badly. During the next six weeks he lost fourteen pounds in weight and was admitted to the hospital November 23, 1912. At that time there was nothing of any importance found on physical examination except that a large mass could be felt in the upper part of the left side of the abdomen, extending from the costal margin downward to the level of the umbilicus, anteriorly almost to the median line, and posteriorly to the midaxillary line. The mass was somewhat tender, was adherent at the old scar, and gurgling of gas could be felt in the colon as it passed in front of the lower part of the tumor.

On November 24, Dr. Crile again operated, removing a portion of the old scar for diagnosis, which on microscopic examination proved to be an adenocarcinoma. No attempt was made to remove the tumor, as it was thought to be inoperable.

The patient made a good recovery from his operation, and was removed to his home four weeks later. During this time there was no rise in temperature above 99.5°. On December 20 the patient had a nasopharyngitis, with an elevation of temperature varying from 100° in the morning to 102.8° on the afternoon of December 22. During the succeeding six days his temperature varied from 99° in the morning to 100° in the afternoon.

Beginning December 31, 1912, he began to feel chilly about noon, and this was followed by a rise in temperature followed by a profuse sweat. After this the patient would fall asleep about 4 P.M., not awakening for four or five hours. This condition continued daily until his death, May 18, 1913. During the first month his maximum temperature after the chill was 101° during the second month, February, 102°, except the 26, when it reached 103°; during March the maximum temperature varied between 103° and 103.6°, and this condition continued about the same during April. On May 1 his temperature reached 104.4°, and on May 2, 104.2°, but throughout the rest of the month the maximum temperature remained between 103° and 104°. Throughout this period the abdominal tumor remained the same size and

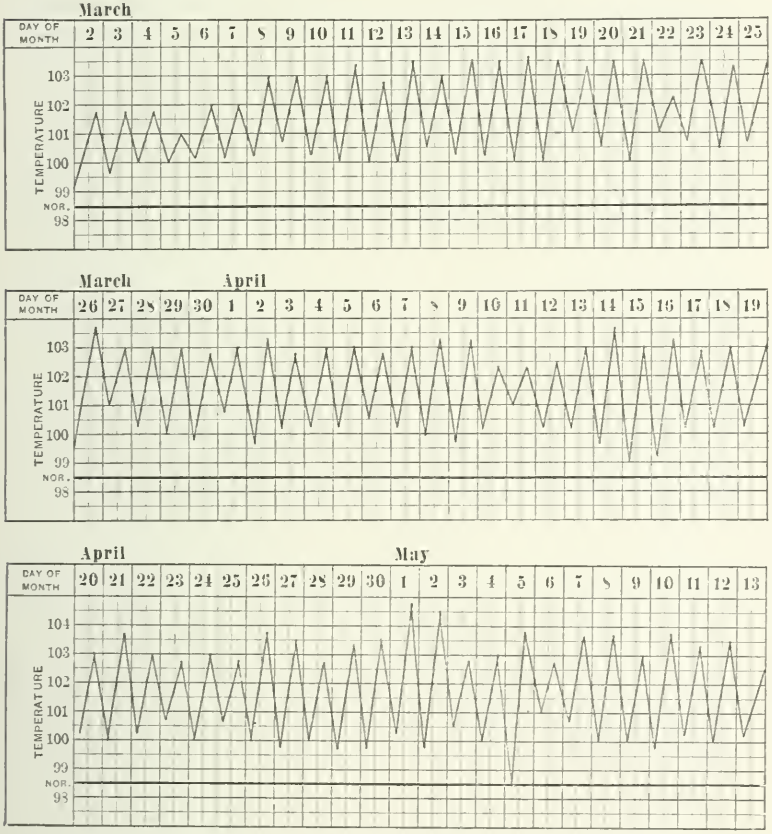
consistency. No evidence of complications could be made out on physical examination. At no time was there more than a moderate leukocytosis, and the blood was repeatedly searched for malarial parasites, but none found; blood cultures were negative. Until April 1 the patient's appetite remained good, and he kept his weight of 195 pounds. After this date he became weaker, lost his appetite, and his weight decreased quite rapidly, though no record



Temperature chart showing continued high fever in a case of adenocarcinoma of the kidney.

was kept, as he could not be weighed, being confined to his bed. The urine was examined twice a week, but showed nothing abnormal beyond a faint trace of albumin during the last two months. Another interesting thing about the case was that there was little tendency to anemia, as the following blood examination will show: February 4: red corpuscles, 5,196,000; hemoglobin (Haldane method), 93 per cent.; leukocytes, 11,200. The differential count

of the stained smear showed small mononuclears, 8.4 per cent.; large mononuclears and transitionals, 7.8 per cent.; polymorphonuclear neutrophiles, 80.4 per cent.; eosinophiles, 3 per cent.; mast cells, 0.4 per cent. The red corpuscles were normal in size, shape, and staining properties. No malarial parasites were seen. Blood cultures and the Widal reaction were negative. February 27: red blood corpuscles, 4,682,000; hemoglobin, 90 per cent.;



Temperature chart showing continued high fever in a case of adenocarcinoma of the kidney.

leukocytes, 14,700. The differential count of the stained smear showed: small mononuclears, 3.7 per cent.; large mononuclears, 2.6 per cent.; transitionals, 2.3 per cent.; polymorphonuclear neutrophiles, 91.3 per cent.; eosinophiles, none; mast cells, none. The red corpuscles were normal in size, shape, and staining properties, and no malarial parasites were seen. There was no growth from the blood cultures, and the Widal reaction was negative.

The patient grew gradually weaker, and died May 18, 1913.

The following is the autopsy report of Professor O. T. Schultz, the postmortem being performed one and a half hours after death:

The body was that of a well-built white male, five feet nine inches tall, weighing approximately 165 pounds. The body was still warm. In the left hypochondrium, about four inches from the median line, was a narrow vertical scar about three and a half inches long, apparently a healed operation incision. A second similar scar of equal length joined this one at its upper end and then extended somewhat obliquely downward and outward. The subcutaneous fat was yellow in color and from one to one and a quarter inches thick. The trunk musculature was of good color and well developed. The pleural, pericardial, and peritoneal cavities were free of excess fluid.

Right lung: The right lung was firmly bound down by old fibrous adhesions. The left lung was everywhere free. The posterior surfaces of both lungs were congested and edematous; otherwise the lungs appeared normal.

Heart: The heart appeared normal in size and consistency. It was not opened or removed.

Abdomen: The stomach was moderately distended, the colon markedly so, with gas. The intestines themselves were everywhere free of adhesions. In the left hypochondrium there were rather easily broken fibrous adhesions between the mesocolon and the anterior abdominal wall. In this region there was a firm, hard mass of tissue extending from the abdominal wall, in the region of the operation wound scars, down deep toward the left kidney region. In the adhesions between the mesocolon and the abdomen was a small mass of tissue made up of cysts measuring 5 to 10 mm. in diameter; these were thin walled and filled with clear fluid. The tail of the pancreas was adherent to the mass of tumor tissue which extended dorsally from the abdominal wall. The pancreas could, however, be readily separated, and when separated showed no involvement. The mesenteric lymph glands were not enlarged. The spleen was about twice its normal size, the free convex surface triangular in shape, with a deep notch in the superior border. The spleen was soft and congested, about half of its substance being occupied by an irregular, triangular, deep red area, whose base was at the capsular surface. Beyond this area the spleen substance was somewhat firmer than normal.

Liver: The margin of the liver came down two fingers' breadth below the costal border on the right side. Upon the inferior surface of the liver, around the region of the hilum, were a number of firm, white nodules measuring from 0.5 to 2 cm. in diameter. In addition, similar whitish areas, softer and more translucent, and varying in size from just barely visible to some 5 mm. in diameter, were scattered in large numbers throughout the liver substance.

Right kidney: The organ showed nothing abnormal except a moderate increase in the thickness of the cortex. The right adrenal was normal.

Left kidney and tumor: The mass of tissue which extended posteriorly from the anterior abdominal wall could be traced directly to the kidney, being attached to the kidney near the pelvis 4 cm. from the lower pole. The kidney could be very readily separated from the posterior abdominal wall and was nowhere adherent except in the anterior middle region mentioned, where the tumor tissue was directly continuous with the kidney. Upon removal, the upper half of the kidney was found to be occupied by a number of cysts measuring from 2 to 7 cm. in diameter. These were thin walled. The contents of some were fluid, dark brown, grumous, apparently made up of broken-down tissue and changed blood. In others the fluid was clearer and contained masses of pale tissue similar to finger-like ingrowths of tissue which extended from the cyst walls into the lumina of the cysts. Still others were almost completely filled with such tissue. The cysts were not adherent externally. At the point of attachment of the mass of tissue which extended from the kidney to the abdominal wall there were a number of firm nodules which had caused some pressure upon the anterior wall of the pelvis of the kidney and had led to moderate dilatation of the pelvis. In the middle region of the kidney, beneath the cystic upper pole, the kidney substance was occupied by a soft, white tissue arranged in rounded nodular areas, from 2 to 10 mm. in diameter. Some of these were opaque and apparently necrotic. The distance from the inferior pole of the kidney to the superior pole of the tumor was 18 cm. The thickness of the tumor in the cystic region was 9 cm. The kidney cortex of the lower pole measured 12 mm. in thickness. From its mesial to its lateral border the tumor measured 12 cm. The posterior surface of the kidney was well outlined and measured 12 cm. from pole to pole; the capsule of the posterior surface stripped readily. The kidney and tumor together weighed 650 grams.

Microscopic Examination. The pancreas is normal. The islands of Langerhans are numerous and well defined. In sections taken from the region where the tail of the pancreas was adherent there is no invasion by tumor tissue.

Spleen: In sections from the dark red middle area the sinuses are widely distended with red blood corpuscles, which are often agglutinated. There is relatively little spleen pulp visible between the distended sinuses; such cells as can be seen still stain well; many of the latter contain finely granular, light yellow pigment. In this region of the spleen the Malpighian bodies are well preserved and stand out prominently in the section. Sections from the more nearly normal appearing spleen tissue show a moderate

general increase in stroma and endothelial cells; light yellow, granular pigment is present in large amounts.

Left kidney and tumor: In sections from cysts the latter are seen to be filled with markedly branched, papillary ingrowths, which are composed of rather dense central fibrous bands carrying thin-walled bloodvessels; these papillæ are covered with a rather tall cylindrical epithelium. Peripherally such cysts show an invassion of the surrounding stroma by small, oval and circular, tubular alveoli lined by a single layered epithelium whose cells are not quite so tall as those covering the papillæ within the cysts. About some of the cysts the stroma is markedly infiltrated with light yellow, granular blood pigment.

In sections from the solid, whitish nodules present in the kidney the papillomatous character of the tumor is not evident. These nodules are composed of a rather dense fibrous stroma in which are closely placed small tubular alveoli similar to those present about the cysts.

The kidney tissue immediately about the cysts and tumor nodules is compressed, the interstitial tissue markedly increased, the tubules decreased in size, and the glomeruli transformed into dense fibrous bodies. In the cortex of the right kidney and in that of the lower pole of the left kidney the convoluted tubules are prominent, the lining cells larger than normal. There is moderate congestion of the intertubal vessels.

In the mass of denser tissue which extended from the kidney to the abdominal wall there are numerous tubular alveoli separated by narrow bands of fibrous stroma. The papillomatous character present in the cysts is entirely absent here and the tissue has the typical arrangement of a cellular adenocarcinoma.

The small mass of cystic tissue found in the omental adhesions is composed of small cysts, some of which are lined by a single layer of cuboidal epithelium and are filled with finely granular, pink stained material; others are filled with papillomatous ingrowths, exactly like those in the cysts of the kidney itself.

Liver: In the larger tumor nodules the stroma is prominent, more here than in any of the other portions of the tumor; the metastases are of the scirrhus rather than the medullary type. The tumor alveoli are small, round, oval, or irregular in shape, and are lined by an epithelium whose cells vary greatly in size and shape. In the smaller liver nodules the amount of stroma is not so great as in the larger ones; these small metastases begin in the interlobular tissue. The latter is moderately increased in amount even where no invasion by tumor tissue occurred, and is infiltrated with lymphocytes. The peripheral portions of the liver lobules are congested and a moderate amount of fat is present.

Anatomical Diagnosis. Papillary adenocystoma of the left kidney; adenocarcinoma of the left kidney; secondary adeno-

carcinoma of the liver; moderate interlobular hepatitis; recent red infarct of the spleen; hematogenous pigmentation of the spleen; moderate compensatory hypertrophy of the right kidney.

Conclusions. There can be no doubt but that the original tumor was a cyst of the kidney which sprung from the middle region of the organ near the pelvis and pointed directly forward. At this time the tumor was most probably benign, and almost certainly there were present other cysts than the one opened at operation. The tumor began as a benign cystadenoma of the kidney. Beginning thus, continued proliferation of the epithelial lining led to a filling up of the cyst cavities with papillomatous ingrowths; from a benign, pure cystic tumor there developed a papillomatous cystadenoma, a tumor with the potentialities of invasion and malignancy. The invasion of the stroma surrounding the cysts is characterized by a loss of the papillomatous nature and a transformation of the tumor into a typical adenocarcinoma. Many of the new-formed tumor alveoli have the appearance of kidney tubules. With this transformation the tumor became definitely malignant, with the property of spreading by direct invasion of surrounding tissues and of producing metastases. At the time of the second operation the tissue removed for diagnosis from the mass which had replaced the wall of the original cyst was unmistakably carcinomatous, and microscopic examination of some of this same mass of tissue removed at autopsy shows it to have the characters which indicate that it had been growing at a more rapid rate than any other portions of the tumor. In spite of the undoubted malignancy of the tumor, as evidenced by the clinical course of the disease, the invasion of the tissue which replaced the original cyst wall, the multiple metastases in the liver, and the microscopic character of the tumor tissue, the failure of the tumor to grow invasively is its most striking feature. The kidney together with its associated primary tumor was most readily removed at autopsy; there was no invasion of the body wall posteriorly or of the overlying tissue anteriorly. The tumor had grown by direct continuity only anteriorly along the cyst wall, which had been stitched to the abdominal wall at the first operation. Metastases were present only in the liver, and there were most probably a development of the terminal four or five months of life.

The other conditions noted in the anatomical diagnosis are all minor ones, secondary to the tumor itself.

The first author to lay stress on the occurrence of fever in cancer was Wunderlich, who, in 1870, stated that in cancer elevation of temperature is comparatively rare, the temperature being usually normal or subnormal, but at times fever is present in the latter stages. He also mentioned the fact that intermittent fever was occasionally noticed in the early stages of cancer and that

its presence suggested a rapidly fatal course. Kühn, in 1875, reported a case of primary carcinoma of the kidney, accompanied by fever, in a child. In this case, however, the febrile periods were associated with such disturbances as hematuria, gastric distress, and softening of the tumor, which might account for the elevation of the temperature. Brinton is quoted by Leube, in 1876, as authority for the statement that fever is not rare as a symptom of malignant disease. Riegel attributed fever to the complications that occurred during the course of cancer. Nothnagel considered it was a symptom of carcinoma itself; and Kraussold reported two cases of carcinoma of the cecum with all the symptoms of acute perityphlitis. Leichenstern stated that entirely atypical cases occur independent of the stage of the disease. This observation has been confirmed by Osler, Rolleston, Russell, and Finlayson. Additional reports of the association of fever with malignant disease have been made by Hampeln, Hawthorne, Freudweiler, Bull, Marchesini, Badnel, and Eichorst. Puritz and others have recorded the occurrence of fever in cases of sarcoma. A few of the cases so recorded were undoubtedly cases of Hodgkin's disease.

Freudweiler, who has made the most complete study of continued elevation of temperature in malignant disease, reviewing the literature, made a systematic study of 475 case histories in which the diagnosis was made with certainty clinically or anatomically during the years 1884 to 1897. In these cases the organs involved were as follows: stomach 265, pharynx and esophagus 105, liver and gall-bladder 38, the colon and rectum 24, the small intestine, omentum, and peritoneum 3, other organs (including uterus, kidney, and prostate gland) 40. Only those cases with a temperature above 38° C. were considered febrile, because if the cases below this were included with the cases of continuous fever this class would be disproportionately large as compared to the class with intermittent and remittent fever. He made the following classification of his cases according to temperature, excluding all cases in which there were complications or other causes to account for fever: (1) Febris continua—variations of temperature within one degree; (2) febris intermittens et remittens; (3) malaria like fever paroxysms; (4) isolated or short periods of elevation of temperature of less than three days' duration. Of the 475 cases of cancer reported by Freudweiler, 189, or 39.8 per cent. had fever. Of the uncomplicated cases 127, or 24.6 per cent. Thus in cancer of the stomach, 265 cases, 61, or 26 per cent., had fever; cancer of pharynx and esophagus, 105 cases, 22 or 21 per cent., had fever; cancer of liver and gall-bladder, 38 cases, 17, or 45 per cent., had fever; colon and rectum, 24 cases, 7, or 29 per cent., had fever; small intestine, omentum, and peritoneum, 3 cases, 1, or 33 per cent., had fever. Other organs,

40 cases, 9, or 22 per cent. had fever. In the consideration of the four different types of fever he deduced the following facts:

1. Febris continua—cases with a variation of less than 1° C. In this form of fever the duration may be only for a few days or weeks. The temperature may then disappear and return with somewhat different daily variations. The cases with continued fever constituted 1.5 per cent. of total cases and 6 per cent. of febrile cases. It occurred in 6.6 per cent. of cases of cancer of stomach.

2. Eight per cent. of cases of cancer of liver and gall-bladder and 14.3 per cent. of cases of cancer of the colon and rectum.

3. Febris remittens et intermittens (the largest class). Once present this type of temperature usually continues until death. Sometimes the intermittent and remittent types may alternate. This class includes 10.1 per cent. of total cancer cases and 41 per cent. of febrile cases. Its occurrence as to organs was as follows: In cancer of the stomach, 34.4 per cent.; in cancer of the pharynx and esophagus, 39.8 per cent.; in cancer of the liver and gall-bladder, 35.2 per cent.; in cancer of colon and rectum, 46.6 per cent., in cancer of other organs, 66.7 per cent.

4. Cases with malaria-like paroxysms. These cases may have chills and sweats lasting ten to twelve hours and recurring every second or third day. In some of these cases the highest temperature, reaching to 39° or 40°, is present in the morning, and in the afternoon it drops to normal. There were 17 cases of this type of temperature in Freudweiler's 475 cases, or a percentage of 3.6 per cent. or 14.5 per cent. of febrile cases. This author has made three subgroups of these cases: (*a*) Those with sudden onset with chills and sweats, the paroxysms lasting from twelve to twenty-four hours; of this type there were eight cases in his series. (*b*) Those in which the onset was slow with a continuous temperature lasting from two to three days and with slow remission. There were no chills or sweats, and of this type there were four cases. (*c*) Those in which the temperature resembles for a time that seen in group (*a*), and the remainder of the time that of the same character as type (*b*). There were five cases in this group.

5. In this group were included those cases in which there was an occasional elevation of temperature, may be as high as 40° C., and which subsides by lysis. Of the total cases, 9.3 per cent. were of this type, or 38.5 per cent. of the febrile cases.

This grouping of Freudweiler is, of course, more or less arbitrary, but one peculiarity of all febrile cases is noted—namely, the great variations in temperature, which may be considered typical, just as we associate the hectic type of fever with suppuration or tuberculosis.

The question naturally arises, What is the cause of the fever? With our present knowledge of bacteriology, infection can be

excluded in a large percentage of these cases. In one-fourth of Freudweiler's cases there was no ulceration. However, infection may exist without tissue change. In many of these cases the condition is analogous to what we see in Hodgkin's disease, in which three different types of temperature have been described: (*a*) the continuous, (*b*) the intermittent or remittent type, (*c*) the recurrent type. This condition was thought to be a form of sarcoma until within the past few years, and recently the infectious origin seems pretty well established by Bunting and others. Hampeln has pointed out two possibilities of the cause of fever in carcinoma: (1) from the growth itself, and (2) from the growth plus malaria. In my case malaria was excluded by repeated examinations of the blood. It would seem that the most reasonable explanation of the fever is that because of the constant degeneration of tumor tissues, products of autolysis are formed which enter the circulation in small quantities, producing systemic disturbances, such as fever. However, though this seems very probable, no such substances have been isolated nor has their presence been demonstrated.

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THE VASOMOTOR MECHANISM IN PNEUMONIA.

By L. H. Newburgh,
BOSTON, MASSACHUSETTS.

(From the East Medical Service, Massachusetts General Hospital.)

Clinicians very generally believe that a failure of the peripheral circulation is a frequent cause of death in pneumonia. This belief rests in part on the assumption that the blood-pressure is abnormally low in most persons dying of this disease—an assumption not supported by clear evidence—and, in part, on certain experiments

which seem to show that the vasomotor nervous mechanism is paralyzed in fatal pneumonia. It is my purpose to examine critically this evidence and these earlier observations in the light of investigation made within the past two years.

The Blood-pressure in Pneumonia. *Earlier Statements.* The feeling that a persistently low blood-pressure is of frequent occurrence in this disease is exemplified by statements of the following nature: "The measurement of the blood-pressure will decide often the question of whether we should look to the heart or the blood-vessels to reëstablish the equilibrium of the circulation. Of eleven fatal cases here reported one-half showed vasomotor paralysis and half did not. A knowledge of the blood-pressure in pneumonia will often be of assistance in judging of prognosis and of treatment."[1]

There are, however, a few clinicians who do not concur in this opinion. Weigert,[2] in 1911, reviewed the work of earlier writers on the subject and added a large number of personal observations. He found the data of his predecessors so contradictory that he could draw no conclusions from them. Among his own 38 cases there were 6 deaths. The blood-pressure in these individuals was not low. He separated the recoveries into several groups. In 8 cases there was no effect on the pressure. In 9 cases the blood-pressure curve showed a gradual fall which reached its lowest point, on the average, nine days after the crisis. In 3 cases there were steep falls which bore no relation to the crisis. In the remaining 9 cases the blood-pressure curve rose progressively. Weigert naturally concludes that no rule can be established for the blood-pressure in pneumonia, and that consequently blood-pressure readings are of no prognostic value.

Even though Weigert's evidence is quite conclusive it did not have the effect it should have had, for clinicians continued to believe that low blood-pressures were common in pneumonia. It accordingly seemed advisable to gather further data. Newburgh and Minot collected such data in 1914.

Observations in 1914. Newburgh and Minot[3] postulated that if it be true that grave symptoms and death in pneumonia are due to failure of the vasomotor apparatus, then it ought to be possible to divide persons ill with pneumonia into two groups:

1. A group in which the vasomotor apparatus is intact.
2. A group in which the vasomotor apparatus is seriously injured.

In the first group, blood-pressure measurements ought to form a curve which does not diverge widely from the normal. In the second group the blood-pressure ought to be low in proportion to the

[1] A. Lambert, Blood-pressure in Pneumonia, Jour. Amer. Med. Assoc., 1911, lvii, 1827.

[2] Ueber das Verhalten deś arterillen Blutdrucks bei acuten Infectionskrankheiten, Vollkmann's kl. Vortrage, 459.

[3] The Blood-pressure in Pneumonia, Arch. Int. Med., 1914, xiv, 48.

gravity of the symptoms, and it should be very low indeed as death approaches.

In order to decide the question, Newburgh and Minot compared the course of the systolic pressure in 19 fatal cases with the pressure in 26 cases which recovered. The resultant curves[4] clearly showed that the systolic pressure in the fatal cases were continuously above the systolic pressure of the persons who recovered.

It appears from the above that persistently low blood-pressures are not of common occurrence in individuals dying of pneumonia. Consequently, failure of the peripheral circulation cannot be a common cause of death in pneumonia.

The State of the Vasomotor Centre. It might seem logically superfluous to discuss the state of the vasomotor centre in pneumonia after demonstrating that the blood-pressure is not abnormally low, since if the vasomotor nervous mechanism were seriously impaired the blood-pressure would of necessity be low. So important, however, is the condition of the vasomotor apparatus in the prognosis and treatment of pneumonia that additional proof of its normal state cannot be unwelcome. Not less important is the examination of the state of the vasomotor arcs concerned in maintaining the normal reflexes by which peripheral stimuli may vary the blood-pressure and thus increase or diminish the blood supply to the lungs and other vascular areas. It is particularly desirable that this evidence be supplied by experiments on animals. Evidence will now be furnished that the vasomotor centre and its afferent and efferent nerves are normal in pneumonia.

The Negative Observations of Romberg. Romberg and his associates[5] attempted such experiments in 1899. In order to test the state of the vasomotor mechanism they made use of the fact that certain stimuli arising in the skin and mucous membranes call forth reflex activity of the vasomotor cells in the bulb. Impulses originating in these cells cause constriction of the small arteries with consequent elevation of blood-pressure. Absence of this reflex is evidence of physiological failure of a portion or the whole of the arc over which the impulses travel, provided experimental errors are excluded.

Romberg and his associates produced a fatal pneumococcus septicemia in rabbits by inoculating virulent cultures of the organism, and then examined the state of the vasomotor reflex in various stages of the disease by observing the effect on the carotid blood-pressure of electrical stimuli applied to the anal and nasal mucous membranes.

[4] The curves in reference will be found in the communication by Newburgh and Minot, loc. cit.

[5] Romberg, Pässler, Bruhns, Müller, Experimentelle Untersuchungen über die allgemeine Pathologie der Kreislaufstörung bei acuten Infectionskrankheiten, Arch. f. klin. Med., 1899, lxiv, 652.

In the early stages of the disease sensory stimuli always caused a marked elevation of blood-pressure. At a later period, when the appearance of the animals suggested the approach of death and the temperature was falling, the reflexes were still present but did not attain the normal height. Finally, when the animal was in a state of collapse and death was imminent no rise of blood-pressure followed peripheral stimulation. As a result of their observations, Romberg and his co-workers believed that they had proved that death in acute infectious diseases was the direct outcome of paralysis of the vasomotor centre in the medulla.

These experiments had a great effect on clinical opinion. Physicians on both continents accepted the new theory without qualifications and began to direct their chief therapeutic efforts in pneumonia against the ever-threatening or already existing vasomotor paralysis. Hence the almost universal administration of strychnin, caffein, camphor, adrenalin, and salt solution in this disease.

But it is to be observed that the evidence upon which this hypothesis is based is of the negative sort. It rests entirely upon a failure to obtain certain physiological responses. It is accordingly exposed to the vital defect inherent in all negative evidence. Such negative testimony is valuable only when positive evidence is lacking.

Positive Observations. Porter and Newburgh[6] have recently completed experiments on animals from which they obtained positive information regarding this problem. They produced not only pneumococcic septicemia in rabbits, but also acute fatal pneumonia in rabbits, cats, and dogs. In order to judge of the condition of the vasomotor apparatus, they measured the vasomotor reflex. But instead of using precarious reflexes from the mucous membranes, Porter and Newburgh exposed and cut the depressor and the sciatic nerves and stimulated the central ends.

Several reasons make blood-pressure data obtained from stimulation of the depressor nerve specially valuable. Since the depressor nerve is composed entirely of fibers which are afferent to the vasomotor centre, impulses pass directly over this nerve to the centre. Other nerves contain fibers of widely different function. In many cases impulses must first pass through the spinal cord where the vasomotor fibers may be exposed to influences not present in the case of the depressor nerve. The chance of error is increased when the stimulating current is applied to the unbroken skin or mucous membrane instead of directly to a nerve trunk. The depressor reflex may be measured in the absence of curare. The latter, unless given with the greatest care, may interfere seriously with the work of the heart and may cause a large fall of blood-pressure. Even under the best conditions, vasomotor reflexes are often absent for

[6] The State of the Vasomotor Apparatus in Pneumonia, Amer. Jour. Physiol., 1914, xxxv, No. 1.

FIG. 1.—The upper line is the carotid blood-pressure recorded by means of a membrane manometer. The lower line is atmospheric pressure. (Reprinted from the Amer. Jour. Physiol., 1914, xxxv, No. 1.)

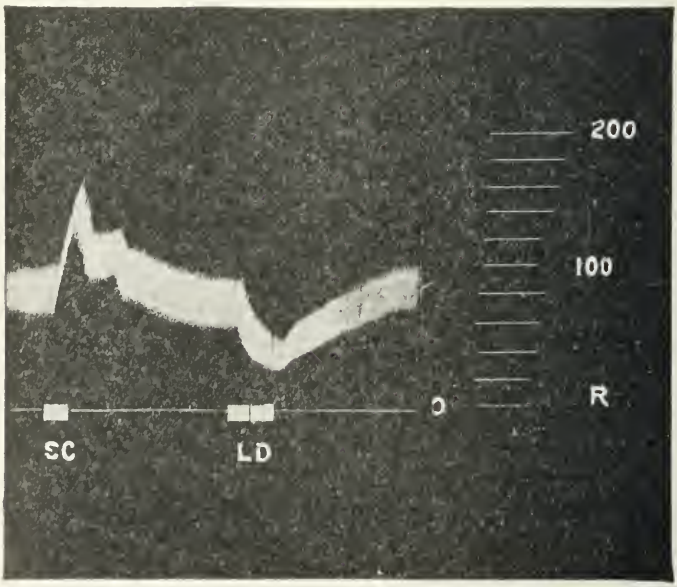


FIG. 2.—Showing the effect of stimulation of the sciatic and of the depressor nerve in a cat near death from pneumonia. (Reprinted from the Amer. Jour. Physiol., 1914, xxxv, No. 1.)

a number of moments after its injection. The use of curare necessitates the employment of artificial respiration with its inherent chances of error. The reflex from the sciatic nerve and from the skin or mucous membranes can be measured only after the administration of curare.

In order to leave no room for doubt in experiments of this type it is obvious that the vasomotor reflexes must be measured when the animals are near death. That Porter and Newburgh actually measured the reflexes of animals in such a state is apparent from the following protocol: Further evidence may be had by consulting their publication in the *American Journal of Physiology*.[7]

Experiment, March 17, 1914, 10 A.M. A cat weighing 3000 grams was etherized and 25 c.c. of a twenty-four-hour culture of the pseudopneumococcus was injected into a bronchus.

March 18, 9.30 A.M. The temperature was 34° C. The respiration was markedly labored and of the type seen in laryngeal stenosis. The animal was relaxed and lying prone and seemed at the point of death. It was immediately placed on the operating board and given a few whiffs of ether.

At 10 A.M. both vagi were cut.

At 10.45 A.M. 1 c.c. of curare was cautiously given. Stimulation of the central end of the left vagus at 11.10 A.M. caused the pressure to fall from 80 to 46 mm. Hg. (Fig. 1).

At 11.55 A.M. stimulation of the sciatic raised the pressure from 45 to 65 mm. (45 per cent.). The animal was now killed.

Autopsy. The total lung area, except the tip of the left upper lobe and the extreme edge of two other lobes, was mottled, gray red, firm, non-crepitant, and voluminous. The cut surface, also gray red, was moist and exuded seropus. Scattered through the lung were may areas of hemorrhage and necrosis. The liver contained very many small foci of hemorrhage. The spleen was large and soft. The pericardium and endocardium showed several small areas of hemorrhage.

These experiments prove that the vasomotor centre was not impaired in any of the examples of fatal pneumonia studied.

SUMMARY. It has been pointed out that there are two main arguments offered in support of the hypothesis that the peripheral circulation is paralyzed in pneumonia. The first argument is based on the assumption that the blood-pressure is abnormally low in fatal pneumonia. It has been shown that this assumption is incorrect. The second argument is that the vasomotor reflexes are absent in fatal pneumococcus septicemia. This has been disproved by positive data showing that the vasomotor reflexes are normal in fatal pneumonia.

The conclusion that the vasomotor apparatus is not impaired in pneumonia is fully warranted.

[7] Loc. cit.

CONCERNING VASOMOTOR AND TROPHIC DISTURBANCES OF THE UPPER EXTREMITIES; WITH PARTICULAR REFERENCE TO THROMBO-ANGIITIS OBLITERANS.

By Leo Buerger, M.D.,

ASSOCIATE ATTENDING SURGEON AND ASSOCIATE IN SURGICAL PATHOLOGY, MOUNT SINAI HOSPITAL; VISITING SURGEON, HAR MORIAH HOSPITAL; INSTRUCTOR IN CLINICAL SURGERY, COLUMBIA UNIVERSITY, NEW YORK.

It is not generally known to clinicians that certain well-recognized vasomotor and trophic disturbances of the extremities may, on the one hand, be the clinical manifestations of occluded vessels, and may also, on the other hand, be associated with arteries and veins that are organically intact. To the latter group belong those interesting symptom complexes which have been described under the name Raynaud's disease, erythromelalgia and acroparesthesia, multiple neurotic gangrene, scleroderma, sclerodactyly, and chronic acro-asphyxia. Considerable attention has been focussed upon these conditions, and attempts have been made to differentiate various discrete syndromes under the above-mentioned appellations. It is conceded that all have one feature in common, *that the arteries and veins have suffered no organic alteration in their patency.* Comparatively little, however, has been written to show that there is a distinct clinical and pathological entity, *thrombo-angiitis obliterans*, with which there may be associated clinical manifestations almost identical with those that belong to these other diseases. It is of no little importance to be aware of this fact and to be able to recognize that there is a disease whose symptoms depend upon vascular occlusion, for the prognosis and treatment of the two types of affections are in no way identical.

A clinical study of 200 cases of thrombo-angiitis obliterans during the last eight years (1906 to 1914) has enabled me to watch the course of this remarkable disease through all its clinical stages. Many of the cases have been followed from five to eight years, and the presence of interesting mutations in the symptomatology could be recorded. It was found that in a certain number of the patients the upper extremities are involved, although it is usually believed that only the lower extremities are affected. And particularly here were patients' histories encountered that singularly emphasized the unreliability of clinical signs alone in diagnosis. Furthermore, as shall be shown in some instances, thrombo-angiitis may, by virtue of the predominance of certain objective phenomena, masquerade as almost any of the true vasomotor and trophic diseases. Yet a careful study of each and every case will almost always make possible the recognition of the nature of the morbid process.

It may be of some clinical interest, therefore, to present here (1) the most striking examples of the various forms in which the disease may affect the upper extremities, where thrombo-angiitis obliterans is most frequently mistaken for other affections, and (2) to point out upon what features the diagnosis of the malady may be made.

A survery of the histories shows that the upper extremities may be clinically involved in the following ways: (1) without subjective symptoms; (2) with vasomotor symptoms predominating; (3) with trophic disturbances alone; (4) with gangrene of slight extent; (5) with extensive gangrene threatening the viability of the extremity; (6) with extensive atrophy of the hand and forearm; and (7) with changes simulating scleroderma and sclerodactyly.

I. Thrombo-angiitis Obliterans of the Upper Extremities Without Symptoms. Just as in thrombo-angiitis of the lower extremities, there are cases in which the radial or ulnar artery, or both, become gradually closed without the patient's experiencing any noticeable symptoms. In some instances, absence of pulsation was discovered during a routine physical examination; in others, where symptoms were present in the lower extremities, investigation of the radial and ulnar vessels had demonstrated their occlusion.

Case I.—J. A., male, aged forty years, Russian, began to have trouble in the right leg ten years ago (1904), pain coming on during walking, subsiding when at rest. Gangrene of the little and of the big toes developed, leading to amputation of the leg at its middle in 1906. Since 1908, similar symptoms involved the left leg, and the first and second toes became ulcerated, also requiring amputation. During the period of clinical observation the right radial pulse gradually disappeared, although no vasomotor or trophic manifestations could be elicited on examination. The patient was lost sight of so that the further course could not be followed.

The symptoms of Raynaud's disease, too, may be closely mimicked, as in the following cases:

II. Cases in which Vasomotor Phenomena Preponderate. Such an instance is described in the following history, where, after about ten years of migrating phlebitis, and the usual circulatory disturbances of the lower extremities, distinct evidences of involvement of the vessels of the arm and hand supervened.

Case II.—A. B., male, aged thirty-one years, Russian, noticed the appearance of small hard lumps under and in the skin of the calf of both legs in 1904 (ten years ago). They were painful, lasted for a few days or a week or more, and would then disappear (migrating phlebitis). For three years similar lumps and strands would come and go over the lower and inner side of the right thigh. About seven years ago he began to experience cramp-like pain in the right foot and calf of the leg on walking. Later the right

foot became "cold." An ulcer developed on the third toe and showed no tendency to heal.

For seven years he has been suffering with similar symptoms in both legs and feet, the typical symptoms of pulseless vessels, erythromelia, ischemia in the elevated position, and gangrene of several toes being present. He now (1914) has already lost four toes of the left foot and two of the right.

Four months ago his right hand began to trouble him. In cold weather it would become very pale, particularly the little finger. On warming the hand, color would gradually return. Of late, however, the tip of the little finger has been bluish for days at a time, although excessive heat seems to bring back a normal color.

Physical Examination, May 6, 1914. The radial and ulnar arteries of both sides pulsate distinctly. Both hands perspire profusely, and are somewhat cold. The tip of the little finger of the right hand is cyanotic and deeply discolored over its palmar aspect. Pressure over this part elicits some pain. Roentgen-ray examination of the hand is negative.

On July 31, 1914, patient says that the little finger and thumb of the right hand feel cold. Scales form on the tip of the little finger, and when these separate, leave a healed depression. He has no pain.

Physical examination shows that both the little finger and the thumb are distinctly cold to the touch, the coldness extending to the base of the fingers. The other hand and fingers are warm. The radial and ulnar arteries pulsate well. On elevation there is no appreciable change in the color of the fingers.

In short we have here an example of thrombo-angiitis in which vasomotor symptoms initiate the onset of the disease in the upper extremities. Previous experience warrants the assumption that we may either expect a complete cessation of the symptoms in the hands, if adequate collaterals be established, or progressive occlusion of vessels until the radial and ulnar arteries become obliterated or until gangrene ensues.

Case III.—J. V., male, aged thirty-four years, Russian, admitted to the Mt. Sinai Hospital (Dr. Lustgarten's service) December 17, 1907, says that three and a half years previously he noticed that his fingers were cold but not blue. The following winter the same symptoms returned, but, in addition, the skin of the tip of the right middle finger became dry and a "wound" spontaneously developed. For the past two years his hands would get blue, cold, and numb on exposure to cold, their natural color returning in a warm room. There was never any pallor. A sort of "sticking" pain in the finger tips would regularly accompany the state of blueness.

Physical Examination, December 17, 1907. Both hands are deeply cyanotic up to the wrist, and very cold. During the examina-

tion bright-red or crimson-colored spots can be seen to appear in the dorsum and palm. Over the back of the hand these red blotches become very distinct and do not shade off into the blue areas. The two distal phalanges remain deep blue. If the hands be observed for a still longer time (five minutes) the red color becomes paler and is mottled with a yellowish-pink; at times a totally different and much lighter shade, variegated with red and blue, will completely replace the deep colors first noted. In the palm the red areas are not so apparent, but they also give way at times to the lighter shades. The terminal phalanges of the ring fingers are enlarged, those of the middle fingers somewhat less so. When the hands are held above the head for two or more minutes the redness disappears, a pale sickly purple remaining. The radials and brachials pulsate well.

In the lower extremity a similar picture is present, but there are evidences of obliteration of the vessels. The right dorsalis pedis cannot be felt, although palpated on many occasions from December 17, 1907, to January 20, 1908. In the left dorsalis pedis there is fair pulsation. There is ischemia in the elevated position of the legs, as evidence of the impaired vascular supply, and bespeaking the presence of the lesion, thrombo-angiitis.

If such an exquisite example of vasomotor disturbance can belong to a case of thrombo-angiitis obliterans, there is little wonder that confusion should exist in the differentiation of the symptoms due to neurogenous and organic lesions of the vessels. What the distinguishing points are upon which the diagnosis must be based will be discussed later in the paper.

III. Cases with Trophic Disorders Only. In some patients, distinctive signs of an affection of the upper extremities manifest themselves as trophic disturbances not extensive enough to lead to gangrene. The disease may be wholly overlooked by the patient and, when the lesion has healed, it may be subsequently referred to by him as a slight "sore" or "ulcer" developing without cause. Were it not for the presence of the disease in the lower extremities and for the changes in the radial pulse the nature of the trophic disorders would be difficult of solution.

Case IV.—T. S., aged thirty-one years, Russian, consulted me in May, 1914, because of the condition of his left foot. Three and a half years previously he experienced pain in the sole of the left foot on walking and was treated for rheumatism. Two years after the onset a sore developed between the fourth and fifth toes of the left foot and another one on the tip of the big toe of the left foot. Since then the foot became red and the little toe gangrenous, falling off about a year ago. About this time his right leg began to trouble him, the symptoms being pain in the calf on walking.

Two and a half months ago there developed a spontaneous ulcer over the middle phalanx of the right hand, not accompanied

by any evidence of inflammation, hardly painful, and not brought about by any injury. He was treated for this for about eight weeks, when the wound healed.

Physical Examination, May, 1914. Over the middle phalanx of the right hand there is an irregularly shaped scar, about 8 mm. in length and 4 mm. in width, evidently the site of the old healed lesion. The right radial pulse is not perceptible.

We have here a typical case of thrombo-angiitis of the lower extremities, first involving the left then the right lower extremity, and three years later manifesting itself also in the hand, with trophic disturbances and obliteration of the radial artery.

IV. Cases with Gangrene of Slight Extent. Not a small number of the patients that suffer with occlusion of the vessels of the upper extremities come to us with a history of having had pain in the tip of one of the fingers for a considerable time. This is followed by a change in the color of the skin, usually reddening of the tip of the fingers, as if it were inflamed. Later there develops a sore or the skin changes color and becomes gangrenous, usually at the tip of a finger, although the lateral margin of the finger may be first affected. The following three cases are examples of this group:

Case V.—L. B., aged forty-eight years, Russian, male, admitted to Mt. Sinai Hospital (Dr. Lilienthal's service), May 1, 1910, says that his left leg was amputated below the knee some ten years ago. Six years later he lost his right leg in the same way. Now for six months the index finger of the left hand has been painful and red at the tip; this has since improved. Four months ago the index finger of the right hand also became red and painful, and during the last three weeks the greater part of the last phalanx has become mortified.

Physical examination shows an old scar at the tip of the left index finger and poor radial and brachial pulse. The terminal phalanx of the right index finger is completely exposed, the dry bone presenting. On elevation of the right hand, marked ischemia occurs.

The right radial pulse is absent, the brachial only faintly pulsating. The gangrenous process is evidently progressing, since a portion of the second phalanx is already involved.

Case VI.—D. B., aged thirty-five years, male, Russian, first examined by me on July 16, 1904, at Mt. Sinai Hospital. He had been treated in the hospital eight years previously for "phlebitis" of the right leg. A portion (five inches) of a large vein was diseased at that time, the history recording that the process was "migrating," moving up and down the thigh. He says that this trouble lasted off and on for two years. In 1903 there were "lumps" in and under the skin of the righ leg and then three months later in the left leg. Such swellings would last a week, develop into

hard, "tender spots," with a covering of red skin, and on one occasion three such spots appeared on the left arm in front of and just below the elbow.

Physical Examination, July, 1904. In the left antecubital region there is a thickened, slightly reddened cord about two inches long. Another is situated on the ulnar aspect of the same forearm near the elbow. The right forearm presents a similar vein about three inches from the elbow; the skin is not reddened. On the inner side of the right cubital space a subcutaneous, adherent nodule can be felt; it is very tender. There are several such nodules in the right calf and smaller ones over the left shin bone. No edema, but slight cyanosis of both legs in the pendent position. A portion of one of the thrombosed arm veins was extirpated for study.

Course. A year later (1905) symptoms referable to an affection of the deep vessels of the left lower extremity manifested themselves, namely, coldness and blueness of the left foot and superficial ulcers on the toes. In February, 1907, he developed a gangrenous patch at the tip of the middle finger of the right hand. His doctor had been treating him for a "felon" of the middle finger of the right hand. His hand had been cold for several weeks and the middle finger painful. Four weeks previously a black, "dead" spot appeared at the tip of the finger, and since then, what with cutting it and self-treatment, he thought that the present intensely painful affection had overtaken him.

Physical Examination, February 1, 1907. A portion of the tip of the middle finger is gangrenous; there is no infection; the distal phalanx seems to take part in the process of mortification.

On holding both hands above the head for some time the right becomes appreciably more ischemic than the left; it does not attain the cadaveric hue characteristic of the lower extremities, but becomes markedly pale, a bluish-red tinge remaining in the distal phalanges. The pain is not increased in this portion. In the dependent position the color rapidly deepens in the left hand, soon assuming a reddish-blue hue, the fingers being particularly discolored. Both radial pulses are felt, the left somewhat small. On the dorsum of the hand, just over one of these veins, there is a bean-sized, indurated area; the skin over it is adherent and tender. About one inch above the wrist, behind the radius, there is a reddened, hard cord more than an inch in length (doubtless a thrombosed vein). The finger improves very slowly.

Here there is most beautifully illustrated that group of cases in which a long period of "migrating phlebitis," first of the lower and then of the upper extremities, dominates the clinical picture. Then, when the signs of impaired circulation of the legs have become well established, the hands, too, show unequivocal marks of the closure of small distal arteries, in the form of small areas of gangrene.

Case VII.—M. S., aged forty-seven years, Russian, was admitted to Mt. Sinai Hospital on June 25, 1907, giving the following history: About eight or nine months ago he noticed that the fourth toe of the left foot was cold, blue, and painful. About four months ago the pain became so severe that he consulted a physician, who told him that an infection had taken place. Since this time a sore developed under the nail and the nail bed became black.

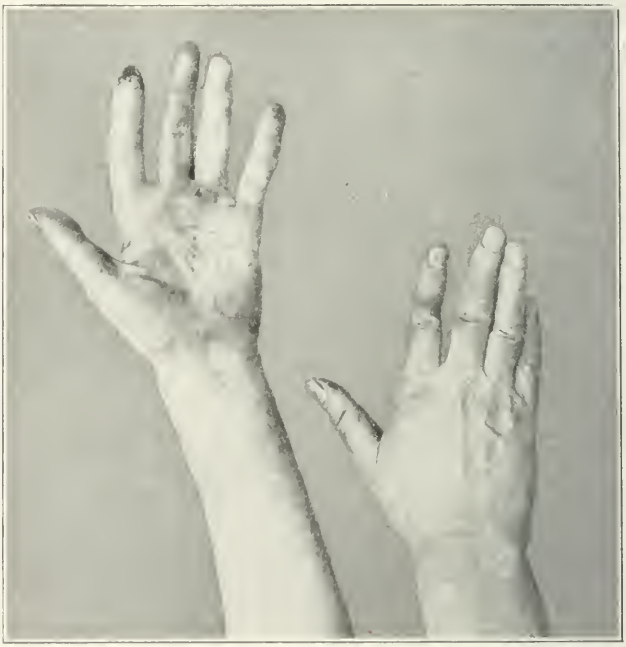


Fig. 1.—Trophic changes in index finger of Case VII.

Physical examination showed complete gangrene of the distal half of the fourth toe of the left foot, absence of pulsation in the dorsalis pedis artery, an area of superficial gangrene of the skin on dorsum of the foot, intense erythromelia (hyperemia of the foot) in the dependent position, and marked ischemia in the elevated position. June 28, 1907, amputation was done by Dr. J. Wiener through the tarsometatarsal articulation. On July 5, re-amputation was done through the middle third of the leg, the wound healing slowly.

In 1910 the disease began to involve the right leg in the same typical manner, leading also to dry gangrene of the fourth toe. When examined in March the popliteal, posterior, tibial, and dorsalis pedis of the right leg could not be felt.

In short we have a typical case of thrombo-angiitis obliterans,

first involving the left lower extremity leading to gangrene, amputation, and some three years later involving the right leg.

In March, 1914, I again saw the patient, who now complains of symptoms in the left hand.

March 18, 1914. For several months he has had pain in the tip of the left index finger and lately the finger has changed color, becoming withered and glossy.

Physical examination shows an ulcer at the tip of the left index finger, the live skin above it atrophied and glossy, the hand somewhat smaller than the other, and the fourth finger of the same hand distinctly shrunken. The radial pulse of this hand cannot be felt (Fig. 1).

We are evidently dealing here with a case in which some seven years after the onset of the disease in the lower extremities the left upper extremity became attacked, as evidenced by ulceration and trophic disturbances.

An interesting group is formed by those patients in whom trophic disturbances and gangrene are the salient features. These are the cases so often confused with Raynaud's disease. In our experience the lower extremities are regularly involved at some time or other, and it is, therefore, necessary to watch carefully for the advent of the typical symptoms in these, so that a correct interpretation of the phenomena in the fingers and hands may be made. The following two histories will well illustrate the cases in which:

V. Extensive Gangrene Threatens the Viability of the Extremity. Case VIII.—A. K., male, aged twenty-seven years, Russian, was admitted to Mt. Sinai Hospital January 4, 1908. About two years previously he had had severe pain in the middle finger of the right hand. The finger became cold, at times very blue, and extremely painful. These symptoms persisted for about two months, when he was told to have the nail removed. Shortly after this was done the tip of the finger became dry and black. After several months the terminal phalanx separated spontaneously, but a wound remained which refused to heal.

For about two months his left hand has been affected, there being excruciating pain in the left middle finger of the left hand, and the fourth finger of the right hand also being somewhat painful for two months. He thinks that the tip of the middle finger of the left hand first became dark blue or purple, and lately has become dry and black.

Physical Examination, January 4, 1906, shows that the distal phalanx of the middle finger of the right hand is absent, the tip of the fourth finger showing a small patch of dry gangrene of the left hand; there is beginning gangrene of the distal phalanx of the middle finger.

Somewhat more than a year later, February 24, 1907, he was again admitted to the hospital, presenting evidences of thrombo-

angiitis of the left foot. The second toe of the left foot had been ulcerated for about three months, and gradually all the toes of that foot, except the fourth, became involved in the same process.

Physical Examination, February 24, 1907. Left foot: On the dorsal and plantar surfaces of the great toe there are ulcers. A similar condition is found at the tip of the second toe and on the plantar and dorsal surfaces of the fifth toe. The skin about the ulcer is sloughing and shows no tendency to heal.

The right foot is negative. The right hand shows an absence of the terminal phalanx of the third finger. Both hands are cyanosed.

March 22. Amputation of the toe. Wound does not heal.

May 17. Re-amputation through the leg, by Dr. C. Elsberg.

Physical Examination, May 20, 1907. The left radial pulse is absent and the artery appears to be converted into a hard cord. In the right radial artery a very faint pulse is perceptible. The brachial artery seems to be much thickened, although the pulsation is good. Ever since amputation of the left leg was done, the stump was painful, discolored, bluish, presenting a wound that failed to heal. Finally, on January 2, 1909, the patient consented to re-amputation. I performed the Gritti-Stokes amputation, the stump healing kindly.

January 3, 1909. The tip of the little finger of the right hand presented a small spot of gangrene about 1 cm. in diameter. The distal phalanx of the little finger is absent. The nail of the fourth finger is deformed and thickened. In the dependent position the fingers become cyanotic, with a slight increase in the normal red color. The left hand is normal as regards color, but the nail of the middle finger as well as the tip of the finger are very much deformed.

The right radial artery is felt as a cord, and no pulse can be detected; the ulnar artery is also pulseless; the brachial pulse is poor. The left radial artery is faint, the ulnar cannot be felt, the brachial also is poor. In the elevated position the right hand becomes somewhat paler than the left, but neither becomes very much blanched.

Lower extremity: The stump is in good condition. The right foot shows evidences of development of thrombo-angiitis, the dorsalis pedis and posterior tibial arteries being absent, and there are other evidences of involvement of that leg.

December 30. The fifth finger of the right hand presents an ulcer at the tip, the result of the separation of a gangrenous patch. He says that he has had pain in that finger for about three months, and that gangrene set in about three weeks ago.

February, 1910. The trophic disturbances, involving the little finger of the right hand seem to be progressive. The tip of the finger shows advancing gangrene, the rest of the finger is swollen and red. In the dependent position the third and fourth fingers

become intensely red and slightly cyanotic. Left hand: Here there has been no progression of the symptoms.

FIG. 2

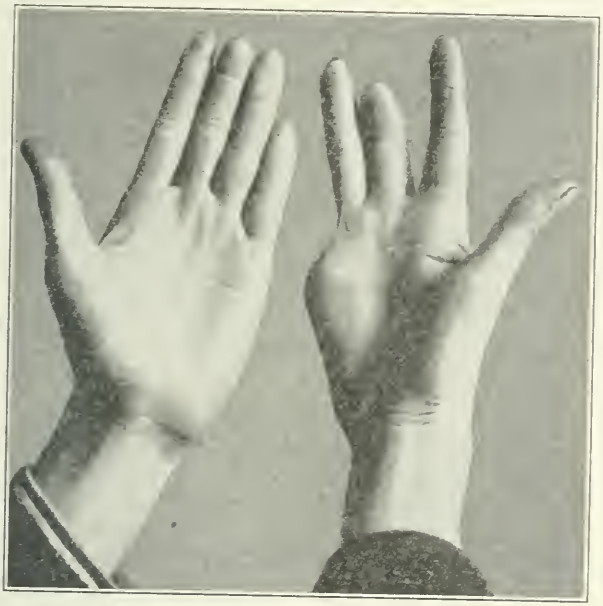
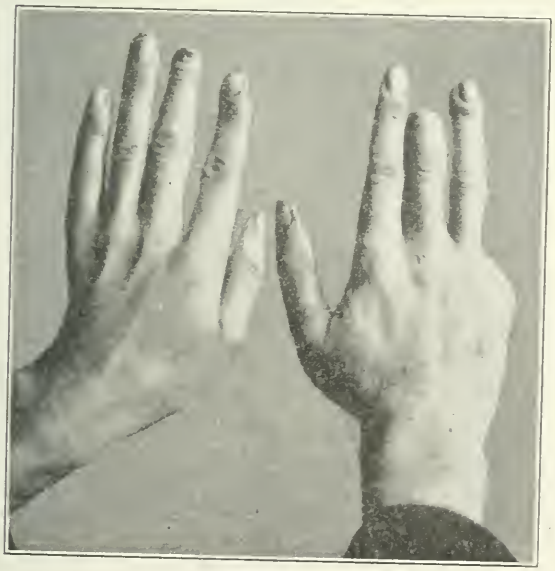


FIG. 3



FIGS. 2 and 3.—Hands in Case VIII, results of gangrene and amputation.

February 2, 1910. The little finger of the right hand was amputated (Figs. 2 and 3).

This is a good illustration of those cases of thrombo-angiitis obliterans in which the symptoms first make their appearance in the upper extremities, are initiated by pain, and followed by trophic disturbances and gangrene. In this case the terminal phalanx of the middle finger and the whole of the little finger of the right hand were lost. During the evolution of these symptoms the disease attacked the left leg, where even greater progress was made than in the upper extremities, amputation being the outcome. Pathological examination of the vessels of the amputated left limb showed the usual lesions of thrombo-angiitis obliterans.

Case IX.—S. A., male, Russian, examined March 23, 1905, gives a typical history of thrombo-angiitis obliterans of the left lower extremity, finally leading to gangrene, for which the leg was amputated August, 1903, and re-amputated September 5, 1903, at the knee.

Fig. 4.—Amputated arm of Case IX. (Photograph taken from specimen after preservation in fixative.)

Eight weeks before admission there appeared symptoms referable to the same disease of the right lower extremity, an ulcer appearing at the inner side of the right heel. On March 21, 1905, the right leg was amputated for advancing gangrene of the right foot.

March 10, 1910. I found evidence of the involvement of the left upper extremity. He says that he has had trouble in his left arm and in the fingers and forearm for several months, there having been pain in the fingers, followed by swelling and redness. Then a bleb appeared at the tip of the index finger, which was incised by a physician. Shortly after this the wound became much worse and sloughing took place. About the same time a black spot

appeared over the back of the middle finger. Neither middle nor index finger has improved, and it is for these that he seeks relief.

After admission the gangrene rapidly spread, the pain becoming excruciating, and the forearm was amputated through its upper fourth.

The ablated forearm (Fig. 4) showed complete occlusion of both radial and ulnar arteries. The typical lesions of thrombo-angiitis obliterans were present.

Four years later, April, 1914, the patient was again admitted to the wards of Mt. Sinai Hospital in a condition of stupor. The notes taken read as follows: "Both legs and the left arm have been amputated. Speech is incoherent and there are evidences either of some cerebral lesion or of an arterial lesion in the brain. The condition of the right hand is of particular interest. Nowhere is there any evidence of ulcer or gangrene. The skin of the right hand is dry and atrophic. The fingers have a tapering apperance. The skin has lost its elasticity, the subcutaneous tissues have withered, and neither the radial nor the ulnar arteries are palpable. The brachial artery, too, gives but the slightest impression of the presence of pulsation."

Here, then, is a case in which two distinct clinical pictures were evolved in the course of the obliterative vascular disease, one exhibiting gangrene of an upper and two lower extremities, and the other demonstrating the unusual phenomenon of extreme atrophy of both hands and forearm.

VI. Cases Simulating Scleroderma and Sclerodactyly. Perhaps most interesting of all are those cases in which the vascular occlusion has led, by virtue of the effects of malnutrition, to a condition of dystrophy, the clinical picture being akin to that of sclerodactyly. In fact we have had occasion to observe a most pronounced example of this manifestation in a patient in whom the diagnosis of scleroderma was made by expert dermatologists.

Case X.—I. L., aged thirty-five years, was admitted to the surgical service of Mt. Sinai Hospital on October 1, 1906, with a typical history of thrombo-angiitis obliterans of the left leg. There was absence of pulsation in the dorsalis pedis and complete gangrene of the second toe, necessitating amputation. Pathological examination of the vessels of the amputated legs showed the typical lesions of thrombo-angiitis obliterans.

June 29, 1907. He was again admitted to the hospital, complaining of intense pain in the right leg which showed the symptoms of ischemia on elevation, redness in the dependent position, but no evidence of trophic disorder or gangrene. The patient begged that the limb be taken off, and the right leg was, therefore, ablated through the middle third. Pathological examination showed here, too, the typical lesions of thrombo-angiitis obliterans.

December 17, 1909. He entered the hospital complaining of trouble with his right hand and arm. For several months he has been unable to use it properly, the muscles having become stiffened. He thinks, too, that a marked diminution of the size of the hand and arm has taken place.

On physical examination the picture presented by the right arm is striking. The fingers have the typical appearance of the skin in scleroderma. Motion of the distal phalangeal joints is markedly impaired in extent. The skin is atrophic and dry and the circumference of the fingers of the right hand is distinctly diminished. Both the radial and brachial pulses are absent. The brachial artery can be felt as a hard cord, and can be traced as far as the axilla. In the axilla there is a distinct pulse.

The left hand shows no trophic disturbances, no ulcers, but the radial and ulnar pulses are absent. The brachial pulse is fairly good.

In order that we may thoroughly comprehend the points that distinguish the vasomotor and trophic disturbances dependent on organic arterial lesions from those of Raynaud's and allied diseases it may be best to pass rapidly in review the salient features of the symptomatology as they were exemplified by the above patients.

Collecting the cases in which vasomotor symptoms predominate we have, on the one hand, those in which the symptoms of thrombo-angiitis obliterans of the lower extremities are well marked and, on the other hand, those in which we are compelled to investigate very carefully in order to elicit evidences of vascular occlusion.

The symptoms simulating Raynaud's disease and acro-asphyxia are cyanosis of the finger tips, coldness of the fingers with or without trophic disturbances, and alternating cyanosis and rubor, involving the fingers or the whole hand. Rather characteristic in the symptomatology of thrombo-angiitis is the apparent dependency of the vasomotor symptoms upon variations in temperature, the chronicity of the manifestations, the absence of pain in some of the cases, and the absence of paroxysmal nature of the attacks so characteristic in Raynaud's disease.

When we turn to those patients in whom the trophic disturbances seem to be unassociated with evidence of vasoconstriction and vasodilatation we note that there is merely a history of the development of a spontaneous ulcer of the fingers. It seems more than likely that in many of these the history of the absence of the vasomotor phenomena would be found unreliable if it were possible to observe the cases throughout the whole course of the disease. Future observations will probably support my belief that here, too, some manifestations of deranged vasomotility do occur.

When we consider the largest group, namely, that in which gangrene of small or greater extent develops, we find that some cases may be mistaken for simple paronychia. Others claim that the development of a gangrenous patch or of the felon was preceded

for a long time by distressing pains in the tips of one or more fingers. The vasomotor symptoms may be absent or the cyanosis and redness may be quite striking. The following sequence of symptoms may be observed and is interesting, because pain and trophic disturbances alone are complained of. The onset is marked by severe pain in the tip of a finger. This is superceded by atrophic changes in the skin, the development of a dry, hard patch, mortification, and also formation of an ulcer. In still other cases the similarity with Raynaud's disease is even more marked, for the symptoms are pain, cyanosis, rapidly followed by gangrene.

More rarely do we meet with those interesting examples of the effects of arterial occlusion in which the development of intense atrophy of a hand or limb or the production of the typical picture of scleroderma and sclerodactyly is the significant feature of the clinical picture.

A careful clinical study of the disease, thrombo-angiitis obliterans, will dissipate all doubt as to the possibility of separating this disease, as a clinical entity, from all those neurogenic varieties of vasomotor and trophic disorders that may be clinically confounded with it. It would be too extensive to dilate upon the symptomatology of thrombo-angiitis obliterans in this paper, and, therefore, I shall confine myself to the consideration of those essential features on which the recognition of the disease depends, and which will be seen to be the effects of the obliterated condition of the arteries.

Thus characteristic for the disease are the following groups of symptoms: (1) the disappearance of the pulses, particularly the dorsalis pedis, posterior tibial and popliteal, more rarely the femoral, radial, and ulnar; (2) the development of typical manifestations of impaired circulation, to wit: blanching of the lower extremities when these are elevated above the horizontal, hyperemia (rubor) or reddening of the foot in the pendent position (a chronic condition which I have elsewhere termed erythromelia) during certain stages of the disease, and trophic disturbances, such as impaired growth of the toe nails, slightly atrophic condition of the skin, ulcers, and gangrene; (3) true vasomotor phenomena of transitory nature, such as alternating syncope, rubor, coldness, apparently independent of those chronic changes that have been cited above and that are distinctly traceable to the occluded condition of the arteries and veins; (4) the symptoms of pain, either in the form of intermittent claudication (pain in the calf of the leg or in the foot on walking with cessation when the limb is at rest) or the severe pain that is associated with the advent of trophic disturbances, especially with ulcers and patches of gangrene; (5) the slow course of the disease, symptoms of intermittent claudication or pain, preceding the development of trophic disturbances for months and years; (6) the fact that more than 99 per cent. of the cases occur in Polish, Galician, or Russian Hebrews, and that almost always young males

between the ages of twenty and thirty are taken with this disease; (7) the onset of symptoms in the lower extremities, one of the legs being first affected; (8) the comparative infrequency of involvement of the upper extremities; (9) the association of a peculiar type of migrating phlebitis in the territory of the external or internal saphenous, less frequently in the larger veins of the upper extremities characteristic in about 20 per cent. of the cases; (10) the slow but steadily progressive course, leading in a large majority of the cases to amputation of at least one limb, not infrequently of both lower extremities, and in rarer instances to amputation of one of the upper extremities as well.

Even a rapid review of the salient symptoms of this interesting malady would seem to suffice to leave the impression that it could hardly be mistaken for other diseases. And were it not for the fact that certain symptoms, closely resembling typical vasomotor phenomena, may persist for weeks and years in this disease, confusion with the true neurogenic vasomotor process would scarcely ever arise. The chronic condition of redness in thrombo-angiitis obliterans can be explained as due to dilatation of the superficial capillaries, this being a compensatory phenomenon making for an adjustment of the impaired circulation. This chronic redness or rubor may be mistaken for erythromelalgia or for the rubor of Raynaud's disease. The fact that it is associated with other evidences of closed vessels and the other characteristic features above mentioned, together with the circumstance that the redness disappears at once upon elevating the extremity, will make the recognition of its nature possible.

In addition to this more or less chronic or permanent sign of deranged vasoconstriction, other phenomena which are truly vasomotor in nature may frequently be associated in thrombo-angiitis, and it is these that must be differentiated from similar phenomena accompanying Raynaud's disease, erythromelalgia, scleroderma, sclerodactyly, and acrocyanosis.

If we do not overestimate the importance of single manifestations of vasomotor irritation, but regard as more significant the clinical course and the symptoms in their totality, we will not fail to separate very clearly in our minds the true vasomotor neuroses from the organic vascular disease attended with vasomotor phenomena.

In order that a differential diagnosis may be clearly presented, let us briefly recapitulate the typical course of a case of Raynaud's disease. Raynaud's disease is an affection whose pathology has not as yet been definitely determined, the lesion doubtlessly residing somewhere in the central nervous system. Its clinical characteristics may thus be summed up:[1] Somewhere in the peripheral portions of the body (so-called acra) there occurs more or less

[1] Cassirer, Die Vasomotorisch-tropischen Neurosen (S. Karger, Berlin, 1912).

severe pain not confined to distinct nerve territory, usually affecting symmetrical parts, attacks of vasomotor disturbance being part of the syndrome. These latter are (1) syncope, asphyxia, or local rubor, and (2) severe trophic disturbances, usually in the form of gangrene of the parts first affected with symptoms. The course is an intermittent one, for there may be completely free intervals; but in some instances, evidences of disturbed vasomotility may persist. The disease may consume itself in one attack or several attacks may occur in succession. Objectively, sensory disturbances are usually absent, as well as paralysis, although other evidences of disturbed vasomotor innervation, such as aphasia, hemoglobinuria, arthropathy, may occur. Usually neuropathic individuals are affected. The organic vascular changes, as well as the lesions of the nervous system, reported occurring in some of the cases, have, doubtless, no causative relation with the disease.

It is true that there are still some who cling tenaciously to the theory that some lesions of the peripheral arteries may account for the symptoms of Raynaud's disease. In support of this view certain anatomical findings have been cited as strong arguments by those who believe that a definite anatomical lesion in the peripheral vessels is irresistible testimony against pure hypothesis. A careful analysis of the cases in question, as made by Cassirer, shows that reported organic alterations in the vessels will not suffice to explain the symptoms any more satisfactorily than the theory of a central nerve affection of the sympathetic system. Whereas in thrombo-angiitis obliterans the territory manifesting symptoms corresponds to that containing the diseased vessels, we find that no such relation exists where vascular lesions are associated with Raynaud's disease.

For the clinical diagnosis of thrombo-angiitis we must depend upon (1) the racial (Hebrew) and sex (male) predilection; (2) the early involvement of the lower extremities; (3) the early symptoms of pain or intermittent claudication; (4) the presence of migrating phlebitis; (5) the evidences of pulseless vessels; (6) the presence of blanching of the extremity in the elevated position; (7) the existence of rubor in the dependent position; (8) the relation of the hyperemic phenomena to posture; (9) the absence of simultaneous, symmetrical involvement; and (10) the slow, progressive chronic course terminating in gangrene.

In Raynaud's disease we will note the following features: A sudden onset of the first stage of local syncope or regionary ischemia involving usually the fingers, more rarely the toes, and occasionally the margins of the ears or the tip of the nose with coldness and blanching; associated sensory phenomena, paresthesia, and pain; a comparatively short duration of the vasomotor and sensory manifestations, their intermittent character with return to normal between the attacks; the symptoms of local asphyxia attended with

local depression of temperature and swelling of the parts involved; the disappearance of the asphyxia with substitution of reactive hyperemia and a third stage of dry gangrene. Characteristic for this disease as well as for the cases of scleroderma and sclerodactyly is the striking atrophy of the ends of the distal phalanges.[2] The changes in the bones can be well demonstrated by Roentgen-ray examination, atrophy and disappearance of large portions of the end-phalanges being distinctive and diagnostic features. In our own experience the alterations in the bones could be detected early in the disease, probably developing simultaneously with the other trophic disturbances.

If we analyze the symptomatology of the cases of thrombo-angiitis cited above we will find, that the differential diagnosis of this condition from the vasomotor neuroses is only difficult in those cases where we cannot rule out the possibility of the association of the two diseases. It will be noted that where coldness and cyanosis are complained of, a distinct dependency on temperature or other environmental condition can often be elicited or that pain is absent. The presence of vessels changes and the history of the involvement of a lower extremity at once clear up the diagnosis.

Where trophic changes alone are present, the absence of symptoms referable to the central nervous system speaks decidedly against nerve lesions. The relation of the vasomotor symptoms to the position of the limb will in other cases be of value in explaining the nature of the symptoms.

How can we explain the occurrence of true vasomotor phenomena such as do not seem to owe their existence to the mechanical effects of impaired circulation? The blanched appearance that is a sequence of an obstructive condition of the arteries, and which can be demonstrated by elevation of the leg, and in bad cases can even be elicited in the horizontal position, is a phenomenon easily explicable on the theory that the avenues of arterial supply are cut off through extensive obturation of the arteries. Many clinical and experimental observations have been gathered that speak in favor of this view. So also is the rubor not a true vasomotor phenomenon, but a sign of chronic vasodilatation of the superficial capillaries and is compensatory in nature.

On the other hand, veritable symptoms of disturbed vasomotility can be associated with thrombo-angiitis obliterans. That these should occur is not surprising when we call to mind that not only have intense and extensive destructive, pathological alterations taken place in the most important arteries of a limb, but that the accompanying nerves are frequently bound down by a dense mass of cicatricial tissue and have undergone severe fibrotic changes. Although the mechanism of the irritative and exhaustive vaso-

[2] Compare with changes in sclerodactyly (Figs. 5 and 6).

motor phenomena is not clear, the total disorganization of the vascular innervation in many of the cases would seem to afford sufficient basis for the possibility of the occurrence of the disturbances which we call "vasomotor" in nature.

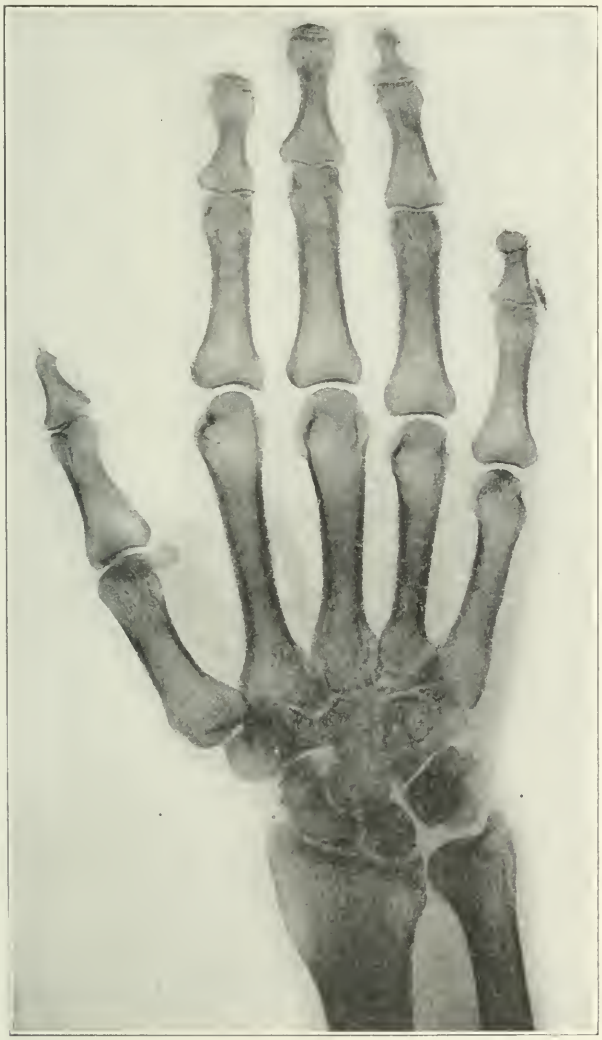


FIG. 5.—Roentgen-ray photograph of a case of sclerodactyly, showing disappearance of the terminal phalanges.

Where signs of thrombo-angiitis of the lower extremities are unquestionably present, and where evidences of vascular occlusion in the upper extremities are lacking, although these are the site of disturbed vasomotor innervation, we may for a long time be

unable to rule out the possibility of the simultaneous occurrence of two different diseases.

The differentiation of true scleroderma from thrombo-angiitis will be rarely difficult to make. In scleroderma and sclerodactyly the first stage with hard edema is characteristic and never simulated by

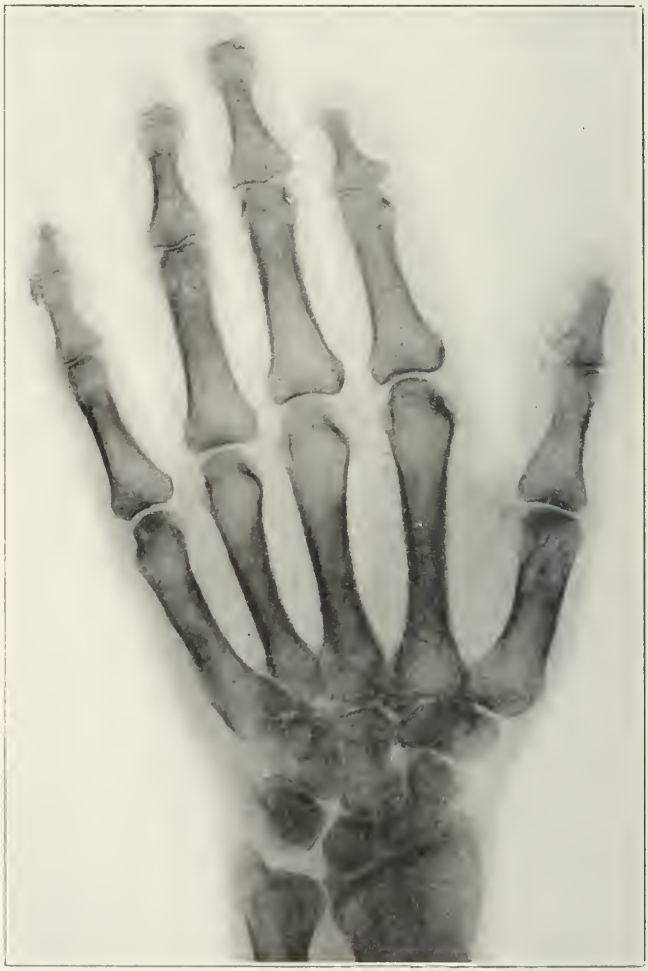


FIG. 6.—Roentgen-ray photograph of a case of sclerodactyly, showing disappearance of the terminal phalanges.

cases of organic vascular disease. The second indurative stage may, however, be almost exactly reproduced by other affections. The form of scleroderma known as "sclerodactyly," because of attendant alterations in the deeper tissues, may be not unlike

thrombo-angiitis. Roentgen-ray examination of the hand in sclerodactyly offers the most valuable means of differentiating the two diseases (Fig. 5 and 6). The phalanges will very early show atrophic changes and disappearance of the terminal portions in scleroderma, sclerodactyly, and Raynaud's disease, while the bones, although somewhat rarefied, will be seen to conserve their outlines throughout the course of the disease, thrombo-angiitis obliterans, until they are disturbed by the effects of gangrene.

So far as our experience permits us to judge, symptoms of scleroderma occur only late in thrombo-angiitis when other signs of vascular occlusion have already become well developed. The recognition of the condition will then depend upon the absence of pulsation in the larger peripheral vessels, the presence of gangrene (or the history of such a condition) and of the other typical signs of obliterated arteries and veins.

In the light of our recent studies on the pathology of thrombo-angiitis obliterans we are able to state that certain characteristic morphological changes in the arteries and veins are specific[3] for this process. These occur in the deep arteries and veins as well as in the superficial veins, when these are the seat of the so-called "migrating phlebitis." Whenever migrating phlebitis is present, therefore, the excision of a portion of vein under local anesthesia followed by microscopic examination will lead to a diagnosis.

It is most probable that in Raynaud's disease and the related affections the seat of the pathological process is to be sought in the vegetative system, that is, somewhere in the vasomotor apparatus. Nor are we likely to be rewarded in a search for any organic change. The frequent return to a normal condition, observed clinically, also speaks against the likelihood of morphological or chemical alterations in the nervous system.

Whereas in thrombo-angiitis obliterans a definite and specific morphological change in the arteries and veins is responsible for the varied phenomena in the superficial capillaries, in Raynaud's and allied diseases the vasomotor and trophic disturbances are the outcome of irritative and exhaustive processes of the sympathetic nervous system.

[3] Surg., Gyn., and Obs., 1914.

THE IMPORTANCE OF THE PARANASAL SINUSES IN THE EXPLANATION OF PAIN IN THE FACE, HEAD, NECK AND SHOULDERS.[1]

By M. A. Bliss, M.D.,

ASSISTANT IN NEUROLOGY AND INSTRUCTOR IN PSYCHIATRY, WASHINGTON UNIVERSITY MEDICAL DEPARTMENT, ST. LOUIS.

Two years ago I reported some observations on the relation of the branches and the ganglia of the fifth cranial nerve to the accessory sinuses of the nose. The material on which that study was made consisted of approximately seventy decalcified heads and parts of heads observed with Dr. Greenfield Sluder.

The work of Ladislaus Onodi,[2] came to our notice about two months later (July 18, 1912) than my report, in which he confirmed these observations, employing a different method.

In the past few years numerous studies of the accessory sinuses have been made, chiefly by rhinologists. These studies, notably those of St. Clair Thompson,[3] deal chiefly with direct extensions of suppuration through dehiscenses in the post-ethmoidal-sphenoidal walls or transference through venous or lymphatic channels of infection to the cavernous or other blood sinuses, or to the meninges.

Our efforts have been to show that the nerve trunks and ganglia are directly or indirectly affected by the air sinus infections and that widespread referred pain springs from this district, pain which is treated without result unless its origin be recognized.

The anatomical relationships described in the above-cited text, I believe explain the mode of production of these pains.

Recently, Dr. C. A. Gundelach, of St. Louis, has devised a method of directly inspecting the interior of the sphenoidal sinuses much in the same way that a bladder is viewed through a cystoscope. This has enabled us to see during life not only the condition of the lining membrane but the position of the Vidian in the floor and the convex elevation marking the position of the second division of the fifth on the outer wall of the sinus.

Our clinical observations, carried on at the same time as the anatomical study, have been very numerous and have served to confirm our belief that the thickness of the sinus walls and the close or remote relationship of the trunks and ganglia to diseased sinuses has a constant significance.

The widespread distribution of the referred pain cannot be explained on anatomical grounds, according to our present knowledge. This phenomenon is still somewhat a mystery in other

[1] Read before the American Neurological Association, May 8, 1914.

[2] Archiv. f. Laryngologie (zweite heft).

[3] Trans. Med. Soc., London, 1906, vol. xxix.

parts of the body also, although much light has been shed upon this subject in recent years by the studies of Dr. Henry Head and others.

In 1908 Sluder published[4] a description of sphenopalatine ganglion neuralgia which runs as follows:

"Inflammation in the nasal structures (accessory sinuses, sometimes nasal membrane) produces by its extension to, or transmission of its toxins, the ganglion, a symptom-complex, partly neuralgic (painful), and partly motor, sensory, and gustatory. The neuralgic picture is pain in the root of the nose and in and about the eye, in the upper jaw and teeth (sometimes lower jaw and teeth), extending backward under the zygoma to the ear, frequently making earache and pain in the mastoid; extending thence to the occiput, neck, shoulder-blade, breast, and when severe to the arm, forearm, hand, and fingers, with sometimes a sense of sore throat on that side. Rarer additions to this picture are itching of the skin of the upper extremity, taste disturbance (parageusia), a sense of stiffness and muscle weakness in the upper extremity, and fortification scotomata."

Mild cases are described as a sense of tension in the face and stiffness or "rheumatism" in the shoulders. It may appear as constant pain with exacerbations or it may stop and reappear cyclically as a migraine; or it may stop and reappear with the stabbing sharpness of a "tic."

The motor phenomena are changes in the appearance of the soft palate. Its arch is higher on the affected side, and the dimple which forms in the rhaphe just above the uvula in the act of gagging is deflected to the well side. The uvula is inclined to the well side.

The sensory phenomena are slight blunting of the tactile sense of the soft palate, pharynx and tonsils, with like condition of the membrane of the nose of the affected side.

The gustatory phenomena are confined usually to a slight blunting of the sense of taste on that side. Parageusia is rare.

Heretofore we have felt that the complete picture was so rare as to be never presented by one case. I have recently found, however, examples of the entire symptom complex. I have also observed a large number of modifications of the complex, depending, I think, upon the anatomical variations present.

The following case, which has been followed since 1905, will serve as a type of the complete picture.

Miss S., aged twenty-seven years, had for several years suffered "off and on" with pain beginning at the root of the nose, involving the upper jaw and teeth (occasionally the lower jaw and teeth), extending backward to the tip of the mastoid, and most intense about

[4] New York Med. Jour., May 23, 1908, pp. 989–990.

5 cm. posterior to this point. When she first came under observation, in 1906, the nose was negative in every particular. Some months later a post-ethmoidal-sphenoidal inflammation developed on the left side. Almost simultaneously the old pain, which had almost disappeared, returned. It involved the root of the nose, the cheek, the mastoid tip and a little behind it, the neck, shoulder-blade, shoulder, and arm—all in greatest severity.

Soaking a strong solution of cocain into the tissues overlying the sphenopalatine ganglion always stopped the pain, and the relief would often last for several days.

The pain was on the left side. The arch of the soft palate was markedly higher on the left; the uvula was deflected to the right. The soft palate and the pharynx down to the level of the lower part of the tonsil were somewhat less sensitive on the left side to contact with a lock of loose cotton. On the floor of the left nostril anteriorly cotton was not so well perceived. In the middle and anterior third of the tongue the sense of taste for sugar, sodium chloride, citric acid, and quinin bisulphate was less acute on the left than on the right.

Many exacerbations and remissions occurred. Many injections of plain alcohol were attempted. The total result has been a cure. The case illustrates not only the characteristic features, but the sometimes extremely discouraging failures one must meet before getting a complete result. For three years she has been well.

We meet with certain cases which are characterized by a sense of tension and soreness in the neck, from the occiput to about the seventh cervical vertebra, radiating into one or the other shoulder, in which there is very slight pain in the face or about the ear. Movement of the head forward or from side to side is painful and there is a sense of lameness and muscle soreness in the shoulder and arm. Both golf arm and violinists' cramp have been diagnosed in such instances.

There is often a sense of depression and irritability amounting to demoralization. I have had men and women of the highest type tell me that although the pain was not intense that the nagging quality of it made it impossible for them to keep control of their emotions. The sensory distress is variously described as clawing, grabbing, pulling, or as tension which never lets loose and fatigue which does not disappear with rest.

Headache, which usually accompanies the neck and shoulder pain, is inconstant. No sensory or motor changes need accompany the picture. The following will serve to illustrate this type:

J. A., aged twenty-six years, a healthy, single man, had suffered, on May 16, 1912, five years with severe discomfort in the left side of the back of his neck. His collar annoyed him constantly on that side. Some months after the pain began it extended into the left shoulder and later to the left arm and hand. Before I

saw him he had sometimes had pain about the eyes, which led him to consult an oculist, but without relief. His left ear sometimes felt "filled up." He never had any discharge from his nose. Cocainization of the area of the sphenopalatine foramen relieved the pain for a time. Injection of the sphenopalatine ganglion with approximately ten drops of a 5 per cent. carbolic in 95 per cent. alcohol was followed by some discomfort at the time, which lasted from seven to ten days. Then followed marked betterment clinically.

The relief, however, was not complete. Reinjection three months later was followed by further betterment. A third injection at about the same interval was followed by a practical cure. A coryza six months later reëstablished his discomforts but in a lesser degree. A fourth injection was given which seems thus far to have completed the cure. For the past year he has been free from pain except a slight degree, which has been provoked from time to time by coryzas of greater or lesser severity.

We could demonstrate no motor or sensory changes in this case which we interpret to have been unquestionably explainable by an exposure of the Vidian nerve itself in the sphenopalatine foramen. This is not an infrequent exposure, as may be very readily determined by an examination of a series of skulls. The Vidian in this class of skulls must proceed farther forward and slightly outward before it reaches the ganglion. It is accessible from the sphenopalatine foramen for cocainization or treatment, and may readily be injected from the foramen itself or from under the tip of the middle turbinate. We have proved this fact by the injection in cadavers, the specimens being injected as in the veritable operation, and subsequently decalcified and sectioned.

We believe this to be a case of Vidian neuralgia. Admitting this, it becomes self-evident that exposure of the Vidian in the floor of the sphenoidal sinus, either by dehiscense of the upper arc of the Vidian canal, or through a thin plate of bone, will produce this same picture, the point of irritation being posterior in this instance to that in the first instance. In the first instance cocainization of the area of the sphenopalatine foramen will stop the pain, but in the second instance will be without effect. In the second instance intrasphenoidal applications of analgesic remedies will be effective.

A type of similar kind is illustrated in the case of Mrs. F., aged forty-seven years. She came under my observation October 8, 1913. For two weeks she had suffered from a painful neck, from the occiput to the seventh cervical vertebra. Movement either active or passive increased the pain. There was tenderness to pressure over the cervical spines and extending over the muscles of the left side of the neck. Later the pain extended to the left shoulder and was so constant and harassing as to demoralize the

patient. Psychically the depression seemed out of proportion to the pain described. This had been a usual observation in this type.

Combinations of internal and local remedies, salicylates, iodides, moist heat, massage, electricity, etc., were thoroughly tried, without effect.

Cocainization of the area of the sphenopalatine foramen, particularly its posterior half, exposure of the Vidian district, very much reduced the pain in ten minutes.

Later examination disclosed a suppurating sphenoidal sinus. Treatment addressed to the sphenoid and to the exposure of the district of the Vidian has resulted in nearly complete relief for the greater part of the time.

The relief has been even more striking psychically than physically, and a sense of well-being and zest in life customary to the patient have returned.

Optic disk swelling associated with headache, vertigo, and nausea is such an important symptom-complex indicative of intracranial tension, and the presence of post-ethmoidal-sphenoidal infection often so obscure, that we may possibly accept a reminder of what may happen, and in doubtful cases direct our attention to the exclusion of this field before we advise a decompression.

The following will illustrate such a case:

S. P. C., a vigorous lad, aged sixteen years, came to me from Dr. Post, ophthalmologist, with a history of pain in the eyes and befogged vision for five weeks. A gradually increasing headache, with vertigo, accompanied the failing vision. There had been no vomiting. Vision was 1/92 in either eye. There was swelling of the disks, four diopters in the right and five in the left. General neurological examination negative.

Rhinological examination at first reported negative, subsequently disclosed post-ethmoidal-sphenoidal suppuration. Post-ethmoidal operation was performed by Dr. Loeb.

There was prompt subsidence of the optic swelling and rise in visual clearness, with disappearance of headache. Vision in five days had risen to 20/24° and the swelling had receded to one diopter in either eye in the same period. This case was seen in August, 1912. The boy recovered and remained perfectly well during the next several months. Not content with the conditions of life in his home he departed for the Pacific Coast and has been lost sight of.

It is well to say that these are not simple and easy cases to manage. They require painstaking investigation for correct diagnosis. Treatment is at first often disappointing. A certain dogged persistency, not always easy to maintain, is required to meet the failures and baffling eccentricities of reaction. Curious reversals of reaction occur, some of which I am laboring with now, and which will be dealt with in a subsequent paper.

My object in this report has been to present three clear types, with which I have had a large experience, and which I have learned to manage with a degree of success that is satisfactory.

They are infinitely more difficult to deal with than tics or neuralgias of the second and third division, which may be cured by injection from the zygoma. The nerve fibers are readily destructible by alcohol, but the nerve cells are very resistent. These points were proved by Dr. Otto May[5] in experiments on cats, dogs, and goats.

Another feature which should be remembered is that the sphenopalatine ganglion is small (5 mm.) and by no means easily struck, whether approached with a straight needle from below the posterior tip of the middle turbinate or by means of a curved needle entering through the sphenopalatine foramen, and whether these attempts be made under the view of the Holmes pharyngoscope, because it is impossible to know the exact position of the ganglion in any individual.

Dr. Sluder and I have proved in a series of experiments on the cadaver that the ganglion or its immediate environment may, however, be struck as an average procedure. Our injections were made with carmine and Prussian blue, the specimens then decalcified and sectioned macroscopically.

It is probable that instillation of alcohol into its immediate environment is efficacious, but not to the same degree that follows when it is placed directly in its substance.

For these reasons I have long since ceased to be discouraged by an incomplete or unsatisfactory result from a first injection.

Some years ago I felt that the result of an injection was complete in ten days. I have since changed my ideas on this subject, and now believe that it requires three months before conclusions can be reached.

These are my feelings since carbolic acid has been added to the alcohol for its analgesic effect. It seems that the effect of carbolic acid is not complete short of three months. At the end of this time I have the case reinjected if the result has not been satisfactory.

It is, of course, self-evident that the shoulder-arm-hand syndrome may be produced by a mediastinal pressure, which must be borne in mind.

[5] British Med. Jour., August 31, 1912.

FUNCTIONAL TESTS IN EXPERIMENTAL TARTRATE NEPHRITIS.[1]

By A. C. Potter,

and

E. T. Bell.

(From the Department of Pathology, Bacteriology, and Public Health of the University of Minnesota.)

Pathology of Tartrate Nephritis. Underhill, Wells, and Goldschmidt[2] succeeded in producing a severe form of acute nephritis in rabbits by subcutaneous injections of racemic tartaric acid. According to these observers, vacuolization of the epithelium of the convoluted tubules is the essential lesion in the earliest stages. Necrosis rapidly follows the vacuolization, so that nearly all the convoluted tubules may soon become necrotic. The glomeruli are practically uninjured. It was suggested by these investigators that tartrate nephritis offers a specially favorable opportunity for physiological studies, inasmuch as the convoluted tubules are practically all destroyed and the glomeruli left intact.

Pearce and Ringer,[3] from a study of tartrate nephritis in dogs, state that the most striking change is necrosis of the convoluted tubules, with fat in the loops of Henle and sometimes in the collecting tubules. They found exudative glomerular lesions in about one-half of the animals in which the tubular lesions were severe. Tartrate nephritis was purely tubular in only about one-half of their cases.

In our series of forty-five cases of experimental tartrate nephritis in rabbits the tubular lesions in the severe cases are essentially the same as those described by Underhill, Wells, and Goldschmidt. A few hours after injection of the tartrate the epithelium of the convoluted tubules may show extreme vacuolization. This condition was pronounced in one animal killed five and a half hours after the injection and in another killed two and a half hours after the injection. (See Figs. 1 and 2). The exact time of the first appearance of vacuolization was not determined. Necrosis and fatty metamorphosis begin the first day and advance rapidly. If the animal lives three or four days, fat may be a prominent feature. It is specially conspicuous in the convoluted tubules, but may be found in any tubule. Rarely there are some fat droplets in the glomeruli.

[1] Aided by a grant from the Research Fund of the University of Minnesota.

[2] Tartrate nephritis, with special reference to some of the conditions under which it may be produced, Jour. Exper. Med., 1913, xviii, 322.

[3] A study of experimental nephritis caused by the salts of tartaric acid, Jour. Med. Research, 1913, xxix, 57.

When necrosis is well established there is usually no suggestion of the original vacuolated condition.

We have found a little hydropic degeneration (vacuolization) after the first day, but it seems to be a prominent lesion only during the first half day.

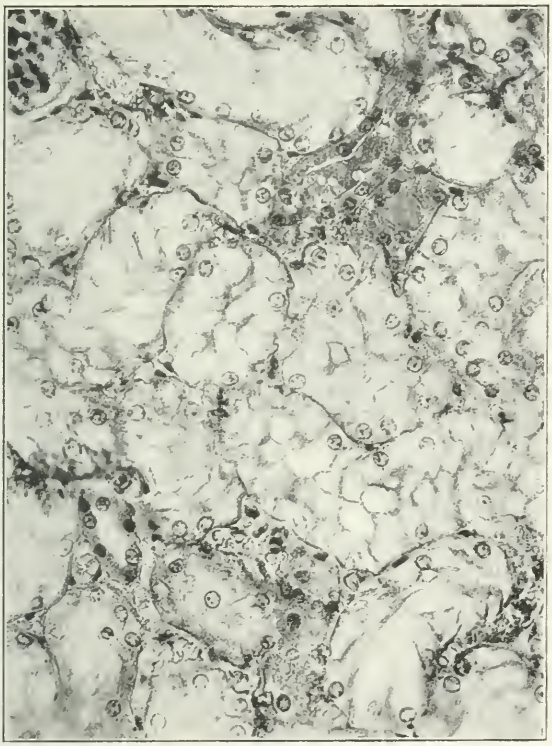


FIG. 1.—Kidney of rabbit five and a half hours after tartrate injection. Zenker, paraffin, hematoxylin, and eosin. Hydropic degeneration is very pronounced. The small tubules of the collecting type show little involvement. Photomicrograph.

The left kidney of a rabbit was removed seven and a half hours after the tartrate injection. This kidney showed extreme hydropic degeneration. Forty-eight hours after the nephrectomy the rabbit was killed. The right kidney showed necrosis of nearly all the convoluted tubules. No sign of hydropic degeneration was to be seen. It is therefore clear that the first lesion in tartrate nephritis is a hydropic degeneration, and that this condition gives place to fatty metamorphosis and necrosis in the later stages.

Hydropic degeneration involves all the convoluted tubules in all parts of the cortex. The first tubules to undergo necrosis are those near the capsule. The tubules in the deep part of the cortex next to the medulla become necrotic only in severe cases, though

they may show marked degenerative changes. When all the convoluted tubules are necrotic there is usually an anuria so that no functional tests can be made. As a rule our functional tests were made on kidneys in which over half the convoluted tubules showed necrosis and the remainder fatty and granular degeneration.

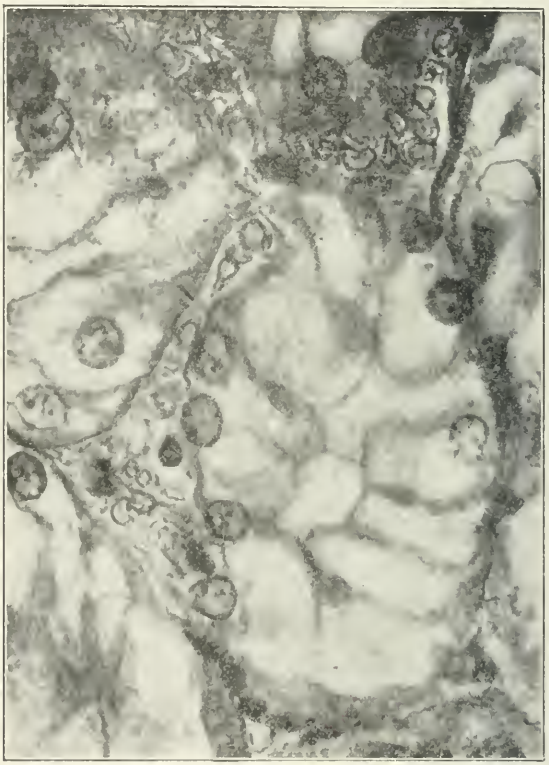


Fig. 2.—Small area from Fig. 1 under high magnification. Photomicrograph.

Some of the cases show swollen, opaque, cloudy kidneys. These have the gross features of cloudy swelling. When crushed specimens of fresh tissue are examined under high magnification it is seen that nearly all the tubules are granular. This granular condition is present in kidneys that are dark and reddish as well as in those that are pale and cloudy. The granules are least conspicuous when necrosis is most extensive. Of course, many of the granules are fat droplets. These may be identified by their insolubility in potassium hydroxide. But the albuminous granules are always present and frequently dominate the picture. These fade in potassium hydroxide but do not completely disappear. They are unlike the granules seen in the normal kidney. This granular condition of the epithelium is constantly present in tartrate nephritis of the mild

as well as the severe types. It is best seen in crushed specimens of fresh tissue. It may be called a granular degeneration. The swollen, cloudy kidneys that show this microscopic appearance would usually be regarded as examples of cloudy swelling.

As regards the glomerular lesions, there were seven animals in our series of forty-five in which precipitated serum could be seen in some of the capsular spaces in every section. To what extent this indicates functional disturbance in the capsular epithelium we cannot determine. The glomerular tufts are often congested and rarely fat droplets can be demonstrated in them; but they are never found necrotic. And even in the most extreme cases of glomerular involvement there are always many in every section that are anatomically intact. It is probable that there is moderate glomerular injury in some cases of tartrate nephritis; but one may exclude these cases and use only those in which there are no anatomical glomerular lesions.

Schlayer and Takayasu[4] believe that the glomeruli may be functionally deranged even though they show no histological lesion. They therefore discard the histological evidence and estimate the glomerular function by testing the amount of contraction and dilatation of the renal vessels and the diuresis in response to stimulation. But as v. Monakow[5] has in part suggested, it is doubtful whether Schlayer's test is any better than the histological appearance. The capsular epithelium of the Malpighian corpuscle might be able to perform its functions even though the bloodvessels of the kidney do not respond to stimulation.

Material and Methods. Experimental tartrate nephritis has been studied in forty-five rabbits. In the latter half of our work we have used only racemic tartaric acid. In our first experiments Merck's dextrotartaric acid was used. Merck's preparation will produce a severe nephritis, but it is much less certain in its action than the racemic acid. It is also easier to produce a complete suppression of phenolsulphonephthalein excretion with the racemic acid. We have usually employed 0.4 gm. to 0.7 gm. of racemic tartaric acid neutralized with sodium carbonate and injected subcutaneously according to the method described by Underhill, Wells, and Goldschmidt. 0.3 gm. of the acid often produces complete suppression of the phthalein excretion, but much larger doses occasionally fail. In general a large dose is much more apt to produce a severe nephritis than a small dose. The animals were fed in the usual way during the experiments.

Some rabbits develop considerable resistance to tartrates. If they recover from the first dose much heavier doses are required

[4] Untersuchungen über die Funktion kranker Nieren, Deutsch. Arch. f. klin. Med. 1909, xcviii, 17.

[5] Beitrag zur Funktionsprüfung der Niere, Deutsch. Arch. f. klin. Med., 1911, cii, 248.

subsequently to produce a nephritis. In one rabbit an initial dose of 0.6 gm. reduced the phthalein excretion to 6 per cent. for the first two hours. After the phthalein excretion had returned to normal, repeated doses of tartrate were given, some as high as 1.5 gm., but no signs of nephritis appeared.

Only those animals have been used for further functional tests in which the nephritis produced was of such a degree as to cause complete or almost complete suppression of phthalein excretion. This condition is usually present as early as three hours or less after the injection of the tartrate, and continues until the death of the animal. An injection of phthalein was given every forty-eight hours during the experiment. Two rabbits that at one time showed complete suppression of phthalein, recovered completely.

Phenolsulphonephthalein. Rowntree, Fitz, and Geraghty[6] have shown that this dye is excreted by the tubular epithelium in the frog's kidney. They have also shown that the elimination of phthalein is greatly reduced in experimental passive congestion whenever the congestion is made severe enough to produce marked tubular injury. In moderate passive congestion there is no marked change in phthalein excretion.

Rowntree and Geraghty[7] and Rowntree and Fitz[8] have given abundant clinical evidence that the excretion of phthalein is decreased in almost all forms of nephritis, and in general that the amount excreted corresponds to the degree of functional involvement of the kidney. Inasmuch as human nephritis never shows complete destruction either of all the tubules or of all the glomeruli it is difficult to decide from this material by what route the phthalein is eliminated.

Eisenbrey[9] found marked reduction of the phthalein excretion in experimental nephritis in dogs, produced by uranium nitrate and potassium chromate.

Austin and Eisenbrey[10] state that in experimental nephritis in dogs the anatomical picture bears no definite relation to the amount of phthalein excreted. These observers had no cases of zero phthalein elimination.

In our experiments twenty-three rabbits showed either no excretion of phthalein or a faint trace for the first two hours. All of these animals had very severe nephritis. In over half of these the

[6] The effects of experimental chronic passive congestion on renal function, Arch. Inter. Med., 1913, xi, 121.

[7] An experimental study of the functional activity of the Kidneys by means of Phenolsulphonephthalein, Jour. Pharmacol. and Exper. Therap., 1909–10, i, 579.

[8] Studies of renal function in renal, cardiorenal, and cardiac diseases, Arch. Inter. Med., 1913, xi, 258.

[9] A study of the elimination of phenolsulphonephthalein in various experimental lesions of the kidney, Jour. Exper. Med., 1911, xiv, 462.

[10] Experimental acute nephritis: The elimination of nitrogen and chloride compared with that of phenolsulphonephthalein, Jour. Exper. Med., 1911, xiv, 366.

animals were not allowed to die of nephritis but were killed immediately after a phthalein test, so that the corresponding anatomical picture could be studied. The lesions in the convoluted tubules are either severe hydropic degeneration, fatty metamorphosis, necrosis, or a mixture of fatty metamorphosis and necrosis. Granular degeneration is associated with all the changes just mentioned. The glomerular changes were discussed above. In tartrate nephritis

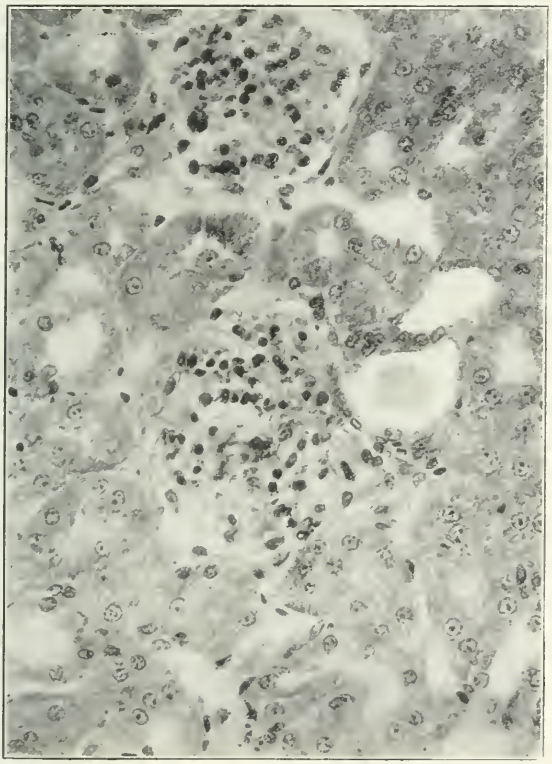


FIG. 3.—Kidney of a rabbit injected with tartrates the preceding day. Zenker, paraffin, hematoxylin, and eosin. The animal was killed immediately after a test which showed a 5.8 per cent. phthalein excretion for two hours. The epithelium is very granular, but there is no necrosis. Photomicrograph.

a trace or a zero elimination of phthalein corresponds always to a very severe injury of the renal tissue. There may, however, be little or no necrosis.

One of our animals was killed immediately after a test which showed 5.8 per cent. phthalein for the first two hours. All the epithelium was decidedly granular, but there was not much necrosis, vacuolization, or fat. (See Fig. 3.) Another animal, killed immediately after a test showing 6 per cent. elimination of the dye for two

hours, had a rather marked hydropic degeneration. These two experiments indicate that different histological pictures may be associated with the same degree of functional derangement. Apparently the excessive accumulation of granules in the cytoplasm interferes with cell function even as vacuoles do.

Large quantities of urine, containing various normal constituents, may be excreted when the phthalein excretion is zero. In many of

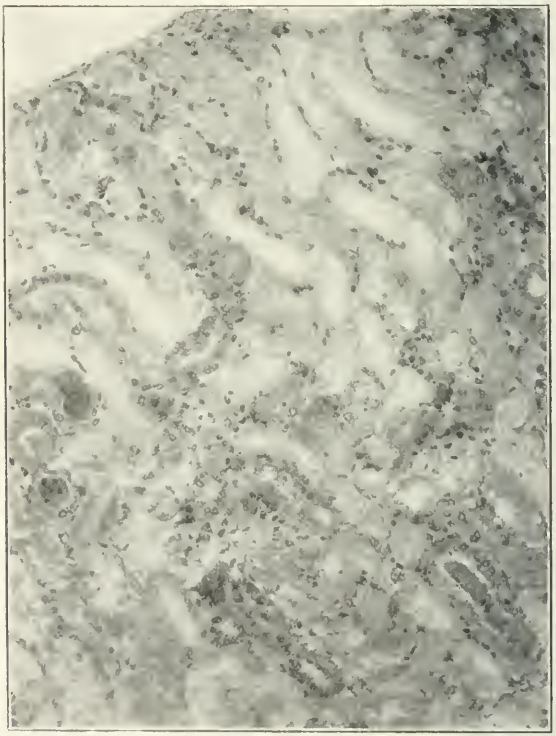


FIG. 4.—Kidney of a rabbit forty-eight hours after tartrate injection. Zenker, paraffin, hematoxylin, and eosin. The convoluted tubules are almost entirely necrotic. The intermediate tubules are granular, but otherwise appear normal. This is the type of kidney we have used to a considerable extent in our functional tests. Photomicrograph.

these cases the lesions are almost entirely tubular. It is, therefore, highly probable that phthalein is eliminated by the tubular epithelium.

A zero phthalein excretion does not necessarily mean a fatal prognosis in tartrate nephritis. Two rabbits showing this condition at one time have recovered completely so far as can be determined by phthalein excretion and general health. Rowntree[11] reports

[11] The study of renal function: The prognostic value of studies of renal function, AMER. JOUR. MED. SCI., 1914, cxlvii, 352.

that he has seen 2 cases of chromate nephritis in rabbits showing zero phthalein excretion recover in a short time.

Indigo-carmine. Rowntree, Fitz, and Geraghty[12] state that there is no additional information to be had from the use of indigo-carmine when phthalein is used, since it is excreted in amounts roughly corresponding to the amount of phthalein and is much more difficult to estimate colorimetrically. Rowntree and Geraghty[13] give a discussion of this test.

Our results also show parallelism between the excretion of phthalein and indigo-carmine. Two rabbits which showed a faint trace of phthalein for one hour were given indigo-carmine immediately. Only a trace of the dye was eliminated in each case. Three other rabbits which showed complete suppression of phthalein for the first hour likewise showed complete suppression of indigo-carmine injected immediately after the phthalein test. Phthalein and indigo-carmine are apparently excreted by the same structures in the kidney.

Methylene Blue. A discussion of this test is given by Rowntree and Geraghty[14] (p. 585). The excretion of this dye is said in general to run parallel to indigo-carmine. In some forms of chronic parenchymatous nephritis its excretion is said to be normal or exaggerated.

In our experiments one rabbit which showed a trace of phthalein for the first hour showed complete suppression of methylene blue. Two rabbits showing suppression of phthalein gave a trace of methylene blue. In two other rabbits both phthalein and methylene blue were completely suppressed. These results agree closely enough to prove that methylene blue is excreted in the same way as phthalein and indigo-carmine.

Lactose. De Bonis[15] injected a 1 per cent. solution of sodium fluoride into the ureter near the renal pelvis (Bottazzi's method). This procedure is said to destroy the medulla and all of the cortex except the glomeruli. More urine usually passes through the injured kidney than through the normal one. De Bonis[16] determined in this way that lactose may be excreted by the glomeruli. Rowntree, Fitz, and Geraghty[17] found that in the frog lactose may be excreted by the tubular epithelium. This experiment was performed by ligaturing the arterial supply of the glomeruli and then testing the renal function. (This method was first used by Nussbaum[18] in a study of renal function.) These authors also found that in experimental chronic passive congestion in dogs, lactose excretion is delayed one to two hours after intravenous injection. Marked

[12] Loc. cit. [13] Loc. cit. [14] Loc. cit.

[15] Giorn. intern, d. Science med., 1907, xxix, 446. (Cited from Rowntree and Fitz.)

[16] Experimentelle Untersuchungen über die Nierenfunktionen, Arch. f. Anat. u. Physiol., physiol. Abth., 1906, 271.

[17] Loc. cit. p. 126.

[18] Arch. f. d. ges Physiol., 1876, xvi, 179; xvii, 580.

delay in the excretion of lactose may occur when the phthalein output is normal.

Schlayer and Takayasu[19] used lactose as a vascular test in their experiments on rabbits. The normal kidney eliminates 1 gm. of lactose when injected intravenously in five and a half to seven and a half hours, average time six hours. In chromium, sublimate, and aloin nephritis lactose excretion is good in the earlier stages while the bloodvessels of the kidney react; but in the later stages when the bloodvessels no longer react its excretion time is prolonged to eight hours. No experiments showed suppression of lactose excretion.

Cases of human nephritis with delayed lactose excretion are regarded by Schlayer and Takayasu[20] as a vascular type. These authors believe that lactose and water are excreted by the glomeruli.

Rowntree and Fitz find lactose excretion delayed in all their human cases of nephritis or chronic passive congestion. In several cases they found a complete suppression of lactose excretion. These were all cases of severe nephritis. Lactose excretion in nephritis does not correspond to that of phthalein. The manner of its excretion is not yet determined.

To test the excretion of lactose we injected 3 gm. subcutaneously. The time required for the disappearance of sugar from the urine of normal rabbits after this injection varied from 13.5 to 23.5 hours in the five animals tested. The average time was twenty hours. Benedict's test for sugar was used. This is much longer than the time required to excrete 1 gm. when given intravenously. This period was found by Schlayer to average six hours in the normal rabbit.

Five animals in which the phthalein elimination was zero were injected subcutaneously with 3 gm. of lactose. The lactose disappeared from the urine in thirty-two, forty-two, forty-three, forty-eight, and forty-eight hours respectively—average 42.6 hours. This, it will be noted, is about twice the normal elimination time.

Several clinical cases reported by Rowntree and Fitz showed lactose excretion prolonged beyond twelve hours (2 gm. of lactose were injected intravenously in their cases). This period is also about twice the normal elimination time.

No case of lactose suppression has been encountered experimentally. Even when practically all the convoluted tubules are necrotic it is still excreted. Inasmuch as the destruction of the tubular part of the renal excretory apparatus is so complete in many cases of tartrate nephritis this condition affords specially clear proof that the glomeruli may excrete lactose. There is, however, no

[19] Untersuchungen über die Funktion kranker Nieren, Deutsch. Arch. f. klin. Med., 1909, xcviii, 17.

[20] Untersuchungen über die Funktion kranker Nieren beim Menschen, Deutsch. Arch. f. klin. Med., 1910–11, ci, 333.

evidence in these experiments that the tubular epithelium cannot perform this function. The delayed excretion may mean that more must now be excreted by the glomeruli since the tubules are destroyed. There is no experimental evidence to explain the complete suppression of lactose observed in some of the clinical cases reported by Rowntree and Fitz. Some light might be thrown upon this question if a form of experimental nephritis could be produced in which lactose excretion was suppressed. Until further evidence is obtained we must agree with Rowntree that the manner of lactose excretion is not completely understood.

Potassium Iodide. Frey[21] studied renal secretion by producing diuresis. He believed that the larger the amount of urine the nearer its composition would approach that of the glomerular excretion. He concluded from his experiments that the iodides are eliminated almost exclusively by the tubular epithelium.

Schlayer and Takayasu found that 0.025 gm. of potassium iodide injected intravenously into rabbits is completely eliminated in twenty-two to twenty-eight hours—average twenty-four hours. In experimental nephritis produced by chromate, sublimate, aloin, or uranium nitrate the iodide excretion is greatly delayed—forty to sixty hours. The excretion of potassium iodide may be greatly delayed, but it is never suppressed. The iodide is used by these authors as a test for the condition of the tubular epithelium, since they believe that it is excreted entirely by this part of the kidney tissue.

Von Monakow obtained indefinite results with potassium iodide. He does not regard it as a satisfactory test. In one of his clinical cases the autopsy revealed that nearly all the glomeruli were destroyed while the convoluted tubules showed only slight changes. In this case the iodide excretion was prolonged to one hundred and eighty hours. The prolongation of the excretion is much greater in this case than in those in which the lesions were mainly tubular.

Rowntree, Fitz, and Geraghty found that the excretion of potassium iodide is usually prolonged in chronic passive congestion of the kidney even in cases in which the phthalein output is normal.

Rowntree and Fitz found no constant relation between the degree of nephritis and the time of excretion of potassium iodide. They regard it, therefore, as of little value as a functional renal test.

Our tests were made by injecting 1 gm. of potassium iodide subcutaneously. Sandow's test was used for its detection in the urine. The time of elimination of this dose in four normal rabbits varied from 19.5 to 23.5 hours—average 21.5 hours.

In two rabbits in which phthalein excretion was permanently suppressed the elimination times for potassium iodide were 85.5

[21] Das Glomerulusprodukt ist ein Blutfiltrat, Arch. f. d. gesam. Physiologie, 1912, cxxxix, 435.

hours and ninety-five respectively. Both animals died the night following the disappearance of the iodide from the urine. At autopsy one showed a considerable amount of necrosis of the tubular epithelium; the other showed extensive granular degeneration, fatty metamorphosis, and some necrosis.

Another rabbit in which the phthalein excretion was completely suppressed was killed sixty-five hours after the iodide injection. The iodide was still being excreted. At autopsy the majority of the convoluted tubules were found necrotic and the others were fatty and granular. The glomeruli were all anatomically intact.

These experiments show that iodide excretion is delayed in tubular nephritis. Schlayer and Takayasu obtained similar results, but interpreted them to mean that the iodide is excreted by the tubular epithelium and not by the glomeruli. Apparently they believe that the functional capacity of the epithelium is decreased but not completely suppressed in tubular nephritis.

But no one has yet reported an instance of suppression of iodide excretion except in anuria; whereas phthalein, which is almost certainly excreted by the tubules, is suppressed when the injury of the epithelium passes beyond a certain degree. Unless we believe that degenerated epithelium incapable of excreting phthalein, indigocarmine, or methylene blue may still excrete iodide, we must admit that the glomeruli take part in the elimination of this substance. It seems more probable that the delayed excretion of iodide in our experiments is due to the fact that it must all be excreted by the glomeruli. Moderate injury of the glomeruli might further decrease the rate of excretion of iodide. The experimental results seem to us to afford good evidence that potassium iodide may be excreted by the glomeruli. The part that the tubular epithelium takes in the elimination of this substance is undetermined.

If we could produce experimentally a destruction of the glomeruli as complete as the destruction of the tubules in tartrate nephritis, valuable additional evidence could be obtained.

We have not made any functional tests with urea or sodium chloride. The discussion of these substances is therefore omitted.

Hemoglobin. This test was performed as follows: 5 c.c. of washed red blood cells from a rabbit were hemolyzed with distilled water, and after the addition of 0.5 per cent. sodium chlorid injected into the ear vein of the rabbit to be tested. In normal rabbits the urine is almost black three or four hours after this injection. Two rabbits with tartrate nephritis, causing complete suppression of phthalein, each gave a slightly colored urine after this test. The benzidene test for blood was strongly positive in these urines, but the color of the urine was very much less dark than in the normal. It is therefore probable that hemoglobin is excreted mainly by the convoluted tubules, but that a small amount may pass through the glomeruli.

Summary. By subcutaneous injections of tartaric acid it is possible to produce in rabbits a form of acute nephritis in which the great majority of the convoluted tubules are necrotic and the rest fatty and granular. The glomeruli and collecting tubules may be anatomically intact.

In kidneys of the type just described the excretion of phenolsulphonephthalein, indigo-carmine, and methylene blue is completely suppressed. The excretion time of lactose is over twice as long as normal, while the excretion time of potassium iodide may be four times the normal. Both potassium iodide and lactose are excreted by this type of kidney.

The evidence obtained suggests that phthalein, indigo-carmine, and methylene blue are excreted exclusively by the convoluted tubules and that potassium iodide and lactose may be excreted by the glomeruli. Hemoglobin is excreted mainly by the tubules, but may pass through the glomeruli slowly.

A REPORT OF THE TREATMENT OF CEREBROSPINAL SYPHILIS BY INTRASPINOUS INJECTIONS OF SALVARSANIZED SERUM.[1]

By A. G. Rytina, A.B., M.D.,

and

C. C. W. Judd, A.B., M.D.

(From the Departments of Genito-urinary Surgery and Clinical Pathology, College of Physicians and Surgeons, Baltimore, Maryland.)

Since the discovery of the Wassermann reaction and the luetin tests, scientific proof has been added to the clinical belief that such affections as tabes and general paresis are not parasyphilitic diseases but true luetic processes.

The discovery of the Spirocheta pallida in these diseases by Noguchi and others not only adds further proof, but establishes the fact that they are active syphilitic affections. One of the things that created the belief that these affections were parasyphilitic diseases was their lack of response, in most instances, to antisyphilitic treatment. The cause, we now know, is due to the peculiarity of the choroid plexus of the dura mater, being more or less impermeable to such drugs as mercury, potassium iodide, and salvarsan. We must admit, however, that occasionally clinical improvement follows the administration of salvarsan, mercury, and potassium iodide given in the usual manner, but

[1] Read before the 116th Annual Meeting of the Medical and Chirurgical Faculty of Maryland, April 29, 1914.

improvement of the spinal fluid from the standpoint of the Wassermann reaction, cell count, globulin test, etc., is extremely rare, indicating that the improvement must be regarded only as temporary. When we further realize that even in the preëruptive stage of syphilis, while the blood still is negative to the Wassermann reaction, the spinal fluid may be positive, it is obvious that the proper method of handling these affections must be by direct applications to the nervous tissue itself. The difficulties that strew our path are not only technical but lie chiefly in the high susceptibility of the nervous tissue to foreign substances. However, that such a mode of attack is practicable has long been exemplified by intraspinous injections of serum in meningitis and tetanus. We have, too, the experience of several observers that even medicinal substances may be injected into the spinal canal without untoward effects.

Fortified by this knowledge and experience, various investigators have tried to improve syphilis of the nervous system by intraspinous injections of the newer antisyphilitic compounds. Salvarsan on account of its irritating alkaline content was out of the question. Wechselmann was the first to inject neosalvarsan in the spinal canal. Since that time Marinescu, Marie and Levaditi, Gennerich, and others have tried this treatment. Wechselmann used aqueous solutions, and after the injections it was found that the patients had violent reactions, consisting of severe headaches, vomiting, marked neuralgic pains in the legs, elevation of temperature, micturitional difficulties, etc. These severe reactive symptoms indicate an irritant action on the spinal cord, and on this account the method has not met with general favor.

Swift and Ellis tried injections of neosalvarsan solutions, but on account of the irritating action of the drug on the spinal cord gave them up and adopted their method of injecting salvarsanized serum. This method has found many adherents and is the method we have followed in our present study with some slight modification. The method of procedure is as follows: The patient is given a full dose of salvarsan intravenously; at the end of one hour 100 c.c. of blood is withdrawn. This blood is then sent to the laboratory. The next day the patient is prepared for the intraspinous injection of the salvarsanized serum by painting well the whole lumber and sacral regions with tincture of iodin. The patient may be sitting or lying, but it is essential that the back be well bowed. A point one-eighth to one-quarter inch to the right of the median line between the third and fourth lumbar intervertebral space is selected, and the needle, which is an ordinary lumbar puncture needle, is directed upward, inward, and forward. The successful entrance is indicated by the escape of spinal fluid. If the fluid is under great pressure an amount sufficient to reduce it is allowed to flow out, otherwise the same quan-

tity of fluid is withdrawn, as we have serum to inject (usually 15 to 30 c.c.). The injections are made by us with a syringe. Some use gravity, others combine both. The fluid is then sent to the laboratory for study. The patient is now sent to the ward and the foot of the bed elevated for two hours. He remains in bed until the temperature and pulse are normal. Some of the patients develop no reaction whatever, and they are allowed to go home the next morning. Others develop a meningismus, characterized by fever, increased pulse rate, nausea, vomiting, severe headaches, and shooting pains in the lower extremities. These symptoms are never alarming, and they pass off within twenty-four to forty-eight hours. Some of the patients feel comfortable so long as they are recumbent, but on standing develop a headache which may be quite severe. This condition lasts several days and then gradually subsides. We have not observed any unfavorable complications or sequelæ.

To date we have given twenty-nine intraspinous injections to 18 patients; 11 patients received one injection each; 4 received two injections each; 2 received three injections; and 1 received four injections. It is our plan, patients consenting, to repeat the injections every two or three weeks, irrespective of the clinical improvement, until the Wassermann reaction becomes negative in all dilutions, the cell count becomes normal, and there is negative globulin test. While some of our patients have shown a decided clinical progress, suggesting a cessation of treatment, the more accurate laboratory check has revealed the necessity of further injections.

At this point, the citation of a few cases from a clinical standpoint may be interesting.

B. F. C. entered hospital suffering with nausea, vomiting, and markedly defective mentality. Neurological examination, Wassermann test of the spinal fluid, etc., established the diagnosis of cerebrospinal lues. The Wassermann test of the blood was negative. Mercury and potassium iodide treatment ineffective. Twenty-four hours after the first intraspinous injection of salvarsanized serum his nausea and vomiting had disappeared and he became perfectly rational. Two weeks later he began again with nausea and vomiting, which was promptly relieved by the second intraspinous injection. He returned to his home in West Virginia feeling perfectly well. Patient returned to us February 9, 1914, feeling fine, having gained considerably in weight and being perfectly rational. He was then given another intraspinous injection.

J. H. A. Complaint: sharp pains in abdomen. At age of twenty-eight years, he had a chancre, followed by secondaries. He took mercury and potassium iodide for one year and was pronounced cured. Well until three years ago, when he began to notice weakness in limbs after walking up and down stairs.

Present Condition: Two years ago began to have sharp, intermittent pains in abdomen and difficulty in walking, until at the time of admission he was unable to walk at all. Examination lead to the diagnosis of tabes.

March 10, 1914. Intraspinous injection of 13 c.c. concentrated salvarsanized serum.

March 11. Patient had no more pains. Left the hospital March 14, 1914.

March 30. Again entered hospital. Given 0.6 gm. salvarsan intravenously, but on account of severe chill, lasting several hours, blood for intraspinous injection was not obtainable.

Again entered hospital April 7, 1914. Patient has no more pains; notices a steady improvement in his legs; 17 c.c. concentrated salvarsanized serum injected intraspinously. Patient, with slight support, walked from the bed-room to operating-room.

April 27. Patient feels fine. No pains; walks with perfect ease, but still notices a slight weakness which improves daily. Has resumed his occupation.

Case XI.—W. C. T. Complaint: violent headaches. Initial lesion October 1, 1913, followed by secondaries. Received four injections of salvarsan, and his symptoms promptly disappeared. Felt well until five weeks following last injection of salvarsan, when he began to have severe frontal headaches. Eye examination negative. Patient received another injection of salvarsan intravenously, which helped headaches for a few days, when they returned with increased severity. Hypodermic injections of biniodid in oil and large doses of potassium iodide proved unavailing.

March 7, 1914. Lumbar puncture made for diagnostic purposes. Fluid under pressure; Wassermann reaction of fluid triple plus; high cell count and positive globulin.

March 11, 1914. Headaches violent as ever, some nausea and vomiting, loss of weight and insomnia. Today 25 c.c. concentrated salvarsanized serum injected intraspinously. Forty-eight hours later, headaches had disappeared and have remained absent ever since. Patient's general condition has also shown marked improvement. Received another injection April 2, and another April 17.

Case VIII.—J. F. B. Initial lesion, 1894; left hemiplegia, 1911. Has received three injections of salvarsan intravenously. Symptoms complained of at time of treatment were scraping of right toe on floor and hemiplegia of right arm. Has received three intraspinous treatments. Now has good use of right arm and scraping of toe practically disappeared.

From a clinical review of our cases we have observed improvement, marked in some, slight in others, in practically every case, excepting one case of tabes in a patient who has been blind and paralyzed for many years, in whom the treatment was given

chiefly to satisfy the patient. We do not doubt that some of these patients may have been benefited by the older methods of treatment, but of this we are certain, that (1) the percentage of improvements would not have been as large, and (2) would not have been in most cases as prompt.

Though in certain respects the laboratory findings did not substantiate the clinical diagnosis of the cases included in this series, they in some cases established a definite diagnosis, often confirmed it, and in the latter event afforded evidence as to the efficiency of the treatment, either temporary or permanent, in the following directions:

1. As regards the globulin content of the cerebrospinal fluid.
2. As to the white blood cell count of the spinal fluid.
3. As to the Wassermann reaction of the blood.
4. As to the Wassermann reaction of the cerebrospinal fluid.

It is a source of great regret that this series did not include the colloidal gold test of Lange, but our work was already well advanced when the advisability of including this test was first seriously considered.

As regards the preparation of the salvarsanized serum the following procedure was employed:

The salvarsanized blood collected directly into centrifuge tubes of 50 c.c. capacity was kept at refrigerator temperature until the morning after collection (usually about sixteen to eighteen hours), when the clot was freed from the sides of the tube and the specimen centrifugalized until the serum was entirely free from cellular elements. Such cell-free serum was then transferred aseptically to other tubes. Except in the first few injections, when the sera were diluted to a 40 per cent. mixture with 0.9 per cent. sodium chloride solution, according to the method advicated by Ellis and Swift[2] we followed the plan employed by Boggs[3] of using undiluted serum. This has the advantage of decreasing the amount of fluid injected into the subdural space. We never experienced any ill effects attributable to this procedure, but rather feel that it is more efficacious and at the same time minimizes cord pressure symptoms. It was only by this means that we were enabled to institute the plan, which has been our recent custom, of giving the comparatively speaking huge doses of salvarsanized serum in the hope of securing a more intensive form of treatment than employed by others. The serum so prepared was inactivated in a water bath at 56° C. for thirty minutes, and when brought to body temperature was ready for administration.

Regarding the laboratory work carried on the following methods were employed: 1. In reference to the globulin content. For the sake of conformity to the method employed by others we used

[2] New York Med. Jour., 1912, xcvi, 53.

[3] Personal communication.

the Noguchi butyric acid test for globulin,[4] rather than at least more agreeable methods. Only such fluids as were entirely free from red corpuscles were utilized in this connection. A clear fluid without white precipitate either as sediment of in suspension was negative (—). An opacity of the entire specimen without any definite white precipitate either as sediment or in suspension was doubtful (±, ∓, or +). An opacity of the entire specimen with a definite white flocculant precipitate in suspension was definite (++). An opacity of the entire specimen with a coarse white flocculent precipitate as sediment and in suspension indicated a great increase (+++). The rapidity of development of the precipitate also influenced the intensity of the reaction, the most marked degree (++++) appearing immediately upon the addition of the alkali.

Globulin, though present in traces in all spinal fluid, is not detectable in normal amounts by the Noguchi method. Though increases occur occasionally in conditions other than central nervous syphilis which now definitely includes general paresis and tabes, its presence in increased quantities is usually associated with such involvement, the intensity of the reaction running roughly *pari passu* with the activity of the process.

2. With reference to the cell count. This estimate was made with a pipette and counting chamber in a manner comparable to that employed in counting the leukocytes of the blood, modified to suit the altered conditions encountered in the spinal fluid.

A cell count of more than eight white cells per cubic millimeter of undiluted spinal fluid was considered abnormal. Roughly corresponding to the activity and severity of a luetic involvement of the central nervous system this number is materially increased, the increase affecting the lymphocytic cell particularly, and the number varying from anywhere above eight to several hundred.

3. With reference to the Wassermann reaction of the blood. This reaction was performed substantially according to the technique which one of us has already described.[5] The exception is that in the majority of cases considered here we used two antigens, one Noguchi[6] antigen and the other a standard cholesterinized antigen.

The relative merits of these two antigens will be discussed by one of us[7] elsewhere.

Reaction of — and ± we consider diagnostically against lues (exclusive of cases involving the central nervous system when not

[4] For method see Noguchi, H., The Serum Diagnosis of Syphilis, first edition, page 118 to 119, Philadelphia, 1910.

[5] Judd, Charles C. W., Maryland Med. Jour., September, 1913, p. 220

[6] Methods of preparation was essentially the same as that described by Kolmer and others. Arch. Int. Med., 1913, xii, 665, for Noguchi Antigen, and Sacks, H., Berlin klin. Woch., 1911, p. 2066, for the cholesterinized antigen.

[7] Judd, Charles C. W., Jour. Amer. Med. Assoc., July 25, 1914, lxiii.

infrequently the blood is negative and the spinal fluid if examined is found positive). Those cases designated as ± and + we consider has having an inconclusive reaction unless there is a revision downward from a positive reaction under the influence of treatment. Finally ++ and +++ are positive reactions and are diagnostic of lues.

4. With reference to the cerebrospinal fluid. The technique of the Wassermann was essentially the same as in the case of the blood, save that not possessing compliment it was not inactivated and, when feasible, smaller and greater concentrations of the fluid were utilized for each test. Selections as seemed most appropriate in the individual cases are made from the following: Undiluted fluid, diluted one in two parts, two in five, one in three, one in five, one in eight, and one in ten. By so doing small degrees of variation in fixative property were detected. In this connection we wish to emphasize the importance of as complete a titration of the spinal fluid as possible, as evidence of the actual influence of the treatment may thus be obtained which in our estimation is at least as important as the lowered cell count and diminished intensity of the Noguchi reaction which has been so heralded by others.

Certain of our cases, which presented clinical evidence of involvement of the central nervous system, in a known luetic, emphasize the probability that such disturbances are not necessarily due to organic implication of brain or cord in the luetic process, since the examination of the cerebrospinal fluid furnished altogether negative results while the blood Wassermann was positive. More probably this was due to some complicating condition, *e. g.*, arteriosclerosis. Our experience, however, is in accord with the suggestion of Bernstein,[8] to this extent at least, that in luetic patients presenting symptoms referable to the central nervous system, despite negative laboratory findings, an intraspinous injection of salvarsanized serum has done no harm and may be of incalculable prophylactic benefit.

Whether as a direct result of this treatment or not the laboratory findings in all of the cases included in this series which we have been enabled to follow have shown unequivocal improvement save in the question of the blood Wassermann. In the improvement there has been no particular uniformity with reference to any special one of these reactions. In no case, though as many as four injections have been administered, has there been a return from pathological conditions to absolute normality of the spinal fluid and blood in all phases of its examination, though in some of the cases there has been a restitution of the cerebrospinal fluid to normal in some respects. At best in well-established cases long

[8] Amer. Med. Assoc., 1914, lxii.

courses of treatment seem inevitable. Despite this the initial results are so far encouraging as to stimulate us to carry this treatment of these therapeutically discouraging cases to the limit in the hope of restoring not only the clinical condition of the patient but also both blood and spinal fluid to a normal condition in respect to all of these methods of examination.

Conclusions. 1. Intraspinous injection of salvarsanized serum, with proper precautions, is a safe treatment.

2. The results obtained indicate its superiority over the older known methods.

3. Treatment must be persisted in until the laboratory findings are negative irrespective of the clinical progress observed.

4. Such clinical and laboratory improvements as have been observed by us have still to go further. The permanancy of the improvement still has to be determined.

We wish to express our appreciation to Dr. Charles E. Simon for placing at our disposal the Wassermann reports of several of the cases herein included.

STUDIES IN THE CONCENTRATION OF BLOOD-SUGAR IN HEALTH AND DISEASE AS DETERMINED BY BANG'S MICRO-METHOD.[1]

By Arthur H. Hopkins, M.D.,

Assistant Instructor in Medicine in the University of Pennsylvania, Philadelphia.

(From the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania.)

This work was stimulated by the current interest in the relation of blood-sugar to diabetes, nephritis, and conditions involving changes in the glands of internal secretion.

A brief outline may be cited of our present knowledge of the relation of blood-sugar to carbohydrate metabolism. The sugars and starches of the food, after conversion by the intestinal enzymes into glucose, etc. pass, by way of the portal circulation, to the liver, where the larger portion remains and is converted into glycogen.

Claude Bernard was the first to suggest the regulatory function of the liver in the sugar supply to the blood, it being warehoused in that organ and given to the muscles as demanded by their work.

[1] Aided by the J. Alison Scott Research Fund. Read before the Pathological Society of Philadelphia, October 8, 1914.

When he produced glycosuria by puncturing the floor of the fourth ventricle, he demonstrated the control of the nervous system over the output of sugar from the liver.

In animals, stimulation of sensory nerve trunks, and in human beings, lesions of the central nervous system produce the same phenomena.

Recent investigations reveal the importance of the ductless glands in the regulation of carbohydrate metabolism. Opie, MacCallum, and others consider that the islands of Langerhans furnish an internal secretion necessary for this metabolism, while Cushing concludes that the posterior lobe of the pituitary gland has an important influence on carbohydrate metabolism, in that any operative disturbance of it is followed by glycosuria and by lowering the assimilation limit of sugars. Increased tolerance follows a deficiency in secretion on the removal of this portion of the gland.

Experimentally, the influence of adrenalin is well established, though clinically there is no organic disease of the adrenals which produces glycosuria or diabetes.

Disregarding further theories concerning glycogenesis and glycolysis, it may be borne in mind that glucose is the principle sugar of the blood, that it is "a food material in transport from the organs of supply to the organs of consumption," and finally that its concentration in normal individuals varies between 0.06 per cent. and 0.11 per cent., it being generally conceded that 0.085 per cent. is the average.

Conditions Causing Variations in Blood-sugar Concentration. Hyperglycemia and glycosuria are the result of a disturbance in equilibrium of that delicate chemical or nervous mechanism which controls the sugar supply from the various glycogen depots. Conditions causing an increase in blood-sugar may be:

Physiological, as alimentary changes, nervous or emotional disturbances, pregnancy and infancy, etc.

Pathological, as diabetes, conditions involving changes in glands of internal secretion, pancreatic and certain hepatic diseases, cerebral injury, tumor or hemorrhage, and finally peripheral nerve diseases.

Experimental, as renal diabetes with intoxication by means of metallic salts, stimulation of splanchnics, asphyxia, and drugs, as adrenalin, diuretics, morphin, strychnin, chloroform, etc.

Total reduction in blood-sugar is less common than hyperglycemia occurring chiefly in exhaustion and phloridzin glycosuria.

The Micro-method of Sugar Determination. Bang[2] introduced this method in his monograph *Der Blutzucker,* in January, 1913, and in November of the same year so modified it as greatly to enhance its value as a rapid bedside method.

[2] Bioch. Ztschr., November, 1913, H. ¾, B. 57.

Technique. Two or three drops of blood, approximately 100 mg. from a prick in the finger, are taken up on a small, specially prepared, and weighed piece of filter paper. The paper with its contained blood is again weighed, the amount of blood thus being accurately estimated. Next the paper is dropped into a test-tube containing 6.5 c.c. of an alkaline potassium chloride solution which has been brought to the boiling-point, and is allowed to remain there for a half-hour, during which time the albumin coagulates and remains in the paper while the sugar diffuses into the solution. The solution is then poured into a small flask, another 6.5 c.c. of the alkaline solution is poured in the original test-tube, thus washing the remaining sugar from the paper. This is then added to that in the flask with 1 c.c. of a specially prepared copper solution. The mixture is brought to a boil by heating for exactly one and a half minutes and boiled for two minutes. When cool a few drops of a specially prepared starch solution is added as an indicator and titrated with $\frac{n}{100}$ iodin solution until the blue iodin starch color reaction appears and persists for a half-minute. The theoretical consideration and the details of the technique are given in Bang's paper.

The small amount of blood required, the ready means of collecting it, the opportunity for repeated and serial estimations without discomfort to the patient, and finally the rapidity and simplicity of the method, afford advantages far greater than any of the older methods.

Though quite new the method has been used by a number of workers, all of whom confirm Bang's findings (Hirsch and Reinbach,[3] Tannhauser and Pfitzer,[4] Jacobson,[5] Leire,[6] Bing,[7] etc.). The test has been successfully controlled by the methods of Fehling, Knapp, Bertrand, Michaelis, and Rona, and we have controlled it with Allihn's method, and with known sugar solutions, with satisfactory results.

My results show that the concentration of sugar in normal cases varies between 0.065 per cent. and 0.1 per cent. In each test two samples were taken, the average of the two being the given result.

Studies in Alimentary Hyperglycemia. Comparatively little work has been done to date in this line. The factors which govern the various stages in the breakdown of sugar may vary considerably in different animal species, hence the results are of greatest value when obtained directly in man.

Much more work has been done in alimenary glycosuria, concerning which Allen[8] states that the results "may be obscured by imper-

[3] Hoppe Seyler's Ztschr. f. Phys. Chem., 1913, Bd. 87, H. 2, S. 122–141.
[4] Münch. med. Woch., 1913, ix, S. 2155.
[5] Biochem. Ztschr., Bd. 56, H. $\frac{5}{6}$, S. 471–491.
[6] Der Blutzucker, Wiesbaden, 1913.
[7] Deutsch. Arch. f. klin. Med., 1914, Bd. 113, H. $\frac{3}{4}$.
[8] Glycosuria and Diabetes, Boston, 1913.

meability of the kidney, and even in diabetes, when renal involvement exists, the reaction may be negative, the sugar merely heaping up in the blood. For this reason examination of the blood is most important to accompany or replace examination of the urine, and the most recent studies concerning lowered assimilation of sugar are based not upon alimentary glycosuria but upon alimentary hyperglycemia."

The most characteristic sign of a disturbance in carbohydrate metabolism is the increase in the sugar content of the blood. The value of the alimenary test is greater than an occasional single test for preformed sugar in that the former, or serial test, may reveal such a disturbance far earlier.

The rapidity of absorption may be controlled by the type of starch, some forms being absorbed much more quickly than others, and by the addition of fat which retards absorption. The rate of progress from the stomach to the intestine is important, the tolerance of ingested sugar being almost doubled by an accompanying meal.

Tachau[9] found only a very slight increase in normal cases after 100 grams of glucose, that amount being recognized as the standard quantity. The lack of uniform results by various workers is striking, a few having failed to get any positive results. There are several factors responsible for this, the most prominent of which are variations in individual reactions, and that the rise in normal cases frequently occurs within a half-hour after oral administration, and by the end of the hour has resumed the normal or almost normal level.

Again, all work done prior to the introduction of Bang's method last year involved the use of much more blood, and consequently but one or occasionally two tests were made in each case. Naturally the conclusions drawn from such limited series are lacking in uniformity and contribute more to the confusion than to the elucidation of a complex subject.

Alimentary Hyperglycemia in Normal Cases. In order to ascertain the degree of fluctuation of the concentration of sugar in the blood, lying within the physiological boundaries, a series of normal cases was studied.

In these tests 100 grams of glucose dissolved in 420 c.c. of water was given before breakfast. Estimations of blood-sugar were then made at frequent intervals, as shown in Table I.

This table illustrates the irregularity in time at which the height of the curve is reached, which may be from a half to two hours. In some cases the normal level may be resumed within one hour. The difference in degree of the individual reaction is also worthy of note. Case 3 was the only one which failed to show a definite rise

[9] Arch. f. klin. Med., 1911, 104, S. 437–447.

in sugar concentration. Case 9 received 20 grams of glucose subcutaneously and no rise occurred until four and a half hours after the injection.[10]

TABLE I.—ALIMENTARY HYPERGLYCEMIA IN HEALTH.

Case.	1, S.R.	2, S.H.	3, B.	4, J.	5, H.	6, Sa.	7, D.	8, L.	9, N.
Preformed Sugar.	0,099	0,108	0,100	0,078	0,075	0,097	0,101	0,065	0,074.
100 gms. glucose.	..	..	..	..	..	..	..	..	20 gms. subcutaneously.
½ hour.	..	..	0,112	0,111	0,149	0,126	0,142	0,143	0,074
1 "	0,127	0,110	0,102	0,106	0,103	0,142	0,108	0,147	
1½ "	..	..	0,108	0,138	0,093	0,115	0,112	..	0,073
2 "	0,141	0,157	..	..	..	..	0,074	0,141	
2½ "	..	..	0,087	0,127	0,099	0,073	..	..	0,058
3 "	..	..	..	..	..	..	0,072	0,123	
3½ "	..	..	0,105	0,091	0,082	0,091			
4 "	..	..	..	..	..	..	..	0,092	
4½ "	..	..	0,084	..	0,076	0,066	0,085	..	0,101
5 "									
5½ "	..	..	..	..	..	..	..	..	0,091
6 "	..	..	0,109	..	..	..	..	..	0,105

So far my findings partially confirm those of Jacobson,[11] who recently published his series of normal cases studied by the same method, in which he found a rise in blood-sugar within five minutes after 100 grams of glucose, the height being reached in a half-hour and the preformed level resumed in approximately two hours.

DIABETES. The most characteristic symptom of this disturbance in carbohydrate metabolism is the increase in the sugar content of the blood.

It is of importance to distinguish between the glycosuria of febrile, toxic, hepatic, or nervous diseases and that of early diabetes, especially when it is borne in mind that a diabetes may be the result of any of the above-mentioned causes of a transient glycosuria. Hyperglycemia may exist for a variable length of time before there is any evidence of sugar in the urine, hence an earlier and more reliable criterion of diabetes is the study of the blood-sugar. In early diabetes, postprandial hyperglycemia is greater and longer in duration than in health, and becomes progressively more lasting until there are no low levels reached in the course of the day, the result of this slow decline being the early stage of a true diabetes. Finally the barriers give way, sugar overflows into the urine, and the disease is well established. For a time the blood-sugar level may remain fairly constant, only to rise again when the toxic effect of the excess of sugar renders the kidneys less permeable to it[12] (Macleod).

Using Bang's method in their recent experiment with intravenous injections of sugar solution, Tannhauser and Pfitzer[13] found that in

[10] A 5 per cent. solution was injected into the thigh, but owing to the pain and discomfort the test was not repeated.

[11] Biochem. Ztschr., Bd. 56, H. $\frac{5}{6}$, S. 471–494.

[12] Jour. Amer. Med. Assoc., vol. lxii, No. 16, p. 1222.

[13] Münch. med. Woch., 1913, ix, 2155.

diabetes the blood-sugar was markedly increased and remained so for hours, there being an accompanying parallel increase in glycosuria

Alimentary Hyperglycemia in Diabetes. Alimentary hyperglycemia was studied in a series of cases of diabetes. Here the method of adminsitration and technique were the same as those used for the normal cases.

Table II.—Alimentary Hyperglycemia in Diabetes.

Case.	1, K.	2, A.	3, D.S.	4, F.	5, P.H.	6, M.	7, S.	8, P.	9, C.	1, K.
Preformed sugar.	0,217	0,192	0,152	0,251	0,306	0,229	0,234	0,243	0,235	0,190
100 gms. glucose.	..	..	..	..	..	..	..	..	..	100 gms. glucose by rectum.
½ hour	..	..	0,226	0,353	0,398	0,372	0,350	0,328	0,267	
1 "	0,365	0,270	0,261	0,355	0,389	0,377	0,348	0,402	0,333	0,182
1½ "	..	..	0,299	0,378	0,343	0,392	0,372	..	0,392	
2 "	0,344	0,370	..	0,429	..	0,325	0,437	0,448	..	0,196
2½ "	..	..	0,265	..	0,359					
3 "	..	..	..	..	..	0,240	0,429	0,503	0,457	0,196
3½ "	..	..	0,216	..	0,319					
4 "	..	..	..	..	..	0,252	0,324	0,467	..	0,269
4½ "	..	..	..	..	0,318					
5 "	..	..	..	..	..	..	..	..	..	0,233
6 "	..	..	..	0,253						

From this table it will be observed that alimentary hyperglycemia is very pronounced, the height of the level appearing at any time from one-half to three hours after the ingestion of glucose, and the duration being greatly prolonged.

In Case 1 it is interesting to note the delay and impairment of absorption when the glucose was administered by rectum.

No marked rise occurred for four hours after the rectal injection. The preformed value was lower here, as the patient had been on a carbohydrate-free diet for ten days. Several patients were unable to retain the glucose solution by rectum, and therefore a larger series is not presented.

Alimentary Hyperglycemia in Various Diseases. These cases were observed as each presented a condition in which a disturbance in carbohydrate metabolism might be suspected if the most recent theories on the subject of sugar regulation are to be accepted. The technique was the same as in the former series.

Table III shows especially interesting results in the pancreatic and pituitary cases. In Case 2 a series of tests were carried out, the first after 100 grams of glucose, the second after 167 grams of bread, representing approximately 100 grams of glucose. In the latter series it will be observed that the rise in blood-sugar was less pronounced and slower than where glucose was given.[14]

[14] At the end of a half-hour the patient was given cócain as a local anesthetic for a slight surgical operation, and this was followed by a definite hyperglycemia.

TABLE III.—ALIMENTARY HYPERGLYCEMIA IN VARIOUS DISEASES.

Case	1, O'B.		2, D. S.		D. S.		3, R. S.		4, Mr. McM.		5, H. C.		6, Miss McM.		7, Sh.		8, My.		9, J. T.		10, E. J.
Diagnosis	Hepatic cirrhosis.	Glycosuria.	Hepatic cirrhosis.	Glycosuria.	Same as case 2.	Glycosuria.	Sub-acute pancreatitis.	Glycosuria.	Pancreatitis.	Glycosuria.	Acromegaly (?).	Glycosuria.	Optic neuritis. Pituitary (?)	Glycosuria.	Tabes (?).	Glycosuria.	Endocarditis.	Glycosuria.	Plumbism.	Glycosuria.	Infantilism. Pituitary (?)
Preformed sugar.	0.081	..	0.072	..	0.108	..	0.066	..	0.093	..	0.104	..	0.078	..	0.078	..	0.125	..	0.086	—	0.085
100 gm. glucose.	...		...	..	167 gms. bread.																
½ hour.	0.138	..	0.166	..	0.112	—	0.180	..	0.183	Dec.	0.120	—	0.136	—	0.180	—	0.211	—	0.149	+	0.185
1 "	0.160	..	0.167	..	0.147	—	0.178	..	0.193	+	0.172	—	0.217	Dec.	0.218	+	0.149	—	0.249	++	0.137
1½ "	0.137	..	0.207	..	.. .	..	0.238	..	0.173	++	0.151	—	0.217	+	0.320	+	0.141	—	0.217	+	
2 "	...	..	...	..	.	..	...	..	0.108	+	...	..	...	..	...	..	...	..	...	..	0.133
2½ "	...	..	...	..	0.128	—	...	..	...	..	0.130	—									
3 "	...	..	0.206	..	...	..	0.183	..	...	..	...	..	0.073	—	0.164	..	0.157	—	0.130	..	0.142
3½ "	0.141	..	...	..	...	..	0.132	..	0.074	Dec.											
4 "	...	..	...	..	0.085	—	...	..	...	..	0.088	—	...	..	...	..	...	..	...	..	0.099
4½ "	...	..	...	..	...	..	...	..	0.079	—											

In 7 of the cases, repeated analyses were made for glycosuria, the results of which are similar to those of other workers in that there is no constant level of hyperglycemia at which sugar appears in the urine.

The height of the curve was reached in the majority of these cases in from one to one and one-half hours, the duration of the hyperglycemia lying between that of the normal and the diabetic.

Nephritis. The following cases were studied owing to the theoretical interest as well as the existing diversity of opinion in regard to blood-sugar values in high tension nephritis. The first observations of a rise in blood-sugar with renal involvement were those of Neubauer, confirmation of which has been furnished by Frank,[15] Leire,[16] Weiland,[17] Rolly and Opperman,[18] and many others.

Neubauer[19] considers an existing relation between increased blood-pressure and hyperglycemia, while others attribute the latter to such causes as uremia, edema with chloride retention, dyspnea, etc.

Bing and Jacobson[20] recently found a slight increase in such cases on admission to the hospital, the tendency being to fall as the stay in the hospital continued.

The following tests were made to ascertain the possible relationship between blood-sugar, blood-pressure, phthalein elimination, congested liver, and edema. Table IV.

This short series of 26 cases is presented merely as a preliminary report. It will be seen that of the 16 cases with a blood-pressure ranging from 180 to 280 the blood-sugar values lay within normal limits in but 5 cases, while the 11 other cases showed a definite, though moderate, hyperglycemia.

In 11 of these 16 cases the phthalein elimination was reduced. The influence of chronic passive congestion upon the phthalein output must be taken into consideration.

In 10 other cases without high pressure, 7 were normal and 3 were hyperglycemic. Of the 19 cases showing a low phthalein elimination, 9 showed a definite rise in blood-sugar.

Where edema was present it has been noted and its presence reveals no association with the blood-sugar level. An enlarged and congested liver might be expected to be the source of some alteration in carbohydrate metabolism, but in the tests for the preformed sugar alone, *i. e.*, not including the alimentary test, the expectations are not borne out.

[15] Deutsch. Arch. f. klin. Med., 1911, p. 103, S. 397.
[16] Der Blutzucker, Wiesbaden, 1913.
[17] Zentralbl. f. d. ges. Phys. u. Path. d. Stoffwechsels, 1910, Nr. 13.
[18] Ztschr. f. phys. Chem., 1913, Bd. 88., H. 2, S. 155–158.
[19] Biochem. Ztschr. 25, 1910, S. 284–295; Arch. f. exp. Path. u. Pharm., 1911–12, p. 67, S. 192–193.
[20] Deutsch. Arch. f. klin. Med., 1914, Bd. 113, H. $\frac{3}{5}$.

TABLE IV.—NEPHRITIS, SHOWING RELATION OF BLOOD-SUGAR TO BLOOD-PRESSURE, PHTHALEIN ELIMINATION, ETC.

Case.	Age.	Diagnosis.	Date.	Blood-sugar.	Blood-pressure.	Phthalein, per cent.	Liver.	Notes.
1 J. B.	39	Cardiorenal.	April 1	0.135	130–60	10	9 cm.*	Four and a half hours after food. Early A.M. Edema.
			April 2	0.073	110–60			
2 J. H.	34	Chronic interstitial nephritis; chronic myocarditis.	April 1	0.060	190–130	40	5 cm.	Edema.
			April 2	0.087				
3 J. M.	48	Cardiorenal.	April 1	0.076	135–98	40	8 cm.	Edema.
			May 22	0.090	155–85			
4 J. W.	45	Chronic nephritis; chronic myocarditis.	April 1	0.090	145–85	45	4 cm.	Edema.
					155–85			
5 N. P.	65	Chronic interstitial nephritis; arteriosclerosis.	April 1	0.121	180–130	35	Negative	Three hours after food.
6 D.	..	Chronic interstitial nephritis; arteriosclerosis; arthritis.	April 7	0.106	200–170			
7 J. J.	56	Chronic interstitial nephritis; arthritis.	April 15	0.132	180–90	—	3 cm.	Four hours after food.
					150–90			
			April 16	0.076	150–90	—		
8 M. G.	54	Chronic interstitial nephritis; endocarditis.	April 30	0.114	190–110		5 cm.	
9 M. W.	28	Chronic interstitial nephritis.	May 2	0.125	262–175	10	Negative.	Gastro-intestinal symptoms; edema; headache.
					225–			
			June 16	0.123	256–163	3		
10 A. P.	49	Chronic nephritis; chronic myocarditis.	May 5	0.159	180–100	15	4.5 cm.	Edema.
11 H. L.	75	Chronic interstitial nephritis (vascular); arterio-sclerosis.	May 5	0.131	160–95	30	5 cm.	
			May 12	0.119	145–85			
			June 4		135–95	29		
12 A. S.	22	Acute nephritis.	May 22	0.095	146–90	36	Negative.	Edema.
13 H. H.	52	Chronic interstitial nephritis.	Mar. 23	0.081	150–125	36	1 cm.	Edema.
					120–80			
			April 2	0.073	120–80			
14 A. W.	70	Chronic nephritis; chronic myocarditis.	Feb. 18	0.161	135–85	—	10 cm.	Edema.
15 G. B.	..	Chronic interstitial nephritis.	Feb. 25	0.082				
			Mar. 9	0.075				
16 C. B.	40	Chronic interstitial nephritis; renal.	Jan. 30	0.146	250–150	14	2 cm.	Headache intense.
			Feb. 14	0.152				
17 C. E.	50	Chronic interstitial nephritis; cerebral hemorrhage; arteriosclerosis.	Mar. 21	0.111	210–100	—	Cloudy. Swollen.	Death same day.
					160–95			
18 J. S.	47	Hypertension.	Mar. 21	0.117	180–130	55	Negative.	
					140–100			
19 L. L.	55	Chronic interstitial nephritis (vascular).	Mar. 23	0.082	225–115	43	Negative.	
			April 2	0.077	160–85			
20 M. C.	41	Chronic interstitial nephritis; chronic myocarditis.	Mar. 30	0.090	152–100	8.5	6 cm.	Edema.
21 L. R.	56	Chronic interstitial nephritis; hypertension.	May 29	0.137	280–	53	1 cm.	
					220–110			
22 E.O.D.	15	Acute nephritis.	May 29	0.122	126–82	30	9 cm.	Edema.
23 S. R.	26	Chronic interstitail nephritis.	June 16	0.121	230–156	22	Negative.	
24 M. R.	27	Chronic interstitial nephritis; hypertension.	June 16	0.117	225–180			
25 P.F.	61	Chronic interstitial nephritis.	June 4	0.074	170–130	24	9.5 cm.	Edema.
					190–110			
26 M. L.	54	Chronic interstitial nephritis; uremia.	Sept. 26	0.127	202–135	67	Negative.	

* Below costal border in midclavicular line.

Alimentary Hyperglycemia in Nephritis. Consider, however, the following table in which nephritics were fed 100 grams of glucose:

Table V.—Alimentary Hyperglycemia in Nephritis.

Case.	1, H.L.	2, J.H.	3, S.R.	4, H.P.
Diagnosis.	Chr. int. neph.	Chr. int. neph.	Ac. par. neph.	Chr. int. neph.
Preformed sugar.	0.119	0.085	0.095	0.074
100 gms. glucose.				
½ hour.	0.200	..	0.179	0.118
1 "	0.172	0.176	..	0.126
1½ "	..	0.218	0.220	
2 "	..	0.161	0.159	0.148
2½ "	0.177			
3 "	..	0.097	0.124	0.114
3½ "	..	..	0.126	
4 "	0.104			
Edema.	—	+	+	+
Enlarged liver.	5 cm.	5 cm.	—	9.5 cm.

In each case the urine was tested for sugar at one-hour intervals, with negative results throughout.

These results emphasize in the individual cases the existence of normal preformed values associated with markedly abnormal values in alimentary hyperglycemia, as do the results in Tables II and III.

Aside from impaired renal function we have to consider altered hepatic function as well as the existence of pancreatitis in a certain proportion of elderly cases. In all cases the rapidity of passage from the stomach to the intestine and rapidity of absorption add somewhat to the uncertainty of the results.

More detailed studies are being carried on in association with Dr. Jonas, in which, in a series of high-pressure cases, the blood-nitrogen and blood-sugar are being studied simultaneously after definite periods of various types of feeding. Chloride retention, blood-pressure, and phthalein elimination with other factors are also being considered.

Pneumonia. In studying the blood-sugar in this series of 17 cases of pneumonia the possible influence of blood-pressure, temperature, and renal changes was observed as well as the associated leukocytosis. Table VI.

In 8 cases hyperglycemia was present, being accompanied by fever in all but 2; 5 of the remaining 7 were convalescent and had no fever.

There was apparently no relation between the blood-sugar values on the one hand and blood-pressure, leukocytosis, and renal involvement on the other, a feature well illustrated by Case 7, which was followed closely from the fifth day to the crisis.

TABLE VI.—BLOOD-SUGAR IN PNEUMONIA.

Case.	Age.	Date.	Diagnosis.	Day of disease.	Blood-sugar.	Blood-pressure.	Temperature.	Leukocytes.	Notes.
1, J.	—	April 7	Lobar pneumonia	8th	0.091	115–65	98.2°	9,600	Crisis
2, M. O'D.	23	April 4	Lobar pneumonia	4th	0.119	155–100	100.2°	23,200	Death next day.
3, D. R.	18	April 4	Lobar pneumonia	23d	0.090	125–65	98.2°	20,000	Convalescent. Leukocytes taken 4 days previous.
4, A. S.	22	April 4	Lobar pneumonia	8th	0.114	140–105	97.4°	8,600	Convalescent.
5, B. J.	70	April 4	Lobar pneumonia	9th	0.158	130–100	98.2°	11,800	Convalescent.
6, A. M.	27	April 9	Articular rheumatism; bronchopneumonia; endocarditis	2d	0.106	115–56	101.2°	9,000	
7, J. M.	34	April 9	Lobar pneumonia	5th	0.138	100–60	102.0°	13,600	Extreme cyanosis.
7, J. M.	34	April 11	Lobar pneumonia	7th	0.139	90–60	102.0°		
7, J. M.	34	April 12	Lobar pneumonia	8th	0.138	80–50	101.0°	28,000	
7, J. M.	34	April 13	Lobar pneumonia	9th	0.084	100–65	100.0°	35,000	Crisis.
8, C. L.	37	April 11	Bronchopneumonia	7th	0.091	—	103.2°	17,500	
9, B. L.	24	April 11	Lobar pneumonia	2d	0.137	—	102.3°	14,300	
10, C. F.	45	April 11	Lobar pneumonia	6th	0.122	116–96	101.0°	16,800	
11, B. McD.	65	April 11	Lobar pneumonia	10th	0.156	140–85	101.0°	9,600	Death.
12, M. H.	30	April 11	Lobar pneumonia	11th	0.086	135–85	97.2°	24,200	Convalescent.
13, P. B.	13	April 11	Lobar pneumonia; empyema	23d	0.093	125–85	97.0°	24,000	Empyema. Pneumonia subsided.
14, H. McC.	14	April 11	Bronchopneumonia; arthritis	5th	0.093	90–60	102.1°	12,900	
15, C. S.	32	April 4	Lobar pneumonia; empyema	14th	0.092	110–85	98.0°	19,800	Pneumonia subsided. Empyema.
16, N. F.	51	April 30	Pneumonia; endocarditis	9th	0.100	135–75	101.2°	21,000	
17, B. N.	52	May 26	Lobar pneumonia	9th	0.113	115–82	103.4°	19,700	Death.

Various Diseases. The micro method was used in the study of blood-sugar values in a series of 64 miscellaneous cases as follows:

Table VII.

Case No.	Diagnosis.	Blood-sugar.
1	Pancreatic diseases	0.066
2	" "	0.093
3	" "	0.119
4	" "	0.081
1	Apoplexy	0.182
2	"	0.118
3	"	0.125
4	"	0.126
1	Primary anemia	0.134
2[22]	" "	0.061
2	" "	0.070
1	Leukemia	0.103
1	Erysipelas	0.155
2	"	0.089
3	"	0.084
4	"	0.104
1	Carcinoma	0.171
2	"	0.181
3	"	0.095
4	"	0.102
5	"	0.111
6	"	0.074
1	Acute articular rheumatism	0.061
2	" " "	0.091
3	" " "	0.106
4	" " "	0.118
1	Hyperthyroidism	0.082
1	"	0.067
1	"	0.080
2	"	0.140
2	"	0.093
2	"	0.108
3	"	0.070
1	Exophthalmic goitre; endocarditis	0.170
1	Typhoid	0.147
2	"	0.122
3	"	0.103
4	"	0.103
5	"	0.105
6	"	0.117
1	Pulmonary tuberculosis	0.074
2	" "	0.087
3	" "	0.094
4	" "	0.141
4	" "	0.116
4	" "	0.135
5	" "	0.139
6	" "	0.100
7	" "	0.103
8	Tuberculous peritonitis	0.115
9	Acute miliary tuberculosis	0.125
10	Tuberculous meningitis	0.127
10	" "	0.091
11	" "	0.080
12	" "	0.117

[22] Where the case numbers are repeated, the tests have been made at various stages of the disease.

TABLE VII—Continued.

Case No.	Diagnosis.	Blood-sugar.
13	Tuberculous meningitis	0.139
13	" "	0.171
14	" "	0.116
1	Neurosis	0.099
1	Tonsillitis	0.075
2	"	0.061
1	Chorea	0.101
1	Epilepsy	0.100
1	"	0.118
1	Hysteria	0.111
1	Psoriasis	0.078
1	Plumbism	0.086
1	Chronic jaundice	0.061
1	Pituitary disease	0.117
2	" "	0.116
3	" "	0.104
4	" "	0.078
5	" "	0.085
6	" "	0.110

Thus it will be seen that hyperglycemia was present in all the cases of apoplexy and typhoid and in 3 out of 6 cases of cancer.

In 14 cases of tuberculosis it was present in 8, being especially pronounced in those having fever or involvement of the meninges.

In nervous diseases, values along the upper normal limit were the usual findings.

CONCLUSIONS. 1. In health a moderate rise in blood-sugar (0.14 per cent. to 0.15 per cent.) occurs after feeding 100 grams of glucose, reaching its height in from one-half to two hours and quickly subsiding.

2. There is no constant blood-sugar level at which sugar appears in the urine.

3. Evidently absorption after rectal and subcutaneous injection is slower than after feeding by mouth, however, owing to the discomfort produced by the former methods this series is too limited to permit of definite conclusions in regard to this point.

4. Where a disturbance in carbohydrate metabolism exists there may be a normal sugar concentration associated with a most pronounced alimentary hyperglycemia.

5. In diabetes, alimentary hyperglycemia is pronounced, the height of the sugar level appearing at any time from one-half to three hours after the ingestion of glucose, and the duration being more prolonged than in other conditions.

6. Pancreatic, nephritic, and pituitary cases all furnish very high figures after feeding glucose, the duration lying between that of normal and of diabetic patients.

7. A moderate hyperglycemia occurs in many high-pressure nephritic cases, and frequently in those with low phthalein elimination. In most cases of nephritis without high-pressure the blood-sugar is normal. Edema and hepatic congestion do not influence

blood-sugar values, though the role they may play in alimentary hyperglycemia, which is pronounced in nephritis, I am at this time not prepared to say.

8. A rise in blood-sugar occurs in pneumonia and may be present in the absence of fever. It is apparently uninfluenced by blood-pressure, leukocytosis, or renal involvement.

9. Hyperglycemia occurs quite constantly in apoplexy, typhoid, and tuberculosis in the presence of fever and in some cases of cancer.

10. The test, owing to its simplicity and accuracy, affords a practical method for early diagnosis and control of dietary therapeusis.

I wish to express my appreciation of the kind assistance given by Dr. A. I. Ringer in the perfecting of the technique of this method and to Dr. Morris J. Lewis for the opportunity to study some of the pneumonia patients who were on his service in the Pennsylvania Hospital.

All the other cases were from the wards of the University Hospital on the service of Dr. Alfred Stengel.

EXTRAPHYSIOLOGICAL OR PUTREFACTIVE UREA.

By G. Delgado Palacios,

PROFESSOR OF PHYSIOLOGICAL CHEMISTRY AT THE UNIVERSITY OF CARACAS, VENEZUELA.

Schematically considered, the destruction of nitrogenous foodstuffs in the animal body end in the formation of the two principal and characteristic organic constituents of the urine, urea and uric acid. Neither, nevertheless, represent the last residue of the gradual disintegration of nitrogenous substances; they originate, on the contrary, through a synthetic process performed principally by the liver from ammonia, which may be considered as the most simple residue of the nitrogenous katabolism. In birds and reptiles the ammonia gives rise to uric acid, and in man and mammalians to urea. The small proportion of uric acid found in the urine of the latter proceeds from a real process of gradual dissociation of nucleins. These substances are disintegrated until xanthic bases result, which, by means of enzymatic oxidation, are turned into uric acid. While in birds and reptiles the introduced urea turns, in its greatest part, into uric acid, in mammalian animals certain enzymes which exist in various organs (Schittenhelm's uricolytic ferments) tend to destroy the uric acid, changing it into urea. Though apparently opposite it is probable that both compounds may proceed in each case from the same physiological process.

How does urea originate from ammonia? This is not entirely

known, but the principal explanation of this biological fact is to be found in the Nencki-Schultze-Schmideberg anhydration theory and in the Hofmeister oxidation theory; both theories suppose the preëxistence of ammonia. It is not well fixed, at present, what part of the truth corresponds to each one of these theories. It is not known also if there are other organs besides the liver which may produce the urea from ammoniacal compounds. Especially interesting is the formation of urea from arginin; here, 50 per cent. of the nitrogen of this substance is directly dissociated by a ferment which has been isolated from the liver, kidneys, thymus, and other lymphatic glands.

The following conclusions can be accepted as well-established facts: (1) the urea proceeds in the body from ammoniacal compounds; (2) the liver is the only organ for which the formation of urea has been experimentally proved; (3) the urea may derivate also from dissociation of other nitrogenous compounds, as, for example, arginin.

Though all nitrogenous foodstuffs which are decomposed in a given animal do not give rise, however, to the production of urea, this principle may be considered as the main nitrogenous product of tissue katabolism, at least in man and mammalians, and therefore it is a substance entirely physiological to the animal body.

In the present article I will endeavor to expose the experimental basis upon which it is possible to establish that, in the common conditions of human life, a part of the urea, as small as it may be, proceeds directly from the intestinal putrefaction; that is to say, it is the product of chemical transformations which takes place outside of the normal tissue katabolism. This part of the urinary urea must receive the name of extraphysiological or *putrefactive* urea. In the sick man, especially in the diabetic, the putrefactive urea increases enormously and plays an essential part in the pathogeny of the malady.

If a solution of an ammoniacal salt of a volatile or inferior fatty acid is introduced into the rectum and its entire absorption permitted the result to be observed is that the twenty-four hours, amount of urea increases. This hyperexcretion of urea is accompanied by two interesting phenomena when butyrate of ammonia is the employed salt. The twenty-four hours' urinary volume increases (polyuria) and the excreted acetone greatly augments upon the normal proportions (acetonuria). If the rectal injections are continued for many days the polyuria and the acetonuria reach a high degree.

One of the experiments has been carried out on a subject specially selected in order that the pharmacological influence of the salt could reach the strongest effect with the least quantity used. The person referred to is a female, weighs 45 kilos, lives in the tropical and Atlantic region (Caracas, Venezuela), and is submitted to a

uniform vegetarian diet very poor in nitrogen. The experiment has been divided into two series: the first series has been preceded by a preparatory period of the same diet. During the second series rectal injections of a watery solution of butyrate of ammonia have been used: 50 c.c. the first two days, 75 c.c. the two following, and 100 c.c. the rest of the series. The proportion of ammonia is exactly determined (3.825 grams NH_3 for 100 c.c.) and pure butyric acid (19.8 $C_4H_8O_2$ for 100 c.c.) is added until neutralization takes place; the rosolic acid has been employed as indicator. The daily quantity is diluted four or five times with water and fractionally injected. The quantitative estimation of the various urinary elements has been made as accurately as possible, employing the most reliable methods. The urinary volume has been determined by weight and density, the pipettes and flasks being graduated at the laboratory temperature (24° C.). For the quantitative estimation of the urea the slightly modified method of S. R. Benedict and F. Gephart[1] has been employed: The urine mixed to its own volume of diluted HCl (1 to 4) has been submitted in autoclave to a pressure of 6 atmospheres (150° to 155° C.), during one and a half hours. The resulting ammonia has been determined by the Krüger-Reich-Schittenhelm[2] method, and the preformed ammonia has been substracted. The uric acid has been estimated by the E. Wörner[3] method: the precipitated urate of ammonia dissolved into a watery solution of caustic soda is placed on a water bath to drive out the ammonia. The remaining nitrogen has been finally determined by the well-known Kjeldahl method. The acetone by the Huppert-Messinger[4] method, and on account of necessary comparative estimations for other purposes the volatile fatty acid has been evaluated by the Strauss-Philippsohn method. The obtained analytical results are condensed in the following table:[5]

First Series. Normal Condition.

Days.	Volume. c.c.	NH_3 gm.	Total N. gm.	Urea. gm.	Uric acid. gm.	Acetone. mg.	Hepatic coefficient. per 100.
1st . . .	1235	0.610	6.003	9.687	0.345	7.0	75.0
2d . . .	1344	0.635	6.523	11.068	0.411	5.0	79.0
3d . . .	1255	0.476	6.036	10.629	0.361	8.0	77.0
4th . . .	1251	0.540	5.827	10.511	0.385	3.0	84.0
5th . . .	1460	0.613	6.428	11.443	0.415	3.0	82.0
6th . . .	1154	0.498	5.722	9.743	0.342	9.0	79.0
7th . . .	1422	0.541	6.645	10.772	0.388	5.0	75.0
Averages	1303	0.559	6.169	10.5504	0.378	5.7	78.7

[1] Jour. of Am. Chem. Soc., xxx, 1760.

[2] Abderhalden, E., Physiologisches Praktikum, Berlin, 1912, p. 130.

[3] Hoppe-Seyler's Handbuch der physiol- und pathol- chemischen Analyse, Berlin, 1903, pp. 448–449.

[4] Strauss, H., and Philippsohn, H., Zeitschr. f. klin. Med., xi, 369.

[5] Delgado Palacios, G., Chimie pathologique tropicale de la région atlantique. Caracas. Lit. y Tip. del Comercio, pp. 219–293, 238, 103–125, 116.

SECOND SERIES. ACTION OF BUTYRATE OF AMMONIA.

Days.	Volume. c.c.	NH_3. gm.	Total N. gm.	Urea. gm.	Uric acid. gm.	Acetone. mg.	Hepatic coefficient. per 100.
1st	1816	0.581	7.753	13.442	0.365	84	80.7
2d	1858	0.411	8.122	14.989	0.410	108	85.9
3d	1928	0.404	8.501	16.701	0.328	132	91.5
4th	2304	0.405	8.533	17.344	0.321	149	94.7
5th	2905	0.362	8.956	17.545	0.344	202	91.2
6th	3044	0.392	9.008	18.042	0.309	235	93.3
7th	2525	0.663	8.898	16.938	0.486	245	88.7
Averages	2340	0.4597	8.538	16.428	0.366	165	89.4

I have already pointed out why the physiologically produced urea in this person is so small, namely, an average of 10.5 gm. with a corresponding volume of 1300 c.c. The greatest excess of urea which has been synthetized by the liver, namely, 8 gm., has developed a very powerful diuretic action. It is interesting to note that this person with a total amount 18 gm. urea has excreted 3 liters of urine, which has the physical appearance of diabetic urine, while it is of common occurrence that the majority of persons with this quantity of urea do not excrete more than half a volume. In all my experiments with a starting physiological amount of urea double this one the butyrate of ammonia has had the same diuretic effect, but not so marked as in this case.

The diuretic action of urea is a constant experimental fact, and all the authors admit it. The increase of acetone or iodoform giving compounds upon the normal deserves, in this case, a closer exaplanation. All authors agree in accepting that the volatile fatty acids, when ingested under certain conditions, are completely oxidized in the body, except in case they contain some inorganic radicle. Otto Porges'[6] memoir on the subject may be quoted as a standard monograph upon the destruction of fatty acids in the organism. When butyrate of ammonia is ingested this salt is transformed into urea and butyrate of sodium, which is totally destroyed by oxidation in the body. If the same salt is absorbed through the rectal mucous membrane it arrives immediately at the liver, where the hepatic cell changes it into urea and butyric acid, with the production of a little quantity of acetone. This last transformation has been realized by G. Embden[7] and his collaborators when they made the artificial irrigation of the liver with blood containing substances capable of giving acetone (acetogenic substances), the butyric acid being the principal between them, and certain of its derivatives. The same production of acetone has been carried out on diabetics by making them ingest acetogenic compounds.

[6] Ueber den Abbau der Fettsaüren im Organismus, Asher u. Spiro, Ergebnisse der Physiologie, 1910, p. 8.

[7] Hofmeister's Beiträge, 1904, vi, 59; Embden, G., and Karberlah, F., Hofmeister's Beiträge, 1906, xxx, 120; Embden, G., Salomon, H., and Schmidt, Fr., Hofmeister's Beiträge, viii, 129.

In this case the real interpretation of observed facts deserves a long explanation which space will not permit. Those interested in the subject may read the chapter Diabetic Pathogeny in a book I have published with the title *Tropical Pathological Chemistry* of the Atlantic region.[8]

From the experiment already referred to and others not quoted, easy to be conducted in man, we are right in concluding that the large intestine absorption of butyrate of ammonia produces the increased excretion of urea, acetone, and urinary volume. All the effects here observed, no doubt, are referable to the chemical nature of the employed salt and the way of introduction.

These premises well established, the question which now arises in the mind is whether or not in the common conditions of human life the intestinal putrefaction which constantly occurs from birth to death does or does not produce more or less abundant quantities of ammonia and volatile fatty acids, whose reabsorption would produce the formation of urea and acetone of putrefactive or extraphysiological origin. Before describing the method I have employed to verify the production and absorption of remarkable amounts of amoniacal salts of volatile fatty acids, it may be well to give a short exposition upon the nature and intensity of the chemical and bacterial phenomena which occur in the large intestine.

The intestinal flora which grows in the intestinal contents unfolds there with such a colossal development that more than 25 per cent. of the total organic matter of the feces are composed of bacterial residue. This intense bacterial life renovates incessantly. On the one hand the foodstuffs and the various excretions from the body through the gastro-intestinal tract bring the necessary aliment to its growth, and on the other the defensive forces of the intestinal mucous membrane and the noxious or antagonistic influences that certain groups of bacteria exercise upon others check this development. These conditions explain how a large proportion of dead bacterial matter may be excreted with the feces every twenty-four hours, as the fact has been evidenced by the Schmidt-Strasburger weight method: 5.3 grams of pure bacterial residue, or more than one hundred billions bacteria (calculated as Bacillus coli commune), are excreted daily.

In the small and large intestines the bacterial life exhibits great differences. While the small intestinal contents suffer the acid fermentation of the carbohydrates, it is five times more richer in water and travels with twenty-five times more rapidity than the large intestinal contents, a true normal fecal stasis taking place in the last portions of the alimentary canal. The matter becomes more and more poor in water and oxygen as a consequence of the

[8] Palacios, Loc cit.

absorption and powerful albuminous putrefaction, which commonly give it the alkaline reaction on account of the production of ammonia.

The intestinal contents have been studied chemically by various physiologists. Edwald,[9] Baumann,[10] MacFadyen, Nencki and Sieber[11] and others have made particular researches in the human intestine. The chemical composition of the small and large intestines differs in the same way as the bacteriological and physiological conditions referred to. The intestinal contents, as it has been collected through an artificial anus established at the distal end of the ileum, presents the following characteristics as they were observed by the last three authors named: the reaction was constantly acid, owing to the presence of organic acids, and notably of acetic acid. Other acids that were present were lactic, paralactic, various fatty acids, succinic, and the biliary acids. The odor but rarely suggested the existence of putrefactive changes. Indol, skatol, and phenol could not be demonstrated. Leucin and tyrosin were not found. Alcohol could always be demonstrated. Of gases, carbon dioxide was observed, and also faint traces of hydrogen sulphide, while methylmercaptan was absent. All these products of fermentation, as well as those originating from the normal action of digestive ferments, are completely oxidized and utilized for nutritive purposes.

In the large intestine, on the contrary, appear various products of the true albuminous putrefaction. The normal products of the digestive and fermentative proteolysis suffer the putrefactive degradation, and the resulting end-products, entirely abnormal in its origin and physiological character, are in greatest part eliminated with the feces or absorbed. It seems to be the biological law that all these products are not assimilated nor in any way utilized by the organisms. They are by their own nature or origin noxious or have toxic properties, and the organism, principally through the agency of its great antitoxic or defensive organ, the liver, tend to convert them into harmless substances as completely as possible. The putrefactive bacteria act on the various constructive stones of proteins, the amino-acids, following certain general chemical processes. The tryptophane or indol-amino-propionic acid, by the action of anaërobic bacteria, loses its amino (NH_2) group as NH_3. After this has been done other bacteria, endowed with some aërobic character, oxidize the remaining side chains, yielding carbonic acid and water. The residual indol or skatol is absorbed into the blood and reappears in the urine as indoxyl or skatoxyl in combina-

[9] Ueber das Verhalten des Fistelsekretes, etc. Virchow's Archiv, vol. lxxv.

[10] Die aromatischen Verbindunges im Harn und die Darmfäulniss, Zeitschr. f. physiol. Chem., vol. x.

[11] Ueber die chem. Vorgänge im menschl. Dünndarm, Arch. f. exp. Path. u. Pharm., vol. xxviii.

tion with sulphuric acid and alkalies as conjugated sulphates. The relative proportions in which these heterocyclic compounds appear in the urine depend upon the class of acting bacteria. According to Herter the Bacillus coli commune can produce indol under certain conditions and traces of skatol, while certain putrefactive bacteria produce this last substance in great abundance. According to the same author the indolacetic acid, another putrefactive or degradation product of tryptophane, is the chromogen of urorosein. Staal, Grosser, Porcher, and Hervieux believe that red skatol and urorosein are identical. Reasoning along these lines it is conceivable that, corresponding to a more remarkable change in the intestinal bacterial flora, other coloring matters may appear in the urine, as this has been observed, as a matter of fact, in the tropical and Atlantic region, where urorosein is replaced by cholerythrin.[12] Analogous transformations take place with other split products of protein. The tyrosin and phenylalanin, after having been desamided by the action of putrefactive bacteria losing ammonia, give various aromatic acids, phenol and cresol, and a small proportion of polyphenols. All these products are eliminated in the urine in the native state or in combination with sulphuric acid, glycocol or other compounds. Finally, leucin, butalanin, alanin, glycocol, asparaginic acid, glutaminic acid, and other non-aromatic amino-acids lose equally ammonia, and give rise in the intestine to various volatile fatty acids, such as capronic, valerianic, butyric, propionic, acetic, succinic, and glutaric acids. A certain part of these absorbed fatty acids may appear in the urine, increasing its amount of volatile acids only when they are absorbed in combination with the calcium, as the fact has been experimentally established.[13] Otherwise they are oxidized and destroyed. The butyric acid, which may be considered as an anaërobic and putrefactive product of the fatty amino-acids, and certain of its superior homologous derivatives yield acetone when they pass through the liver in combination with the ammonium, as the fact has been also established experimentally.

As has been summarily explained above, the production of putrefactive ammonia is a phenomenon of universal occurrence in the human large intestine. It is closely related to the formation of other putrefactive products, which are also absorbed into the blood, transformed by the liver, and excreted in the urine. As a matter of fact the presence of ammonia in the large intestinal contents has been verified by all investigators after the first Brauneck[14] researches. Therefore it is a reasonable and scientific hypothesis, in accordance with all our knowledge upon physiological

[12] Delgado Palacios, G., Why Yellow Fever is Endemic in the Tropical and Atlantic Region, Medical Record, July 25, 1914.

[13] Palacios, loc. cit.

[14] Brauneck, Mitteilungen aus der med. Klinik zu Würzburg, vol. ii.

and chemical phenomena, this reabsorption of putrefactive ammonia and its transformation into urea. If the formation of putrefactive urea really occurs in the common conditions of life, it must be accompanied by the production and excretion in the urine of a corresponding amount of acetone, the two substances originating from the same biochemical transformation, as the above experiment suggests. The two phenomena are, however, by no means indissoluble, because other ammoniacal salts of putrefactive origin may be transformed into urea without the production of acetone, such as acetate or propionate of ammonia, and others.

The quantitative estimation of ammonia in the feces has been rarely performed. Schmidt and Strasburger[15] in their fundamental work upon chemical and bacteriological composition of human feces do not mention any quantitative estimation of this substance. This may be explained by the fact that the intestinal ammonia is generally considered as an obliged phenomenon of the intestinal putrefaction without importance and intended to be eliminated in the feces. I have made quantitative estimations of fecal ammonia on many occasions. I shall only quote here those estimations which I have performed with the purpose of establishing the reabsorption of ammonia in the large intestine. The estimations have been made by two methods at the same time, the formol titration and the Krüger-Reich-Schittenhelm method. The figures obtained by the two methods are nearly equal in every case, and therefore may be accepted as reliable. The following table shows the amounts of ammonia and volatile acids obtained in those persons who were submitted to the comparative experiment:

Names.	Feces weight. gm.	Ammonia. gm.	Volatile acids n 10. c.c.
A. C.	85.5	0.0756	89.8
L. E.	144.2	0.1485	81.3
B. de T.	121.2	0.1108	139.7
P. A.	90.6	0.0539	60.8
R.	169.2	0.1900	100.3

The method I have employed to establish that ammoniacal salts of volatile fatty acids of putrefactive origin are effectively absorbed in the large intestine is founded upon the action of saline and drastic purgatives. It is well known that the first ones are absorbed in the stomach and first portion of the small intestine and afterward are excreted through the large intestinal mucous membrane. The second class of purgatives pass along the gastro-intestinal canal and appear to operate more especially by a mechanical and irritative action. The special precaution has been taken to receive into ice the watery evacuations so as to prevent the

[15] Die Fäzes des Menschen, Berlin, 1910, p. 228.

ulterior putrefactive fermentation. The following table shows the results obtained in the same persons by the use of saline purgatives:

Names.	Feces weight. gm.	Ammonia. gm.	Volatile acids n/10. c.c.
A. C.	933.4	0.1433	215.5
L. E.	881.9	0.1734	
B. de T. . . .	1038.4	0.2124	252.4
P. A.	431.0	0.1223	155.6
R.	1213.5	0.2734	290.1

The drastic purgatives have produced a more pronounced action in the same individuals:

Names.	Feces weight. gm.	Ammonia. gm.	Volatile acids n/10. c.c.
B. de T. . . .	514.9	0.3167	452.0
P. A.	529.0	0.1521	184.3
R.	898.3	0.3167	552.0

These experimental researches prove evidently that there is present in the large intestine, in a given moment or during a certain time, a greater amount of ammonia and volatile fatty acids than the quantity which goes out with the feces every twenty-four hours. The differences reach easily 100 milligrams and more; and it is greater for the fatty acids.

Although these figures are quite remarkable, there are many reasons to believe that they are really greater. The production and absorption of fecal ammonia are continual and concomitant phenomena. When the intestinal contents pass the Bauhin valve and enter the large intestine the matter suffers the ammoniacal putrefaction and is five times more rich in water than when it goes out. The purgative surprises the matter as it is contained in the large intestine, in a given moment, and carries it away. Hence it is easy to infer that the drastic evacuation, although less rich in water and weight, contains a greater proportion of ammonia than the saline evacuation, as the reported figures demonstrate. The ammonia which is violently expelled through the agency of the purgatives corresponds to the ammonia produced during the time of their action, eight hours more or less, that is to say, three times smaller than the twenty-four hours' produced ammonia. And this evaluation manifestly represents a minimum, because very probably the purgative action interferes with the ammoniacal putrefaction, and the production of this substance is less pronounced than when the matter is quietly left to its anaërobic stagnation and putrefaction. The amount which is quantitative estimated in the feces represents only the residue which has not been absorbed. The difference between the two quantities corresponds to the amount which would be absorbed, in the supposition that the purgative would not have interfered with the intestinal putrefaction,

and that normal conditions of the intestinal contents would have been the same.

In the purgative evacuations from mellitus or insipidus diabetics I have determined a greater quantity of ammonia than in the normal condition. The amount of volatile fatty acids by the same method reach enormous figures in the same diseases. In these patients a greater proportion of volatile fatty acids has been also verified in the urine. I cannot explain in detail why, in these patients, the volatile fatty acids increase in so large amounts in the urine, while they do not augment above the normal when they are introduced directly into the rectum in combination with the ammonium as in the experiment refered to. I can only say that this depends upon their combination with the calcium, and that I have obtained experimentally this augmentation.[16]

The fecal reabsorption of volatile fatty acids is a known and admitted fact for a long time, and has been verified in man by the same direct method, that is, the action of drastic purgatives. Schmidt and Strasburger[17] says: "In the same person it has been possible to establish that during a three days' constipation (through voluntary checking of the urging to stool) the amounts of volatile fatty acids diminish in the feces, while the quantity of the same acids in castor-oil evacuations becomes three times larger. The observed difference proceeds evidently from quantitative changes of the fecal reabsorption." On the other hand, H. Strauss and H. Philippsohn,[18] by means of their method of estimating volatile fatty acids in the urine, have obtained the highest value in constipation comparatively with the normal condition.

The conclusion may be drawn, from the above experiments and those of other investigators, that it is scientifically correct to establish that, in the common conditions of human life and in normal subjects, a minimum of 300 mg. of ammonia is produced every twenty-four hours in the large intestine as a result of putrefactive processes; in some cases this quantity has amounted to twice as much (case B. de T.); and that this ammonia, after having been absorbed into the blood, appears in the urine as a minimum of 0.5 gram and even 1 gram of putrefactive urea. To this daily amount of putrefactive urea corresponds normally the production of several milligrams of acetone.

I cannot enter, in the present article, into all the details that this great question of putrefactive urea requires to be scientifically criticised and to be put in accord with all admitted physiological and pathological facts. I can only say that the phenomenon of putrefactive urea is not in contradiction with our knowledge on nutrition researches. The fact may have passed unnoticed even

[16] Palacios, loc. cit.
[17] Loc. cit.
[18] Neubauer-Huppert, Analyse des Harns, Wiesbaden, 1910, p. 190.

in the most strict nutritive balances. The comparison between the three values, fecal nitrogen, urinary nitrogen, and alimentary nitrogen, may have been realized without the putrefactive urea phenomenon being disclosed.

The production of acetone in the animal body is a question which actually is too far from its definitive solution. The experimental researches of Embden and his collaborators closely relates this production to butyric acid and some other simple compounds. But from what classes of substances or processes this butyric acid or compounds proceed is not known at present. Various physiologists believe that the destruction of proteins is the principal source of acetone; others attribute their origin to fat destruction. A well-observed fact is the counteraction of carbohydrares upon the production of acetone (anticetoplastic action) and also the constant increase of this substance in man during fast. The scientific criticism of all these questions would lengthen the present article beyond its proper scope; but all these facts and hypotheses may find, in the production of putrefactive acetone, a new and satisfactory explanation. The production of a small amount of acetone in the normal state, intimately related with the production of a certain amount of putrefactive urea, can receive from this conception an entirely more satisfactory explanation than its doubtful and obscure nutritive origin.

I hope the present ideas, founded on experiments carried out on man and corresponding to the common conditions of human life, will be of great importance to physiology and pathology. It would be also very satisfactory to the author to have laboratory men confirm the described experiments.

REVIEWS

A Text-book of Pathology. For Students of Medicine. By J. George Adami, M.A., M.D., F.R.S., Strathcona Professor of Pathology, McGill University, and Advisory Pathologist to the Montreal General and Royal Victoria Hospitals, and John McCrae, M.D., M.R.C.P., Lecturer in Pathology and Clinical Medicine, McGill University, Montreal, etc.; Senior Assistant Physician, Royal Victoria Hospital. Second edition, revised and enlarged; pp. 878; illustrated with 395 engravings and 13 colored plates. Philadelphia and New York: Lea & Febiger, 1914.

The new edition of this work needs no introduction to the medical profession. Adequate proof of this is to be seen in the reception that was accorded the previous edition. There are a few changes and modifications in the text, and several important additions containing the results of recent work on cellular activity and bacterial endotoxins have been added. The syllabus at the beginning of each chapter aids in reference, and many new and excellent colored plates and illustrations have been inserted.

The introductory chapter on the cell as the basis of pathology gives a very concise statement of our present knowledge of the principles underlying the structure, physiology, chemistry, and growth of the cell and its relation to the other cells composing the living organism. Considerable stress is laid upon the more recent work of Vaughan and Abderhalden on the bacterial endotoxins and the part that the specific enzymes produced by the body cells and acting upon the bacteria play in the production both of specific symptoms of a given disease and of anaphylactic shock.

It is interesting to note that the old controversy as to the pathogenic streptococci bids fair to be settled by Rosenow's recent work, in proving that a particular strain of streptococcus may be so modified by growth as to react similarly to pneumococcus, S. rheumaticus, etc.

In writing on the gastro-intestinal tract, the authors emphasize the fact that "auto-intoxication" is a "stupid misnomer" for the symptoms arising in cases of chronic constipation in which there is not the slightest evidence of indol production either by the tissue cells or digestive juices, but which usually arise from absorption of toxins produced by a low grade intestinal infection.

A new classification of neoplasm based on histogenetic principles is advocated. The more common classifications, according to histological characteristics, are held to be less scientific, because a large proportion of new growths, and clinically the most important of them, possess the character not of fully formed tissue elements but resemble one or other stages in the development of one or other tissue. Another advantage is that it tends to give the student a clearer conception of the nature of the different neoplasms, and of their derivation from the various primary germinal layers.

The authors apparently accept Mallory's views as to the morphology of the leukemias. They are classed among the atypical blastomas.

In treating nephritis, the authors use a very simple classification, because clinical observations on the basis of albumin, casts, and edema are so often at variance with pathological findings. "In the present state of our knowledge it is not often safe to predict what kind of kidney is going to be found in any given case. We have some admiration for a certain pathologist of eminence whose pathological diagnosis rests content with the simple statement that the kidneys indicate Bright's disease."

The volume is written in a style so simple and clear that, aside from its worth as a text-book, its perusal is a distinct pleasure, and it will be found of equal value to the practising physician as to the student of pathology. P. McC. K.

Case Histories in Obstetrics. By Robert L. Denormandie, A.B., M.D., Associate in Obstetrics, Harvard Medical School; Physician to Out-Patients, Boston Lying-in Hospital, Pp. 516. Boston: W. M. Leonard, 1914.

This work represents a recent addition to this now well-known series by a group of Boston authors. The increasing popularity of books of this nature is significant of the value of teaching medical subjects by example, as in clinical conference rather than by didactic lectures. In the volume under consideration the author has detailed the histories of seventy-three cases, each of which serves as a paradigm to illustrate some essential problem in obstetrics. When one recalls the clinical dissimilarities in a group of cases of sepsis or eclampsia, all of which must be classed under the general diagnosis of that group, it would appear that too few cases have been described. This seeming deficiency has been overcome by the addition to each section of a summary in which the principle in question is discussed at some length, the nature and presence of indications governing operative interference brought out, the prognosis and treatment reviewed, and finally the conclusions to

be drawn from the whole section stated. Collectively the summaries form a valuable compend of practical obstetrics.

By a logical arrangement of the twenty-eight sections the reader follows the child-bearing process from the diagnosis of pregnancy through normal pregnancy, labor, and the puerperium, and then takes up the abnormalities and complications of each period. There are also sections devoted to scopolamin-morphin anesthesia in labor, the use of hydrostatic dilating bags, puerperal insanity, and the care of the baby.

The book should be of value to the practitioner by stimulating him to a critical reviewing of his own cases, methods, and results; and to the student in the opportunity offered to consider the origin of indications for operations and the well-advised management of typical obstetrical cases. P. F. W.

A Clinical Study of the Serous and Purulent Diseases of the Labyrinth. By Dr. Erich Ruttin, Privatdocent in the Otological Clinic, University of Vienna. Authorized translation by Horace Newhart, A.B., M.D. Pp. 232; 25 illustrations. New York: Rebman Company, 1914.

To those who have studied under and admired the work of Dr. Ruttin in the Vienna Clinic this work will be most welcome, the more so since it is only the second complete work on the labyrinth in English. This work, as stated in the foreword by Prof. Dr. Urbantschitsh, is a presentation of the present position of that great school on the questions which are not yet thoroughly worked out or free from dispute. Unlike the other work mentioned above, Dr. Ruttin takes for granted that his readers are sufficiently advanced in the study of otology to know the normal anatomy and physiology of the labyrinth, and therefore opens his subject with the functional examination of the ear. The whole subject is treated in a very concise and brief manner; too brief and concise to be of great help to one who has not previously studied the subject, or, on the other hand, to one who has studied it deeply. For instance, but two pages are given to the examination of the cochlear function, and no definite instructions are given for making the tests or interpreting them. The work is evidently the result of the author's own experience and studies, and the only labyrinth operation mentioned is his own modification of Neumann's. Over half of the book is taken up with case histories, 108 in number, which are given in considerable detail, and which are well worth close study. The book is well illustrated, and, though written in the characteristic German style, will be of great value to otologists.

G. M. C.

The Ileocecal Valve. By A. H. Rutherford, M.D. (Edin.) Pp. 62; 44 illustrations. New York: Paul B. Hoeber, 1914.

The contents of this book constitutes a thesis for the M.D. degree submitted to the University of Edinburgh. Its chief interest and value concerns observations on a case with an artificial anus in the cecum 8 centimeters long, through which the ileocecal valve could be seen from time to time and carefully studied. The literature of the subject is reviewed, the valve studied in the dog and in thirty-two human specimens hardened in formalin. An excellent half-tone photographic illustration of each of the thirty-two human specimens is presented, the other illustrations also being good. It is interesting to learn that in addition to preventing regurgitation of feces from the large into the small bowel, the ileocecal valve has a sphincter action like that of the pylorus and internal anal sphincter to regulate the flow of semifluid feces from the small to the large bowel. Of more practical interest is the probability that enemata act not only as a foreign body, but as a stimulus to the peristalsis not only of the large intestine but also of the small intestine. The book is a valuable contribution to the literature. T. T. T.

Local and Regional Anesthesia. By Carroll W. Allen, M.D., Instructor in Clinical Surgery in Tulane University. Pp. 625; 255 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

The ever enlarging field which is the subject of this volume is here treated in a thorough and efficient manner. Not only has the author given his readers a clear conception of the methods by which local analgesia may be obtained, but he has given them as well, in the first part of the book, an excellent summary of our knowledge of the character, uses, and relative value of the various substances which have been introduced from time to time for the purpose of producing anesthesia in limited areas of the body. Not the least valuable section of this portion of the book is that which deals with the relative toxicity of anesthetizing agents.

The greater part of the book deals with the methods of securing anesthesia in different parts of the body. The location of the nerve carrying sensory impulses is described in great detail, together with the method of reaching them with the anesthetizing needle. The descriptions are of a character which should enable the average surgeon to perform the operations in question with but little difficulty, provided he has the requisite gentleness and is willing to pay attention to detail.

Spinal analgesia and epidural injections of anesthetic agents are described, but receive less attention than does the use of peripheral injections; the comparatively recently introduced and as yet little used paravertebral anesthesia likewise receives brief consideration. For use in the spinal canal the author seems to favor the use of solutions of high specific gravity as being more easily controlled and more reliable in their movements within the canal than those of lower concentration than the cerebrospinal fluid; glucose is recommended as the means of securing this condition.

While many procedures are described which would probably not be used except by men who have had special experience in this kind of work, the general tone of the work is one of conservatism, and caution is given against attempting certain operations under the influence of a local anesthetic, as those for extensive malignant disease.

It has evidently been the author's intention to write a book which would serve as a reference volume rather than a hand-book of condensed information. In this effort he may have erred in the way of quoting too extensively from his sources of information (experimental investigations, etc.) instead of merely summarizing and giving his conclusions and individual opinions; those of his readers who are in search of ready information, and are content to trust the judgment of one with special experience rather than to make their own deductions, would have appreciated the addition of such summaries in certain instances. Yet when a sufficiently comprehensive view is taken of the work all doubt as to the author's position on the majority of these subjects disappears. S. W. M.

Local Anesthesia. By Dr. Arthur Schlesinger, Berlin. Translated by F. S. Arnold, B.A., M.B., B.Ch. (Oxon.) Pp. 202; 22 illustrations. New York: Rebman Company.

The field for local anesthesia has been greatly widened in recent years and the contributions on the subject have been numerous and valuable. Only recently has it begun to appear in the clinical curriculum, so that most men in general practice are not familiar with the newer and better methods. This book will acquaint them with these methods and their technique. A chapter on the history of ths subject shows how many methods have been used and abandoned and which have prevailed. It is predicted that Bier's venous anesthesia is likely soon to displace other methods in major operations on the large joints and on the large tubular bones of the extremities. The commanding position attained by novocain among general surgeons is emphasized, and that the right of the

patient to a painless operation requires that the risks of general anesthesia should not be unduly exaggerated in favor of local. Most physicians will find it advantageous to familiarize themselves with the newer methods of inducing local anesthesia, and will find this book well adapted for the purpose. T. T. T.

Clinical Examination of the Blood and its Technique. By Professor A. Pappenheim, Berlin. Translated and adapted from the German by R. Donaldson, M.A., M.B., Ch.B., F.R.C.S. (Edin.), D.P.H., Pathologist to Royal Berks Hospital, Reading; late Assistant Pathologist Royal Infirmary, Bristol, and Demonstrator of Pathology, Universities of Bristol and Sheffield. Pp. 87; 5 illustrations. New York: William Wood & Company, 1914.

This small book, by one of the most noted hematologists, first appeared in 1911 as a chapter in Carl Neuberg's *Handbuch der Ausscheidungen und Körperflüssigkeiten*. It was later in the same year published in book form in the German, and is now presented to us in English with minor alterations to conform to the more recent publications of the author. It is essentially a manual for students and practitioners, and deals only with those things which are of primary importance in clinical methods of blood examination: staining, counting of cells, and hemoglobin estimation. The respective features of normal blood and those facts in the semiology which explain pathological blood pictures are described briefly and yet clearly. Two very helpful colored plates of normal and pathological blood cells are introduced. The index is quite exhaustive. The book is a brief summary of the important practical things known about the blood at the present time, and as such it may be highly recommended. T. G. M.

Diseases of Infancy and Childhood and their Dietetic, Hygienic and Medical Treatment. By Louis Fischer, M.D., Attending Physician to the Willard Parker and Riverside Hospitals, New York City; Attending Pediatrist to the Sydenham Hospital, etc. Fifth edition. Pp. 935; 301 illustrations and 43 plates. Philadelphia: F. A. Davis Co., 1914.

The chief impression after reading this book is the wonder that such a mediocre production, to say the most, should have reached a fifth edition within eight years. To mention but a few of the

many defects of the book, we find that the classification, that much debated point, does not admit even the few facts which are generally recognized; that etiology, pathology, and symptomatology are illogically mixed; that the same diseases are described under different headings; that there is a widespread reversion to old fashioned subdivision and nomenclature of diseases, for example: cerebral pneumonia, diphtheroid, pseudo-appendicitis, lithemia, and so on; that most of the literature quoted likewise belongs to the distant past with a curious avoidance of many of the best authorities; and finally that the accounts of many diseases are by no means accurate or entirely trustworthy.

The articles on the acute exanthemata and diphtheria are the best in the book and give evidence of the author's wide experience with these diseases. The appendix contains much information of a practical nature, such as common laboratory technique, dietetics, local remedies, etc., which, coupled with the fact that diseases of all the special organs are considered, makes a book with a wide range and consequent strong appeal to the practitioner.

J. C. G.

The Tonsils; Faucial, Lingual, and Pharyngeal, with Some Account of the Posterior and Lateral Pharyngeal Nodules. By Harry A. Barnes, M.D., Instructor in Laryngology, Harvard Medical School; Surgeon in the Department for Diseases of the Nose and Throat, Boston Dispensary; Assistant Laryngologist, Massachusetts General Hospital. Pp. 143; illustrated. St. Louis: C. V. Mosby Company, 1914.

This book, devoted solely to the tonsillar tissues, consists of 143 rather small pages of printed matter and numerous full-page illustrations, and covers the whole subject from embryology to the various methods of operating. It is not sufficiently detailed, however, to make it the last word on the subject of the tonsils, and the lack of systematic bibliography deprives it of some value as a book of reference. For the student and for the general practitioner it is exceedingly good, giving in a concise form the important facts concerning the tonsil. The embryology, anatomy, and the physiology are well dealt with, and show that the author's knowledge has been gained from actual experience as well as from literature. While, on the whole, the representations are trustworthy and agree with the general view of these structures, we do find a few dogmatic statements to which we must take exception; such as the author's conception that the lymph follicles of the posterior pharyngeal wall "can never be considered normal structures in the mucosa,"

and again we read "chronic abscess formation in the parenchyma of the tonsil is not uncommon."

The reproduction of the photomicrographs are good and clear, and the drawings illustrative of operative technique are even more elaborate than is absolutely necessary. G. B. W.

Die Immunitätswissenschaft. Eine Kurz Gefasste Ubersicht über die Biologische Therapie und Diagnostik für Aerzte und Studierende. Von Dr. Hans Much. Oberarzt am Effendorfer Krankenhause. Second completely revised edition. Pp. 286; 6 plates, 7 figures and many tables in the text. Würzburg: Curt Habitzsch, 1914.

This work presents in brief form our present knowledge of the principles of immunity and their practical applications to diagnosis and treatment. Theoretical discussion is in the main avoided and bibliographical references are not given.

To the general principles of immunity and virulence, including anaphylaxis, 128 pages are devoted, and to immunological diagnostic reactions 85 pages. A few pages are devoted to chemotherapy, and the work closes with a chapter of 67 pages devoted to the application of the principles of immunity to specific diseases. In this last chapter a wide range of diseases of both man and animals, of bacterial and protozoan origin, are discussed as well as the application of immunity to the study of tumors. The up-to-date character of the revision is shown by the inclusion of an account of Abderhalden's protective enzyme methods and a reference to Friedmann's turtle bacillus treatment of tuberculosis. Descriptions of technique are numerous and complete. Excellent colored plates illustrate the opsonic-index method and the tuberculin and Wassermann reactions. R. M. P.

Dreams and Myths. By Karl Abrahams, M.D., Berlin. Translated by William A. White, M.D., Washington. Pp. 74. New York: The Journal of Nervous and Mental Disease Publishing Co.

To those who have followed step by step the development of Freud's ideas, and those of the followers, Jung and Bleuler, this monograph on dreams and myths will appear as further evidence in corroboration of the brilliant work done by this school.

Those who have opposed these theories will find only newer absurdities, inconsistencies, and untruths.

Freud has already shown to a certain degree the psychological analogies between certain folk legends and individual phantasy. The present monograph is an attempt to compare the early myths with the phenomena of dreams. According to the author, certain phases of dream work elaborated by Freud, such as condensation, distortion, displacement, and wish fulfilment may also be noted in the myths, and the author uses the Prometheus saga in illustration.

In all times myths have been a field for speculation. Philosophers found in them a philosophic attribute, religion a moral idea, and now in turn, science seeks its interpretation and finds an answer. Abrahams has logically and clearly found a parallelism between myths and dreams. S. L.

Les Nouveaux Horizons de la Science. By H. Guilleminot, Chef des Travaux de Physique biologique à la Faculté de Médecin; Président de la Société de Radiologie médicale de Paris. Pp. 429; 55 illustrations. Paris: G. Steinheil, 1914.

The present volume, which is the third in this series of scientific publications, concerns itself with the science of living matter, especially with chemistry and morphology. In the first fifty pages the author reviews briefly the contents of the first two volumes, devoted chiefly to physics and electricity. The first half of the present volumes covers organic chemistry and the principles of metabolism, while the second half is occupied with a briefer discussion of comparative morphology. The book is distinctly not for the layman, and yet will scarcely appeal to one trained in chemistry. For it is not only not systematic but also fails of being complete. If one desires to familiarize himself with scientific French and increase his vocabulary, no book could be more satisfactory, for it is well written, clearly expressed, and typographically satisfactory. O. H. P. P.

A Doctor's Table Talk. By James Gregory Mumford, M.D., Lecturer on Surgery, Harvard University. Pp. 257. Boston and New York: Houghton Mifflin Co.

These table talks are between an elderly, wide awake country doctor, a city physician of large general and consulting practice and Scriba, the author, who is of course a surgeon. The topics under discussion are of professional and general interest, the three view points offering an abundance of material. The common sense conclusions to which these talks lead are refreshing.

Many topics of interest are threshed out by the "talkers." Among them may be found reference to the specialist, medical research, medical organization, the nurse, resident, and so on.

Lest one feel that all a doctor's interest is in things medical, political, and other questions of recent significance are rehearsed.

This book is one which may well help the physician to regain the right perspective of his life and in other hands may do much to clear up such misapprehension as exists between the medical profession and the people. A. A. H.

Étude Clinique du Sérum Antituberculeux de Vallée. Le Docteur Boureille, Ex-interne de la Maison de Nanterre, Directeur du Preventorium Antituberculeux du Boulevard Garibaldi. Pp. 50. Nemours: Bouloy.

This pamphlet contains a brief discussion of the serum treatment of pulmonary tuberculosis with special reference to Vallée's serum which it is claimed is "antimicrobic, antitoxic and antiendotoxic." The author briefly describes the results of the use of this serum in eight cases of tuberculosis of the lungs and temperature charts are given in full. It is worthy of note that alarming anaphylactic reactions occasionally followed the injections and that the author does not claim that this treatment is a cure for pulmonary tuberculosis, but only that it has a distinctly beneficial influence upon the temperature, weight and general condition in many cases.

O. H. P. P.

The Diseases of Children. By Henry Enos Tuley, M.D., Late Professor of Obstetrics University of Louisville Medical Department. Second edition; pp. 684; 109 illustrations. St. Louis: C. V. Mosby Co.

The book occupies the middle ground between the compend and the more thorough and complete work on pediatrics. In the main, it is a safe guide for the physician who desires the rudimentary knowledge requisite for practice, although the author evidently has not followed current pediatric literature very closely. He is particularly well qualified to speak upon the question of milk production, while the chapters on malaria and pellagra, and the sections on nervous and dermatological diseases possess some merit. As the second edition has been reached, this book must fulfil some useful function. J. C. G.

Applied Pathology in Diagnosis and Treatment. By Julius M. Bernstein, M.B., D.P.H., M.R.C.P., Assistant Physician (late Pathologist) to the West London Hospital. Pp. 395; 5 colored plates; 46 illustrations. London: University of London Press.

This book is designed to present to the practitioner a survey of the methods of the clinical laboratory, their general principles, their value, their interpretation, but not the details of their technique.

To the practical worker in the clinical laboratory the book is of little value; to the practitioner who desires a knowledge of merely the general nature of the various laboratory methods for the diagnosis and treatment of disease and a discussion of the conclusions that may be drawn from the laboratory reports, the book should be of much value.

The subjects considered are the blood, urine, stomach contents, feces, puncture fluids, serology, specific agglutination, complement-fixation and allergic tests, bacterin therapy, serum therapy and chemotherapy. No mention is made of methods for enumerating cells in the spinal fluid nor of the phenolsulphonephthalein test of renal function, both methods of much clinical value. Roentgen-ray studies and renal pyelography are not considered. The author's unqualified recommendation of spleen puncture for diagnostic purposes in splenomegaly will receive condemnation from many. On the whole the author presents the most important and generally accepted views in clear and readable form. J. H. A.

Diseases of the Rectum. By P. Lockhart-Mummery, F.R.C.S., Senior Surgeon to St. Marks Hospital for Cancer; Surgeon to Queen's Hospital for Children, etc. Pp. 343; 102 illustrations. New York: William Wood & Co., 1914.

There is much in this book to commend it to the thoughtful reader. It is full and adequate without being padded, and is well illustrated by original drawings and sketches, mostly the author's own work. In the chapter on examination and diagnosis he gives a full description of the proper method of making a digital examination of the rectum, which, to one to whom it is unfamiliar, is useful knowledge, the application of which would certainly be appreciated by patients. His description of the important method of dilatation of the sphincter is also worthy of note.

On page 277 he draws attention to the fact that the failure to make an early diagnosis of malignant disease of the rectum is largely due to lack of examination on the part of the physician.

The descriptions of the operations for the various troubles are full and comprehensive. This is especially true of hemorrhoids, fistula in ano, and for malignant disease. As to etological factors in abscess about the rectum, he correctly states that only a small percentage are due to tuberculosis. He states that while fistula in ano is common in phthisical patients, it is also true that the great majority of patients with fistula in ano are not tuberculous.

He emphasizes the wisdom of cutting back the skin edges of the incision when operating for fissure and fistula in ano, so as to have no overhanging edges to interfere with drainage, and states that such wounds heal more quickly and leave less scar. Every physician should read the chapter on malignant disease, especially the part starting on page 278: "The early symptoms of cancer of the rectum."

All in all this book is a valuable addition to our shelves, and that it has the virtue of a personal narration of a man of broad experience.

G. G. R.

FOOD PRODUCTS. By HENRY C. SHERMAN, PH.D. Professor of Food Chemistry in Columbia University. Pp. 594; 36 illustrations. New York: MacMillan Co., 1914.

THIS book is devoted to a discussion of the important foods considering in connection with each: (1) its production, preparation for the market, and economical importance; (2) its proximate composition and general food value; (3) questions of sanitation, inspection, and standards of purity; (4) its digestibility and importance in nutrition. To the first of these is devoted in all about one-half the book; to the second, one-fifth; to the third, including chapters on food legislation, about one-fifth; to the fourth, about one-tenth of the book.

A full consideration of the subject of food legislation and inspection in the United States with important related court decisions is given.

The tables showing the composition of the foods include the content of water, protein, fat, carbohydrate, ash, refuse, calcium, phosphorus, iron, excess of acid or base, and caloric value. In addition the percentage of the various amino acids present in certain important proteins is given.

In discussing the nutritive value of the various foods the result of recent scientific investigations of Osborne and Mendel, Stepp, and McCullom and Davis and others are outlined, showing the peculiar value for growth and nutrition of certain fats and proteins and the importance of these in the arranging of dietaries.

The work is liberally supplied with references, and is well indexed.

All references to the chemistry of the foods are of the most elementary type and do not pre-suppose in the reader any considerable familiarity with physiological or organic chemistry. It is a book that can be heartily recommended for the medical student or practitioner as well as for those interested in food sanitation and food economics. J. H. A.

Guiding Principles in Surgical Practice. By Frederick Emil Neef, B.S., M.L., M.D. Pp. 167; 7 charts. New York: Surgery Publishing Company, 1914.

Surgical practice in this monograph refers to the cases operated on and, almost exclusively, to the common clean operations, one chapter being devoted to the treatment of unclean wounds. A logical working outline of the method of conducting a clean operation is given, as well as chapters on general considerations, the preparation for operation, and the post-operative care of the patient. The iodin disinfection of the field of operation is emphasized, preference being given to a combination with a second methyl salicylate solution for cleansing the field of operation, the iodin having been applied the evening before. The writer's preference for anesthol chloroform modified to increase its safety without impairing its anesthetic usefulness is not likely to meet with general approval. With few exceptions the contents of the book will appeal to most surgeons as a good working guide for the performance of most operations. T. T. T.

Golden Rules of Diagnosis and Treatment of Diseases. By Henry A. Cables, B.S., M.D., Professor of Medicine, College of Physicians and Surgeons. Second edition. Pp. 318. St. Louis: C. V. Mosby.

Revised and rewritten in part with the addition of a section on infectious diseases, this second edition is presented. It is found to consist of numbers of medical facts which when grouped by the reader comprise the cardinal symptoms and physical signs of typical diseased conditions. It is offered as a means of ready reference and the goodly number of prescriptions add to its attraction in this respect.

The field of usefulness of the book must be small and if used beyond modest limits has the potentiality of more harm than good, as such conditions as gastric cancer, gastric ulcer and tuberculosis are not reducible to the statement of some dozens of facts.

The section on acute infections is well conceived and not open to like criticism. A. A. H.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLINTON SPRINGS SANATORIUM AND HOSPITAL, CLINTON SPRINGS, NEW YORK.

Case of Diabetes Insipidus.—R. Fitz (*Arch. Int. Med.*, 1914, xv, 706), after reporting in some detail the reports of the first two cases of diabetes insipidus published, reports a case which has been under his personal observation, and particularly by reason of the fact that the application of the modern studies in renal function may throw considerable light upon the condition. The Wassermann reaction on the patient's blood serum was positive but negative in the spinal fluid. All of the modern tests for renal function were carefully carried out on the case. The author concludes that the original definition given by Frank still holds good, namely that diabetes insipidus is a long-continued, abnormally increased secretion of non-saccharine urine which is not caused by a diseased condition of the kidneys. There are three theories at present in vogue to explain the condition: (1) that it is due to faulty concentration power on the part of the kidney; (2) that it is a primary polydipsia with normal kidney function; (3) that it is a symptomatic polyuria induced by stimulation of the kidney from a variety of causes and in a certain number from hypersecretion of the hypophysis. The condition is a chronic disease not readily amenable to treatment and is apparently frequently of syphilitic origin. Each case, in the author's opinion, must be treated individually, particularly with reference to the evidence of substances which exaggerate the polyuria. Renal function tests in this case showed that the kidney was apparently normal but gave findings indicative of vascular hyposthenuria in which the bloodvessels were over-sensitive to the stimulation of sodium chloride, while other diuretic substances were inert. The case in question was not due apparently to any primary lack of ability to concentrate on the part of the kidney.

Resistance of the Erythrocytes to Saponin.—Numerous studies have shown that the varying degrees of resistance of the erythrocytes of different animals to saponin is dependent upon the cholesterin content of the cells. Investigations by May (*Ann. de med.*, Paris, 1914, i, 605) in various diseases have led to a similar result. Thus in pulmonary thrombosis, or typhoid fever, in which the cholesterin content is low, the resistance to saponin is diminished, as well as in ordinary jaundice cases, while in hemolytic jaundice the resistance is now increased, now lowered. It is normal in those conditions then, in which there is no abnormality in the cholesterin content of the blood. Hence by means of saponin resistance studies it may be possible to establish a group of diseases characterized by an anomaly in the lipoid content of the erythrocytes. It is probable that not colesterin alone, but the relation of cholesterin and lecithin which influences saponin resistance.

The Abderhalden Reaction in Carcinoma and Tuberculosis.—E. Frankel (*Deutsch. med. Wochenschr.*, 1914, xl, 589) has studied the sera of patients suffering with carcinoma and tuberculosis, using appropriate substrata. He has followed rigidly the directions given by Abderhalden in the third edition of his work in carrying out the tests. With cancer substratum from operative and autopsy material, 129 sera were examined. With a sarcoma substratum 62 sera were tested. A number of tuberculous and other sera were tested with tuberculous substrata. The results obtained were far from being specific. In fact, the reaction seemed to be unreliable for diagnostic purposes. The author is unable, as yet, to explain why his results have proved unreliable, while others have had satisfactory experience with this reaction. Possibly, he suggests, the kind of cases examined may have had something to do with the results obtained.

Spinal Fluid Cell Counts in Untreated Cases of Cerebrospinal Syphilis.—Having noted the great fluctuations in the cell counts of cases being treated by the Swift-Ellis method, Mitchell, Darling, and Newcomb (*Jour. Nerv. and Ment. Dis.*, 1914, xli, 686) made some comparative counts at regular intervals upon untreated cases, thus to ascertain the extent of fluctuation in the pleocytosis. The cases chosen were chiefly paretics in all the various stages of the disease: 34 patients in all are included in the series, upon whom 300 counts were made at intervals of two weeks. A brief history of each of the cases is given. In reviewing the results the following features become apparent. A count of three or less was found at some time in all but two of the 34 cases. These two were both far advanced paretics. Seven cases with high average counts were excitable grandiose paretics, but similar high counts were observed in those showing pronounced depression or the apparent remission of active symptoms. In several cases great variation was shown in the counts at two week intervals without there being any demonstrable change in the patient's symptoms. Low average counts may occur in all stages of the disease. The authors conclude that great variation in the cell count may be found at short intervals in any stage of paresis and that both high and low average counts may persist for months at a time in the various

stages of the malady; that the low or falling count is common but not universal before death. Since a reduction in the cell count to a normal limit frequently occurs in progressive untreated cases, a reduced cell count following treatment but accompanied by a persistent positive Wassermann reaction cannot be regarded as having valuable prognostic significance.

The Specific Cause and Cure of Pyorrhea Alveolaris.—Bass and Johns (*New Orleans Med. and Surg. Jour.*, 1914, lxvii, 456) have examined the material taken from the lesions in 87 cases of pyorrhea and have found amebæ in 85 of them. This finding was stimulated by an observation made earlier in the year at which time the same authors had observed amebæ in 7 cases of Rigg's disease. In addition to the above cases in which there could have been no mistake as to the diagnosis, the authors have examined material from the gums and teeth of 100 other normal individuals and were unable to find amebæ in a single instance. The technique for examining for amebæ is very simple and consists in the introduction of a suitable instrument such as a tooth pick or platinum loop underneath the gum, remembering that the amebæ are most numerous at the bottom of the lesion. The material removed is diluted on the slide and promptly examined with the microscope. The amebæ that have thus far been seen vary in size from about that of a leukocyte to three or four times this size. They do not possess a contractile vacuole but do contain refractile nutritive particles. There is a sharp differentiation between the endo- and ecto-sarc. Stained specimens show numerous inclusions of tissue of cellular remains, fair indications of the pathogenicity of the amebæ. Recognizing that ipecac has been employed with much success in the treatment of the amebic dysentery, the authors have experimented with the use of emetin given in doses of from $\frac{1}{2}$ to 1 grain a day hypodermically. The dosage has been repeated daily for three or four days. Their results have been most gratifying. In several cases no amebæ could be found the next day after the first dose was given. The authors are unable to state yet the exact nature of the infecting organism nor how long they will be absent following emetin treatment. The length of time necessary to secure an absolute cure will doubtless depend upon many other factors and careful attention to the dental requirements of the patient.

The Early Diagnosis of Measles.—M. Grumann (*München. med. Wochenschr.*, 1914, lxi, 132) adverts to the importance of Koplik's spots in the early diagnosis of measles. The author has observed another early manifestation of the disease. On the tonsils there may be seen punctate or linear, white efflorescences approximately 3 mm. in length in the region of the lacunar depressions and also on the protuberances of the tonsils; in the latter situation linear efflorescences are more common. The author has noted that Koplik's spots and these appearances described above often appear simultaneously in the initial stages of measles. In many cases Koplik's spots alone are seen and not infrequently the tonsillar manifestations are the only early evidence of measles. The development of the rash makes the significance of the phenomena described above perfectly clear, the author says.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL

Report of the Committee on the Treatment of Structural Scoliosis to the American Orthopedic Association, June, 1914.—(*Amer. Jour. of Orthop. Surg.*, 1914, xii, 5). The committee reached the following conclusions: Overcorrection of the deformity is apparently possible by means of Abbott's method in cases of severity corresponding to grade B and perhaps occasionally of grade A. If sufficient overcorrection is not secured or is not maintained long enough, partial or complete relapse usually follows, rather rapidly, the release from the corrected position. The period of retention in overcorrection, necessary for a cure is longer than formerly claimed; just how long cannot now be stated. Abbott's method has apparently given much better results in his own hands than in others although his technique appears to have been carefully followed. Forbes' method is apparently successful in overcoming rotation in some cases; the effect on the lateral bend has not yet been determined nor has it been shown that the improvement as regards rotation can be maintained. The method of Lovett and Sever shows no decided gain over older methods. A longer period of study and the inspection of a larger series of cases by the committee is desirable in order to determine accurately the value of the newer methods.

Concerning the Symptomatology and Treatment of Fracture of the Patella.—Haeberlin (*Zentralbl. f. Chir.*, 1914, xlii, 1585) reports a case in which he applied the observation of Dreyer (*Zentralbl. f. Chir.*, 1914, No. 22; for abstract see Amer. Jour. Med. Sci., September, 1914, p. 448). By the application of an extension apparatus to the thigh and excluding the effect of the quadriceps femoris, Dreyer determined whether the lateral expansions of the quadriceps at the knee were completely torn or not. Haeberlin confirmed the value of Dreyer's observation. In Dreyer's case the quadriceps was not completely torn and he obtained bony union without operation. In Haeberlin's case the quadriceps was completely torn and after the application of the extension apparatus the patient could not extend the knee and raise the leg as in Dreyer's case. The separation of the fragments in Dreyer's case was 1 cm. (less than $\frac{1}{2}$ in.) and by the extension this was reduced to 2 mm. In Haeberlin's case the fragments were separated about one and a half fingers' breadth, and the fragments and torn

margins of the quadriceps were approximated by strong iodine catgut sutures. The extension apparatus was applied and 12 pounds weight employed. Primary union occurred. On the sixth day, with only 4 pounds weight extension, careful attempts at flexion of the knee were begun. Nine days after operation, 120 degrees of flexion could be obtained. Eighteen days after operation, the patient walked with a cane and at the end of twenty-eight days walked much better without a cane. Thirty-three days after operation there was still some thickening at the site of operation, the scar moved freely on the underlying tissues, the union of the fragments was apparently bony, according to the Roentgen rays, the patella was freely movable and there was no fluid in the knee-joint. The leg could be raised from the bed by the quadriceps.

Disappearance of Recurrent Mammary Sarcoma after the Removal of the Ovaries.—Toreck (*Annals of Surgery*, 1914, lx, 476) says that about ten years ago he reported a series of 7 cases in which he had done Beatson's operation, for the removal of the ovaries for mammary cancer. As a rule, the improvement, though striking, was but temporary; but in a few cases cures have been obtained. He now reports a case with cancerous nodes in the skin and subcutaneous tissue of the region of the operation for the removal of an advanced cancer of the breast which had been performed about four and a half years previously. The woman, aged fifty-seven years, returned more than five years after the operation, suffering from a fibromyoma of the uterus. A panhysterectomy was performed by Dr. Seeligman, after which the patient make an uninterrupted recovery. Toreck saw her about eight and a half months later when not a trace of the cancerous nodes could be found. At least a dozen of these had been counted before the last operation. The larger ones were slightly reddened, the smaller ones had not changed color. In his former series of cases there was improvement in every case; in one of them the tumor had disappeared almost entirely. The tumors, however, began to grow again after the lapse of six or seven months, sometimes sooner, in every case except one. In that case it had been firmly fixed to the chest wall, and became so loose after the removal of the ovaries that, about two months after this operation, he performed the radical breast operation. Fifteen months later, no signs of recurrence of the cancer could be detected. She was then suffering from severe headaches and died suddenly a few months later. It is possible that this case was cured. Toreck considers that the operation should not be entirely relegated to the heap of therapeutic rubbish, where most of us have placed it, but should be remembered in cases where we are unable to do anything better.

Linear Osteotomy.—Bradford (*Amer. Jour. Orthop. Surg.*, 1914, xii, 169) reports his results with linear osteotomy for hallux valgus, forward bending of the tibia, flexed knee, midtarsal deformity, operative dislocation of the hip-joint disease, weak ankles, multiple deformities, and round shoulders. He does not dissect down to the bone before inserting the osteotome but makes the instrument cut its way down through the soft tissues as well as the bone. He emphasizes the

advantage of a relatively small osteotome, narrower than the width of the bone to be cut. In hallux valgus linear osteotomy has the same advantage over wedge-shaped resection, as it has at the knee where the Macewen linear osteotomy is known to be preferable. The deformity of hallux valgus can easily be corrected, without mutilation of the head of the first metatarsal, in the following way: The sole of the foot is placed upon a sand bag, a small osteotome is driven from above down into the head of the first metarsal by means of a mallet and the bone divided by a linear division through its thickness and nearly through its width, the side of the concavity being the portion where the division of bone is most complete. No dissection of the skin is needed. The division of the bone should be close to the joint. The extensor tendon should be avoided as can easily be done. After this is done the toe is grasped and forced inward, securing a fracture of the remaining undivided portion of head of the metarsal. If necessary, any projecting exostoses can be removed by the osteotome on the dorsum or side of the bone and a transference of the tendon or a tenotomy of the extensor propius can be performed, if needed, though for this skin incisions are needed. Thoroughly satisfactory results both in correction and in terminal results can be expected.

Experimental Studies on Lung Extirpation.—Kawamura (*Deutsch. Zschr. f. Chir.*, 1914, cxxxi, 189) says that dogs continue to live in good health after the extirpation of a whole lung. If the animals are relatively young, they continue to grow, gradually, without noteworthy disturbance. Some dogs have withstood well the removal of a part of the remaining lung. The chief difficulty in lung extirpation is concerned with the care of the bronchial stump. The burial of the stump by the Willy Meyer method is a dependable procedure, but is not to be employed when the main bronchus is too short or the animal not a large one. In many dogs he amputated the lung between two large clamps, forcibly ligated the larger vessels and bronchi by perforation, and by a continuous suture made an exact closure of the wound surfaces with excellent results. The expansion of the remaining lung, which was slightly perceptible at the end of the operation, reaches its maximum at the end of thirty to sixty days. The space left by extirpation of one lung, within this time, was compensated for by displacement of the heart, enlargement of the remaining lung, elevation of the diaphragm, sinking in at the upper thoracic aperature and flattening or sinking in of the chest wall on the side operated on. The spine curved strongly to the side with its concavity on the operated side. Notwithstanding the fact that the positive pressure apparatus was employed, no fluid was observed in the thoracic cavity, as stated by Sauerbruch. Soon after the operation the remaining lung shows the picture of an acute vesicular emphysema, and after a long period a vicarious emphysema. An actual compensatory hypertrophy of the lung was always found, never a hyperplasia. The elastic fibers were much increased. The lung vessels in the beginning are distinctly dilated and later new ones are formed. The alveoli communicate with each other in a normal manner by means of pores in their walls. No enlarged or coalesced pores were found in the hypertrophied lungs. The macroscopically enlarged heart did not show demonstrable microscopical changes.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Use of Caramel in the Diet of Diabetics.—Grafe (*Münch. med. Woch.*, 1914, lxi, 1433) has had excellent results with the use of grape-sugar caramelized at a temperature of 140° to 150° C. to supply carbohydrates to diabetics. The average daily amount used by him was from 150 to 200 gm., and this amount was given in brandy or coffee or in puddings. He found that grape-sugar caramel was better borne than cane-sugar caramel. The caramel is best given in fluid form and should not contain more than 3 or 5 per cent. of sugar. Grafe generally gave the caramel for periods of from two to four days, repeating it if necessary after interposed vegetable days. He reports 25 cases of diabetes treated on this plan with usually a marked beneficial action on the acidosis without appreciably increasing the glycosuria. By giving the average daily amount diabetics may obtain from 600 to 800 calories in the form of a utilizable carbohydrate. At times diarrhea was observed to follow the use of the caramel; if this occurs, it should be controlled by astringents. The author states that coma and enteritis are the only contra-indications to these large amounts of caramel.

Some Errors in the Salvarsan Treatment of Syphilis.—Kromayer (*Deutsch. med. Woch.*, 1914, xl, 1736) says that it is admitted that mercury, in the great majority of cases of syphilis, removes the clinical symptoms of the disease with surprising promptness. In order to cure the disease it must be given intensively and for considerable periods of time and when so given mercury produces 90 per cent. of cures. With regard to salvarsan, Kromayer says that it is an undoubted fact that salvarsan removes the clinical symptoms of the disease in much the same way as mercury. After a single large dose of salvarsan or after a series of several high doses in succession, severe syphilitic relapses of a kind previously not observed may occur. He speaks especially of the so-called neuro-recidives in this connection. Death has not infrequently followed the injection of salvarsan; in some cases the injection has been immediately followed by a fatal result and in others death occurred after a considerable interval. In order to prevent untoward effects Kromayer strongly advocates that salvarsan be given in small doses over a considerable period of time. His practise is to give a total dose of two to three grams of salvarsan over a period of four to six weeks, dividing the total amount in ten or fifteen single doses. The results of such a course of treatment are fully as good as those of an intensive course of mercury of the same duration. Intensive treatment with mercury is very apt to cause loss of weight and is frequently interrupted by untoward symptoms of overdosage with the mercury, while the salvarsan treatment with these small

doses, improves the general condition and the patients gain weight. The author believes that salvarsan is contraindicated in diseases of the heart, bloodvessels, kidneys, liver, and brain, unless it be given in very minute initial dosage and increased with great caution. By giving initial doses of from 0.02 to 0.05 gm. salvarsan, he has had very encouraging results in such cases without any toxic effects. Kromayer says that his patients did not seem to do well with combined salvarsan and mercurial treatment, so now he prefers to alternate courses of each. He says there are two great drawbacks to the use of salvarsan: its high price and the inconvenience of intravenous administration. For these reasons, salvarsan ranks below mercury, in practical importance.

The Development of Artificial Pneumothorax.—Balboni (*Boston Med. and Surg. Jour.*, 1914, clxxi, 147) points out that success in the use of this method of treatment depends on the manner in which the pneumothorax is produced and maintained. It is best to produce the pneumothorax gradually by frequent injections of nitrogen, and to bring it slowly up to the desired volume and pressure. The rapid production of a pneumothorax by large quantities of nitrogen is dangerous as it does not give the adjacent organs time to adjust themselves to the changed conditions; furthermore, the expulsion or sudden evacuation of large quantities of purulent matter may infect the sound lung. The only exception to this is in unilateral hemoptysis where it is desired to control the hemorrhage quickly. It is essential to have a free pleural cavity or one that can be made sufficiently free by subsequent injections to allow complete collapse of the lung. The other organs must be in such a condition as to be able to withstand the extra work thrown upon them. The patient ought to be in a sanatorium under the complete control of the physician. Frequent Roentgen-ray examinations are essential for the treatment. Artificial pneumothorax is not an indifferent procedure and should be undertaken only after the careful consideration of each case. The patient should be informed that the treatment is long, tedious, troublesome and expensive, and not devoid of danger.

The Treatment of Heart Involvement in Syphilis.—Brooks and Carroll (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1456) write concerning the treatment of syphilitic heart infections based on a study of 300 cases. They state that cases of heart involvement in early syphilis may be fully cured irrespective of the character of the lesion by vigorous specific treatment alone and independent of circulatory measures. Even well-established and late cases usually respond to treatment with care, or marked, though perhaps temporary, benefit. In most tertiary instances purely circulatory measures produce but slight benefit unless preceded by or combined with specific medication. Interrupted or inefficient treatment establishes an immunity or resistance on the part of the lesions against the specific drugs employed. Hence the importance of vigorous and carefully systematized treatment. They say that the most satisfactory treatment is one which combines the use of salvarsan with mercury and the iodids. Combined treat-

ment may be unnecessary in early cases but it is essential in late ones. Salvarsan, preferably old salvarsan, produces in most instances the quicker results. It is capable, however, of inducing serious symptoms, and in untried cases of heart involvement it should be administered in small doses until its action has been ascertained, particularly in those lesions characterized by disturbances of rhythm. The authors state that mercury alone may produce apparent cure. Best effects are secured with this drug when its form is from time to time changed. Its use appears to be indispensable in all well-established cases. The iodids are valuable adjuvants in the treatment of these cases, especially in their late stages, but they are apparently without specific action. Permanent injury to the heart must be assumed to have taken place in late cases, even though prompt response to treatment and apparent cure occurs. Successful treatment rests primarily on the recognition of the cause of the disease and on its specific treatment.

The Serum Treatment of Tetanus.—v. Behring (*Deutsch. med. Woch.*, 1914, xl, 1833) says that the symptoms of tetanus are due to the action of the tetanus toxin on the central nervous system. The tetanus toxin is able to reach the spinal cord by way of the nerves only by reason of its special affinity for nerve tissue. The transmission by way of the nerve is not rapid and in consequence symptoms are often delayed for considerable periods of time when the path by way of the nerve is a long one. In any case of tetanus the local focus should be excised and tetanus antitoxin should be immediately given in order to neutralize any free toxin. The passage of toxin by way of the nerves should be blocked by resection of the nerves. It is not necessary to amputate the entire limb when interruption of the nerve tract is all that is necessary. The prophylactic treatment by injections of antitoxin may simply delay the development of tetanus which may begin to actively manifest itself when the effect of the antitoxin has worn off. This fact suggests that the repeated administration of antitoxin in suspicious cases is necessary and advisable in order to control the disease.

The Roentgen Treatment of Exophthalmic Goitre.—Sielmann (*Münch. med. Woch.*, 1914, lxi, 2132) reports 21 cases of exophthalmic goitre treated systematically with the Roentgen rays over periods of from six weeks to six months. The dosage must be very carefully controlled and must be regulated so as not to produce a dermatitis. He recommends this method of treatment when medical treatment fails to benefit before resorting to surgery. In case of no result and if surgery should become necessary the Roentgen treatment may be of great value in supplementing the operative treatment. He reports a number of cases in detail, and states that in his experience of five years with 21 cases only one patient failed to show improvement following the Roentgen treatment. He calls attention to the fact that thyroidectomy may not remove the cause of the disease, since, as yet the part played by the ovaries, the pituitary body and other glands in exophthalmic goitre may be a very important one.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M D.,

OF PHILADELPHIA.

Study of the Heart in Diphtheria.—W. E. Hume and S. J. Clegg (*Quarterly Jour. of Med.*, 1914, viii, 1) investigated cardiac irregularities occurring in diphtheria by polygraphic records on 70 cases. Of these 70 cases 30 were found normal. Of the 40 cases showing irregularity, 22 showed the characteristics of a sinus arrhythmia with normal cardiac signs. The remaining 18 cases form the basis for this report and are divided into three groups, clinically, depending on the severity of the symptoms. In the first group of six cases the infection was virulent, with pallor, prostration, extensive membrane, high toxemia, etc. In this group dilatation of the heart was always obvious before the sixth day, the tension in the radials being very low. Premature contractions in auricles or ventricles usually preceded grave types of arrhythmia. The rythm of the heart frequently changed from day to day. Autopsy findings in 4 of these cases showed excess of fat in auricular muscle with increased vascularity. Ventricular muscle showed a very large quantity of fat. Group II shows clinically a marked toxemia and a copious septic membrane. Two of the cases died after six weeks and the remainder were seriously ill for long periods. The cardiac irregularities shown by these cases were auricular or ventricular extrasystoles, reversal of normal beat. In this group the heart beat remained rapid throughout the course of the disease and each case showed dilatation of the heart. The autopsy on one of the cases showed an absence of the increase of fat shown in the first group, but shows scattered patches of interstitial myocarditis in the ventricular muscle. The third group of cases showed no toxemia and the throat condition was not severe. Irregularities in the heart occurred in all of them. These included permature systoles, compensatory pause. It is impossible to correlate the pathological lesions of Group I with the individual instances of arrhythmia. Types of arrhythmia in each individual case may vary from day to day, depend on varying pathological processes in the heart. Any form of arrhythmia of the heart except sinus arrhythmia in diphtheria indicates that heart muscle or nerves are involved in a pathological process however mild the illness may be and special precautions necessary to keep patient recumbent.

Anaphylaxis and Status Lymphaticus: Their Relation to Disease in Infancy and Childhood.—C. McNeil (*Edinburgh Med. Jour.*, 1914, xiii, 38) discusses intensified pneumonia and tuberculosis in childhood which are described by the word "hypersensitiveness," and in which were found postmortem evidences of status lymphaticus. The propositions discussed are as follows: (1) that these fulminant types of illness are clinical illustrations of the pathological condition, anaphylaxis;

(2) that the status lymphaticus which was present is essentially connected with the distorted and intensified type of illness. McNeil describes anaphylaxis as a bodily condition in which abnormal reactions follow repeated injection of a substance which at first injection produced no apparent disturbance of health. Under clinical examples of general anaphylaxis he mentions serum disease, with its ordinary accelerated and immediate reactions, food anaphylaxis such as urticarias and edemas, pollen asthma as in hay fever and acute infectious diseases, the smptoms of onset of which Von Pirquet, Schick and others regarded as anaphylactic. McNeil emphasizes that both in the ordinary and the fulminant pneumonia the symptoms of onset are anaphylactic. Under clinical examples of local anaphylaxis the cutaneous and conjunctival tuberculin reactions are cited and the author submits that in the local reactions of scrofula we have an exaggerated form of local anaphylaxis, similar to the general anaphylactic reaction in fulminant pneumonia. These alleged instances of clinical anaphylaxis are similar pathologically accepted instances of anaphylaxis whose leading pathological features are vasomotor paresis, constriction of certain types of non-striped muscle, edema of the loose connective-tissue, destruction of the more delicate body epithelia and the production of these changes by very small doses of virus. The pathological similarity is here described separately and in detail using fulminant pneumonia and scrofula as examples. Discussing the weakness of the virus the disproportion of cause and effect is seen in human anaphylaxis, as in the sting of an insect or the local reaction by tuberculin or by the tertiary stage of syphilis, of which McIntosh says, "the extensive lesions without Spirocheta pallida in any number must be due to minute quantities of syphilitic toxin on highly sensitized tissues." The author claims that in fulminant pneumonia the virus is weak because of the great number of similar non-fatal cases also observed and that the fatal issue was due to hypersensitive condition of the body (anaphylactic) and not to a virulent poisoning. As to scrofula, the ordinary, normal reaction of tuberculin is accepted as an anaphylactic reaction; the intense reaction in scrofula is heightened anaphylaxis. In these various features, then, of fulminant pneumonia and scrofula, which show evidence, not of intensification of the virus, but of intensified reaction to the virus, the special stamp of pathological histology and physiology is identical with that of the phenomena of anaphylaxis, both experimental and clinical.

Empyema in Children.—H. G. Melville-Dunlop (*Edinburgh Med. Jour.*, 1914, xiii, 4) gives an analysis of 98 cases of empyema in children. During the period covering these cases 861 cases of pneumonia were treated, making a proportion of one case of empyema to every 8 or 9 cases of pneumonia treated on a childrens' ward. Almost all effusions in the pleura of children under three years are of a purulent character. The liability to purulent effusion lessens from three to ten years when the tendency to serous effusion is usually established. In 79 cases under ten years, 68 were purulent; in 67 cases at ten years and over, 28 were purulent. The pneumococcus was present in pure culture in 53 per cent. of all the cases, giving pus of an opaque, greenish color, of creamy consistence and with large masses of fibrin.

Streptococcal infection came next in 16 per cent., and caused a much thinner pus with a whitish-gray deposit on standing. Mixed infection with pneumococcus and streptococcus occurred in 14 per cent. of cases. The staphylococcus alone was present in 3 per cent. of cases. The tubercle bacillus occurred in 3 per cent. of cases, but being hard to find the percentage is probably slightly higher. The fluid in the latter cases was of a turbid character. Dunlop believes that primary forms of empyema are exceptional. In only 7 per cent. of this series was there no history of an antecedent cause for the empyema. The effusion generally occurred with, or followed lobar pneumonia and was invariably purulent. It was much less frequently associated with bronchopneumonia, but frequently developed subsequently to the infectious diseases as scarlet fever, etc. In most of the cases the effusion occurred within a few days of the crisis of a pneumonia. Empyema is often overlooked and the case treated as one of atrophy or miliary tuberculosis. It should be a routine practice to examine from time to time every case not making satisfactory progress. The symptoms of the advent of empyema are usually fever, cough, vomiting, quick breathing, sweating, restlessness, and delirium. Languor, a short paroxysmal cough and rapid emaciation are more especially the symptoms in older children. Especially, the child in almost every case looks seriously ill, has an anxious, pinched appearance and is profoundly anemic. Dyspnea, as found in pneumonia does not usually occur. Leukocytosis is usually from 20,000 to 30,000. Absolute, boardy dullness at the base with a boxy percussion note at the apex and harsh exaggerated breathing above the dullness is very suspicious of pleural effusion. Loud tubular breathing is common over a purulent effusion. The commonest complication was purulent pericarditis present in 40 per cent. of the fatal cases. Exploratory puncture is frequently necessary and is attended by little risk. Under two years the prognosis is grave but after two years the mortality diminished. Pneumococcal cases over two years usually recovered but in streptococcal and mixed cases the prognosis was not so good. Early evacuation and drainage is imperative if good results are to be looked for. Where the fluid is only turbid or the infant very young and unable to stand a serious operation aspiration is best used.

Pyloric Obstruction in Infants. — C. H. Miller (*Lancet.*, 1914, clxxxvii, 987) discussed a series of 9 cases of pyloric obstruction in infants. The ages varied from sixteen days to eighteen weeks. There were three deaths, two from intercurrent conditions and of the six recoveries five have become perfectly normal children. Sudden, forceful vomiting is characteristic. In these cases it was noteworthy that if peristalsis was violent the treatment was much easier and progress steadier. Peristalsis is a variable sign. Visible peristalsis may occur without any hypertrophy of the stomach. It should be regarded as a sign of obstruction rather than of hypertrophy. Peristalsis of the stomach is seen also in infants with vomiting and colic in which the condition is satisfactorily treated by castor oil and eliminating milk curd from the diet for a few days. These are instances of "pyloric spasm." The presence of a palpable pyloric tumor Miller is rather skeptical of,

although he has felt a cylindrical tumor in some cases during gastric peristalsis. He regards this sign rather as one of wasting than of pyloric hypertrophy. The medical treatment consists of careful and skilful nursing, keeping the patient warm, washing out the stomach, and feeding with predigested milk. To keep the patient warm a fracture cradle covered with blanket and equipped inside with an electric lamp and a thermometer is a good method. Washing out the stomach should be performed twice a day, after a week once a day. Solutions used for this purpose are warm tap water or solutions of bicarbonate of soda. Liquor pancreaticus is preferred for the purpose of digesting milk. The milk is given a teaspoonful at a time every half hour, increasing the quantity and interval according to tolerance. Virol and albulactin are valuable as additional foods later on in the treatment. For colicy pain tincture opii $\mathfrak{m}\frac{1}{4}$ or chlorodyne $\mathfrak{m}$i three times a day are used. Belladonna is useless in this disease. Phenolphthalein is the most useful drug to use regularly for constipation. In the very cases medical treatment only can be recommended. If the child is seen early and the diagnosis is definite Miller would recommend surgical treatment provided the child had sufficient strength. Some cases can only be treated by the physician, some are better treated by the surgeon but the after-treatment becomes again medical; in either event neither will be effective without the care of a specially skilled nurse.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Acute Tetany in the Newborn.—Kruger-Franke (*Zentralblatt f. Gynäkologie*, 1913, No. 2), reports the case of a patient admitted to clinic forty hours in labor. She had in a previous confinement given birth to twins, of which the first was born in breech presentation, and ten years previously she had had an operation for vaginal fixation of the uterus. When admitted to hospital the os was partly dilated, the cervix obliterated, and the child was presenting by the breech, which was high above the pelvic brim. Uterine contractions were very weak and in efficient, and full dilatation was not obtained until seventeen hours after admission to hospital. When the breech could be reached delivery was attempted, and a male child, dead and macerated, was delivered The amniotic liquid was foul smelling and stained with meconium. The second twin presented by the head, which was high above the pelvic brim, the membranes were ruptured and the child delivered by version. It was asphyxiated and had inspired some of the foul amniotic liquid, which was removed by the tracheal catheter. On the following day the child was somnolent, cried only occasionally, and had tonic cramp-like contractions of the muscles. Trismus was absent,

but opisthotonus was present. The extremities were partially flexed. The child's skin was moist and resembled wet blotting paper to the touch. The child vomited foul material and could retain nothing in the stomach. In spite of gastric lavage with salt solution, the child did not improve, and died on the evening of the second day. A complete autopsy could not be obtained, but the abdomen was opened and a piece of intestine carefully removed and sent for bacteriological examination. Streptococci were found in the bowel. The mother's puerperal period was without complication. The cause of infection was evidently the foul and infected amniotic liquid swallowed by the child during the version which preceded its birth.

The Immediate Treatment of Depressed Fractures of the Skull in the Newborn.—While this treatment is sometimes carried out in hospitals, it is not employed as often as it should be, and on each report of success it calls the attention of obstetricians to the value of the method. Kosmack (*American Journal of Obstetrics*, February, 1913), reports 3 cases in the Lying-In Hospital of the City of New York, in which depression occurred in the cranial bones of the fetus at birth. The first patient was a primipara, aged thirty-six years, beyond term, and the transverse diameter of the head was wedged into the brim. The promontory was sharp and the anterior posterior diameter could not be readily measured. It did not seem over 10 cm. The arch of the symphysis was moderately contracted, and also the distance between the tuberosities of the ischia. The pelvis was flattened with a tendency toward the funnel-shaped. The patient had been long in labor, with the escape of amniotic liquid, and the lower uterine segment was firmly contracted over the head and neck. The cervix admitted five fingers and seemed unusually firm. It was thought best to apply the forceps, practically the high application, and after several attempts the head was finally brought through the midpelvis to the outlet, after which the blades were removed and the head delivered by expression. The child was well developed and apparently normal, weighing $9\frac{1}{2}$ pounds. It made no effort to cry, but the contractions of the diaphragm were regular but slow. On examination a depressed fracture involving the left frontal bone and a furrow over the parietal region showed where the promontory of the sacrum has pressed upon the head during delivery. The face was very slightly bruised. The genital tract in the mother had been somewhat lacerated, and this was repaired. The child's breathing was slow and labored and the heart action very slow. An attempt was made to raise the depressed fracture by inserting a corkscrew, but this failed; then a single tenaculum forceps was hooked into the depressed portion through a small puncture wound. In spite of the condition present the child recovered, and some time afterward was found in good condition without cranial deformity. In the second case there was a marked depressed fracture of the left frontal bone, and the overlying area was edematous. Eight hours after birth the child's condition was good and respirations regular—about eighteen to the minute. It did not cry, the lids remained separated, the pupils were equally contracted, with a very slight reaction to light. After sterilizing the skin over the site of the fracture, the hook of a single bladed Bullet forceps was inserted into the skin over the fracture and

carried down to the bone. The depressed fragments were readily raised, and on the following day the child seemed normal and made a complete recovery. In the third case the depressed fracture was concealed by a large caput, so that several days elapsed before a diagnosis was made. The outlet of the mother's pelvis was considerably contracted. It was suspected that the child had sustained injury after delivery. The operation was done as in the preceding case, but the operation was not performed until ten days after the birth of the child, when elevation was secured by a hook introduced through the cleft in the bone. The child did well and only a slight ridge could afterward be felt along the line of fracture.

Infection by the Bacillus Coli Communis Complicating Pregnancy and the Puerperal State.—Simpson and Bernstein (*British Med. Jour.*, April 4, 1914) found that in this condition the diagnosis must be made between bacilluria, sapremia, septicemia, and septic phlebitis. The diagnosis is made by examining the blood and the urine taken by catheter, and the contents of the interior of the uterus and the cervix, obtained by swabs. If the serum be examined the agglutination reaction is often well developed with the Bacillus coli diluted to four-hundredfold. As regards treatment the pyelonephritis of pregnancy is recognized as a grave condition which may require local treatment. In general infection vaccines may be employed, the results may usually be divided into three groups: (1) where cure follows, the bacilli disappearing from the urine; (2) the symptoms are relieved and the bacilli disappear so long as the patient is kept under treatment, but to maintain the improvement vaccines must be given at increasing intervals of time; (3) the condition may subside and the bacteria remain in the bladder as harmless saprophytes. The usual methods of treating the urinary tract are described and the writers in using autogenous vaccines do not believe that they can be of value when stock vaccines of the Bacillus coli communis are employed. To be successful, vaccines must be prepared from the organism of the patient, because the Bacillus coli communis undergoes essential change when it leaves its usual location in the intestine. Three cases are described, treated successfully by these methods. In preparing vaccines the cultures were made immediately, and in ten hours sufficient growth was obtained to proceed with the preparation of the vaccines. The first doses were diluted with 0.5 per cent. lysol in normal salt solution and sterilized at 60° C., incubated for a few hours, and again heated to 60° C., and were thus ready for use within twenty-four hours after seeing the patient. The three cases reported were private cases and the most of the work done in the houses of the patients, thus demonstrating the advantages of modern methods in private practice.

The Management of the Third Stage of Labor with Special Reference to the Manual Removal of the Placenta.—Ahlfeld (*Ztschrft. f. Geb. u. Gyn.*, Band 76, Heft 1, 1914) concludes from his study of this subject that the less the uterus is disturbed after the expulsion of the child, the more perfectly does the separation proceed, with but normal and physiological hemorrhages. The uterus does not virtually contract until from one and a half to two hours after childbirth. During this

time the expression of the placenta by external pressure can almost always be carried out with a minimum of disturbance. When there is no indication for shortening this period, one may wait until the uterus contracts and the placenta descends into the pelvis for any reasonable time. With primiparæ this method is sufficient in 89 per cent., with multiparæ in 75 per cent. In cases where there is the history of previous complications in labor, it may be best to shorten the third stage. This is especially true in multiparæ. Where active interference is not demanded the condition of the uterus should be watched by placing the hand upon the abdomen, and the normal separation of the placenta be observed. Where there is no external bleeding, and the uterus contracts at intervals efficiently, separation and descent of the placenta are usually complete in from one and a half to two hours, and the placenta can then be readily espressed. When sudden hemorrhage develops the discharge should be observed every five minutes and fresh gauze used, to watch the quantity of blood. The manual removal of the placenta is seldom necessary and is to be conducted, under strict antiseptic precautions, as a surgical procedure.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Gummatous Ulceration of the Vagina.—An unusual case of syphilitic lesions in the vagina is reported by Bollag (*Cor.-bl. f. Schw. Aerzte*, 1914, xliv, 1068). The patient was a nullipara, aged forty-four years, who admitted having contracted a venereal disease at the age of twenty-one. She complained of pruritis and ulceration about the vulva, and on examination showed the presence of several old scars on the vulva and inner sides of the thighs, with two partly healed ulcers in the vagina. Between these was a ring of marked contraction, evidently due to scar tissue. One of the vaginal ulcers was excised, and showed merely inflammatory tissue. It was possible from the microscopic examination to exclude absolutely tumor formation; the histologic appearance showed nothing characteristic for any specific type of inflammation, however, such as tuberculosis or syphilis, but in spite of a negative Wassermann, the clinical appearance so strongly suggested the latter condition that an energetic antiluetic treatment was begun, whereupon the ulcers promptly healed, although they were of long standing, and had resisted local treatment. The author therefore considers their syphylitic etiology as fairly certain, and believes them to be manifestations of the tertiary stage, in other words, gummatous in nature, the vaginal stricture being also undoubtedly the result of a healed lesion of similar origin.

Urinary Disturbances in Women of Nervous Origin.—Schwartz (*Zeitschr. f. Urol.*, 1914, iii, Beiheft, 346) says that while we must be very careful not to attribute disturbances of micturition to nervous conditions until we have exhausted all the modern methods of diagnoses to exclude the possibility of some local lesion, there are certain cases in which no such disturbance can be demonstrated. These women often complain of great urgency and frequency of urination except during the menstrual periods, at which times they are free of the trouble. Schwartz thinks that in many cases of this type the disturbance lies in the sympathetic innervation of the bladder, and is the result of an insufficient internal secretory activity on the part of the ovary. He believes that the internal secretion of the ovary exerts a marked influence on the pelvic nerves of the sympathetic system, and that when this secretion is present in insufficient amounts, disturbances ensue. The explanation of the relief of symptoms during menstruation is explained by the fact that at this time the ovary is at the height of its functional activity. In proof of the justice of this assumption, he says that a number of cases of this type have been completely cured by the administration of ovarian preparations.

Radium Cure of Urethral Carcinoma.—Quite a remarkable case, both because of the result produced and of the thoroughness with which it could be studied, is reported by Legueu and Chéron (*Rev. prat. d. maladies d. org. genito-urinaires*, 1914, xi, 86). The patient was a girl, aged twenty-six years, with a hopeless and extensive squamous-cell carcinoma (proved by examination of excised piece of tissue), completely surrounding the urethra, and involving all the anterior portion of the vulva and vagina. Operation was out of the question, but following a series of vaginal and intra-urethral applications of radium the tumor completely disappeared, and was replaced by a slight amount of soft, non-painful scar tissue. Unfortunately, however, as a result of the urethral applications, the entire urethra was destroyed, including the internal sphincter, leaving the girl with a permanent incontinence. She gained weight, and in spite of the incontinence remained in perfect health for two and a half years, when she absolutely insisted on operation for relief. Legueu therefore implanted both ureters into the rectum, considering any attempt at plastic work futile. The operation was followed by peritonitis, to which the patient succumed at the end of a week. A most careful autopsy was performed, numerous microscopic sections being made of the pelvic tissues and associated lymph nodes, without the slightest trace of anything suggestive of malignancy being discoverable.

Vaginal Carcinoma Following the Use of a Pessary.—In view of the large numbers of pessaries which are worn by women, who often neglect to present themselves at proper intervals for examination, it is rather surprising that we do not oftener hear of the development of malignant tumors as a consequence. The vagina seems to be an organ which is but very slightly inclined to the primary production of new growths; that such can occur, however, as the direct result of a neglected pessary, is shown by a case reported by Edelberg (*Zentlbl. f. Gyn.*, 1914, xxxviii, 265). The patient was a woman in the late sixties, who had worn

a pessary uninterruptedly for twelve years, having become tired of returning to a physician for periodic examination. At the end of that time a bloody discharge developed, as a result of which she sought medical attention, and on examination was found to have an inoperable squamous-cell carcinoma of the vagina, the growth having evidently originated on the basis of a deep ulcer at the point of impaction of the posterior limb of the pessary. As the uterus was entirely free, the growth was certainly not an extension from that organ.

Cervical Cancer in Young Girl.—A most unusual case of a well-developed cancer of the cervix in a young girl, who had never borne children, is reported by AYRES (*Amer. Jour. Obst.*, 1914, lxix, 698). The patient was seventeen years of age; she had menstruated regularly from her thirteenth year up to a few months before coming under observation, when her periods became increased in amount. Not suspecting the true condition, a physician treated her with ergot, following which she improved somewhat. The bleeding soon became uncontrollable, however, and a gynecologic examination revealed a large cauliflower mass occupying the cervical region, microscopic examination showing it to be a typical carcinoma. A radical Wertheim operation was performed, and several months later the girl was known to be in apparent health.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,

OF PHILADELPHIA.

Case of Spontaneous Retrogression of Cancer of the Larynx.—PUGNAT (*Arch. internat. de lar., d'otol. et de rhinol.*, Mai-Juin, 1914) reports a case of spontaneous retrogression in cancer of the larynx. Such cases are rare but are occasionally encountered. The disease occurred in a man, aged sixty years, who had been hoarse for several months. An oval, red tumor the size of a bean occupied the entire left arytenoid region and extended upon the left vocal cord which it masked entirely. A submaxillary ganglion on the left side was found enlarged to the size of a small nut and was of hard consistence. Clinical diagnosis of malignant growth was confirmed by microscopic examination of a fragment removed with cutting forceps. Surgical interference was declined by the family. Warm sprays of an aqueous solution of adrenalin 1 to 10,000 were prescribed to be used five or six times a day; and every two days instillations were made into the larynx of an oily adrenalin solution. After some weeks it was noted that the tumor had diminished notably in volume and appeared to be

atrophied; the voice had become nearly normal; the anterior two-thirds of the left vocal cord had become visible, and finally at the end of three months there was no more hoarseness. At the close of the following month the larynx had become absolutely normal and there was no trace of the tumor evident. The patient's color had become natural, the mucous membranes were no longer anemic, while the patient had regained his strength and recovered his proper weight. The submaxillary gland, however, had not diminished in volume and had even become more indurated. For several months everything continued well, but the submaxillary ganglion was still in evidence. Eleven months after the entire disappearance of the laryngeal growth, the patient returned with a submaxillary growth the size of a mandarin orange at the same place where the enlarged gland had been noted in the first instance. The larynx had remained perfectly normal. The ganglionary tumor soon acquired enormous dimensions and provoked circulatory troubles by compression of the large vessels of the neck, and at the same time the patient became feebler and cachectic. Sudden death occurred from hemorrhage of the carotid artery. Autopsy was refused. It is to be regretted the gland had not been removed before it began to enlarge.

Teratoma of the Pharynx.—Eves (*The Laryngoscope*, September, 1914) reports and depicts a teratoma removed from the pharynx of a male infant, aged fourteen months. It had been first noticed protruding from the mouth after an attack of vomiting when the child was three weeks old. Its attachment to the pharynx was by a pedicle to the right side of the posterior wall just behind the upper end of the post tonsillar pillar. It was readily seized with a hemostat on making the child gag, and was cut loose at its base with curved scissors without an anesthetic, with very little hemorrhage. Inspection forty-eight hours later revealed only a small white area about the size of a pinhead.

Tuberculosis of the Parotid Gland.—Carmody (*The Laryngoscope*, October, 1914) describes and depicts the facial appearance of a case recently under his care in a Russian-Jewish males ubject, aged twenty-four years. He also gives a resumé of all that has been written upon the subject, including reports of 4 cases in this country and 11 cases abroad, comprising all that are known so far as his knowledge extends.

Nasal Hemorrhage.—Thomfson (*The Laryngoscope*, October, 1914) reports an uncommon case of recurring nasal hemorrhage in a man, aged sixty-three years. The right inferior turbinated body was all angiomatous tissue, and there was a suppurative caries of the right middle turbinate and anterior ethmoidal cells. A number of operative procedures were practised during a period of thirteen months, including the removal of the right middle turbinate body and eventually a submucous resection for the purpose of relieving hemorrhage from the diseased septal cartilage. Since this last operation there have been no hemorrhages. The author states that if anyone has ever done a submucous resection for the cure of hemorrhage before, he has not seen a report of the case; although one case has been reported where frequent nose-bleeds were stopped by a submucous operation, but the operation had not been done for the purpose of checking them.

Bullet Wound of the Frontal Sinus and Brain.—Mackenzie (*Pennsylvania Med. Jour.*, April, 1914) reports a case of a male, aged forty-seven years, who was shot in the middle of the forehead at close range with a 32-caliber revolver. Skiagraphy showed the bullet located in the head about one and one-quarter inches deep, while the inner wall of the sinus was splintered and depressed. The bullet was removed by operation and the inner wall of the frontal sinus was found to be fractured with the splinters presenting inward toward the brain. Two half-inch long spicules of bone had penetrated the dura and were buried about half an inch in the brain substance. These fragments were removed and the patient made an uneventful recovery.

Intermittentl Claudication of the Larynx.—Garel (*Ann. des. mal. de l'oreille, du lar., du nez et du phar.*, No. 6, 1914) reports a case of intermittent aphonia in a clerical patient, aged forty-eight years, who was at the same time a subject of claudication of the right leg. At an earlier stage of his infirmity the intermittent aphonia ensuing upon speaking did not occur during singing, but should he sing false or below the tone necessary to retain his vocal powers, he would soon be taken with a constriction of the throat followed by an aphonia of long duration. Similarly, aphonia brusquely ensued should he address a reprimand to a scholar. Within two months a new fatigue of eyesight had supervened, making it at times difficult to read or write even large characters such as are used for illustration. The writer calls attention to the analogy with the syndromes of bulbospinal myasthenia as recognized by other observers mentioned.

Radical Treatment of Stenosis of the Larynx Due to Permanent Median Position of the Vocal Cords.—Citelli, in an elaborate paper (*Ann. des mal. de l'oreille, du lar., du nez et du phar.*, June, 1914), defends his method of cordectomy by external access as preferable to all others suggested, and cites cases and authorities in evidence.

Excision of the Vocal Cord for Recurrent Laryngeal Paralysis.—Voislawsky (*Pennsylvania Med. Jour.*, November, 1914) reports a case of bilateral paralysis following an operation for goitre. After various other unsuccessful efforts, the larynx was cocainized and a Jackson bronchoscope introduced and the left vocal cord excised with a Cordes punch. For several days subsequently the patient was intubated, and he was discharged from the hospital after the wound had healed. Breathing was made easier, there was improvement in talking and the crowing was replaced by an ordinary snore. At the time of the report a white band of scar tissue replaced the excised left vocal cord and this band approximated with the right vocal cord on phonation.

Bronchopneumonic Complications After Pharyngotomies, Thyrotomies and Laryngectomies.—Castex (*Ann. des mal. de l'oreille, du lar., du nez et du phar.*, June, 1914) sums up the complications of four fatal observations as due to reflex pulmonic congestion toward the second day, rapid septic pneumonia from the fourth to the eighth day, pneumonia from chill, and slow bronchopulmonic infection which drags

along for from three to five weeks. These complications are especially liable to occur in alcoholic subjects. For prevention of such sequels the following technique is advised: (1) Antiseptic sprayings during three days previous to the operation; (2) putting the teeth into good condition; (3) no general anesthesia with chloroform; (4) local anesthesia; novocaine for the exterior, and cocaine for the interior; (5) operation in two sittings for laryngectomies, with attachment of the trachea to the skin; (6) a little delay after opening the trachea, in holding it open to permit the patient to expel the blood which has entered the respiratory passages, and if this be not sufficient, insufflation of air through a soft cannula; (7) no cannula to be allowed in the trachea if possible to avoid it; (8) an esophageal tube to be allowed to remain in position for eighteen days; (9) suturing of bleeding surfaces as much as possible; (10) touching with tincture of iodine the raw surfaces not coaptible; (11) dressing and draining with aseptic gauze and frequent change of the dressing; (12) seating the patient in bed and allowing him to get up when it seems reasonable.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL,

AND

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

Experimental Arterial Lesions and Cholesterin Steatosis.—A considerable work has been done in an attempt to produce arterial lesions in animals comparable to the spontaneous diseases of man. Periodically the methods to obtain these results have changed and with each new series of experiments much hope has been expressed that the human disease could be reproduced. Pressure producing drugs (adrenalin, digitalin, barium chloride, nicotin), infectious agents (B. typhosus, Staphylococcus aureus, streptococcus), organic and inorganic intoxications and mechanical alterations of the blood stream have each had their turn in occupying the interest of those studying the diseases of the arteries. More recently MANOUELIAN (*Ann. de l'Institut Pasteur*, 1913, xxvii, 7), and others, TODD (*Lancet*, 1913, May 17) have again suggested the possible influence of the sympathetic nervous system in having much to do with the arteriosclerotic process. However, a more interesting series of experiments in which positive results were not difficult to obtain in experimental animals, have been developed by the Russian school of workers. As the method consists in feeding animals with unusual diets the resulting processes in the arterial walls are spoken of as a "dietary arteriosclerosis." The lesions thus obtained

appear quite distinct from the adrenalin type of medical necrosis. Ignatowski (*Virchows Arch.*, 1909, excii) first demonstrated in rabbits the production of arterial lesions by offering the animals a foreign diet. The rabbits were fed on various animal tissues and it was the author's belief that the arterial lesions resulted from the absorption of unusual protein substances. It was, however, soon demonstrated by Stuckey (*Centralb. f. allg. Path.*, 1912, No. 21) that the protein substances had far less effect in causing arterial lesions than fatty bodies present in the tissues. His best results were obtained by feeding egg yolk or brain substances to rabbits. This author further demonstrated that neutral fats of animal or vegetable origin produced no lesions in the vessels. Equally negative were also the experiments of Wesselkin (*Russki Wratsch.* 1912, No. 21) with pure lecithin. Thus of the fatty substances in egg yolk there remained the important cholesterin constituent as the possible factor in bringing about the lesions in the arteries. The previous work of Chalatow (*Virchows Arch.*, 1912, ccvii) indicating liver changes with cholesterin deposits in the liver cells following the ingestion of egg yolk or brain substance, made this seem very probable. The common observation of finding cholesterol-esters in the fatty areas of the human aorta also lent support to this view. Anitschkow (*Ziegler's Beiträge*, 1913, lxv) experimented with pure cholesterin and by dissolving it in sun-flower oil was able to reproduce the lesions described by Ignatowski and Stuckey. The cholesterin oil mixture was fed to rabbits by means of a catheter for a period of one to four months. The lesions appeared as macroscopic yellow plaques upon the surface of the aorta. The media was not involved. An actual thickening of the intima with the development of new cells was seen. The reaction lay on the inner side of the internal elastic lamina and on close analysis was found to consist of an unusual collection of large endothelial cells which had loaded themselves with fat. The fatty substances were doubly refractile and simulated cholesterol-esters. It would appear that the reaction in the intima was developed mainly through the aggregation of a large foreign cell and that the individual tissue elements of the intima played little part in the lesion. Inflammatory cells are wanting and there does not appear to be any evidence of hyperplasia of the connective-tissue. In the later stages the neighboring elastic tisues show degeneration and splitting of their fibres. A comparison of these experimental arterial lesions with the human types is possible only in so far as particular scleroses are concerned. There are met with in the human arteries, lesions which have similar cell and fatty changes. It must, however, be remembered that the human scleroses are of a very diverse character and that the etiological factors vary greatly. The development of peculiar arterial lesions in rabbits by cholesterin feeding must not be too hurriedly accepted with broad significance in the human.

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ORIGINAL ARTICLES

THE FUNDAMENTAL PRINCIPLES INVOLVED IN THE USE OF THE BONE GRAFT IN SURGERY.[1]

By Fred H. Albee, A.B., M.D., F.A.C.S.,

PROFESSOR OF ORTHOPEDIC SURGERY, NEW YORK POSTGRADUATE MEDICAL SCHOOL, AND UNIVERSITY OF VERMONT, ETC.

Cellular life may be quite independent of organic or somatic life, and under favorable conditions tissue cells may retain their viability long after being detached from the living organism. The duration of this cellular life depends largely upon the means of preservation of the detached parts, or, in the case of organic death, the preservation of the whole cadaver, and also the amount of disintegration from the cause of death. It is on account of this phenomenon that detached portions of living tissue can be successfully transplanted. The higher the specialization of the cell the less marked are its resisting and proliferating powers. This is especially well illustrated in the case of tissue grafts. The lower order of tissues, which need less nutrition, continue to live for days on their own substance which is contained in the serum that permeates them; but the more highly specialized ones are liable to necrose in a short time unless nourished by a blood circulation.

The most favorable tissues for grafting purposes are the simpler connective tissues, such as bone, fat, fascia, etc. Muscles and nerves are most unfavorable. Autogenous grafts, or those derived from the same individual into which they are engrafted, are by

[1] The Mütter Lecture, delivered before the College of Physicians of Philadelphia, December 4, 1914.

far the most trustworthy. The fluids and tissues of every individual vary in degree from those of every other, and while this incompatibility may be slight, it is sufficient cause for using, whenever feasible, the individual's own tissue for the repair of his defects.

With primary union and in the absence of infection, autogenous bone grafts, properly contacted, are always successful, and even infection does not necessarily indicate failure. The exact knowledge of the histological role which the bone graft plays is fortunately immaterial to its clinical usefulness, whether it serves as an osteoconductive scaffold or as an active osteogenetic force. The extensive experiments and histological studies of Ollier, Macewen, Frangenheim, Cotton and Loder, McWilliams, Phemister, and the author have proved the viability and osteogenesis of the grafts when inserted by the proper technique.

Homoplastic grafts are those which are derived from another individual of the same species, and when composed of the lower order of tissues, such as bone or facia, they may be employed successfully, but not with the same certainty as autogenous grafts; when they consist of the more highly specialized tissues, they result in failures. Homoplastic grafts are often difficult to obtain, and there always exists the danger of transmitting disease from the donor to the host even when the greatest care has been exercised.

Heteroplastic grafts are those which are obtained from an individual of another species. Living grafts from different species usually die when implanted into man or the higher animals. The graft in these cases acts more as a foreign body, and if there is infection it is liable to slough out immediately. In the event of no infection it either becomes encapsulated or disappears, and is slowly substituted by the proliferation and migration of the tissues in which it is embedded. This process may require months in the case of the bone graft, and thus it follows that the graft may be a success clinically, though histologically it undergoes partial or even complete absorption, or, in other words, it acts as an osteoconductive scaffold.

There are certain fundamental rules which should always be observed in the transplantation of all tissues. These rules must be adhered to as closely in the animal as in the vegetable kingdom. The science of grafting in the plant kingdom is centuries old. The most important rule of the process of grafting in the vegetable kingdom is the contacting of the alburnum of the scion or graft (which in a way corresponds to the periosteum) to the alburnum of the stock, or the part grafted. The contacting of the corresponding histological layers is not so paramount in the grafting of bone as it is in vegetable life, but the importance of its observance is unquestionable.

The more closely these rules are adhered to the greater will be the percentage of clinical successes. In the case of the bone trans-

plant, nature is confronted with the following problems: (1) the rapid establishment of cellular nutrition and blood supply, which is brought about by the extension of bloodvessels, by the cellular assimilation of the serum in which the graft is immersed; (2) the union of the graft to the contacted bones or fragments of bones by osteogenesis on the part of the graft or the recipient bone, or both; (3) the adaptation in form and increased strength of the graft to its mechanical requirements through the influence of Wolff's law. If nature is to succeed in accomplishing these problems it is quite essential that both the graft and the recipient bone should be favorable to cellular life and proliferation. The surgeon can do much to aid nature by minimizing the trauma to all the tissues involved, by avoiding cellular death through either bruising or comminuting with hand tools, or by frictional heat from motor-driven instruments; by the avoidance of traumatism, thus guarding against necrosis of portions of the graft and lessening the danger of wound infection; by the proper protection and preservation of the graft bed and the graft itself from drying and possible infection; by wisely arranging his skin incision so that it will not come directly over a superficially placed transplant, as this lessens the danger of necrosis and infection; by excising, if possible, extensive scars from the field of operation, as their poor blood supply is likely to interfere with the establishment of nutrition to the graft; by closely fitting and contacting bone surfaces, which should, whenever possible, include the accurate coaptation of periosteum of graft to periosteum of recipient bone, cortex to cortex, endosteum to endosteum, and marrow to marrow; by properly suturing muscle origins and insertions to the proper mechanical locations on grafts which replace skeletal bones or portions of them (this is important if muscle control is to be reëstablished); by securing sufficient hemostasis in the graft bed, with repeated applications of hot saline solutions, and by careful tying of bloodvessels (a hemostoma not only favors the development of infection but also interferes with the early nutrition of the transplant by the permeating serum; a small amount of blood clot, however, is desirable); by including in the graft the periosteum, endosteum, and marrow, which not only contain active osteogenetic elements, but on account of their loose structure are more favorable than compact bone to a rapid reëstablishment of the blood supply with the recipient tissues of the graft bed, from whence nourishment rapidly reaches the compact part of the graft through the numerous bloodvessels passing from these enveloping membranes into the compact bone. In other words a bone graft consisting of all its elements approaches more closely a complete physiological unit, which is obviously an advantage.

Stöhr states in his text-book on *Histology:* "The bloodvessels of the bone, the marrow, and the periosteum are in the closest connection with one another and also with the surrounding struct-

ures. Small branches (not capillaries) of the numerous arteries and veins of the periosteum enter the Haversian and Volkman's canals which on the inner surface of the bone are in communication with the bloodvessels of the marrow. The latter is supplied by the nutrient artery, which on its way through the compact substance gives off branches to the same, and in the marrow brakes up into a rich vascular network."

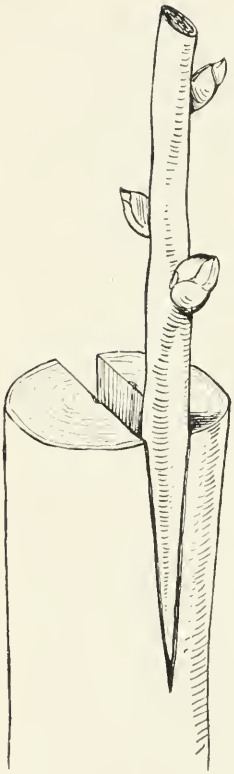

Fig. 1.—A diagram illustrating the method used most frequently in grafting fruit trees. It will be noted that it is an inlay graft and that the three elements of the graft or scion (namely, the bark, alburnum (sap) and wood) are closely coapted with their corresponding elements of the stock or recipient branch. This contact of individual tissue layers is most essential in tree grafting, and it is believed to be analogous to bone or other animal tissue grafting.

The bone contact should be of generous extent, and always to healthy vascular osteogenetic bone—the more unfavorable the bone the greater should be the area of contact. Careful suturing as well as accurate coaptation should be secured, when early use is to be made of the part, in order to obtain the benefits of functional irritation. In many instances early bony union may be enhanced by the interposition of numerous small grafts or fragments of bone. These coalesce with each other, and also with graft and recipient bone.

The ideal contact of these bone elements can only be secured by the employment of the inlay principle of procedure, which should always be carried out as carefully as circumstances permit. Examples of the various modifications of this principle are the inlay spinal graft for Pott's disease, the bone graft wedge for the correction of deformities, and the inlay for fresh and ununited fractures.

Bone grafts have been successfully applied by other methods, but the following are some of the obvious advantages of the inlay method besides the approximation of corresponding bone elements of graft to recipient bone which this procedure makes possible. Its modifications meet practically all mechanical requirements; it is as applicable to fracture of the small bones of the forearm as of the tibia or femur; it controls the deformity of the foot as well as of spinal caries. Its inherent mechanics favor the fixation of the graft as well as the immobilization of the fragments into which it is inserted. Its technique is not difficult because it has to do with plane surfaces.

A thorough understanding of the *modus operandi* and theory of Wolff's law is imperative. The influence of this law upon the success of bone-grafting procedures of all kinds cannot be too strongly emphasized. It not only influences the graft to proliferate and strengthen to an almost unlimited degree, if the new mechanical environment of the graft requires it, but this law also causes the

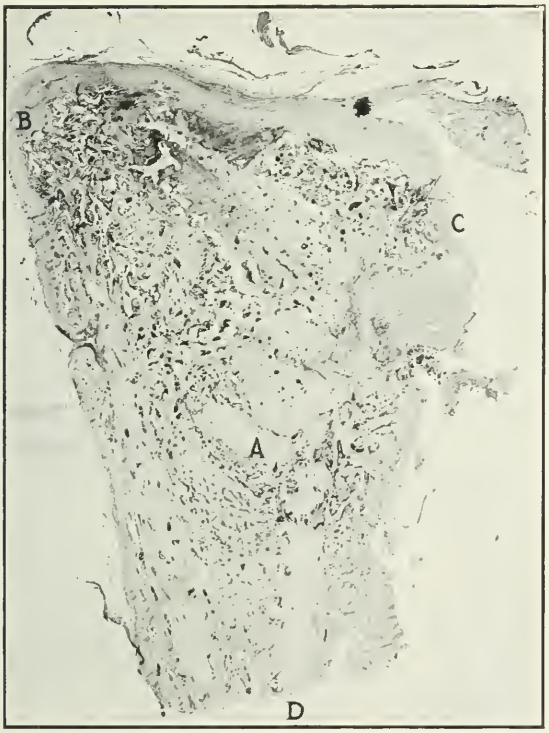

FIG. 2.—Photomicrograph of section through the long axis of spinuous process of a dog with a cross-section of an autogenous ulnar graft (*A*, *B*, *C*) thoroughly united by new bone two months after the graft was inlaid into the split tips of three spinous processes. The analogy to the technique of the tree graft (Fig. 1) is apparent. A careful microscopic study of this section has failed to disclose dead bone cells. The corners of the graft are indicated by *A*, *B*, and *C*. *D* indicates base of spinous process. The author's surgical experience in over 250 cases, as well as a large amount of animal experimental work, has convinced him that the inlay method of insertion affords by all means the most favorable graft environment, as this and many other microscopic sections have proved.

bone from which the graft was removed to be restored to its original strength. This same influence also causes internal reconstruction of not only the trabeculæ as the mechanical forces demand, but also of the general histological character of the bone, *i. e.*, cortical bone ultimately becomes spongy bone if implanted in or contacted with bone of that character, and *vice versa*.

A brief statement of Wolff's law is as follows: "Every change in the form and position of the bones, or of their function, is followed by certain definite changes in their internal architecture, and by equally definite secondary alterations of their external conformation, in accordance with mechanical laws."

The external shape of the bone is the result of functional adaptation. The bone is strengthened and thickened at those points where most stress and pressure come upon it, and is weakened at the opposite points. Such transformations have the object of enabling the bones or grafts in their altered positions and relationships to meet the new and abnormally directed stress thrown upon them.

Local or general hypertrophy of a graft may occur.

FIG. 3.—Skiagram of two grafts, each three inches long, inserted by the author for a tibial defect from the removal of two-thirds of its shaft for sarcoma. It was necessary to amputate the leg just four weeks after the insertion of the grafts, on account of the recurrence of the sarcoma, and in this short time the grafts had become firmly united (at *C*) by solid bone, although the diameters of the grafts both above and below the union remained the same as when implanted. These proliferating callus bone cells could have originated from no other source than the two graft ends, thus proving conclusively the active osteogenesis of these free grafts. The efficiency of the bone graft could not be better demonstrated than by this specimen. *A*, indicates where firm union has occurred between the upper graft and the upper remaining end of the tibia; *B*, where the lower graft has become united to the lower fragment of the tibia; *C*, indicates firm bony union between the two graft ends which were contacted in the centre of the leg far away from any possible source of new bone.

Local hypertrophies may occur in consequence of increased strain upon certain parts of a graft, either directly or through muscle pull.

Recognition and full appreciation of these important conclusions of Wolff constitute the foundation of the treatment of deformities and the application of grafts of all kinds. It is obvious that it is always advisable to allow the graft to functionate as early as possible by bearing mechanical stress within the limits of safety. This is highly favorable to osteogenesis, establishment of blood supply, and bony union. This functionating period should be preceded by the most efficient fixation of the parts grafted for an interval of not less than five weeks.

Although not advisable, many liberties can be taken with the

bone graft without interfering with its success. It has certain bacteria-resisting properties.

The author's experimental grafts were kept in normal salt solution for varying periods up to one week, with successful results following their implantation. In other cases, sepsis occurred immediately after insertion of the graft (experimental); nevertheless, parts of the grafts became united to recipient bone, while the rest of the implant sequestrated.

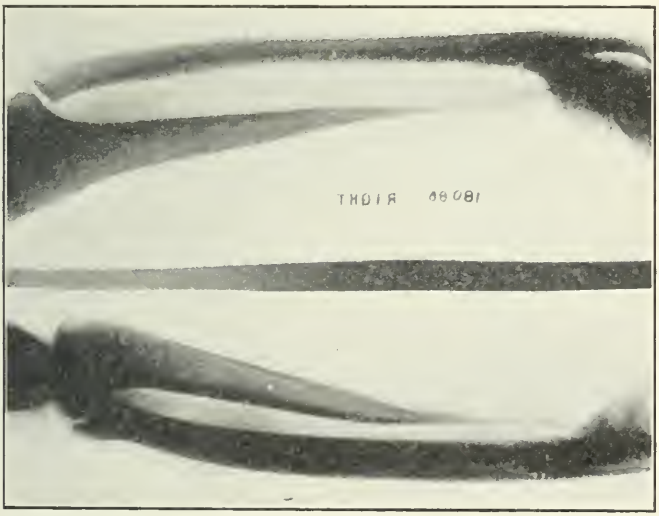

FIG. 4.—This is a skiagram of a case of loss of the lower one-third of the tibia one year before from osteomyelitis. The remaining periosteum attempted to reform the shaft and a small interrupted thread of bone can be seen. It, however, either became broken in two places or a complete bridge of bone was never produced; therefore, the influence of Wolff's law did not operate to stimulate bone proliferation as it would have if there had not been a solution of continuity. The potency of this same Wolff's law, however, could not be better demonstrated than it is in this same skiagram, as shown by the enormous hypertrophy of the fibula, which has become the size and strength of a normal tibia. This is a physiological property of bone, and shows itself as strikingly in bone grafts under functional stress as it does in complete skeletal bones. Therefore, as stated elsewhere, at the same time the graft is proliferating, in order to be of sufficient strength for its new environment, the tibia from which it was removed proliferates under the stimulus of function until it has returned to its normal strength and size.

Human autogenous grafts have been repeatedly so placed that they extended through, at their middle portion, tubercular foci, and in no case has primary union or taking of the graft failed. Likewise grafts have been so placed as to span attenuated pyogenic infected areas, and here the grafts have been equally successful.

Experimental grafts taken from long bones, such as the tibia or ulna, showed evidence of greater osteogenesis than those taken from vertebral spinous processes. Bone from which the periosteum

had been removed proved equally satisfactory to bone grafts on which the periosteum had been retained.

It is deemed advisable, as stated elsewhere, to always include the periosteum, endosteum, and marrow substance, when possible, on the graft.

The bone graft acts always as a stimulus to osteogenesis to the bone into which it is engrafted or to which it is contacted. This

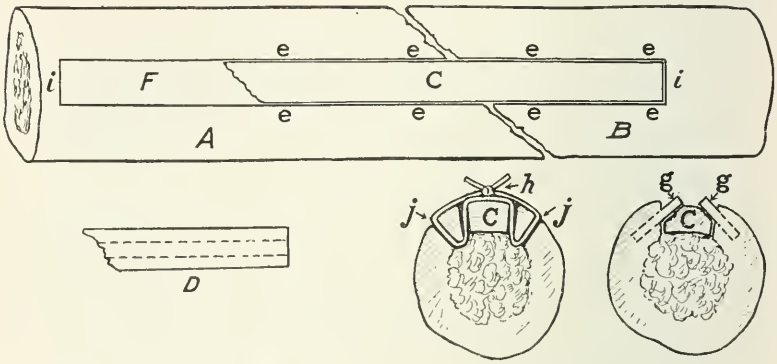

FIG. 5.—Diagram illustrating the author's application of a sliding-inlay-graft to an oblique fracture of a long bone as a substitute for a Lane's plate. The inlay should always be inserted, when possible, on the side of an oblique fracture, as indicated in this drawing. Over-riding of fragments and shortening of the limb are thus prevented by virtue of the mechanical property of the inlay, with the author's twin-circular motor saw adjusted, as to distance apart, according to the diameter of the bone. Parallel cuts to the marrow cavity are made extending into the upper or, if necessary, the long fragment (*A*) for a distance varying from four to six inches. The cuts are then extended into the lower fragment (*B*) one-half the distance, or two to three inches. These strips of bone are cut off at *i* with a small circular saw. The short strip of bone *D* from the lower fragment is then removed, producing a cortical gutter, and the longer strip *C* from the upper fragment is reversed ends and slid into the gutter in the lower fragment. It then remains to choose between heavy kangaroo tendon or bone dowel pegs to hold the inlay in place and thus immobilize the fracture-fragments. *D* is cut longitudinally along the dotted lines with a motor saw into two or three fragments, which are pushed through the author's motor-surgical-lathe and turned into perfectly round dowels each two to three inches long. These are cut with a motor saw into short pegs (*g*) and are placed in drill holes over the graft as indicated at *g* and *e*. These holes are made with a motor drill which is the counter-part, in size, to the dowel cutter. Therefore the fit must be accurate. If kangaroo tendon is chosen, *h* indicates the tendon tied at that point. *j* and *e* indicate the location of the drill holes through which the tendon is passed.

is a constant and important factor, and may be depended upon toward securing results. If the graft is placed in a location where there is no mechanical function for it to perform its cells retain their vitality, but nearly always there will be few or no proliferative changes in the transplant. On the other hand, if it is transplanted into a defect where there is a demand for it to perform a mechanical function, proliferative changes are usually marked, and it rapidly becomes united and similar in structure to the part to which it is

grafted. This is the law of functional irritation as laid down by Roux. The more perfect the technique of transplantation the greater will be the effect of this law of irritation.

The bone graft, when well contacted, becomes immediately adherent to the recipient bone by newly formed tissue, which usually changes to solid bone within four weeks. This, in the author's opinion, together with the graft's bacteria-resisting property,

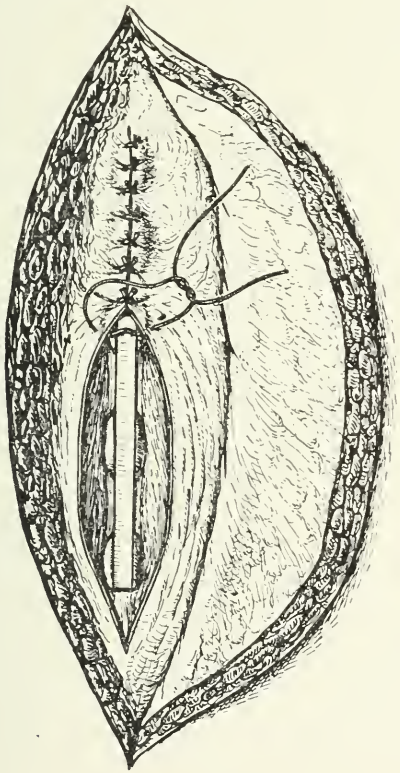

FIG. 6.—Drawing demonstrating the author's inlay bone graft inserted into five split spinous processes for vertebral tuberculosis. In the lower part of the wound the split supra- and intraspinous ligaments have been drawn over the lower end of the graft by means of heavy kangaroo tendon.

strongly favors, when feasible, the employment of the bone graft in place of any metal internal splints, especially when it is appreciated that metal has an effect opposite to that of a graft in that it inhibits callous formation, produces bone absorption, and favors infection.

The dowel, the inlay, and the wedge bonegraft fulfil all mechanical requirements and afford a means of repairing and remodeling the skeleton which the surgeon has not hitherto possessed.

Preservation of the Bone Graft. Various methods have been suggested for the preservation of bone-graft material, but in the experience of the author the following have proved most convenient and reliable.

The temporary emersion in normal salt solution is most satisfactory, and even this is not usually necessary, as, when possible, the graft bed should always be prepared prior to the removal of the graft, and the graft is immediately implanted in the prepared bed. This sequence of the operation is important, because (1) it assures an interval of time for the more perfect hemostasis in

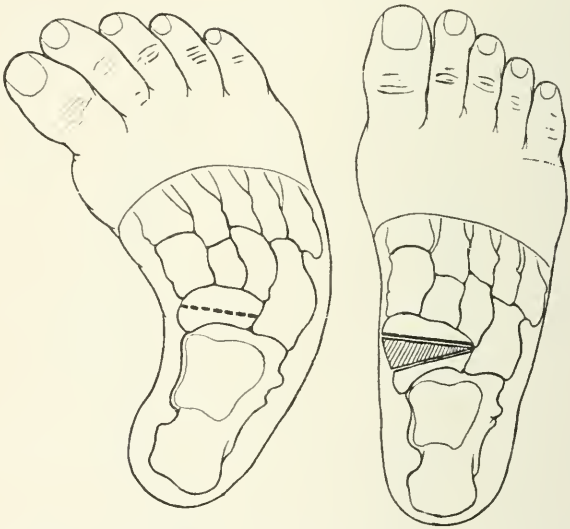

Fig. 7.—Diagram illustrating an inlay wedge bone graft removed from the crest of the tibia or the cuboid of the other side of the foot and placed into the split scaphoid for the purpose of permanently remodelling the tarsus of a congenital club-foot. In this deformity the inner side of the tarsus is shorter than its outer side, and the graft is inserted to overcome this distortion in older children and adults. The advantage of guarding against relapse by remodelling the bony tarsus is also augmented by lengthening the foot, which is always short.

the graft bed; (2) it enables the surgeon by means of calipers and flexible sterile pattern rod to obtain the exact size and contour of the graft required, thus avoiding unnecessary traumatization from holding forceps in reshaping a graft after its removal. Even in grafts where drill holes are necessary it is far preferable to drill the graft before loosening it from the bone from which it is obtained. A graft should always be used as soon after its removal as possible, but if it is necessary for any amount of time to elapse before it can be used, normal saline solution is not satisfactory as a preserving medium because of its evaporation and the consequent toxic effect. In both experimental and human work of the author, sterile vaselin

has proved a most satisfactory medium in which to keep the graft. It is not only perfectly non-toxic, but it is an efficient preventive of drying. The graft should either be immersed in a jar of vaselin or wrapped in gauze smeared with the same and placed in cold storage at a temperature of 4° to 5° C. Freezing is not desirable, as the resultant contraction and expansion damages the cellular content of the graft. Human grafts removed from cadavers and from other individuals have been successfully kept by the author for forty-eight hours on ten different occasions.

Emphasis should again, however, be laid upon the importance of using autogenous bone grafts whenever possible, as they are the most reliable; and as they are always used immediately, no preserving medium is necessary.

The surgical status of the value of the bone graft has now become so thoroughly established that the surgeon should be ready and equipped to make the best use of it in every individual case requiring boneplasty, where it may be indicated. An unabridged enumeration of the indications for the employment of the bone graft would be most difficult, and the following tabulation serves only as a suggestion of its broad field of usefulness:

General Indications. 1. To immobilize and stimulate osteogenesis in certain tuberculous joints.

2. To repair traumatic bone injuries.

3. To replace bone destroyed by infection.

4. To supply bone congenitally absent.

5. To strengthen or replace bone weakened or destroyed by benign or malignant growths.

6. To correct congenital or acquired deformities of the face.

7. To establish joints congenitally absent and restore those destroyed by disease.

8. To fix in place certain dislocated joints, acquired or congenital.

9. To close bone foramina in neuralgias.

10. To correct congenital or acquired deformities of extremities of trunk.

More specific indications for the bone graft are:

1. To immobilize, support, and stimulate repair in spinal vertebræ whose bodies are infected with tuberculous or other chronic infections where mechanical treatment is indicated. It is also applicable in cases of persistent non-union following fracture of the spine, presenting pain, disability, and increasing deformity, and should be inserted as for Pott's disease. Further indications are for certain fresh fractures of the spine; spondylitis traumatica (Krummell's disease) and neuropathic spine (Charcot), where, on account of a rarefying osteitis, crushing of the vertebral bodies and increasing deformity is likely to produce cord compression.

2. In the support and immobilization of cases of tuberculosis of the sacro-iliac joint, in certain desperate cases of tuberculosis

of the tarsus, and in the form of inlays to hasten or insure bony union in erasure or excising operations for adult tuberculosis of the knee or the hip.

3. In certain cases of paralytic scoliosis to support the weakened spine and prevent lateral deviation, due to superincumbent weight and unbalanced muscle pull.

4. To immobilize and support or replace bones of the tarsus or carpus destroyed, or partly destroyed, by tuberculosis.

5. To correct deformity or restore balance in congenital club-foot and acquired deformity from local disease or paralysis.

6. As a substitute for all metal plates, screws, nails, spikes, and wires, as used in the internal fixation of fractures and other conditions. The graft is in the form of inlays and various sizes of nails or pegs, and is employed by the author in all types of fractures, such as fresh and ununited fracture of the long bones and neck of the femur.

7. To produce a permanent closure of nerve foramina after nerve resection for neuralgia (Kanavel).

8. As a prevention to luxating or slipping patellæ by raising the low femoral condyle by inserting a graft in the form of a wedge.

9. To aid, in the form of numerous small grafts, rapid bone union where joint resection has been done or where a large graft has been used.

10. To strengthen and prevent lordosis or other deformity of the spine, in cases of spina bifida, where a large amount of bone is congenitally absent.

11. To replace the head and neck of the femur, when previously destroyed by disease, the head and neck of the astragalus being used as the graft (Roberts).

12. In congenital and paralytic dislocations of the hip where the acetabulum is shallow and the femoral head will not remain in place. The upper half of the meager rim of the acetabulum is separated with a chisel and forced out and down, forming a pronounced rim. The cuneiform cavity thus produced is filled with wedge grafts.

13. To produce an ankylosis of the ankle joint in sever paralytic cases, or tuberculosis in the adult, by placing a bone-graft peg through the os calcis and into the lower end of the tibia (Lexer).

14. To replace bone removed for osteomyelitis, tuberculosis, and spina ventosa.

15. For deformities of the nose by contacting graft with nasal bones. If the skin incision is made in the tip of the nose the scar is not noticeable (Carter).

16. To replace or repair defects of the lower jaw.

17. In intra-articular fracture-dislocations the head of the humerus or femur, etc., should be replaced, at an open operation, as a graft.

Summary. The bone graft is a trustworthy surgical agent, as proved by my uniform success, in its use in over 350 surgical cases. Also by a careful study microscopically, macroscopically, and by the Roentgen rays of its results, when used experimentally, both in the presence of primary union and sepsis. The cortical graft's field of usefulness is distinctly enhanced because of its resistance to tubercular and attenuated pyogenic infection.

Its field is also enlarged by the use of the author's motor-driven instruments, circular saws of different sizes, the adjustable twin saws, and the lathe or dowel instrument with different adjustments for making various sizes of bone graft inlays, nails, or spikes as they are needed.

By the use of this motor outfit and its products in conjunction with kangaroo tendon I have been able to avoid entirely the use of all metal in the form of screws, nails, Lane's plates, wire, etc., for internal bone-fixation purposes during the past two years. This has been made possible, largely, by making the best of well-known fundamental mechanical devices hitherto rarely, if at all, used in surgery, such as bone inlays, wedges, dowels, tongue and groove joints, mortised and dove-tail joints.

GASTRIC ULCER.[1]

By John B. Deaver, M.D.,

PHILADELPHIA.

I have thought it of sufficient interest to bring before the College certain questions relative to the treatment of gastric ulcer which have interested me very much, and which I have worked out to my own satisfaction along lines not universally endorsed perhaps by surgeons doing this work, but which I feel sure will prove to be the solution of certain vexing problems.

The experience of the last few years of activity in gastric surgery has shown both brilliant successes and dismal failures. It has shown that no one operation will fit all cases, that variations in situation, chronicity, and complications demand different methods of treatment, until finally, by the slow evolution of clinical experience and observation, we are in a position to draw some conclusions as to the principles which should underlie the surgical treatment of gastric ulcer.

Speaking of gastric ulcer in general, we must all agree that the treatment is aided by understanding both the predisposing and provocative causes which are responsible for the condition. Greater

[1] Read before the College of Physicians, Philadelphia, January 6, 1915.

knowledge along the latter lines enables us so to base our treatment as to attack the root of the evil. Direct traumatism, nervous and vascular conditions aided and abetted by the digestive and erosive action of the gastric juice, particularly when over-acid, have been the basis of the most advocated theories of the cause of this special form of ulcer. None of these explanations has stood the test of clinical parallel or sufficed to explain the revelations which have been brought about through the medium of the aseptic scalpel.

That peptic ulcers are at the outset due to some form of toxemia or infection there is no doubt in my mind. The clinical arguments in favor of toxemia and infection being the causative factors are devious, and may not in themselves be conclusive, yet, as is often the case with such beliefs, evidence of a more satisfactory nature has appeared after a time. We know that experimentally (Turk) gastric ulcer has been produced by intravenous injection of the colon bacillus. Recently, Rosenow has demonstrated that certain strains of the streptococcus when inoculated into the blood of experimental animals produce ulcers of the stomach and duodenum with great uniformity. Gundermann has produced both acute and chronic ulcers of the stomach by ligation of the left hepatic branch of the portal vein, concluding that an hepatic toxemia is the cause of the ulceration. Experimental evidence, therefore, is not lacking as to the role that toxemia, whether metabolic or bacterial in origin, may play in causing gastric ulcer.

Appendicitis is by far the most common intra-abdominal disease. If we admit that appendicitis is always caused by infection, and that it is the most common intra-abdominal disease, we must also admit that the appendix, therefore, is the most common avenue by way of which infection reaches the abdominal circulation, be it through the blood or lymphatic current. Granting this is true, we have the keystone of the arch of the knowledge of intra-abdominal diseases which always are the result of an infection. I believe the appendix is responsible for liberating the infection, which in turn causes gastric as well as duodenal ulcer and other forms of upper abdominal disease in an overwhelming majority of instances.

In my clinics at the German Hospital I have observed the almost constant association of chronic appendicitis and gall-bladder disease with duodenal and gastric ulcer. Paterson also calls attention to this point. Graham, in the Mayo statistics, gives 23 per cent. of duodenal ulcers and 20 per cent. of gastric ulcer coexistent with disease of the appendix and gall-bladder. The focus of infection need not necessarily be the abdomen, though it seems that it is here the association is more evident.

That infection from the mouth, as occasioned by pyorrhea, for example, may be the exciting factor in causing gastric ulcer is true perhaps in a small percentage of cases. Doubtless there are many portals of entry for infection, but it is sufficient to say

that we are warranted in assuming that chronic or acute infections with the toxemia or bacteremia consequent thereon are capable of producing and do, under clinical conditions, produce gastric and duodenal ulcerations. Furthermore, the common association of chronic disease of the appendix with gastric and duodenal ulceration is significant of a causal relation between the two through the medium of toxic products and infection liberated from the appendix.

We are concerned equally as much with the factors that keep the ulcer from healing as with those that give rise to it. Among these are the conditions of the general health, the continuance of exciting causes in the muscular activity of the stomach, the action of the gastric juice upon eroded surface, and infection that implants itself upon the bed of the ulcer. That there is a strong natural tendency for simple gastric ulcers to heal there can be no doubt, as there is abundant evidence of such healing in the human. Experimental ulcers usually close rapidly.

Well-directed medical treatment will succeed in healing most acute ulcers and a fair percentage of those on their way to chronicity. In the absence of severe complications, medical treatment should always be given a fair trial before resorting to surgery.

Ambulatory treatment will rarely be successful except in the simple form of ulcer. If anything is to be expected of medical treatment in the chronic types of ulcer it must be radical, demanding four to eight weeks rest in bed and most careful feeding. The entire remission of all symptoms, which is a characteristic of ulcer, has been productive of much misunderstanding and harm. It must not be forgotten that ulcer is productive of symptoms, as a rule, only when it is in an inflamed and active state. When the bed of the ulcer is covered with insensitive granulation tissue, and its walls are not inflamed, pain and distress are abolished, and unless adhesions or cicatricial deformity are present, the patient feels quite well and the incautious physician may be led to believe that the ulcer is healed. It is not difficult to lull an inflamed ulcer into quiescence, but it takes time, patience, care, and coöperation on the part of the patient to await the time necessary to reinvest the ulcer with epithelium. In this quiescent stage many a patient has been placed asleep in the eternal rest of the grave.

The explanation of recurrent attacks extending over many years is to be found in the fact that at no time was the ulcer healed. Circumstances render it impossible in many instances for the patient to submit to the rigorous regimen necessary for cure, and in many other cases it is equally impossible to secure the coöperation of the patient in the tedious process. Attempts at healing by medical treatment with the best means available is justified in all except those cases complicated by perforation, recurrent hemorrhage of sufficient moment to cause material drain upon the patient's health,

or in the presence of persistent indigestion that does not yield after a fair trial of medical treatment, by which I do not mean indefinite temporizing. We must not forget the marked tendency of cancer to develop on a chronic ulcer base, and all such cases are properly to be rated as the most disastrous medical failures.

Admitting the conditions just stated to be the correct clinical indications for operation, we come to the consideration of surgical procedures, about which there is not as yet unanimity.

There is a difference of opinion among surgeons as to the correct procedure in perforation. Some contend that only the perforation should be closed. Others believe that a simultaneous gastro-enterostomy not only aids permanent cure, but also increases the chances of recovery in acute perforative conditions. While it may appear on the surface that simple closure of the ulcer would suffice for the immediate emergency, and that the less surgery the greater likelihood of recovery, nevertheless it is my belief that a primary gastro-enterostomy is far more likely to be followed by immediate recovery, and certainly the prospects of future relief are much improved. The mortality of those who combine gastro-enterostomy with closure of the ulcer is superior to that of those who practise only closure. I have reported thirty cases of acute perforation of gastric and duodenal ulcer in which gastro-enterostomy was done as a primary procedure, with one death. Since then I have had three additional cases, with recovery.

Hemorrhage, whether massive, recurrent, or occult, will furnish different indications according to the lesion believed to be present, its duration, the amount and seriousness of the loss of blood. Profuse gastric hemorrhage in the young without previous symptoms of ulcer may be due to mucous erosions or hemorrhagic gastritis. The cause of these so-called Dieulafoy's ulcers may not be clearly understood, yet clinical experience shows that they are not ordinarily fatal, tend to clear up spontaneously, and often are followed by no sequel of any kind. Gastro-enterostomy has been advocated for these conditions, but the evidence, in my opinion, does not warrant its use in every case. On the other hand, massive hemorrhage from erosion of the base of a chronic ulcer is a dangerous condition and urgently calls for intervention At the same time it is not wise to operate upon a patient in an exsanguinated state. The first hemorrhage rarely kills, and with proper treatment some reaction may be expected. On the other hand, reaction with restored blood-pressure is apt to excite fresh hemorrhage, which is more likely to be fatal than the first. It becomes a question of nice surgical judgment therefore to decide when to operate. I have regretted my decision n both directions, and do not feel able to advise in any other than the most general terms. It is too hazardous to wait for the reformation of blood to take the place of that which was lost, as that is a matter of some days and even weeks. This

being the case, it seems wise to wait only for the subsidence of shock, the refilling of the bloodvessels by the body fluids, and by water administered and the restoration of the blood-pressure to approximately normal level. Direct transfusion of blood will occasionally have a field here.

In these cases one's difficulties are not over with the selection of the best time for operation. The location of the actual erosion in the vessel is a matter of the greatest difficulty. It is difficult to determine which artery is affected. Direct ligation is, therefore, theoretically desirable, but practically well-nigh impossible. Complete excision of the ulcer is almost invariably too much of an operation for these patients to stand. Simple gastro-enterostomy may be helpful but does not provide absolute security against recurrence of bleeding.

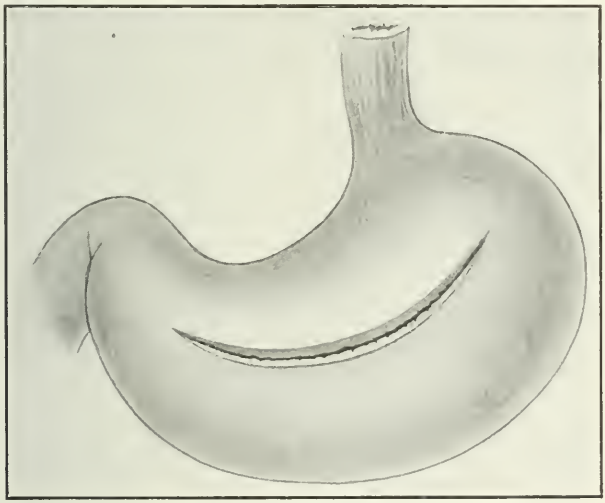

FIG. 1.—Incision through anterior wall of stomach.

A plan which I have followed successfully appeals to me as sufficiently radical. After opening the abdomen and locating the ulcer the stomach should be opened and the base of the ulcer inspected. If the vessel is seen it should be ligated directly by transfixion. If, as is more commonly the case, no erosion or vessel is seen a stitch of catgut should be whipped around the base as well as the edges of the ulcer, with the object of occluding the vessel supplying it. The stomach may then be closed and gastro-enterostomy quickly performed. I liken this procedure to hysterotomy, of which I am a strong advocate.

Further, it is my practise, where the ulcer cannot be located by inspection and careful examination of the exterior of the stomach, to open widely the stomach through the anterior wall and inspect

its interior throughout, which can be done satisfactorily, as I have frequently demonstrated. The latter treatment, as a matter of course, applies to chronic ulcer more than to acute ulcer. That the danger in opening the stomach in chronic ulcer cannot be great is proved, moreover, by the fact that I have operated upon thirty-three cases of acute perforation of the stomach and duodenum with but one death. In these cases there is much more soiling of

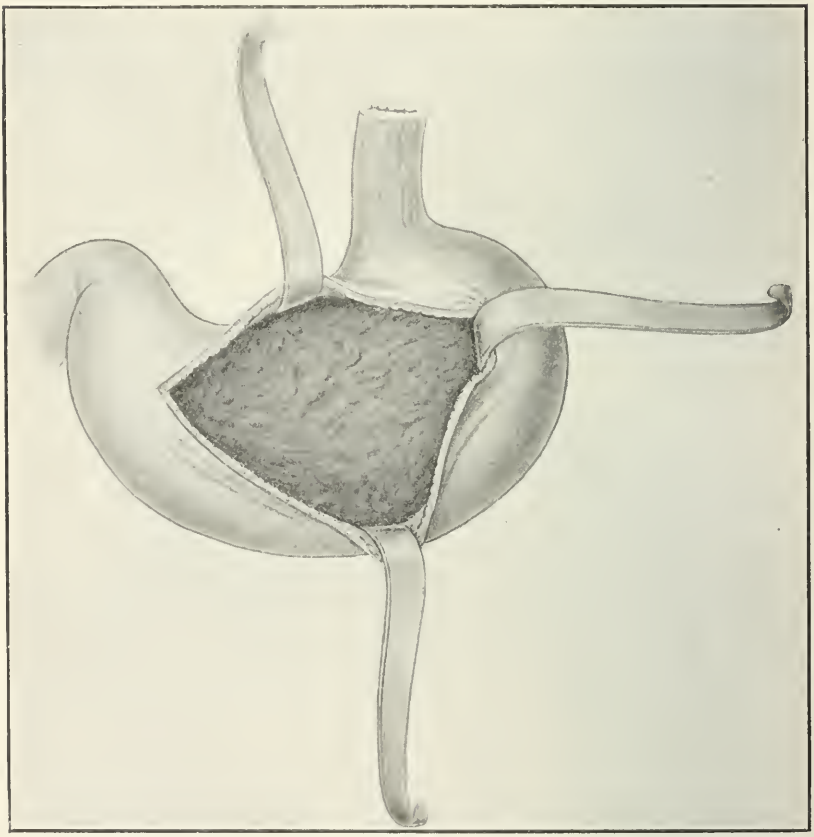

FIG. 2.—Margins of incision retracted, showing interior of stomach.

the peritoneum by gastric contents than could result from a properly performed gastrotomy.

The degree of fibrosis in the wall around a gastric ulcer varies. It may be so slight that the ulcer is not easily felt; this is particularly so when it is situated close to the pylorus (pyloric ring). This is one of the reasons why I open the stomach in cases where I cannot satisfy myself as to the presence of a lesion. The area of open ulceration is not necessarily related to the extent of sclerosis of

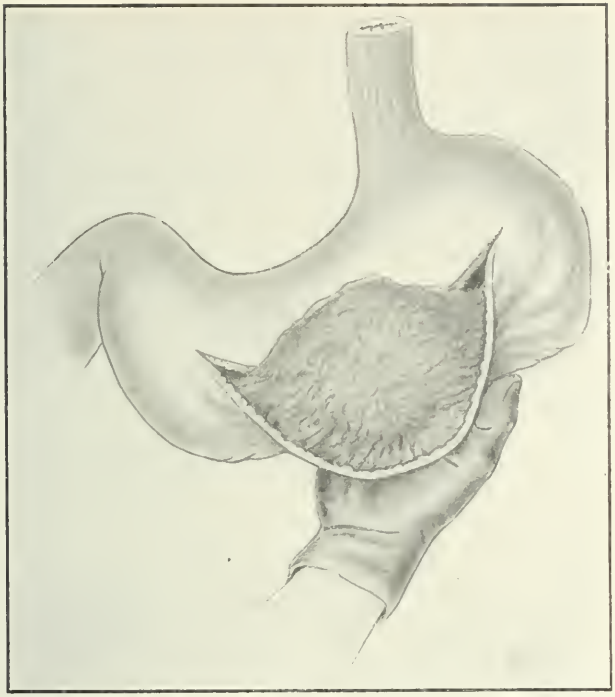

FIG. 3.—Wall of stomach everted through gastrotomy incision.

FIG. 4.—Ulcer, posterior wall.

the wall of the stomach. The physical character of an ulcer has an important bearing on the question of excision. Ulcers on the posterior wall of the stomach are more frequently adherent to surrounding structures than those on the anterior wall.

The effect of gastro-enterostomy when ulcers are some distance from the pylorus is often disappointing. Gastroduodenostomy has an important field in surgery of ulcers close to the pylorus. The latter operation positively excludes pyloric spasm and retention, two most important phenomena in gastric ulcer. Excision is influenced by the site of the ulcer, adhesions, and the general condition of the patient.

Smaller hemorrhages, if persistent, also strongly indicate surgical measures, since we cannot determine just what artery is being

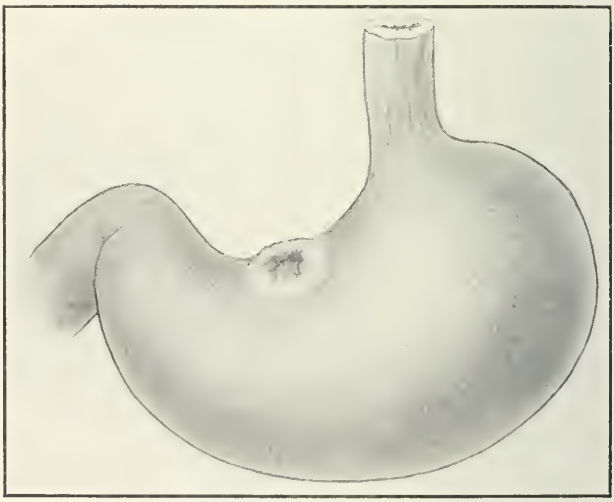

Fig. 5.—Ulcer, lesser curvature of stomach.

attacked; and even if it is not a precursor of serious hemorrhage the patient's vitality is much affected by constant loss of small quantities of blood.

Chronic ulcers situated along the lesser curvature of the stomach I always excise. This is accomplished by first opening the lesser peritoneal cavity through the upper layer of the gastrohepatic omentum, tieing the coronary artery to the left and the pyloric artery to the right, then opening directly through the anterior wall of the stomach, exposing the ulcer, cutting it out with scissors, closing the stomach, and finishing the operation by posterior gastro-enterostomy and plication of the duodenum. I have done several of these operations and up to the present without a fatality.

I have recently performed a transduodenal excision of an ulcer in the internal posterior wall of the duodenum in its second portion.

The crater-like fibrosis around the excavation of the ulcer was felt through the anterior wall of the duodenum, where it lay on the head of the pancreas which at that point showed induration and evidence of chronic inflammation. Through a longitudinal incision in the duodenum the ulcer was exposed and was then excised with the scissors and knife. The defect in the posterior wall was brought together with stitches of chromic catgut and the opening in the anterior wall closed with chromic gut and linen thread. A posterior gastro-enterostomy was made and the patient recovered. This I believe is the first instance of such an operation for duodenal ulcer. It is applicable only to ulcers similarly situated which have not eroded completely through the wall into the adjacent tissues.

This case shows what may be done early in the history of gastric or duodenal ulcer. The later the case, the more widespread is the

FIG. 6.—Ulcer, internal posterior wall of duodenum.

ulcer and its consequences, the more difficult is the surgery and the less satisfactory the results.

Ulcers of the posterior wall of the stomach distant to the lesser curvature I expose by opening the stomach and the lesser peritoneal cavity which affords oportunity to deal with the ulcerated area with the least difficulty, following the latter with a posterior gastro-enterostomy. In ulcer of the pyloric portion of the stomach, unless very small and not indurated, I perform pylorectomy.

If perforation or conspicuous bleeding are absent at what point does a gastric ulcer cease to be a medical condition? Clearly, it seems to me, when it is seen that such medical treatment as can be employed fails in a reasonable time to cure the ulcer. *Cure* should be sharply distinguished from *remission* or improvement of symptoms. Recurring ulcer symptoms mean only one thing, failure of cure, and to incur the risk of the grave complications which are

likely to follow chronic relapsing ulcer is an unjustifiable assumption of responsibility. We must not stop short of surgery if the ulcer is refractory to other methods. One relapse after thorough treatment, two or at the most three relapses after treatment imperfectly carried out should convince one that chronic ulcer of a refractory type is present.

The question of the proper surgical treatment of a gastric ulcer can be decided only after the abdomen has been opened and the condition present thoroughly explored, which often means that the stomach must be opened widely to make the exploration thorough,

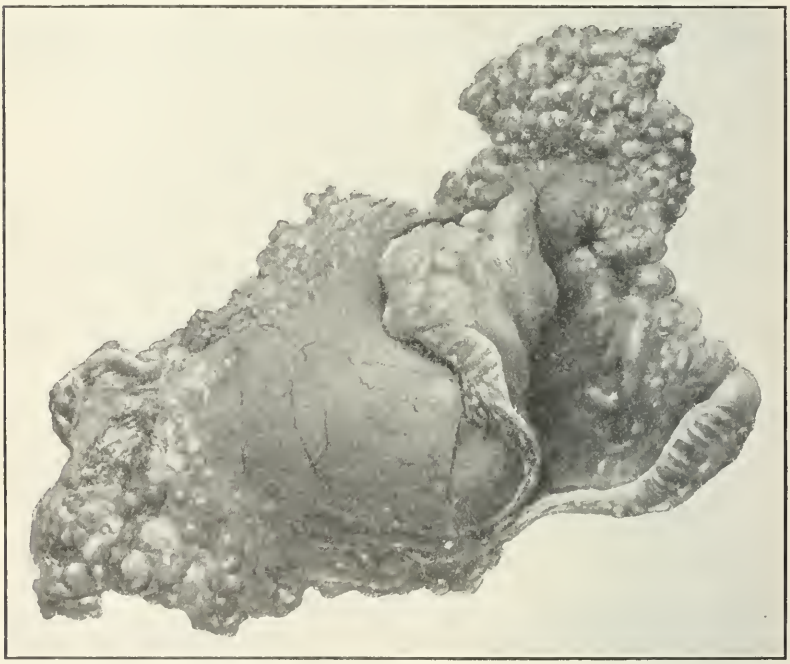

Fig. 7.—Ulcer, lesser curvature.

as I have referred to above. Complete excision of the ulcer may be spoken of as the ideal treatment, but, like ligating an eroded vessel in an ulcer bed, or many other measures theoretically ideal, it can seldom be accomplished. Localized saddle ulcer on the lesser curvature, ulcers strictly limited to the pylorus or small punched-out ulcers elsewhere in the wall, are those which are best adapted to excision. Given a patient in good general condition, and an ulcer that can be so removed that subsequent closure can be made without undue distortion of the stomach, and without tension and danger of leakage, excision is the method of choice. If such an ulcer be unusually hard and suspicions of malignant degeneration

there is the greatest need for excision, or better still, subtotal gastrectomy. If excision has been done it is best to make a gastro-enterostomy even though the pylorus has not been encroached upon. A method of removing the ulcer completely is the so-called exclusion, which consists in placing occluding ligatures through all the thickness of the stomach wall, encircling the ulcer completely, and cutting off its blood supply so that it separates as a slough by ulceration into the interior of the stomach. The occluding ligatures having been tied the walls of the stomach immediately adjacent

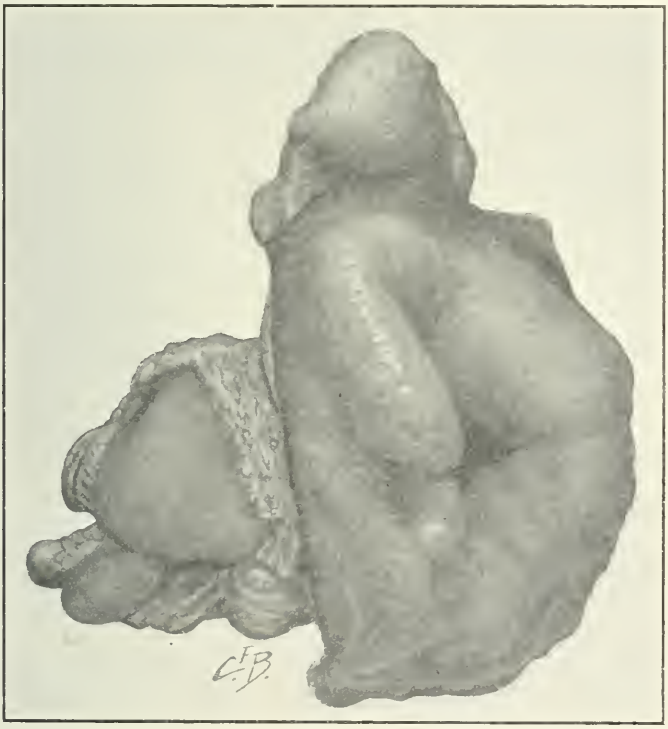

FIG 8.—Ulcer, pyloric end of stomach.

are apposed. This method should be ideal in bleeding ulcers, as hemostasis is at once affected by the ligatures. In many situations, however, it is impossible to apply this variety of ligature, and I believe that this method is of little real utility. I have never done this operation.

Ulcers high up in the fundus of the stomach are the most difficult to treat. Gastro-enterostomy fails to effect a cure. Excision is usually impossible because of its difficulties and the great operative hazard. These may be treated best in an indirect manner

by jejunostomy, which gives absolute rest to the ulcerated surface and favors healing.

One of the most important points to be noted in connection with this subject is the fact that the sufferer from gastric ulcer does not belong to either the internist or the surgeon exclusively. The physician should make the first attempt at cure, and in the event of failure or sudden catastrophe the patient becomes surgical. If he can have his ulcer excised he may be through with his physician so far as this particular condition is concerned. If, as more often happens, the surgeon finds it impossible or unwarrantably dangerous to excise the ulcer, he employs an operation which depends for its efficacy chiefly upon rest for the affected area. The patient should then return to his physician, who will so direct his diet and mode of life as best to assist in this object. Right at this point

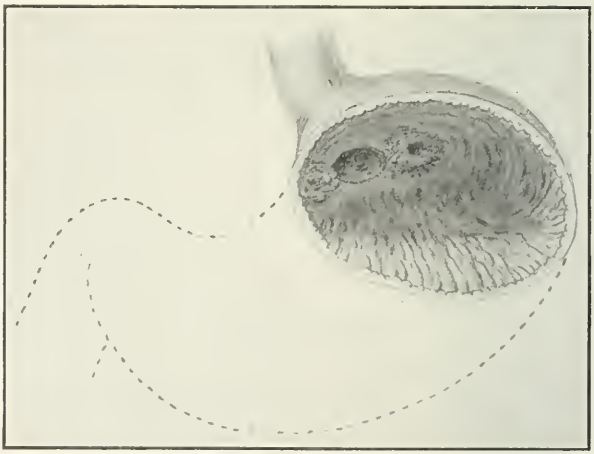

Fig. 9.—Ulcer at esophageal opening of stomach.

many failures occur. Either the physician fails to appreciate the importance of careful supervision or the patient, completely relieved of his symptoms, believes that he is cured, and can indulge his appetite as freely as he wishes. This is particularly true of patients who have had more or less pyloric stenosis. Their relief is so great and their hunger in their half-starved condition is so compelling, that if not restrained they will go to extremes in eating that no sound man could endure. In this case the ulcer may be deprived of its rest and protection and fails to heal, or in still other cases additional ulcers form elsewhere. A goodly percentage of recurrences are due to such failure of the patient or his physician to carry to completion the work only begun by the surgeon.

Finally, in view of the fact that prevention is greater than cure, and particularly because it is seen from this brief review of certain

mooted points in the surgical treatment that cure is difficult and perhaps impossible, I would urge the propriety of acting on a well-reasoned suspicion that a small inhabitant of the right iliac fossa is responsible for much of the serious diseases of the upper abdomen. In other words, search diligently for evidences of chronic disease of the appendix in all digestive disorders and treat it to a drum-head court martial at the first sign of insubordination.

PAIN AND OTHER SENSORY DISTURBANCES IN DISEASES OF THE SPINAL CORD AND THEIR SURGICAL TREATMENT.[1]

By Charles A. Elsberg, M.D.,
NEW YORK.

(From the Surgical Department of the New York Neurological Institute and the Third Surgical Service of Mount Sinai Hospital.)

The tremendous development of abdominal surgery has brought with it a great advance in our diagnostic acumen. Not a few books and monographs on the special subject of abdominal pain and abdominal tenderness have been published. Strange to say, however, the authors have devoted little attention to the neural origin of many cases of persistent abdominal pain. The more one keeps in mind the possibility of this source of origin the more one will meet with cases in which the symptoms will be found to be due to a lesion or disease of nerves, nerve roots, or nerve centres, and the more important will become this aspect of the subject.

The abdominal symptoms of locomotor ataxia are well known, yet in not a few cases, operations upon the stomach have been performed for supposed gastric disease when the real trouble was gastric crises in the course of tabes. During the past five years two patients have been sent into my service in one of the hospitals in New York with the diagnosis of acute appendicitis; in both instances the patients had Pott's disease with irritation of spinal nerve roots and areas of skin and muscle tenderness in the right iliac region. I have personal records of three patients in whom various operations had been performed, a floating kidney anchored, the appendix removed, the gall-bladder operated upon, in one case a hysterectomy performed for pain and tenderness in the lumbar, right iliac and right hypochondriac regions; finally they were found to have a spinal tumor or a neuritis of the nerves of the cauda equina. A patient was operated upon by me for supposed

[1] Read before the College of Physicians of Philadelphia, November 4, 1914.

gangrene of the toes with severe pain shooting down the leg; she was finally relieved of some of her painful symptoms by an operation for spina bifida occulta. The areas of gangrene on the toes were trophic ulcers due to the spinal disease. Many patients are treated for a "neuritis," brachial, sciatic, peroneal, etc., for long periods of time, until finally the diagnosis of spinal disease, tumor, gliosis, or malignant disease of the vertebræ is made. We now know that painful sensory disturbances referred to the extremities frequently occur in disease of the optic thalami and corpora striata.

On account of the importance of this subject, therefore, it may be of interest to recount some of the experiences that I have had and some of the conditions I have met with during five years of spinal surgery, the anatomical conditions found at operation, and the surgical methods by means of which relief was given.

Pain in the Extremities Due to Spinal Disease. In order to understand the distribution of painful symptoms in the extremities a few words regarding the anatomy of the spinal nerve roots may be of value. As I have elsewhere shown, there is a marked difference between the cervical and upper dorsal and the lower dorsal and lumbosacral posterior roots. In the latter the nerve fibers which originate from the cord soon unite to form one bundle, the posterior nerve root; in the former, however, the bundles of fibers which originate from the cord along a line from 1 to $1\frac{1}{2}$ cm. in length do not unite to form the posterior root until near to where they perforate the dura. As a result a tumor may press upon some of the nerve bundles without compressing the entire spinal root. This anatomical arrangement enabled us to understand the early symptoms of a patient from whom I removed an extramedullary tumor of the spinal cord between the seventh and eighth cervical segments, whose first and for a long time only symptom was a painful pin-and-needle sensation in the index finger of the left hand. At the operation the tumor was found to have pressed upon only the lower nerve root bundles of the seventh cervical posterior root, as shown in Fig. 1. From several cases of this kind I feel justified in making the statement that of the nerve bundles which make up the seventh cervical posterior root the lower supply the index finger and the upper the thumb, an interesting fact for finer spinal localization.

I have operated upon a patient whose only complaint was excruciating pain on the upper and outer side of the right thigh. She had been thrown out of an automobile about one year before, but was unaware that she had injured her back. There was an area of superficial hyperalgesia extending over the posterior and outer surface of the thigh, outer surface of the knee, and anterior and inner aspect of the leg. This and another similar case allowed me to map out a somewhat different area of supply of the fourth posterior lumbar root than that heretofore described. At the

operation upon this patient a ruptured ligamentum subflavum was found to have compressed the fourth lumbar root, and with the excision of the ligament the pain disappeared.

Abdominal Pain in Spinal Disease. As a preface a brief consideration of some aspects of abdominal pain may not be out of place. There are many abdominal disturbances that patients suffer from which are but little understood. Physical examinations only too often will fail to demonstrate anything excepting tenderness perhaps most marked in one or the other part of the abdomen. Some of the patients are neurasthenic or have become so, but very

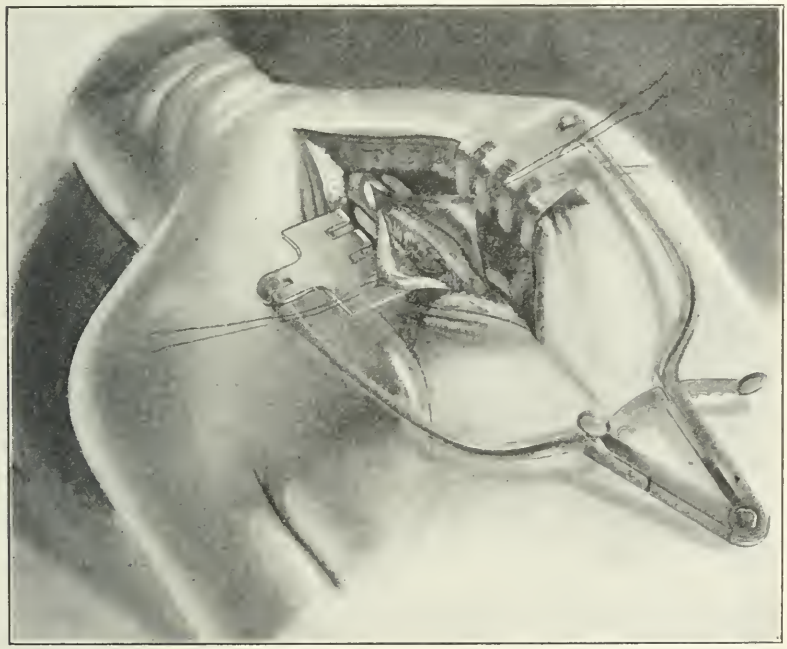

Fig. 1.—An extramedullary spinal tumor which pressed upon the lower root bundles of the seventh posterior spinal root and caused a painful sensation in the index finger of the left hand. (The tumor has been drawn too low by the artist.)

many are normal and well-balanced individuals. It is wrong to tell these patients that they have nothing the matter with them and to send them away after unsuccessful treatment, often into the hands of quacks, Christian scientists, or faith healers. Nor does it help to characterize the condition by vague names, to speak of painful aortas, of neuralgia of the sympathetic (Buch). Not a few of the patients are finally operated upon and too often without benefit. An appendix, perhaps not quite normal, is removed, the gall-bladder is explored and perhaps a few calculi extracted, various operations done upon the female adnexa and uterus. After these

"surgical decorations," as Mayo calls them, the patients are often as badly off as ever. There are fads in medicine, and the latest is to explain the symptoms by a mobile cecum (the German point of view) or a membrane which prevents freedom of peristalsis (the American point of view). Of course, the one or the other of these views may sometimes be correct, but probably in most instances both are wrong. In passing I would say that in my experience those who have changed from an active to a more sedentary life are peculiarly apt to suffer from a variety of abdominal disturbances. Many of these patients are subjected to operative interference, but I have again and again found that the abdominal disturbance will disappear after the patients again take regular exercise.

If we see this type of patient we should never omit to make or to have made a careful neurological examination. In my last 100 laminectomies for spinal disease I have performed six operations on patients who had been treated for long periods for abdominal symptoms. In four of the six patients I found and removed extramedullary or extradural tumors from the spinal cord. Therefore, in every case of indefinite abdominal pain and tenderness it is advisable to make certain that we are not dealing with a cutaneous hypersensitiveness which so often simulates real abdominal tenderness.

Mrs. W., aged forty-three years, was first seen by me in 1912. For two years she had been having frequent attacks of pain in the lower abdomen on the left side. The patient was married and had a number of children; cystocele and rectocele operations had been done in the attempt to relieve the pain; the appendix had been removed. She had been Roentgen-rayed and cystoscoped and her ureters had been catheterized; she had received a great many remedies, but the abdominal symptoms were unrelieved. Otherwise she complained of no symptoms.

The patient was a stout woman, looking the picture of health. Careful examination revealed the fact that the abdominal pain and tenderness were really due to a superficial skin tenderness and that this was limited to the distribution of the twelfth dorsal root on the left side. The patient had a slightly exaggerated knee jerk on the left side with a slight tendency to ankle clonus. On the right side there was slight hypesthesia and hypalgesia over three toes with a diminution in the acuity of deep muscle sense in the right big toe. The Wassermann reaction and Roentgen-ray examination were negative, and the spinal fluid showed a normal cell count. The diagnosis of a small tumor pressing upon the twelfth dorsal root was made. With the removal of a fibroma of the size of an almond the patient recovered. For almost one year she complained of slight pain over the area where she had had pain before the operation, but this pain gradually disappeared.

I have several times observed this persistence of slight root pains after the removal of a spinal tumor, no doubt due to changes in the nerve which had been long pressed upon. It is advisable, therefore, in a case of this kind, to divide the spinal root in question. The division of such a posterior root will not give rise to any symptoms and will of certainty prevent the neuritic pain. There are, however, some painful disturbances which may persist for some weeks after the removal of an extramedullary or intramedullary new growth which must be considered as central pain, protopathic in character.

The relief of the gastric crises of tabes by means of division of posterior roots was first recommended by Foerster, of Breslau. As is often the case the first results that were reported were successes; then the frequency of failure caused the operation to be modified and extended. In the beginning Foerster recommended that three to five spinal roots should be divided, later he advised that eight posterior roots, the fifth to the twelfth dorsal, should be cut. Even this extensive root section (requiring an extensive laminectomy) often failed to control the attacks, and the vagus was blamed for the failure. The present status of the matter is that extensive root division will often benefit the patients, but in only a small percentage will a recurrence of the gastric and intestinal crises be prevented. I believe that before doing a root section for gastric crises the surgeon should always give the patient a preliminary intraspinal injection of stovain; by this means one can gain a fair idea of the prospects of success from the division of posterior roots.

I can not pass over the subject of pain in spinal disease without paying a tribute to the Philadelphia neurologist and surgeon who originated a valuable operative method for the relief of severe pain of peripheral or of spinal origin. There is nothing more horrible than the pain suffered by unfortunates with metastatic malignant disease of the spinal column. The patients may remain alive for months or years, the amount of relief afforded by drugs and anodynes is small, and division of posterior roots will seldom permanently stop the pain. It is well known that division of posterior roots for the relief of pain will often, no matter how extensive the root division, fail to be of benefit. When, a few years ago, Spiller and Martin proposed that the anterolateral tracts in the spinal cord, those tracts in which lie the pathways for pain, be divided, a real advance in therapeutics was made. My experiences with the operation of Spiller and Martin have been small up to the present time. I have had only two cases; the result in one of the patients was satisfactory. The method is based upon a sound anatomical and physiological foundation, great relief has been afforded the patients, in most of the cases in the literature, and the future for the operation is a bright one. In several cases

in which the operation was not entirely successful the division of the anterolateral tracts was not made high enough in the cord or the tracts were not completely or not correctly divided.

The Sensitiveness of the Cord and Meninges. An interesting subject, and one concerning which up to the present time but little is known, has occupied some of my time and attention. Is the spinal cord sensitive to pain? Or is it insensitive like the brain?

I have carefully watched and questioned a large number of patients upon whom a lumbar puncture was done. I have further made some observations in patients upon whom a spinal operation was done under local anesthesia. Finally, I have attempted to learn something on this subject in the course of some experiments upon animals.

The outer surface of the dura is insensitive to touch or when it is rubbed or scratched with a needle. The inner surface is, however, very sensitive, and gentle handling is felt as a painful sensation by the patient. The dentate ligament is insensitive; it can be grasped with a forceps and cut without any complaint by the patient. The surface of the cord is not sensitive to pain excepting along the line of origin of the nerve bundles which unite to form the posterior spinal roots. An incision can be made into the cord without the patient feeling it, but in one instance in my experience the patient complained of a burning sensation in one leg while the cord was being pulled upon. This may have been due to traction on a spinal root, or may have been one of those central pains of which I have already spoken.

The most sensitive part of the posterior spinal roots is just at the point where they perforate the dura. This may be contributed to by the peculiar course of the nerve roots at this point. I have recently called attention to the peculiarities in the course of many of the nerve roots. At many levels they are bent at a more or less acute angle as they pass through the intervertebral foramina. In the cervical and upper dorsal regions the nerve bundles unite to form the posterior root and pass out of the dural sac at almost a right angle to the cord. They perforate the dura and enter the posterior ganglion. From the ganglion each root passes outward with a slight inclination upward. From the eighth cervical to the middorsal region the course of the posterior roots is a different one. Each root has an inclination downward until it nears the dura; it bends upward at an angle just as it perforates the dura. In the middorsal region this angle is often very acute, 40 to 45 degrees. Taking into account the peculiar course of the nerve roots just mentioned and the sensitive dura it is easy to understand why a small metastatic focus of malignant disease in the posterior and lateral part of the body of a vertebra may cause those agonizing root pains from which the patients suffer, which may defy even the largest doses of morphin, and which can only be relieved by the division of the anterolateral

tracts of the cord recommended by Spiller and Martin. It is easy to understand also that only a slight inflammatory process near the dural opening may cause very marked root pains.

A Peculiarity in the Sensory and Motor Symptoms in Some Cases of Spinal Tumor. In the later stages of spinal compression the typical Brown-Séquard syndrome, motor symptoms on the same and sensory symptoms on the opposite side to that of the lesion can no longer be recognized. But in slight compression of the cord the clinical picture may be clearly outlined. In some cases in the literature and in several patients whom I have operated upon, the root pains and the loss of sensation below the level of the lesion were on the same side as the tumor, and the paralysis and

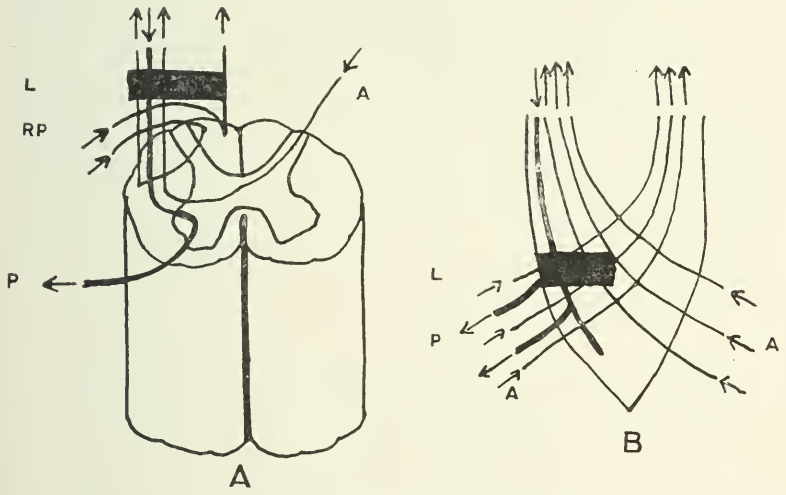

Fig. 2.—*A*, the Brown-Séquard syndrome; *B*, the explanation for the occurrence of marked sensory symptoms on both sides of the body in unilateral disease of the lumbosacral cord; *P*, paralysis; *A*, anesthesia; *RP*, root pain; *L*, lesion.

other motor symptoms mainly on the opposite side. In other words the motor symptoms were on the side on which most sensory symptoms usually occur and the sensory disturbance on the usual motor side. How can such a condition of affairs be explained? In the lower lumbar and sacral cord, the explanation is easy (Fig. 2, *B*). Here the cord segments occupy so little space and lie so near together that a tumor will usually compress most of the nerve tracts which have already crossed and will also catch those that pass to the other side. At higher levels of the cord, however, the segments are longer, and hence in early compression of the cord a more or less well-marked Brown-Séquard syndrome can occur. In one patient from whom I removed an extradural tumor from the mid-dorsal region the root pains were on the side of the tumor as was

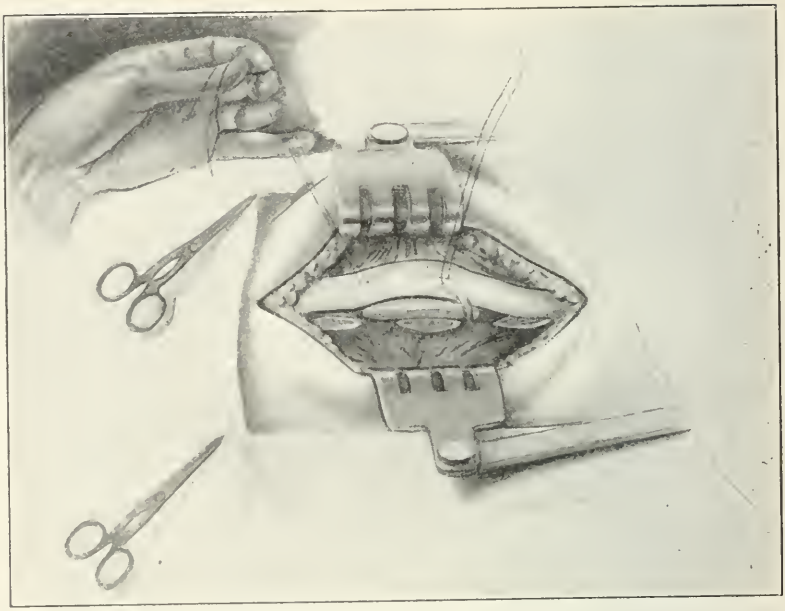

FIG. 3.—An extradural spinal tumor in the middorsal region in which the most marked symptom were on the opposite and the most marked sensory loss on the same side as the tumor.

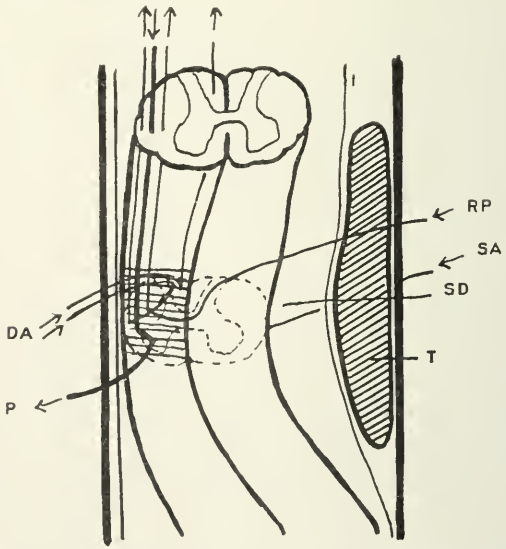

FIG. 4.—The explanation for the reverse Brown-Séquard symptom-complex in the patient with an extradural tumor. *DA*, deep anesthesia; *RP* and *SA*, root pains and superficial anesthesia; *P*, paralysis; *T*, extradural tumor; *SD*, subdural (subarachnoid) space filled with fluid pushing the cord to the other side against the wall of the spinal canal.

also the anesthesia below the level of the lesion. Most of the motor disturbances were on the opposite side. At the operation I found the explanation for the symptoms. The tumor had pushed the cord over to the other side so that it was compressed against the wall of the spinal canal, the cord was partly protected from direct pressure by the tumor by the large amount of fluid within the arachnoid on that side of the cord. (Figs. 3 and 4). In other words the same thing happened as we sometimes see in tumors in the posterior cranial fossa, where a right-sided cerebellar neoplasm may push the cerebellar lobes to the other side so that the left facial nerve is pressed against the petrous portion of the temporal bone, with a resulting left facial paralysis.

If we study the symptoms due to compression of the spinal cord from this point of view, we shall learn not a little regarding the pathological mechanics of spinal compression.

This may lead to a more intensive study and comparison of the sensory and motor disturbances which occur on each side of the body when the spinal cord is pressed upon by a new growth or as a result of an inflammatory or traumatic lesion. With this object in view I have presented these few rather fragmentary remarks upon the symptoms of pain and of other sensory disturbances in diseases of the spinal cord.

SEVERE JAUNDICE IN THE NEWBORN CHILD A CAUSE OF SPASTIC CEREBRAL DIPLEGIA.[1]

By William G. Spiller, M.D.,

PROFESSOR OF NEUROPATHOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Among the many causes of arrest in the development of the brain, and consequently of spastic cerebral diplegia, severe jaundice of the newborn child does not appear to have been recognized. The ordinary mild icterus neonatorum need not be considered, but occasionally the jaundice is severe and death threatens. I have observed four cases in which severe jaundice was believed by the parents to have had an etiological relation to cerebral diplegia.

An interesting family reported by Pitfield demonstrates that severe icterus in the newborn may be indicative of a condition which in turn is responsible for arrest in the development of the brain. Intracranial hemorrhage may be produced by some abnormal condition of the blood which may cause hemophilic jaundice. All severe jaundice in newborn children is not necessarily of this

[1] Read before the Philadelphia Neurological Society, October 23, 1914.

character, and other conditions than hemorrhage may cause arrest of the brain development. The icterus possibly may be indicative of the degree of intoxication of the cortical cells of the brain, but the various conditions that lead to icterus may themselves be responsible for the arrest of the brain development.

Pitfield's[2] cases were as follows: The first child in the family was born naturally, but soon after birth became very yellow, vomited black material, and passed stools of a dark, tarry nature, which probably were mostly blood. With this condition there were fever and rapid loss of weight. At the end of eighteen days the icterus was so intense that the death of the child was expected. At this time the skin was a dark coffee brown. Finally he recovered, and was at the time of the report a sturdy, healthy child.

The second child became icteric on the third day. Subdural hemorrhage was supposed to have quickly followed on account of coma and convulsions, but recovery occurred. At five years the child could hardly walk, and was mentally defective. His powers of coördination were very poor. A cranioplastic operation done later revealed adhesion of the dura over the cerebellum. It seems that hemorrhage was possible in this case, but it is also possible that the icterus was the cause of the convulsions and coma.

The third child was icteric when born and became profoundly so when forty-eight hours old, and died from subdural hemorrhages before he was seventy-two hours old. Subdural hemorrhages were found at the necropsy.

A fourth child became icteric a few hours after birth, and the process was arrested by injection of blood serum from another person.

In the chapter on diseases of the liver in the second edition of Osler and McCrae's *System of Medicine*, written by A. O. J. Kelly and revised by William Pepper, on page 454 the effects of jaundice on the nervous system are described as follows: "Grave disturbances of the nervous system occur in many cases of jaundice; on the one hand there are manifestations of depression, such as general neuromuscular weakness, asthenia, headache, vertigo, mental depression (that may progress to melancholia), insomnia, etc., on the other hand, there are manifestations of irritation, such as severe headache, active delirium, coma, convulsions, etc. These manifestations are more common in cases of acute toxic or infectious jaundice (associated with fever) than in the more protracted cases of obstructive jaundice; but they may supervene in any case of jaundice and not uncommonly lead to the fatal issue. They are commonly described under the name *cholemia*, but it is difficult to separate from one another the symptoms due to bile acidemia, to interference with the detoxifying function of the liver, and to the initiating toxic

[2] Arch. Ped., 1912, p. 761.

or infectious process. The condition is not cholemia in a restricted sense—that is, it is not due to bile acidemia—since the symptoms may occur when the bile acids are not in excess in the blood, as well as in cases of disease of the liver (such as cirrhosis) unassociated with jaundice. The condition is most likely an acid intoxication, due to disturbances of the detoxifying function of the liver, which may be brought about by disorganization of the hepatic parenchyma, such as occurs in severe forms of toxic and infectious jaundice, acute yellow atrophy of the liver, phophorous poisoning, Eck's fistula, starvation, diabetes, etc., or by an excessive formation of enterogenic toxins the consequence of absence of bile from the intestine."

A. E. Taylor, in the same *System*, vol. II, page 520, speaks of the effects of jaundice as follows: "Bile acts as a tissue poison, particularly to the renal, hepatic, and muscle cells. There is further evidence that it exerts a hemolytic action. Possibly this may be related to the hemorrhagic tendency so frequently noted in jaundice. The body temperature is reduced, the pulse and respiration retarded, apparently on account of peripheral influences, since the effects occur following the local application of bile to the surface of the heart after section of the vagus in the curarized frog. There is dilatation of the peripheral capillaries. Large doses cause coma, convulsions, and paralysis. In jaundice we observe, clinically, retardation of the pulse, somnolence, albuminuria, sometimes emaciation and cutaneous disturbances, occasionally hemorrhages directly corresponding to the experimental findings."

Acute hemoglobinuria of the newborn according to E. P. Davis,[3] was first clearly described by Winckel, who reported 23 cases of the disorder. It is characterized by swelling of Peyer's patches and the mesenteric glands, blackish-red staining of the pyramids of the kidneys, with stripes of hemoglobin coloring, fatty degeneration of the liver and other viscera. Hematogenic icterus is present, the hemoglobin being extensively changed into bilurubin. The urine is dark, brown-reddish in color, contains hemoglobin, epithelium, casts, and micrococci. Chemical poisons as a cause were excluded in diagnosis. The mothers showed no infection and the children were usually well developed. The mortality was 19 out of 23. The cause of the disorder is not clearly demonstrated. It is undoubtedly an infection which attacks the blood, resulting in hemoglobinemia. Prophylaxis and treatment, beyond the faithful employment of antiseptic precautions, are practically without avail.

Hematogenic jaundice accompanied with multiple oozing of blood has been described by Partridge. In the case reported recovery ensued.

Pfaundler and Schlossmann[4] say that in case the icterus increases

[3] An American Text-book of the Diseases of Children, edited by Louis Starr.
[4] The Diseases of Children, English translation, vol. ii.

in intensity toward the end of the second or even the third week we may well assume that we are not dealing with that variety of icterus termed icterus neonatorum, but rather with an icterus due to some other and usually more serious disease. This disease, in most cases, is sepsis, in the clinical picture of which icterus plays a prominent role. In case sepsis can be excluded, and if toward the end of the first month of life the icterus becomes more pronounced, consideration must be directed toward the possible presence of an obstructive jaundice. The latter condition is, in general, rare in the newborn, and may be due to various causes, one of which is a congenital obliteration of the bile ducts, with which condition the feces are only slightly colored, and the icterus increases in intensity from day to day until the skin takes on a yellowish green color.

The relation between disease of the liver and alteration of the brain has received much attention in recent literature. A remarkable progressive disease of the central nervous system was observed by Schütte[5] and a diagnosis during life was impossible. The liver at the necropsy was found to be much diseased, and the frontal lobe of the brain showed extensive destruction of nerve fibers and nerve cells and overgrowth of neuroglia. The changes were most intense in the frontal lobe, but were not confined to this part. The vessels were little affected and there was no evidence of syphilis in them. Schütte believed that the disease of the liver stood in some relation to the disease of the brain, and there are other cases in the literature which justify this assumption, such as those recorded by S. A. K. Wilson. Schütte does not detail the manner in which the liver disease affects the brain, but he states that in the developing organism the effect of disease of the glands with its resulting metabolic change is especially intense on the development of the brain.

Fleischer and Völsch have described a condition with brownish pigmentation of tissue, especially of the edge of the cornea, with cirrhosis of the liver and implication of the spleen, allied to the pseudo-sclerosis of Westphal and Strümpell. The condition has been studied in this country especially by Holloway.[6] A recent case of this disease is reported by Westphal,[7] and in reporting it he discusses the possibility of toxins or infection as the cause of the disease of the liver and spleen; but an examination of the liver did not disclose any metallic poison. Westphal cannot explain the relation of the disease of the liver to the brain alteration, but he suggests that the hepatic cirrhosis may be embryonal.

Bostroem,[8] in reporting a case of pseudo-sclerosis, comes to the conclusion that the changes in the nerve cells of the brain and the

[5] Archiv f. Psychiatrie, vol. li, p. 334.
[6] American Journal of the Medical Sciences, 1914, cxlviii, 235.
[7] Archiv f. Psychiatrie, vol. li, p. 1.
[8] Fortschritte der Medizin, 1914, Nos. 8 and 9.

overgrowth of neuroglia, as well as the alteration of the liver, are certainly caused by intestinal intoxication, depending on a functional disturbance of the gastro-intestinal tract. In 6 cases of pseudo-sclerosis there was chronic intestinal catarrh and in 4 cases diabetes. In these disorders gastro-intestinal disturbance and alteration of the liver in the form of cirrhosis are often observed. If more attention had been paid to gastro-intestinal disease in pseudo-sclerosis, Bostroem thinks, such disease probably would have been detected oftener. The peculiar condition of the liver occurring in this disease, he says, certainly is caused by an enterogenous toxin, although other causes may assist the gastro-intestinal condition in producing pseudo-sclerosis.

The conditions described above have been observed in adults, but if a relation between disease of the liver and alteration of nerve cells of the brain is possible in adults, much more likely could such a relation exist in a newborn child.

The cases I have observed in which severe jaundice seemed to be in etiological relation to the spastic cerebral diplegia are as follows:

Case I.—E. K. was brought to me December 7, 1910. She was then three years old. She was the fifth child, and all the other children were healthy. The labor was not difficult, was at full term, and forceps were not used. She was supposed to be a normal child until severe jaundice developed, when she was one week old and her entire body became very brown. She probably was unconscious during this attack. The jaundice disappeared after three days. She had a slight attack of measles in the second week of life. She was unable to hold up the head for a year. Until three years old she was unable to rise to a sitting posture when lying on the floor. When I first saw her she was unable to walk alone, and all movements of the upper and lower limbs were awkward. She was unable to talk.

She was brought to me again May 14, 1914. At that time she was able to say "Papa" and "Mamma" and sometimes put two words together, but did not form any sentence and speech was very indistinct. It was difficult to determine the degree of intelligence. Choreiform movements were seen in the whole body and in the muscles about the mouth, and at times she had choreiform jerking of the upper lids and head. The head at times was held to the left. All the limbs were poorly developed and rigid. Both feet turned inward, and she wore out the toes of her shoes. She fell easily. The case was one of spastic ataxic diplegia.

Case II.—L. K., aged sixteen months, was referred to me by Dr. William Muhlenberg, of Reading, November 21, 1912. He was born prematurely, possibly at the seventh and a half or eighth month, but in normal labor. Jaundice began on the fourth day, was very severe, and lasted about six weeks, and the child nearly

died. When recovering from the jaundice the mother noticed that the head frequently was drawn backward. The left upper and lower limbs were paretic six or seven months, but at the time of my examination they were not weaker than the right. The digestion had been poor. He showed much incoördination in attempting to grasp objects. He was unable to sit up or to hold up the head, and if not supported the head would fall backward or to one side. He could move the head from side to side voluntarily. The upper limbs were moved freely and the grasp of each hand was fair. The biceps and triceps reflexes were not distinct. The upper limbs were not spastic. The lower limbs were moved freely and were somewhat rigid, and attempts to obtain the patellar reflexes increased the rigidity of these limbs. The premature birth complicates this case, but it does not explain the left hemiparesis.

Case III.—H. A. A., was seen in consultation with Dr. David Riesman, September 30, 1913. She was born June, 1911, in normal labor without injury at birth. Severe jaundice developed a few days after birth, and for weeks the child was very ill and not expected to live. When I saw her she had been walking for six weeks. She was able to say a few words. She saw well and seemed to understand what was said to her. She was able to walk without support and apparently with no more incoördination than a normal child of the same age. The head could be moved voluntarily in all directions, but she had much hypotonia of the neck muscles, and the head would fall first in one direction then in another, but fell chiefly to the left and backward. She had formerly drooled much. The facial muscles did not appear to be weak, but the eyes had a tendency to roll upward slightly. The limbs were very little if at all spastic.

Case IV.—M. E. H., was referred to me by Dr. L. J. Wenger, of Reading, September 2, 1914. She was three years and ten months old. She was the second child, healthy at birth, and born in normal labor. Severe jaundice began on the third day and lasted about three months. When five months old she had general convulsions. She had never held the head up. The mouth was held open and the head inclined forward or to one or the other side. She could not speak at all, and it was impossible to determine whether she could understand. The back was weak and she was unable to sit without support. She was badly nourished and appeared sickly. She did not try to hold anything in her hands, and sometimes would grasp the mother's fingers. She was able to swallow without difficulty, but had had much difficulty at the time I saw her in swallowing. All the limbs were very rigid and emaciated, and the spasticity prevented the obtaining of the tendon reflexes. The bowels were very constipated. She had bilateral talipes equinovarus.

PREVALENT FALLACIES CONCERNING SUBACROMIAL BURSITIS. ITS PATHOGENESIS AND RATIONAL OPERATIVE TREATMENT.

By Walter M. Brickner, M.D., F.A.C.S.,
associate surgeon, mount sinai hospital, new york.

Since the publication of Codman's[1] classic description of subacromial bursitis as "the common cause" of shoulder disability ("stiff and painful shoulder"), various articles on the subject have appeared in journals and text-books. It is curious to note in almost all of these, and in the conceptions of the condition held by surgeons and roentgenologists generally, here and abroad, that gross fallacies prevail—despite the precise observations of Codman as to some of them, and in the evident absence of critical study concerning all of them.

These fallacies are:

1. That thickening of the bursal walls casts a shadow in the roentgenogram.

2. That the calcareous deposit found in many of the cases is *in* the bursa.

3. That subacromial bursitis often arises from vaguely conceived bacterial or "toxic" irritation.

4. That subacromial bursitis is marked by decided swelling in the deltoid region.

5. That there is a characteristic point of tenderness over the outer aspect of the shoulder just below the acromion margin, and that the absence of this sign indicates, clinically, absence of bursitis.

6. That the routine operative treatment to be recommended is "excision of the entire bursa."

Based on a personal study of over one hundred cases of shoulder disability, including nineteen that showed this calcareous deposit radiographically, seven of which I operated upon, this communication is written to correct these fallacies.

1. The Roentgen-ray Shadow. As may be demonstrated by radiographs after operation (*vide infra*) a much thickened bursal wall casts no shadow, and with the removal of the calcareous deposit the shadow disappears.

2. The Calcareous Deposit. This is *not in* but entirely *beneath* the bursa, in or in and upon the supraspinatus tendon or,

[1] On Stiff and Painful Shoulders; The Anatomy of the Subdeltoid or Subacromial Bursa and its Clinical Importance; Subdeltoid Bursitis, Boston Med. and Surg. Jour., 1906, cliv, 613. Bursitis Subacromialis or Periarthritis of the Shoulder-joint (Subdeltoid Bursitis), Boston Med. and Surg. Jour., beginning October 22, 1908, clix. "Stiff and Painful Shoulders" as Explained by Subacromial Bursitis and Partial Rupture of the Tendon of the Supraspinatus, Boston Med. and Surg. Jour., 1911, clxv, 115.

occasionally, the infraspinatus near its insertion. To be sure Painter,[2] who was the first to record the calcareous formation in subacromial bursitis, reported four cases with shadows in the radiographs, in two of which, he says, the bursa contained lime-bearing, cheesy material. But in the other two he found no deposit in the bursa, did not look beneath it, and assumed that the shadow was produced by the thickened bursal wall, which he excised—an assumption which he failed to control by a subsequent radiograph. Codman was present at one of Painter's operations, and noted in his own article[3] that the calcareous material seemed to him to have come from beneath the bursa. He reported[4] three cases operated upon by himself, in all of which the deposit lay just beneath the floor of the bursa. It is not difficult for one who has performed the operation to understand why Painter made this faulty observation. If the dissection is not made with this point in mind it is easy, especially in adherent cases, to inadvertently cut into the floor of the bursa with the same incision that divides its roof, thus allowing the often cheesy deposit beneath to flow out apparently from within the bursa.

My series of seven operations amply corroborates Codman's finding and the observation, in a single case, of Wrede.[5] In three of my cases the deposit lay on the supraspinatus tendon and underneath the bursal floor. In one case it was completely imbedded in the *infraspinatus* tendon near its insertion in the tuberosity. In three cases it was entirely concealed in the supraspinatus tendon —one (semifluid) near, and two at a considerable distance from its insertion. In three of these cases of intratendinous deposit and in one of extratendinous location (Fig. 3), the material was dry, gritty, and composed of rough, sand-like granules, in color and appearance much resembling shad roe or yellow tartar when scraped from the teeth. Here and there in the mass may sometimes be found slightly larger, smooth bodies resembling miniature sesamoid bones. An analysis of all these tiny bodies from one case, made by Dr. S. Bookman, physiological chemist to Mount Sinai Hospital, showed them to be composed "chiefly of calcium oxalate, with smaller amounts of calcium carbonate, magnesium carbonate, blood fibrin, and serum albumin." The calcium salts vary, however, in their presence and proportions.

In the other three cases, one acute (16 days) and two chronic (several months), the deposit was semifluid—small and whitish in two cases, large and yellowish in one case. These are the accumulations that Codman quite pictorially describes as "wen-

[2] Subdeltoid Bursitis, Boston Med. and Surg. Jour., 1907, clvi, 345.

[3] Codman, loc. cit., second article.

[4] Codman, loc. cit., second and third articles.

[5] Ueber Kalkablagerung in der Umgebung des Schultergelenks und ihre Beziehungen zur Periarthritis scapulo-humeralis, Arch. f. klin. Chir., 1912, xcix, 259.

like." He is wrong, however, in referring to them as cysts and in speaking of their sac. They are not cysts, and in neither the extra- nor the intratendinous variety has the deposit any sac or limiting membrane. The semifluid material from a case of four months' duration, examined by Dr. Celler, associate in pathology to Mount Sinai Hospital, was found microscopically to consist of "broken-down cellular material, many fat cells, a small amount of lime; no leukocytes; no tubercle bacilli or other bacteria in spreads; cultures sterile after seventy-two hours; guinea-pig inoculation, negative." Baer[6] stated, however, that "if the process is a tuberculous one the cavity may be filled with a dense, cheesy material," which we know now to be an error, as well as is his statement that "when the bursa is replaced by dense scar tissue there is a shadow

FIG. 1.—Linseed-sized shadow in a case of semifluid extratendinous deposit as large as a finger-nail.

to be seen in the radiographs." When yellow and quite fluid, the material is easily mistaken for pus, as by Cumston.[7]

The roentgen-ray appearances of these deposits vary. The shadow is usually close to or even in contact with that of the greater tuberosity of the humerus, but it may be at some distance from the tuberosity in the line of the supraspinatus, or separated by a wide space from the bone margin. The shadow may be very small (Fig. 1) or quite large (Fig. 2, from a case in which the calcareous material removed would thickly cover a fifty-cent piece). Usually single, the deposit is sometimes multiple (Fig. 3). The dry

[6] Operative Treatment of Subdeltoid Bursitis, Bull. Johns Hopkins Hospital, June, July, 1907, p. 282.

[7] Acute Suppurating Bursitis of the Subdeltoid Bursa, Annals of Surgery, 1913, lvii, 143.

deposits correspond in size with their shadows. The fluid deposits, containing but a relatively small amount of lime, are much larger

Fig. 2.—Unusually large, cap-like, dry extratendinous deposit.

than their shadows. Thus in the case of which Fig. 1 is the radiograph the deposit was the size of a finger-nail.

Nor is the lime formation a slow or late process. In the acute case referred to its presence was revealed by the radiograph ten days after the undoubted trauma that originated the symptoms

Fig. 3.—Multiple calcareous deposits.

(lurch of the body while hanging to a street-car strap), and it was demonstrated at the operation six days later. In another acute

case two large shadows were shown by the roentgenogram eleven days after a fall on (?) the shoulder, and these two dry calcareous deposits were removed from within the supraspinatus tendon on the seventeenth day after the injury. In another case a deposit was found by the roentgen rays on the fifth day after trauma.

In none of my cases (all, however, operated upon within a year and a half after the onset) was there any infiltrating calcification of the tendon, or ossification. The deposit occurs in a discrete mass or masses, readily removable with a blunt spoon.

In all three cases of extratendinous deposit I found a small transverse tear in the supraspinatus near its insertion, such as Codman[8] so clearly describes, without deposit, as associated with the bursitis. The rupture was of variable depth, in one case extending through the thickness of the tendon and exposing the joint capsule. Within the rent lay more of the deposit. In one of these, an acute case, both the infra- and the supraspinatus tendons were swollen and deeply hemorrhagic. In the four cases in which the mass of lime salts was concealed within it, the surface of the tendon appeared normal.

As a result of contusion or tear of the tendon, there is a formation of granulation tissue, necrosis of tendon substance and deposition of lime. This corresponds with the histologic findings, to be published, in sections made from tendon fragments of my cases by Dr. E. Moschcowitz, pathologist to Beth Israel Hospital, New York. The deposition of lime in necrosed and inert tissues is a common phenomenon in pathology, *e. g.*, in tuberculous processes, scars, corpora Albicantia, etc. But its frequent, early, sometimes multiple appearance in the spinatus tendons after mild traumata has no parallel, as far as I know, in the human body. Its unique features present several interesting problems in the pathology of tendon injuries and of lime formation, the elucidation of some of which I hope to publish later.

3. The Etiology. The condition is one of adult life. The assumption of a bacterial or toxic origin for subacromial bursitis has never been substantiated by any evidence. If such an etiology were common, we ought to find a similar affection in the olecranon, trochanteric, quadriceps, and other bursæ.

Excluding the rare tuberculous form described by Bilhaut[9] (of which I have seen but a single instance), and the purulent type, occasionally occurring metastatically in septic processes (of which I have operated upon three cases), I believe that subacromial bursitis is of traumatic origin, and that it is produced by bruising the structure between the acromion and the greater tuberosity (over which latter the adhesions and the thickening of the bursal wall

[8] Loc. cit., second article.

[9] Observations de Kyste à Grains Riziformes de la Bourse Sereuse Sous-deltoidienne, Ann. d'Orthop. et de Chir. prat., 1892, cx-iii, 6.

are most often found). When, as is frequently the case, the underlying tendon is likewise contused or torn, the lime salts deposit in the area of necrosis that develops in this poorly vascularized tissue. Compression of the bursa and tendon between tuberosity and acromion is easily demonstrable at operation by abducting the arm.

To be sure, a history of injury is often obtained with difficulty and sometimes not at all. This is because the trauma is usually a comparatively mild form of internal violence, such as hanging from a car-strap or flying ring, throwing the weight of the body on the outstretched arm while scrubbing the floor, or forcibly abducting the arm to throw a ball or to strike at an object with a stick. Such common movements are often not associated by the patient with his developing shoulder disability, not only because they *are* so commonly performed but also because the pain, and especially the stiffness, may not seriously attract his attention for a few days thereafter. But we must not depend entirely upon careful anamneses of these cases for evidence that such forms of internal violence can seriously injure the bursa and the tendon. Codman[10] has reported two cases he operated upon of complete rupture of the supraspinatus tendon and tear of the bursal floor, produced, respectively, by throwing a heavy blanket over a clothesline, and by tightening a saddle-girth. In both cases something was felt to snap in the shoulder, and the arm fell limp.

Another, still milder form of internal violence has been described as causative of subacromial bursitis, and I have a few probable instances in my own series. This consists in repeatedly performed occupational movements, such as cello-playing, hammering, and machine operating. I am not at all sure, however, that in these cases the real cause was not some unduly forcible abduction movement.

Two types of external violence are also productive of subacromial bursitis. One of these is a fall upon the outstretched arm, which, it would seem, jams the head of the humerus against the acromion process, bruising bursa and tendon. The other is a fall or blow on the deltoid region. This latter injury may cause an irritation of the subdeltoid portion of the bursa, but it seems to me it is not very apt to tear the supraspinatus tendon. It may and often does, however, cause a tearing out of a portion of the supraspinatus insertion, *i. e.*, a small fracture of the greater tuberosity; and this condition closely simulates, clinically and radiographically, bursitis with calcareous deposit.

4. Concerning Swelling. In the early stage there is probably always an effusion of serum into the bursa (Flint[11] aspirated 3

[10] Complete Rupture of the Supraspinatus Tendon; Operative Treatment with Report of Two Successful Cases, Boston Med. and Surg. Jour., 1911, clxiv, 708.

[11] Acute Traumatic Subdeltoid Bursitis, a New and Simple Treatment, Jour. Amer. Med. Assoc., 1913, lx, 1224.

to 4 c.cm. in two acute cases); and *sometimes* this is sufficient in amount to produce an appreciable swelling in the deltoid region. In the later stage (and it is very often after several weeks or months that the patient first seeks relief) there is, in my experience, no swelling whatever. On the contrary, there may be a decided flattening of the deltoid from atrophy of that muscle, with which there may also be atrophy of the spinati. The electrical reactions remain normal, however.

5. Point of Tenderness; Diagnosis. In easily recognized cases there is, indeed, localized tenderness over the outer aspect of the shoulder just below the acromion. But most instances of subacromial bursitis, in my experience, are not "typical," and I have found this sign as often absent as present. It is absent sometimes even in acute cases. Nor is the sign pathognomonic. It may be one of several points of tenderness in some other form of shoulder disability, or even when this is the only tender spot, it may be a manifestation of a fracture of the tuberosity, an inflammatory process in the bone or periosteum (tuberculosis, syphilis), etc.

The site of tenderness I find most constant in subacromial bursitis is anteriorly, *over the lesser tuberosity*, or a little above it; but this, too, is not pathognomonic. Sometimes the only, or the greatest tenderness is posteriorly, over the line of the infraspinatus. In some cases of long duration there is no point of noteworthy tenderness.

Dawbarn's sign—disappearance of the typical point of tenderness when the bursa is carried under the acromion by abducting the arm —I find only occasionally positive. This tenderness, when it is present, very often does not thus disappear.

A sign I described[12]—pain referred to the outer deltoid region on gently pressing the circumflex nerve against the inner aspect of the humerus—is also only occasionally present. Greater or less limitation of abduction and of internal rotation is a striking feature of the typical cases. But I have found dense adhesions in the bursa of two who could abduct and rotate the arm fully, although with some effort. I have radiographs, too, showing large calcareous deposits in patients who complained only of annoying pains in the shoulder, and had had no limitation of motion in any direction.

Of the typical cases the signs and symptoms have been admirably described by Codman[13] (although his classification into three types is open to criticism) and, less fully, by others. Of the larger number of less characteristic and atypical cases the diagnosis is to be made, not by a few clear-cut signs and symptoms, but by: a careful

[12] Brickner, W. M., Shoulder Disability (Stiff and Painful Shoulder), Amer. Jour. Surg., 1912, xxvi, 196.

[13] Loc. cit., second article.

history of the onset and development; an inquiry concerning traumata of the kinds above described; a consideration of the incidence, location, and radiation of the pain, and its behavior at night and on resting the arm; a painstaking inspection and palpation of both shoulder girdles; tests of all the shoulder movements, active and passive; the exclusion of such lesions as arthritis, cervical rib, bone inflammations, true brachial neuritis (extensive brachial neuralgia may be due to subacromial bursitis), and forms of shoulder disability other than bursitis; and, finally, roentgen-ray examination.

A radiograph is of the greatest importance in all cases. When a bursitis has been diagnosed clinically, the picture may show, instead, a localized periostitis, tuberculosis or syphilis of the head of the humerus, a small fracture, or other lesion. *Per contra*, in cases in which the signs and symptoms suggest some other form of shoulder disability the roentgen-ray plate may reveal tell-tale calcareous deposits. A normal radiographic appearance of course does not exclude a bursitis without lime deposit.

6. "Excision of the Bursa;" Operative Treatment. I shall not here describe the non-operative treatment nor, in detail, the indications for operation. In acute cases, if there are severe and increasing pain and loss of function and a radiograph shows lime formation, open operation affords the promptest relief; indeed, if I may generalize from two cases, it speedily aborts a condition that would otherwise be very prolonged. In less severe acute cases, without evidence of tendon injury, treatment by rest, preferably in bed, with the arm abducted, should be given a full trial.[14] In long-standing cases much can often be done by persistent conservative measures; but none of my cases with lime deposits has been relieved of pain except those operated upon. If the pain and loss of function seriously interfere with sleep and work, if the muscles are undergoing atrophy and, especially, if there is a deposit, operation provides the surest means of early cure. The breaking of bursal adhesions under narcosis is a more uncertain and far more risky procedure for, as Codman[15] reports, it is not without danger to the large vessels, the brachial plexus, the muscles, and, I would add, the bone itself.

The recommendation in text-books to "excise the entire bursa" is evidently based on this advice in the articles of Baer and Painter, each of whom reports cases in which they performed this operation. They both speak of the bursa as "the size of a silver half-dollar" and refer to its apparently easy removal through a five-centimeter incision, by Painter, through "an incision of small extent," by Baer. It is quite clear, therefore, that they had merely excised the sub-

[14] Brickner, A Simple, Easily Regulable Method of Applying Abduction in the Treatment of Shoulder Disability, Medical Record, January 2, 1915.

[15] Loc. cit., second article.

deltoid portion, which is still rather generally supposed to be a separate sac. Küster[16] had previously shown, and Codman has subsequently emphasized, that this is not so.

The subacromial is one of the largest bursæ in the body. Above, it is adherent to the under surface of the acromion process and the coraco-acromial ligament, wherefrom it is reflected onto the joint capsule. Below, it is adherent to the inner surface of the deltoid muscle, extending fully one and a half inches distad to the greater tuberosity. Anteriorly and posteriorly, it encircles almost one-half the circumference of the humerus, and is attached by its under surface to the bone, the joint capsule, the biceps sheath and the tendons of the subscapularis and the spinati. Surely the complete removal of this extensive, intimately attached structure would be an imposing task! For an attempt to perform it I can conceive but a single indication—tuberculosis.

The removal of even the subdeltoid portion is, it seems to me, quite unnecessary—theoretically, because a person ought to have as good function with a thickened bursal area as with an absence of that lubricating surface; practically, because, in my experience, there are prompt relief of pain and early restoration of function after the following operation.

Operation. The patient is turned partly on his side, and a cushion is placed under the affected shoulder to conveniently expose its outer surface. The forearm and hand, which may be laid across the body, are wrapped in sterile towels or pillowcase so that, if necessary, an assistant can manipulate the extremity.

A two-and-a-half- to three-inch vertical incision is made from the outer border of the acromion process downward over the greater tuberosity, *i. e.*, toward the external condyle (Fig. 4). The exposed deltoid muscle is split in the same line, largely by blunt, partly by sharp dissection. Retraction of the muscle exposes the roof of the bursa. This is drawn up, away from the bone, with two forceps, and freely divided between them, in the line of the muscle incision (Fig. 5). With retractors in the bursa its interior is thus freely exposed where it is usually most affected, viz., over the greater tuberosity (Fig. 6). Adhesive strands or bands are divided with scissors or excised. "Villous" or "papilloma-like" masses, as described by Painter and Codman, if found, are cut away. With curved scissors, concavity toward the humerus, the sac is then explored below (toward the deltoid insertion), anteriorly, posteriorly, and above (under the acromion), and any further adhesions are divided. The bursa is then explored with the finger, the arm being rotated backward, then forward, and pulled down upon, to facilitate this palpation, if necessary. At the site of maximum

[16] Ueber Bursitis Subacromialis (Periarthritis Humero-Scapularis), Arch. f. klin. Chir., 1902, lxvii, 1013.

injury the bursal wall may be more or less thickened. I have not seen it thick enough to suggest the necessity of excising even small areas.

FIG. 4.—The incision. The lateral-supine position of the patient is not indicated.

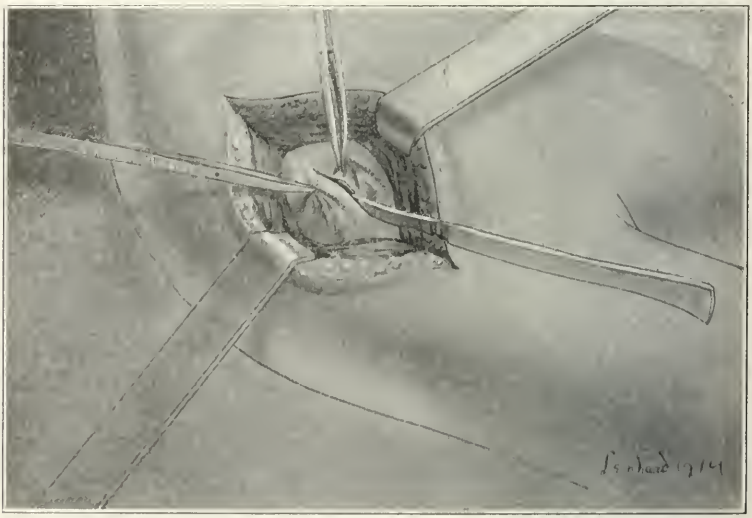

FIG. 5.—The deltoid separated by retractors. The roof of the bursa is drawn up by toothed forceps and divided between them.

The floor of the bursa is now incised, in the same dissection line, over the greater tuberosity and the supraspinatus insertion, and

dissected up from the tendon. If a deposit, fluid or solid, is thus found, it is removed with a blunt spoon (Fig. 7). The tendon thus exposed will reveal a superficial injury or a distinct small trans-

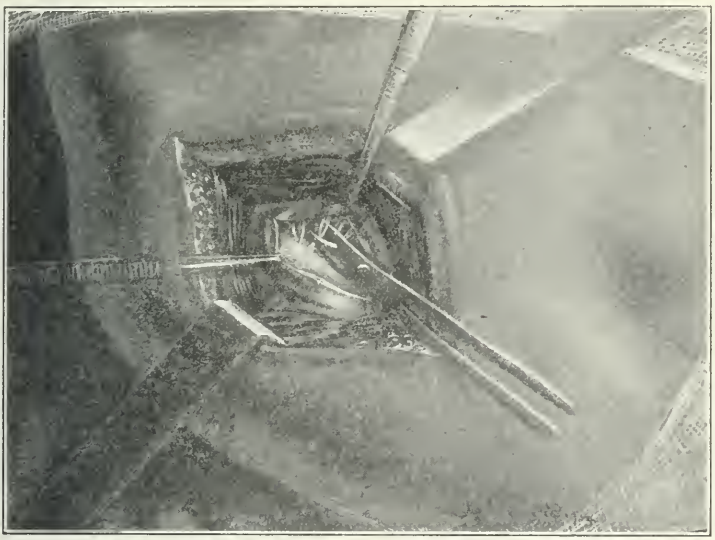

Fig. 6.—The bursa is held open and adhesions are divided.

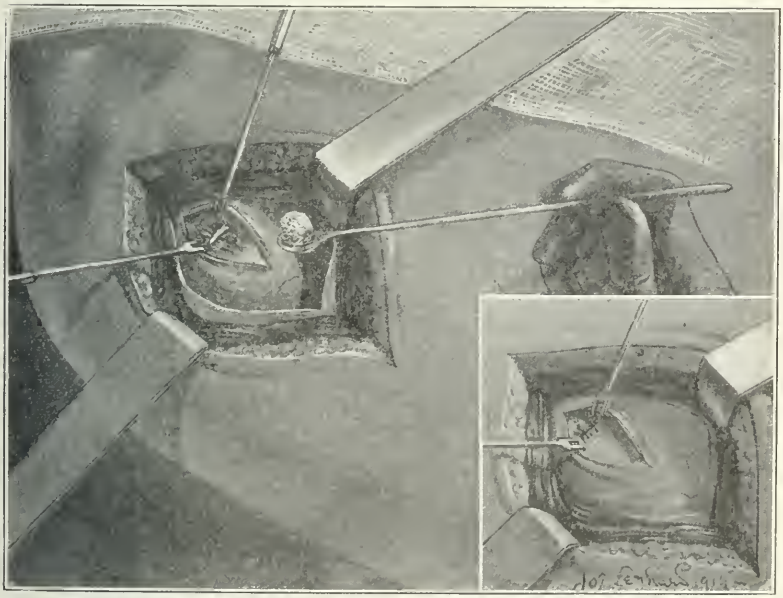

Fig. 7.—The floor of the bursa is incised, dissected up and retracted. An extra-tendinous deposit is removed with a spoon. The small tear in the tendon is sutured after trimming the edges.

verse tear, within which is more of the solid or cheesy material. The edges of the rent are trimmed with a scalpel to remove adhering granules and frayed fibers. The tendon wound is then closed

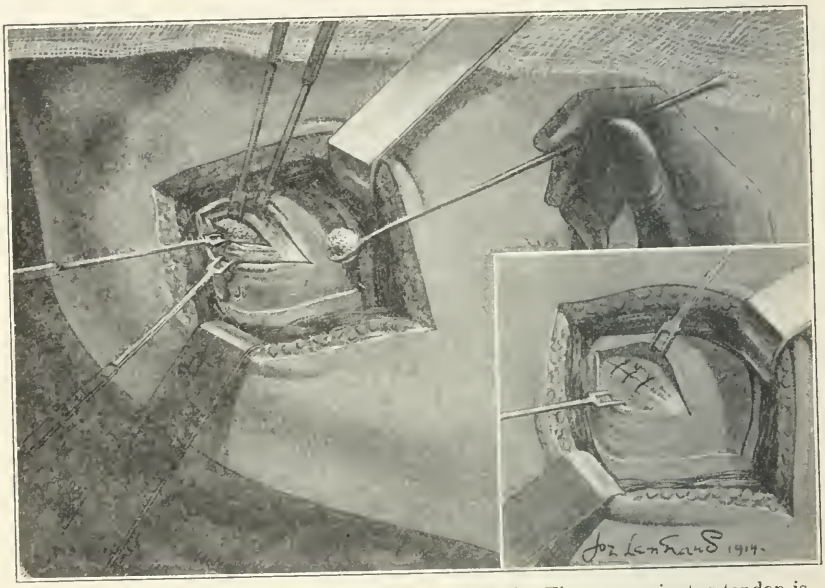

FIG. 8.—The divided floor of the bursa is retracted. The supraspinatus tendon is split and held open and the intratendinous deposit is removed. The split tendon is reunited with chromicized catgut sutures after trimming away the fibers surrounding the lime.

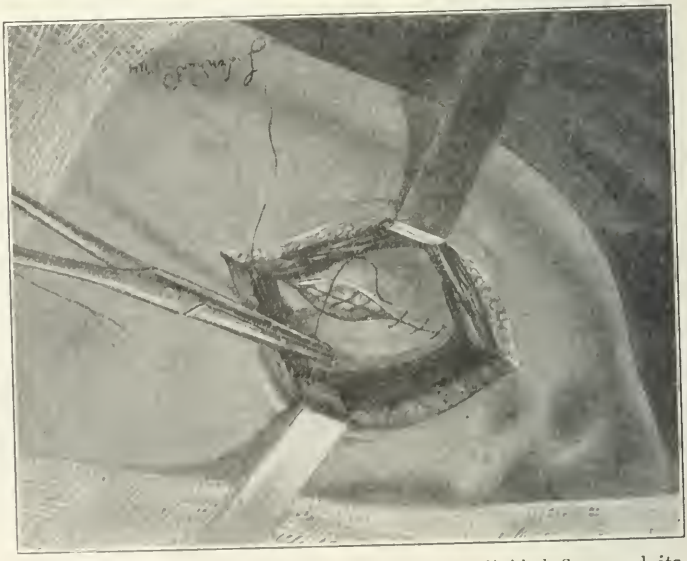

FIG. 9.—Reconstruction of the bursa by suturing its divided floor and its roof.

with a couple of vertically placed chromicized catgut stitches (Fig. 7). If no extratendinous deposit is found, the supraspinatus tendon is opened axially at the point suggested by the roentgenogram, if necessary enlarging upward the incision in the floor of the bursa. The tendon wound is retracted and the deposit is spooned out (Fig. 8). The tissue immediately surrounding the deposit is trimmed away with the granules adhering to it. The tendon is sutured with transverse stitches of chromicized catgut (Fig. 8). If no deposit is found in the supraspinatus the infraspinatus is opened, axially, and the material removed therefrom in the same way.

The above paragraph refers to those cases in which the roentgenogram shows a shadow or shadows. In all cases, however, I think it

FIG. 10.—The arm is kept in abduction by a light plaster-of-Paris spica.

worth while to examine the tendons for a possible tear, through a small incision in the floor of the bursa.

The incision in the bursal floor is closed with fine catgut sutures. In some cases of very adherent extratendinous deposit, these cut edges of the bursa are so frayed at this site, after it has been dissected up, that it cannot be entirely approximated over the tuberosity.

A thin layer of vaseline is spread over the lining of the sac with the gloved finger or a smooth instrument. No small lump of the lubricant is left in, lest, by encystment, it might cause adhesions. In spite of this theoretical objection to the vaseline, I have found that it behaves well in these cases, and I believe that it probably

prevents the immediate reformation of the adhesions. The roof of the bursa is sutured completely with catgut (Fig. 9). Codman thinks it advisable to leave both layers of the sac unsutured so that fluids may drain through. I see no advantage in this practice; it has the perhaps theoretical objection that through gaps in the bursa adjacent structures may become adherent to the opposite wall.

The deltoid muscle is allowed to fall together. I usually insert a few catgut stitches. The skin wound is closed without drainage. The arm is dressed in abduction of about 120 degrees, in a light plaster-of-Paris spica (Fig. 10).

The abduction is continued until the first dressing—eight to ten days. Painter sees no advantage in the primary abduction and Codman abandoned it. I think it quite important. It relaxes the sutured supraspinatus; it relaxes the bursal walls and puts them in the position of maximum separation; it stretches the contracted periarticular structures (muscles chiefly), and assures at once a certain amount of abduction capacity, thus, I believe, reducing the period of after-treatment. It is a position by no means insupportable, and though some patients find it irksome, their discomfort is a small price to pay for the service it renders.

After the cast is removed the healed wound needs but a bit of gauze and adhesive plaster or collodion; and the patient is free to move his arm about. He is instructed to move it but little and gently at first, to rest it in a sling when sore or fatigued, and at night to abduct it as much as he comfortably can on pillows, or with a bandage carried from the wrist to the head of the bed. In the third week after the operation more active movements are instituted, if necessary. The length of time needed for full restoration of shoulder function depends upon how much and how long it had been previously interfered with. In cases of moderate disability, cure may be complete, or nearly so, within a month. In more severe cases, it will take two or three months to effect restoration of *full* mobility, by means of light Indian-club exercises, etc. Long after abduction is fully restored, there is apt to persist some limitation of internal rotation (inability to quite touch the opposite scapula across the back).

THE CLINICAL INTERPRETATION OF THE WASSERMANN REACTION WITH SPECIAL REFERENCE TO CHOLESTERINIZED ANTIGENS.[1]

By John A. Kolmer, M.D., Dr.Phil.,

PROFESSOR OF PATHOLOGY IN THE PHILADELPHIA POLYCLINIC AND COLLEGE FOR GRADUATES IN MEDICINE,

AND

Jay F. Schamberg, A.B., M.D.,

PROFESSOR OF DISEASES OF THE SKIN IN THE PHILADELPHIA POLYCLINIC AND COLLEGE FOR GRADUATES IN MEDICINE.

(From the Laboratories of the Philadelphia Polyclinic and College for Graduates in Medicine.)

It is now well proved that the antigen in the Wassermann reaction is not necessarily biologically specific, but may be furnished by a variety of different lipoids from normal or syphilitic tissues. While it is true that extracts of a normal liver are generally inferior to extracts of syphilitic liver as antigen in this reaction, it is equally true that alcoholic extracts of normal human heart may be equal or superior to alcoholic extracts of syphilitic liver, indicating that alcohol serves to extract from heart muscle a lipoid similar in its antigenic properties at least to that found in liver which is due to the presence and activities of Treponema pallidum.

The serum of a syphilitic is characterized by the presence of an antibody-like substance, which has a great affinity for lipoids (lipodotropic), and in a mixture with them will cause the absorption or fixation of complement to a well marked degree. The old conception of the reaction which regarded the antigen as specific is erroneous; rather the nature of the antibody constitutes the specific character of the reaction because of its ability to absorb or fix complement in the presence of a lipoid. This antibody or "reagin" will, however, react better with some lipoids than with others and hence the necessity of finding that lipoid or combination of lipoidal substances which possesses most affinity or antigenic sensitiveness for the lipoidophilic antibody regardless of whether these lipoids are derived from syphilitic or normal tissues. In other words, the main principle and all that is definitely known of the syphilitic reactions is that while lipoidal extracts, as well as normal and luetic serums, may separately absorb or fix small amounts of complement, a mixture of a suitable extract and syphilitic serum is capable of fixing larger amounts of complement. Therefore, while the antigen is not biologically specific nor the

[1] Read before the College of Physicians, Philadelphia, October 8, 1914.

antibody endowed with the property of reacting with but one lipoidal substance, the Wassermann reaction is, nevertheless, highly specific because a similar lipoidophilic antibody is found practically in two other diseases, namely, frambesia and leprosy. When these may be excluded the Wassermann reaction becomes highly specific and one of the best diagnostic aids known in modern medicine. Most efforts of late, therefore, have been made to increase the delicacy of the Wassermann reaction and yet keep it specific by attention to technical points in the hemolytic system and by attention to the tissue extract used as antigen.

'Since Sach's[2] originally proposed alcoholic extracts of beef heart reinforced with cholesterin as antigens in the Wassermann syphilis reaction, most observers who have employed these antigens have reported them as being quite sensitive and superior to all others. Thus McIntosh and Fildes[3] found cholesterinized heart extracts much superior to a plain extract of normal heart, to alcoholic extracts of syphilitic liver and to the lecithin-cholesterin mixture of Browning, and on account of their sensitiveness and the constancy of their qualities believe that they fulfil the requirements of a standard antigen. Walker and Swift[4] have reported equally favorable upon cholesterin heart extracts, having found them superior to alcoholic extracts of syphilitic liver, simple in preparation and of constant antigenic value. One of us (Kolmer) with Laubaugh, Casselman, and Williams[5] has been interested in this subject for several years and has made a study of cholesterinized extracts as compared with a number of other well-known antigens, particularly alcoholic extracts of syphilitic liver and acetone-insoluble lipoids. Our studies proved quite conclusively that a cholesterinized alcoholic extract of normal heart constitutes the most delicate antigen of the large number of extracts studied, acetone-insoluble lipoids coming second and proving the best non-cholesterinized extract. As compared with alcoholic extracts of syphilitic liver the cholesterinized extracts gave 29.4 per cent. stronger reactions, and what is more important yielded positive reactions in 23 per cent. of cases where the reaction with an alcoholic extract of syphilitic liver was negative. In an analysis of these cases it was found that the positive result was generally correct and but an expression of the higher antigenic sensitiveness of the cholesterinized antigens. This was true in cases yielding 50 per cent. or more inhibition of hemolysis. In a number of cases, however, the cholesterinized extracts yielded 25 per cent. or less inhibition of hemolysis with complete negative reactions with alcoholic extracts of syphilitic liver, and such cases have given us

[2] Berl. klin. Wochnschr., 1911, xlviii, 2066.
[3] Ztschr. f. Chemotherap., Orig., 1912, pp. 1, 79.
[4] Jour. Exper. Med., 1913, xviii, 75.
[5] Archiv. Int. Med., 1913, xii, 660.

much concern as to the proper interpretation to be made of the results. Using the serums of normal persons we found 5 to 10 per cent. of these cholesterinized extracts would yield pseudo-reactions of about 10 per cent. or less inhibition of hemolysis. In other words strong positive reactions with cholesterinized extracts indicate the presence of syphilis even though the reaction with alcoholic extracts of syphilitic liver were clearly negative; but weak positive reactions are more difficult to interpret and the chief object of the present communication deals with this class of reactions based upon a group of cases tested with different extracts and carefully studied from the clinical aspect.

Additional reports upon cholesterinized extracts as antigens in the Wassermann reaction have been made by Field,[6] Thompson,[7] and Judd,[8] all of whom compared them with other antigens as alcoholic extracts of syphilitic liver and acetone-insoluble lipoids, and reported favorably upon the superior qualities of the cholesterinized heart extracts. Thomas and Ivy[9] secured a relatively large number of what they considered pseudo or false positive reactions and are opposed to their use.

The main purposes of this communication are fourfold:

1. To further study the antigenic value of cholesterinized alcoholic extracts of normal heart as compared with alcoholic extracts of syphilitic liver and acetone-insoluble lipoids.

2. To study with particular care those cases reacting only with cholesterinized extracts and negatively with other antigens in order to determine the specificity of the reaction with cholesterinized antigens.

3. To study the question of weak positive reactions with cholesterinized extracts and the serums of persons who deny syphilitic infection and who present no evidences of the disease.

4. To study the value of the Wassermann reaction performed with cholesterinized extracts as a control on the treatment of syphilis.

Technique and Method of Study. There is general agreement among those who have employed cholesterinized antigens regarding the remarkable sensitivity and antigenic value of these extracts. Not all observers, however, have mentioned the possibility of obtaining slight degrees of inhibition of hemolysis with an occasional serum from a person who denies syphilitic infection and who presents no clinical evidences of the disease, although it is practically impossible to rule out latent hereditary syphilis with absolute certainty in all instances.

The antihemolytic activity of cholesterin is well known and unless the extracts reënforced with this substance are carefully standardized the tendency to obtain varying degrees of inhibition

[6] Jour. Amer. Med. Assn., 1914, lxii, 1620.
[7] Ibid., 1458. [8] Ibid., lxiii, 313. [9] Ibid., lxii, 363.

of hemolysis with normal serum becomes more and more in evidence. In using these extracts, therefore, the first requirement is a careful titration of their antigenic and anticomplementary values; in the Wassermann reaction we use two or three times the antigenic unit as one dose, providing that this amount is at least eight or ten times less than the anticomplementary unit.

If exactly one unit of complement and one unit of hemolytic amboceptor are employed in a technique the percentage of pseudo-reactions with cholesterinized antigens is likely to be relatively high because of the natural antihemolytic activity of cholesterin in addition to the anticomplementary action of the alcoholic extract and patient's serum themselves. This influence may be overcome in a large percentage of cases by using at least one and a half or two units of complement or hemolytic amboceptor in conducting the reaction. It is important to remember this antihemolytic tendency of cholesterin and provide for it in our hemolytic system if antigens reënforced with cholesterin are being employed. As expected old serums, those containing appreciable amounts of thermostabile anticomplementary bodies, are more likely to show their anticomplementary condition with cholesterinized than with plain extracts.

With antigens which are carefully standardized at frequent intervals we have for several years used one and a half or two units of complement or hemolytic amboceptor in conducting the Wassermann reaction. Our usual custom is to use 0.05 c.c. (1 c.c. of 1 to 20 dilution) of fresh guinea-pig serum as a unit of complement and after titrating the hemolytic amboceptor with the complements and corpuscles used in the day's work to employ one and a half or two units of the amboceptor in the antigen titration and in the Wassermann reactions. The results of the reactions herein recorded were conducted in this manner. Even under these conditions we have found a small percentage of cases denying syphilis and showing no clinical evidences of the disease to yield slight (10 per cent. or less) inhibition of hemolysis with the cholesterinized extracts; possibly a portion of these may have been avoided by using larger amounts of complement or amboceptor; at least the importance of not using more of the antigen than is necessary and of using more than one unit of complement or amboceptor are to be emphasized.

The use of multiple units of complement or amboceptor up to two or three units does not appear to impair the delicacy of the reaction of cholesterinized extracts with syphilitic serums and lessens the effect of the antihemolytic action of the cholesterin and the tendency for false positive reactions with normal sera. It is peculiar of these reënforced extracts that when they inhibit or fix complement with syphilis antibody the degree of fixation is usually quite marked and not so readily masked by an excess

of complement or hemolytic amboceptor as when plain antigens are employed.

For several years it has been our custom to use at least three different antigens with each serum in conducting the Wassermann reaction. The two main reasons for this practice are, first, to better study cholesterinized extracts as compared with plain extracts with a check upon the possibility of pseudo-reactions; and secondly, because we have reason to believe that the lipodophilic reagin or syphilis antibody in different serums concerned in the Wassermann reaction, has a different affinity for lipoidal extracts, and that these differences are independent of any changes in the antigens themselves. With the serum of active syphilis most any extract will serve to fix complement and yield a positive reaction, but when the amount of antibody is small, as in long standing or vigorously treated cases, the question of antigen and technique becomes one of considerable importance. It is in such cases that we have noted the varying degrees of reaction with different antigens of equal efficiency, and it was not uncommon to find a negative reaction with one antigen and a positive with the others. In not a few cases dependence on a single extract would have led to false negative reactions with serums of cases where treatment was being guided by the serum reactions. This is especially true of alcoholic extracts of syphilitic liver; less true of acetone-insoluble lipoids and least likely to occur with cholesterinized extracts.

It is the practice of one of us (Kolmer) to employ a cholesterinized alcoholic extract of human or beef heart, an alcoholic extract of syphilitic liver and an extract of acetone-insoluble lipoids in conducting the Wassermann reaction with each serum. As recorded by one of us in the paper previously mentioned, acetone-insoluble lipoids was found the best non-cholesterinized or plain antigen. The results of several hundred of reactions performed since then substantiate this observation. In other words, we have found cholesterinized alcoholic extracts of normal heart most sensitive; an extract of acetone-insoluble lipoids second in the order of antigenic sensitiveness and alcoholic extracts of syphilitic liver somewhat less sensitive than the other two.

Materials Used in This Study. *Antigens.* Two kinds of cholesterinized extracts were used, namely, alcoholic extracts of human and beef heart reënforced by the addition of 0.4 per cent. pure cholesterin. Human heart extract has been found superior to that of beef heart and guinea-pig heart. An alcoholic extract of syphilitic liver and suitable extracts of the acetone-insoluble lipoids from human and beef heart were used in a comparative study with the cholesterinized extracts.

Serums. In all the serums from 434 persons have been tested during the past seven months. These were mostly secured from

cases in private practice and from the wards and out-patient clinics of the Polyclinic Hospital. In one series are collected 239 cases in which a history and clinical diagnosis were available; in a second series are listed 175 cases in which the diagnosis was incomplete or not given. We have excluded from this series all cases which reacted with cholesterinized extracts only because without a history they are not available for critical study.

1. A general examination of these series of cases shows that with 214 of the 414 serums the reactions were negative with all antigens including the cholesterinized extracts. In a further study of the question of false positive reactions with cholesterinized extracts we shall have occasion to refer to them in more detail.

2. With 200 serums a positive reaction was observed with one or more of the antigens. With 164 serums the reactions were positive with all three antigens but the degree of the reaction was not equal with all. Thus with 82 serums or exactly 50 per cent. the results are equal and in the remaining 50 per cent. the reactions with the different extracts varied to some degree. These are worthy of further analysis in order to study the relative sensitiveness of the different extracts.

3. Even a cursory examination of these series will suffice to show the greater antigenic sensitiveness of cholesterinized extracts; that they serve to give positive reactions with luetic serums reacting weakly or negatively with alcoholic extract of syphilitic liver and acetone-insoluble lipoids and that the tendency to produce pseudoreactions with normal serums is slight.

Antigenic Value of Cholesterinized Extracts as Compared with Alcoholic Extracts of Syphilitic Liver. 1. Of 155 serums in which a positive reaction was observed with both extracts, in 81 or 52.2 per cent. of cases the reactions were equal in both.

2. In 74 or 47.8 per cent. of cases the cholesterinized extracts gave a stronger reaction.

3. In no instance were the reactions negative with the cholesterinized and positive with the alcoholic extracts of syphilitic liver.

4. In 21 or 10.5 per cent. of 200 cases the reactions were positive with the cholesterinized extracts and negative with alcoholic extracts of syphilitic liver. These cases are worthy of further study and will be later considered in detail; here it may be stated that while the diagnoses were mostly made in the clinics and the patients were not directly under the observation of the authors, in at least 14 the history strongly suggested syphilis.

Antigenic Value of Cholesterinized Extracts as Compared with Extracts of Acetone-insoluble Lipoids. 1. Of 169 serums in which a postive reaction was observed with both extracts, in 120 or 71 per cent. of cases the reactions were equal in both.

2. In 48 or 28.4 per cent. of cases the cholesterinized extracts yielded stronger reactions.

3. In only one case (No. 233) the reaction with a cholesterinized extract was very slightly weaker than that observed with acetone-insoluble lipoids.

4. In no instance was a reaction negative with a cholesterinized extract and positive with acetone-insoluble lipoids.

5. In 21 cases or 10.5 per cent. the reactions were positive with a cholesterinized antigen and negative with acetone-insoluble lipoids.

In the majority of these the reactions occurred with the serums of persons in whom the history and findings were strongly suggestive of syphilis.

These results, which correspond quite closely with those previously reported by one of us[10] indicate the superior antigenic sensitiveness of cholesterinized antigens as compared with other extracts which are in common use.

It may be stated, therefore, that cholesterin appears to have a more marked affinity for the lipodophilic reagin or syphilis antibody than other lipodal substances and consequently is capable of absorbing or fixing complement with this antibody to a well-marked degree. The increased sensitiveness of reënforced antigens may be due in part to the antihemolytic activities of cholesterin in a manner comparable to the increased sensitivity of serums containing thermostabile anticomplementary bodies. Or if the Wassermann reaction is interpreted as a colloidal reaction, cholesterin may be regarded as peculiarly suited for the formation of new compounds with the syphilis antibody with consequent absorption of complement to a well-marked degree. Whatever may be the explanation the fact remains as well proven that the addition of cholesterin to alcoholic extracts of normal organs and particularly of heart muscle, increases the antigenic sensitiveness of these extracts for syphilis antibody. The important question at issue, however, is in regard to the possibility of these reënforced extracts yielding false positive reactions with normal serums, that is, of its power to fix or absorb complement with some constituent of normal serum as is present to a well-marked degree in normal rabbit serum[11] and increased as a result of syphilitic infection. This is the point we have studied with particular interest.

Concerning the Specificity of the Wassermann Reaction with Cholesterinized Antigens. As just stated, most interest centres about the small percentage of cases which reacted only with the cholesterinized extracts. In practice these are the cases

[10] Kolmer, J. A., Laubaugh, E. E., Casselman, A. J., and Williams, W. W., Archiv. Int. Med., 1914, xii, 660.

[11] Kolmer, J. A., and Casselman, A. J., Jour. Med. Research, 1913, xxviii, No. 2, p. 369.

which give us most concern in the clinical interpretation of the reaction, especially when the degree of inhibition of hemolysis is slight. When there is 50 per cent. or more inhibition of hemolysis with a cholesterinized extract we regard the reaction as positive even though the reactions with alcoholic extracts of syphilitic liver and acetone-insoluble lipoids are clearly negative.

The following is a list of cases from the Polyclinic Hospital and included in one series which reacted only with cholesterinized extracts. Cases 234, 235, 236, 237, 238, and 239 were observed in the skin clinic of the Polyclinic Hospital under the eye of one of the authors.

Case 10.—W. E., aged forty-two years. Primary optic atrophy. Had an accident to one eye in childhood. At present has Argyl-Robertson pupil. The blood reaction is as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+++	−	−

Case 25.—E. B., aged two years. Diagnosis: enuresis; hereditary syphilis. Nothing in family history suggestive of lues. Physical examination shows occipital and cervical lymphatic glands are palpable. Has ptosis of the right eyelid. Had suspicious rash during winter.

	Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
July 27, 1914	++−+++	−	−
July 31, 1914	+++	−	−

Case 35.—S. B., aged twenty-one years. Diagnosis: tumor of breast. Nothing in history suggestive of syphilis. Patient has a mass in the breast that appeared to be tuberculous. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 55.—M. C., aged sixty-eight years. Diagnosis: carcinoma of liver or cirrhosis of liver. Patient had failure of health four years previous to admission. Was married, had three children; all died in early life. One was stillborn; one died at age of one and a half years and one died at age of fifteen years. Causes not stated. Father had paralysis before he died. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
++	−	−

Case 85.—H. S., aged two years. Infantile hemiplegia; nothing in history suggesting lues; present sickness came on with chills, fever, and convulsions, followed by a paralysis of left arm and leg, also could not speak. Regained power of speech, but cannot walk. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 106.—H. R., aged four years. Diagnosis: acute cardiac dilatation and chorea. Nothing in family history suggestive of lues. Mother had no miscarriages; no stillbirths. Physical examination shows that all the superficial lymphatic glands are enlarged and not tender. Present sickness began with a chill, fever, and pain in the wrists. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble. lipoids.
+	−	−

Case 127.—T. M., aged fifty-eight years. Primary diagnosis: locomotor ataxia; secondary diagnosis: gastritis. Patient denied any luetic infection. Nothing in history suggesting syphilis. (There was quite a dispute as to the diagnosis in this case.) Knee-jerks were quite suggestive of gastric crises. Tabes was the diagnosis severally suggested. The blood reaction is as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 134.—A. M., aged fifty-six years. Primary diagnosis: acute dementia; secondary diagnosis, neurasthenia. Patient had eleven children, all dead but three; causes not stated. Patient complains of indefinite pain in all parts of her body. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
++	−	−

Case 168.—S. G., aged forty-three years. Primary diagnosis: osteitis (luetic?). The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 174.—R. G., aged nineteen years. Nothing whatsoever in history suggestive of lues. Patient suffering from nausea, loss

of weight. Patient was put on protiodide on July 16, 1914, but no data as to results of the treatment. Girl has suspicious patches on tongue. The reaction of the blood was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
++++	−	−

Case 200.—E. H., aged twenty years. Diagnosis: psychosis. Nothing in history suggesting syphilis. Patient became melancholy for no apparent cause. Refused to talk, walk, or eat. Was afraid to be touched and refused all assistance. Was in the hospital but three days. A complete family history was not obtained. Right-sided paralysis. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 201.—B. D., aged forty-two years. Diagnosis: chronic gastritis; arteriosclerosis. Pain in epigastrium for past year. Nausea and sometimes vomiting. History of chancre; enlarged epitrochlear glands. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble. lipoids.
++++	−	−

Case 205.—M. T., aged two months. Diagnosis: gastro-enteritis and malnutrition. Child healthy at birth. Bottle fed. First birth. No history of lues. Mother states that child had blebs on soles of feet and palms of hands at birth. No skin eruption. At time patient was admitted there was a distinct shedding of the skin on the palmar and plantar surfaces. The blood reaction was as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
++++	−	−

Case 207.—W. S., aged forty-five years. Diagnosis: carcinoma of stomach. Nothing whatsoever suggestive of syphilis in the history; however, there was no negative statement as to luetic infection. Pain in epigastrium. The blood reaction was as follows:

	Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
May 10, 1914	±	−	−
May 12, 1914	±	−	−

Case 214.—T. K., aged thirty-six years. Diagnosis: acute neuritis. Nothing in history or physical examination suggestive of syphilis. This patient was put on KI gr. VII t.i.d. and on the

second day after taking medicine patient developed a severe coryza which quickly cleared up upon withdrawal of the drug. Pain in legs about course of anterior and posterior tibial nerves; weakness after standing. The blood reaction is as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 234.—I. A., aged ten years. Lues hereditaria. Patient had extensive ulcerative and vegetative lesions on the right arm and hand. His serum reaction on was as follows:

Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Under appropriate specific improvement a striking improvement in the eruption was brought about.

Case 235.—F. McL., aged fifty years. Was treated several years ago for a squamous syphilide of the palm of the hand. Had been under internal treatment for some years. On April 10, 1914, his reaction was as follows:

Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 236.—Mrs. K. Developed an initial lesion on the lip in April, 1913. Husband was being treated for lues. This patient had had salvarsan and mercurial inunctions. Her serum reactions were as follows:

	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
June 29, 1914	+	− (D. H.)	−
September 16, 1914	++	−	+

Case 237.—O. R., aged fifty-nine years. Slight treatment at the dispensary for pruritus of the genitalia. It was noticed that he had luetic scars on the forehead and blood was taken for a Wassermann reaction.

Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

Case 238.—P. McG., aged forty-four years, presented himself with an eruption upon the lower lip of suspicious character. Duration two years. His Wassermann reaction yielded the following result:

Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+++	−	−

Case 239.—D. M., aged thirty years. Patient has been under observation with a rebellious and severe sycosis vulgaris involving the cheeks, chin, and lip. There is no history of lues and the patient's general health is good. On April 2, 1914 his serum reacted as follows:

Cholesterinized beef heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble. lipoids.
+	− (D. H.)	− (D. H.)

In this case we are not persuaded that the reaction indicates lues; the possibility of a latent lues hereditaria, however, can never be quite eliminated, and the interpretation of the reaction in this patient must remain open.

The list above given representing ambulatory hospital patients might readily contain inaccuracies of diagnosis such as not infrequently occur in dispensary practice. It will, perhaps, be more valuable therefore to study a series of patients in private practice. Below is appended a list of 20 such patients who have been under the observation of one of the authors for from one to six years. All of these patients are luetic subjects, and multiple serological tests have been made on practically all. These patients have shown at times a positive Wassermann reaction with the alcoholic extracts of syphilitic liver and an extract of acetone-insoluble lipoids, but have at other times been negative with these and positive only with the cholesterinized antigens. The persistence of negative Wassermanns in these cases would have suggested an extinction of the spirochetic infection and consequent cessation of treatment, had not the cholesterinized antigen been employed. Most of these patients were in the secondary and tertiary stage. Some of these patients after exhibiting positive reactions only with the cholesterinized antigens later gave frank positives with an alcoholic extract of syphilitic liver. One patient with a four-year-old infection had had several negative Wassermanns reported by a competent serologist. He presented himself for treatment with an annular nodular eruption upon the side of the chin; he was much surprised and shocked when he was informed that the patch was syphilitic for he was hopeful that he had been cured. A blood test was again made and was negative with alcoholic extract of syphilitic liver, but weakly positive with the extract of syphilitic liver and strongly positive with the cholesterinized extracts, and intravenous injection of salvarsan effected a rapid disappearance of the patch.

A brief history of these cases is appended:

Case 1.—J. W., aged thirty-two years. Infection in 1901. Treated by his physician with internal remedies for two years. He has since July, 1913, received ten intravenous injections of salvarsan and neosalvarsan and a course of gray-oil injections and is entirely free of any manifestations of disease. The record of his blood test is as follows:

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
December 30, 1913	±	±	−	−
February 11, 1914	+++	....	++	±
April 27, 1914	+++	−	−(D. H.)	−
June 13, 1914	−	−	−(D. H.)	+
September 6, 1914	+++	....	±	

It will here be seen that when the patient came first under observation the serum test with the alcoholic extract of syphilitic liver and acetone-insoluble lipoids was negative, with positive reactions only with the cholesterinized extracts. As indicating that the latter tests meant spirochetic activity, the tests later became positive with the other antigens.

CASE 2.—W. S., aged fifty-five years. Infection dates back to early manhood. Patient has arteriosclerosis. Wife treated ten years ago for placques on tongue. The record of the serum test is as follows:

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
March 4, 1911	....	....	Weak +	Weak +
September 26, 1911	....	....	++	++
November 24, 1911	....	....	−	±
May 23, 1912	....	....	+	+
Octo ber23, 1912	....	....	+	++
March 14, 1913	....	....	−	−
May 8, 1913	....	....	−	−
June 12, 1913	+	+	−	±
November 13, 1913	+	±	−	−
June 24, 1914	+++	....	−	−

This patient has had seven intravenous injections of salvarsan and neosalvarsan, in addition he received mercurial injections. His health has been much improved. The five tests above indicated that are negative with the alcoholic extract of syphilitic liver do not persuade us that infection is eradicated.

CASE 3.—J. K., aged thirty-three years. Infection dates back five years. Had an entirely inadequate treatment during the secondary period. Patient came under the care of one of the authors in December, 1912. A blood test taken about three weeks after the cessation of mercurial inunctions was negative. The serum reactions are herewith appended:

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
December 2, 1912	....	....	−	
September 27, 1913	++++	++++	++++	++++
April 7, 1914	+++	−	−	−
June 27, 1914	++	....	+	+

The first test when the patient came under our observation was made by a very competent serologist in this city; it doubtless had

been influenced by the preceding treatment. The patient received while under our care thirteen gray-oil injections, five intravenous injections of neosalvarsan and other treatment.

Case 4.—S. H., aged thirty-two years. Had a suspicious sore three years ago, the nature of which was not determined by his physician at that time. The patient came under observation in the autumn of 1913, at which time he had numerous ulcerative lesions on the thighs and legs. His blood reactions were as follows:

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
October 21, 1913	++++	++++	++++	++++
March 24, 1914	+	+	−	−
June 2, 1914	++	++	−	−

The ulcerations healed up under two intravenous injections of neosalvarsan. The patient received in all eight intravenous injections of neosalvarsan and salvarsan and eight gray-oil injections. He is at present free of symptoms, but is still under treatment.

Case 5.—F. G., aged twenty-six years. Had an initial lesion followed by atypical secondaries in June, 1912. Received mercurial inunctions and other treatment.

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
March 5, 1913	....	....	−	−
September 13, 1913	++++	++++	+++	+++
March 10, 1914	−	....	−	−
May 5, 1914	−	....	−	−
July 19, 1914	++	....	−	−

On September 19, 1913, he received 0.45 gram salvarsan intravenously, a second dose on September 28, 1913, and a third on October 3, 1913; this was followed by a course of gray-oil injections. Salvarsan intravenously on July 15, 1914 and July 22, 1914. The patient is free of symptoms.

Case 6.—S. F., aged five years. Father treated for affection some years ago; child has mild degree of luetic cachexia; no florid symptoms. The blood reactions are as follows:

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
February 2, 1911	....	....	−	+ faint
May 23, 1911	....	....	−	
September 7, 1911	....	....	±	
September 27, 1911, while taking KI and Hg. bichlor.	....	....	+	+

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
December 2, 1912	±	+	−	−
September 16, 1913	−	−	−	−
November 14, 1913	−	−	−	−
February 11, 1914	−	−	−	−

On May 21, 1914, the luetin test was slightly positive.

From October 9, 1911, to September 18, 1914, this patient received nineteen gluteal injections, each containing 100 milligrams of salvarsan in oil.

CASE 7.—Miss H., aged thirty years; luetic infection in 1909. No active symptoms during past three years. Had a positive Wassermann before presenting herself for treatment. Received intravenous injections of salvarsan on March 27, 1913, April 7, 1913, October 27, 1913, and November 10, 1913 in addition to other treatment. On October 1, 1913, her serum test was:

Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	+	−	−

The patient is free of symptoms of lues.

CASE 8.—Mrs. S., wife of a patient (Case 2). Had persistent placques on tongue over ten years ago.

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
May 19, 1913	....	....	−	±
November 11, 1913	+	++	−	−

The patient received salvarsan and gray-oil injections, after which her reaction became negative with all antigens.

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
April 14, 1914	−	−	−	−

CASE 9.—W. C., aged thirty-six years. Initial lesion four years ago. Treated by his physician with pills for two years. He then had several negative Wassermann reactions. In the late Spring of 1914 he developed an annulonodular patch upon the side of the chin which was readily diagnosed as a syphilide. His blood at this time gave the following reaction:

		Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
May 21, 1914	....	+++	−	−

An intravenous injection of salvarsan effected a disappearance of the patch; this was followed by two other injections; later the reaction with the alcoholic extract of syphilitic liver became positive.

		Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
June 27, 1914	....	++	+	+
September 18, 1914	....	++++	+	++++

The patient is now free of symptoms.

CASE 10.—P. V., aged fifty-five years. Infected at age of twenty-eight. Very little early treatment. Later extensive ulcerations of leg. Treatment by mouth then given for three years by patient's physician. This patient had some neuritic pains in arm. On April 27, 1914, his blood showed the following:

Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	−	−

He was then given three intravenous injections of salvarsan; two months later the reactions was as follows:

	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
June 24, 1914	++++	−	−

Since this time further treatment has been instituted.

CASE 11.—F. S., aged forty years. Infection at age of twenty-one years. Insufficient early treatment. The patient has premature arterial fibrosis. He has had five intravenous injections of salvarsan, gray-oil, and cacodylate of mercury injections and other treatment. He has had negative serum reactions on a number of occasions only to be followed by a swing to a positive reaction. The reactions for the past two years are herewith appended:

	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
February 19, 1913	....	−	−
April 4, 1913	....	−	−
June 17, 1913	+	−	−
November 11, 1913 ...	±	−	−
February 1, 1914 .. .	+	−	−
May 4, 1914 ..	−	−	−
July 11, 1914 ...	+++	−	−
September 28, 1914 . .	−	−	−

It will be seen that the alcoholic extract of syphilitic liver and the acetone-insoluble lipoids have given negative reactions for over a year, but with the cholesterinized antigens the serum has given positive reactions from time to time. In support of the contention that the latter indicates that the spirochetal infections is not extinguished may be cited the fact that on March 20, 1914, after the Wassermann had been negative for almost a year, there was a strongly positive luetin reaction and that on May 7, 1914, the luetin reaction was again positive, although this time the lesion did not go on to pustulation.

CASE 12.—H. G., aged forty-two years; infected over twenty years ago. Inadequate early treatment. Patient has arterial

changes, loss of sexual power, and certain other symptoms suggestive of incipient paresis. The complement-fixation test on September 14, 1914, was as follows:

	Cholesterinized human heart.	Alcoholic extract of syphilltic liver.	Acetone-insoluble lipoids.
....	++ to +++	−	−

Several intravenous injections of salvarsan have greatly improved the patient's condition.

Case 13.—A. F., aged thirty-eight years; infection seven years ago. Has been thoroughly treated by salvarsan and mercurial injections. On June 4, 1913 the serum reaction was:

Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
±	+	−	−

Case 14.—J. K., a college student, aged twenty-two years; infected six years ago. On October 12, 1912, the complement-fixation test was as follows:

Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
++++	++++

After treatment the reaction became negative on March 20, 1913. On June 6, 1913, the following reaction was obtained:

Cholesterinized guinea-pig heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	+	−	−

The patient did not return for treatment; in the Autumn of 1913 he entered a Western University; his blood examined at that time was frankly positive with the alcoholic extract of syphilitic liver, according to a communication received from one of the professors in this institution.

Case 15.—Dr. X., aged thirty years. Digital chancre three years ago. Intravenous injections of salvarsan and other treatment. On February 28, 1912, the serum reaction was:

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
February 28, 1912	....	....	+	+
May 9, 1912	....	....	+++	+++
June 25, 1912	....	....	±	+
October 24, 1912	....	....	Weak +	Weak +
December 8, 1913	....	....	−	±
February 24, 1913	....	....	Weak +	Weak +
June 30, 1913	±	−	−	−
October 14, 1913	+++	++	+	±
January 4, 1914	−	−	−	−
February 11, 1914	±	−	−	−
May 4, 1914	....	−	−	−

Treatment was continued as long as positive reactions were obtained.

Case 16.—Mrs. A., aged forty-five years. Infection fifteen years ago. Had tertiary ulcerative lesions on elbow when she fitst came under observation. The patient was treated by salvarsan intravenously and mercury iodides by mouth.

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
January 19, 1914	++	+ to ++	−	−

The patient lived out of town and did not continue the treatment after the above test was made. The reaction, however, indicates the need of further treatment.

Case 17.—A. H., aged fifty-three years. Infection sixteen years ago. Patient presented himself with a tertiary ulceration of cheek. Intravenous injections of salvarsan and internal treatment.

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
November 11, 1913	+	−	−	−

The patient has not returned for treatment since the above test was made.

Case 18.—Mrs. W., aged thirty years. Husband treated for lues. Anemia and failure of health. This patient has been treated with salvarsan and mercury. The serum reactions are as follows:

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
November 2, 1911	....	....	±	+
November 15, 1912	....	....	±	Weak +
November 25, 1913	± to +	−	−	−
April 8, 1914	....	....	−	−

Case 19.—M. G., aged forty-eight years. Infected twenty years ago; early treatment inadequate. Recently treated by salvarsan and mercury.

	Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
October 22, 1913	−	+ to ++	−	−
June 24, 1914	−	....	−	−

Case 20.—Mrs. C., aged forty-eight years. No history of lues. Has had several years recurrent sores in mouth. The serum reaction was as follows:

Cholesterinized beef heart.	Cholesterinized human heart.	Alcoholic extract of syphilitic liver.	Acetone-insoluble lipoids.
+	+	−	−

A gluteal injection of salvarsan was followed by marked improvement.

Of these 41 *cases, no less than* 20 *were known to be definitely syphilitic and in at least* 14 *others the diagnosis of lues was most probable. In other words, in* 34 *or about* 83 *per cent. of these cases, the positive reactions with the cholesterinized extract were in all probability correct and an expression of continued spirochetal activity. What is of great importance is the fact that if these extracts had not been used either a diagnosis of syphilis would not have been made or treatment would have been interrupted before spirochetal activity had ceased.*

In 7 cases, however, the reactions were negative with an alcoholic extract of syphilitic liver and acetone-insoluble lipoids, but weakly positive with cholesterinized heart extracts. In none of these cases, as far as the available records are concerned, was there clinical evidence of syphilis, although the dispensary physicians did not record careful family histories with the possibility of congenital syphilis in mind.

These cases are typical of the difficulties of interpretation of the Wassermann reaction with cholesterinized extracts. All weakly positive reactions with these antigens cannot be disregarded, for there is a possibility that such reactions are true positive reactions. Especially is this true of cases of syphilis under treatment and also of cases of latent tertiary syphilis.

Not infrequently serums are encountered which react strongly positive with cholesterinized extracts and negatively with alcoholic extracts of syphilitic liver and acetone-insoluble lipoids. We have found that these are almost invariably from luetic persons and have learned by experience to interpret them as positive reactions. The chief difficulty is with serums which react weakly with cholesterinized extracts and negatively with plain extracts. According to our experience most of these are from luetic persons and the reactions are to be regarded as positive; but this at the present time cannot be claimed for all such reactions so that the result must be interpreted in the light of the history of symptoms and a physical examination. If there is a reasonable suspicion of syphilis we have found it well to administer antiluetic treatment, as in several instances persons yielding these doubtful reactions have shown marked improvement in their clinical condition followed in some instances by a stronger Wassermann reaction.

This is called a "provocative" reaction and is similar to the clinical Jarisch-Herxheimer reaction. We may state that an extended experience with cholesterinized extracts has steadily increased our confidence in their value; we desire, however, to make a reservation concerning the possibility of cholesterinized extracts delaying hemolysis or even yielding weakly positive reactions with the serums of persons who are apparently non-syphilitic.

In the presence of such a reaction, namely, a weak positive with a cholesterinized extract and clear negative with alcoholic extract of syphilitic liver and acetone-insoluble lipoids, the result should be interpreted according to the history and clinical symptoms of the patient. If the history is suggestive of lues the reaction should be in the interests of the patient interpreted as a positive; if the patient is a luetic subject under treatment, further treatment is indicated. In a number of instances of such reactions in persons in whom infection was denied, marked clinical improvement followed the administration of salvarsan and mercury.

III. Concerning the Question of Pseudoreactions with Cholesterinized Antigens. In a previous paper one of us had directed attention to the possibility of obtaining weakly positive reactions of 10 per cent. or less inhibition of hemolysis with 5 to 10 per cent. normal serums. At that time we were using with the cholesterinized extracts a hemolytic system which did not permit of a sufficient excess of complement or hemolytic amboceptor to overcome the increased antihemolytic action of these extracts due to the presence of so much cholesterin. As already pointed out it is necessary to carefully standardize the antigen and to use no more than necessary and to use more than a single unit of complement or hemolytic amboceptor.

Of the serums of 434 persons submitted for Wassermann reaction and included in this study, 214 reacted negatively with all antigens including the cholesterinized extracts. It is possible that some of these were luetic but the number of negative reactions with cholesterinized antigens and the serums of persons who were apparently healthy or showing no signs of the disease and with a negative history of infection is such as tends to minimize the likelihood of false positive reactions with these extracts.

In 7 out of 41 reacting only with cholesterinized extracts there was no adequate evidence of syphilis, but as already stated there was no rigid inquiry made as to the family history by the dispensary physicians who sent the blood for diagnosis, and the possibility of a latent infection cannot be absolutely set aside. We do not feel justified in regarding these cases as luetic but a final judgement as to the interpretation of such reactions must be left to the future.

IV. The Use of Cholesterinized Antigens in the Wassermann Reaction as a Therapeutic Guide. We hold that the alcoholic extract of syphilitic liver, the usual antigen employed in the Wassermann reaction, is not sufficiently sensitive to detect minute amounts of "reagin" in the blood. Many reactions are reported as negative with this antigen in which the use of cholesterinized antigens gives positive reactions. That in the vast majority of cases these latter positives indicate spirochetic activity, we believe is proven by the accompanying case reports. In patients

known to have had syphilis, positives with cholesterinized antigens definitely demonstrate that the patient is not cured.

The interpretation of weak positive reactions with the cholesterinized antigens and negative with luetic liver extract will depend somewhat upon collateral evidence. Where the patient is known to have had syphilis, weak positives with cholesterinized extracts, to our minds, indicate the persistence of spirochetic activity. This opinion is based (1) upon the fact that some of these patients, particularly when treatment is interrupted, will later show frank positives with other antigens; (2) that some patients with obvious luetic lesions present such serum reactions; (3) that some of our patients with such reactions have given positive luetin reactions; (4) that certain patients with such reactions, exhibiting no definite syphilitic manifestations, but such symptoms as anemia, failure of health, ocular or nervous diseases of undetermined character, respond often in a surprising manner to specific treatment, and (5) finally, that the persistence of specific treatment in patients with weak positives with cholesterinized extracts, will often extinguish such reactions. One of the authors has had 25 luetic patients in whom he was able to secure a negative reaction with all of the antigens employed.

It is obvious that when the "reagin" in the blood has been reduced to a point where it is no longer discoverable by the use of luetic liver extracts but only by more sensitive antigens, the patient is in the best position to have his infection eradicated, provided treatment is not suspended. This is a practical consideration upon which we wish to place emphasis.

A luetic person under treatment will react negatively with alcoholic extracts of syphilitic liver and acetone-insoluble lipoids for some time before the reaction becomes negative with cholesterinized extracts. In other words, it requires more treatment to extinguish a reaction with reënforced antigens than with plain extracts. We have several reasons for believing that treatment should be continued as long as the serum reaction with cholesterinized antigens remains positive to the slightest degree and a number of our cases in private practice have proven that with sufficient treatment the reaction may be rendered negative with all antigens. We have had several "Wassermann fast" patients whose serum reactions cannot be altered by persistent or rigorous treatment. One patient with an old lues has received 19 injections of salvarsan and neosalvarsan in addition to other treatment and still has a ++++ reaction. Such cases usually react positively with all antigens but rather more strongly with the cholesterinized than the plain extracts.

Discussion. Not infrequently the statement is made that the diagnosis of syphilis should never be made in the laboratory. In not a smaller proportion of cases, however, especially cases of

latent and hereditary syphilis the diagnosis cannot be made otherwise. Indeed, the Wassermann reaction has its chief usefulness in this class of cases. Persons may be sincere in denying knowledge of infection and the symptoms may be of such an indefinite character as to make a clinical diagnosis impossible. It is generally conceded that the Wassermann reaction serves as an important guide to treatment; this is based upon the assumption that a positive reaction indicates the presence of living spirochetes within the tissues, although these may not be sufficiently active or numerous or so situated as to produce obvious symptoms.

With these considerations in mind it may be granted that the reaction should be made as delicate as is possible within the limits of specificity. In the diagnosis of syphilis by the Wassermann reaction every possible precaution should be taken in the technique to avoid error. Such a diagnosis, pregnant as it is with the infliction of mental suffering and at times domestic unhappiness, should be made only after the establishing of conclusive laboratory evidence or after a mature consideration of conjoint laboratory and clinical data. In doubtful cases it is better to err on the side of announcing the reaction as negative. The physician submitting the blood for diagnosis should, however, receive a supplementary statement to the effect that the absence of syphilis cannot be conclusively demonstrated, and, that any suspicious symptoms should be submitted to the therapeutic test.

In using the reaction as a guide to treatment the technique should be as delicate as is compatible with specificity in order to detect the minutest amounts of antibody present. The persistence of ever so few living spirochetes in the body may later give rise to serious manifestations.

According to our experience cholesterinized antigens are the most delicate with which we are acquainted. A negative reaction with a good cholesterinized extract as antigen excludes syphilis more definitely than is possible with any other extract. Furthermore, this antigen will detect a larger proportion of latent luetic infections than any other antigen. Cholesterinized antigens necessitate more prolonged and more thorough treatment of syphilitics than when plain antigens are used in the technique. All of these are advantages, as they tend to more accuracy in diagnosis and greater thoroughness in treatment.

It is to be emphasized, however, that this delicacy renders these antigens dangerous in inexperienced hands. They must be frequently and carefully tested and standardized and used with a hemolytic system embracing more than a single unit of complement and amboceptor. After an experience of a number of years with all of the better-known extracts, we would hesitate to report upon a Wassermann reaction unless at least one satisfactory cholesterinized extract was used as an antigen in the test.

Conclusions. 1. Cholesterinized alcoholic extracts of normal heart constitute more sensitive antigen in the Wassermann reaction than alcoholic extracts of syphilitic liver and extracts of acetone-insoluble lipoids. The latter extracts are superior to alcoholic extracts of syphilitic liver and rank second to the cholesterinized extracts in antigenic sensitiveness.

2. Of 41 cases reacting only with cholesterinized antigens no less than 20 were known definitely to be syphilitic and in at least 14 the diagnosis of lues was most probable. In other words, in 34 or about 83 per cent. of the cases the positive reactions with the cholesterinized extracts were in all probability correct and an expression of continued spirochetal activity, even though the reactions with alcoholic extracts of syphilitic liver and acetone-insoluble lipoids were negative. What is of great importance is the fact that if these extracts had not been used either a diagnosis of syphilis would not have been made or treatment would have been interrupted before spirochetal activity had ceased.

3. We are of the opinion that cholesterinized extracts are best employed in conjunction with non-cholesterinized extracts in performing the Wassermann reaction and very slight positive reactions with the cholesterinized extracts should be interpreted in conjunction with a clinical study of the patient. With a person known to be syphilitic these slight reactions are to be interpreted as positive and as an indication for further treatment.

4. The large number of negative reactions with cholesterinized antigens and the serums of persons in good health or those known to be suffering from non-luetic conditions is evidence that false positive or pseudoreactions with these extracts are rare.

5. In using cholesterinized antigens it is not advisable to work with single units of complement and amboceptor because of the well-known antihemolytic properties of cholesterin, and the corresponding increased likelihood of obtaining false reaction.

6. Cholesterinized alcoholic extracts of heart are easily prepared and are quite stable. It is advisable, however, to retitrate them at frequent intervals as is usual with other antigens.

7. Cholesterinized alcoholic extracts of human heart are probably better than those of beef and guinea-pig heart. The latter extracts are particularly prone to become anticomplementary.

8. Cholesterinized extracts constitute the best antigens when the treatment of syphilis is being guided by the Wassermann reaction reaction, because they are the most delicate and serve to indicate spirochetal activity after the reactions with alcoholic extracts of syphilitic liver have become negative. It requires more treatment to extinguish the Wassermann reaction when cholesterinized extracts are employed. This result, however, can be achieved, and when the reactions so performed continue to be negative, the test constitutes the best evidence of the cure of syphilis that we possess.

COLONIC AND PERICOLONIC ABNORMALITIES.

By Glenn I. Jones, M.D.,
MEDICAL CORPS, U. S. ARMY.

A classification of the conditions to be considered under this title, to be of scientific value, can be made only on a pathological basis. We meet with a distinct syndrome manifesting itself definitely, and progressing relatively with the degree of mechanical obstruction. This results in exosmosis, absorption, colonic and pericolonic exudative inflammation, and local or diffuse membrane formation, in the order named.

The ultimate results are sacculations, diverticula, pericolonic membranes, visceral kinks, local and general splanchnoptosis, all caused by stasis, from causes within or outside the intestine.

Recent studies of the right iliac region have given us a more accurate understanding of pericecal dyscrasiæ. This has led to a more logical consideration of other abdominal conditions, characterized by adhesions and membrane formation.

Doubt still exists as to the causes producing adhesions around the colon. Many investigators seem to be of the opinion that such new formations are the result of faulty development subsequent to embryonal defects. They are more probably due to a degeneration of the physique resulting from disregard of the organs of digestion.

There are three important factors that are productive of colonic conditions with membrane formation, viz.:

1. Nervous, producing colonic atony, and producing colonic tetany.
2. Inflammatory.
3. Mechanical.
    (1) Sacculation.
    (2) Diverticulum.
    (3) Ptosis.
    (4) Kinks.
    (5) Stasis.

These all result from, accentuate, and produce further colonic stasis.

The diminished function of the colon may be etiologically a myasthenic, a neurotic, an arteriosclerotic, or (rarely) a digestive abnormality. I am of the opinion that it rarely if ever is, except in young infants, at which age its recognition is unusual, a congenital malformation.

All of us are familiar with the vagaries in location and adhesions following one or more attacks of acute appendicitis without perforation or rupture. The malposition of the appendix at operation

for its removal has been repeatedly commented upon. Do these adhesions form as the result of bacterial or toxin invasion of the peri-appendicular tissues? Cannot a *locus minoris resistentiæ* in the colon enhance the virulency of organisms of decomposition contained therein, and in the subnormal condition of the colonic tissues, permit passage of such bacteria through the gut wall to the surrounding peritoneum?

The sequence of the formation of pericolonic membranes and adhesions seems to be as follows:

1. Local colonic stasis.
2. Fermentation and decomposition of the contents of the colon.
3. Dilatation and ptosis.
4. Inflammation with increasing stasis.
5. Bacterial invasion and toxin osmosis into pericolonic tissues with the formation of protective or anchoring local adhesions, or diffuse pericolonic membranes.

The clinical aspects depend upon the degree and extent of the process. Early and middle cases present medical aspects only. Late ones, with or without prolonged medical treatment, finally come to the surgeon.

Persistent, prolonged constipation is rarely the result of embryonal defects. It is commonly dietetic. It is the primary productive factor in intestinal intoxications with the ultimate formation of colonic malformations and false membranes.

It is illogical and confusing to reason that a condition normal to man (*i. e.*, the upright posture) should be the prime or even a contributing factor to a diseased condition. Stasis is the result of continued abuse in some form.

Symptomatically the manifestations are as varied as the exact pathology is indefinite.

Acute attacks of colic in the lower abdomen with preference for the right side with only slight or moderate elevations of temperature, little or no disturbance of digestion, immediate relief after thorough bowel evacuations, the tendency to irregular diarrhea, the absence of physical signs, except acute tenderness immediately over the pubes, or over the right subhepatic or iliac region, without marked disturbance of nutrition, are indicative of stasis with acute inflammatory reaction. Proper hygienic and dietetic management, exercise, and occasional use of tonics generally relieve these symptoms.

The persistence of dull, indefinite pain over the entire course of the ascending or transverse colon, attacks of localized or migratory acute pain in the right iliac or subhepatic region, colonic distention and flatulency, undigested stools, the absence of diarrhea, more or less severe digestive and nutritional disturbances with the development of neuroses, neuralgias, arthropathies, and endogenous depression, retardation in the passage of cecal contents, the presence

and persistence of organic elements of decomposition in the urine, indicate deformity or membrane formation.

In advanced cases the attacks of acute pain are not influenced by catharsis. Arthritis and neuritis are frequent concomitants of advanced cases. Not infrequently dull pain in the sacro-iliac region and thighs, accompanied by slight tenderness over the lower dorsal vertebræ, is a source of complaint.

William J. Mayo, in a masterly article on this subject, emphasizes the fact that the deductions of the operators, as to the nature and result of treatment, are confusing, when he propounds the query, "Have the profession in regular medicine, with their accurate observations, no conclusions which depend on authentic data?" I should add, Have the operators made accurate observations and scientific analyses of such cases with the view to logical and unbiased deduction?

Arbuthnot Lane, Coffey, and others have given an excellent foundation upon which to proceed, but the surgeon should not ignore the fact that most of his cases have had long observation and treatment by the internist.

It is important in making an analytical study to determine the frequency, cause, etc., of colonic membranes and deformities that the race, social position, age, habits, and previous medical history immediately bearing on the case be noted.

Parallel investigations should be conducted at autopsies. Unless we are to conclude that these conditions are caused by a beginning physical degeneration, it seems they would be equally common in races leading a simple, fairly well-regulated life.

The embryonal development and descent of the abdominal viscera are certainly not different in the various races.

The less enlightened and less dissipated races certainly do not have intestinal intoxication and its results as frequently as those further advanced in dietetic abuse and other abnormalities of habit. All maintain the erect posture. Dietetary intemperance rarely enters as a factor productive of stasis and its sequelæ in the so-called inferior or uncivilized races.

Let us not content ourselves with a discussion of the relative merits of medical and non-medical treatment of crippling colon conditions. The recognition and management have always an embarrassment to the internist, and have given encouragement to faith healers and "masseurs."

Surgeons have theorized, experimented, and made many well-founded logical deductions, but most of them seem willing to admit their confusion.

If surgeons would give us their facts, internists their opinions and deductions, physiological chemists their experimental results, without influence of bias or personal equation, the problem of causes would be solved, and early recognition and prevention are then natural and early sequences.

The most important factor in the prevention and treatment of this, as of all conditions which are to be anticipated as the result of an established and preventable cause, is that the race from childhood should so mould its career as to conserve its organs of nutrition and excretion in a state of maximum efficiency. More attention should be paid to the education of the child in intestinal hygiene.

Induced defecation inhibits and abolishes normal activity, and further lowers the resistance of the intestinal wall to invasion from within.

The location of the obstruction is of importance. Obstructions and bacterial decompositions in the colon at or beyond the hepatic flexure rarely give other than local manifestations. Stasis at or near the cecum usually results in serious intoxication, and not infrequently reverses peristalsis. The intestines and stomach are slower in evacuating their contents, and the condition existing in the lower bowel is transmitted to the small intestine. This naturally only occurs in late cases, or those with marked obstruction, and is preceded by insufficiency in the ileocecal valve.

There can be no doubt that surgical intervention with the view to extirpation of false membranes, without attempt at restoration of normal bowel function, will fail in many cases unless non-surgical treatment is kept up after operation. This may be due to the inadvertent destruction of such anchoring peritoneal folds as those described by Jonnesco, Juvara, Treves, and the genitomesenteric fold of Douglass Reid.

Those who are skeptical as to the exogenous functional disorders of the nervous system will in many neurasthenics find the beginning of the solution by the correction of primary intestinal intoxications, as the means of curing the nervous, and the prevention of pericolic inflammation and resulting membrane and colonic deformity.

It is further of importance that operators, when they have done skilful work in removing obstructions, and doing fixation and anastomotic operations for the correction of colonic abnormalities, reinforce their results by the establishment of such dietary and habit management as to assure greater percentage of cures than they now obtain after one or more operative procedures. It is imperative that the colon be reëducated to normal processes by every means available after corrective operations.

Colonic plications, removal of membranes and adhesive bands, anastomotic and fixation operations, will give small promise of permanent cure if the patient reverts to the same dissipations which were the original causes of the trouble.

Nerve, lymphatic, circulatory, and muscular tone should be restored and equilibrated; digestion and absorption encouraged and nutrition improved.

Too great emphasis cannot be made to the end of recognition of conditions leading to membranous pericolitis. If we assume that stasis is the precursor to the sequence which I have attempted to analyze, it seems that early recognition and prevention is to be desired. Unfortunately but few cases are seen sufficiently early to prevent a more or less temporary disabling deformity.

Several points are of importance in determining the degree of disability and the hope for recovery with non-surgical treatment; and certainly a very large portion can be cured without laparotomy.

There are three indices to progress under non-surgical management.

1. Symptomatic.
2. Radiography.
3. Urine content of indican and sulphur ethers of decomposition.

In well-developed cases of acute pericolitis the manifestations are never alarming. Intermittent constipation, intestinal flatulency, fulness in lower abdomen, digestive disturbances of upper bowel, the usual evidences of intestinal intoxication producing local or general polyneuritis or arthritis are suggestive. On examination tenderness is found to exist above the site of stasis or accumulation, but rarely over it. Palpation reveals a colon distended with gas and feces.

SYPHILIS OF THE STOMACH.

By William Gerry Morgan, M.D.,

PROFESSOR OF GASTROENTEROLOGY AT THE GEORGETOWN UNIVERSITY HOSPITAL, WASHINGTON, D. C.

In a paper published eight years ago I stated that syphilitic manifestations in the stomach were quite rare, and up to that time I think only a few cases had been recorded. At the present time we know that syphilitic gastritis is often seen. Many cases, no doubt especially in women, go unrecognized for obvious reasons.

Andral, in 1834, was the first to definitely call attention to gastric syphilis, reporting in detail two cases. From that time on cases were reported with increasing frequency until at the present time the histories of several hundred cases may be studied. Not all the cases reported can be accepted as gastric syphilis.

A study of the report of autopsies made by Chiari and Stolper upon 329 individuals affected by syphilis is of considerable value. They found four cases of organic gastric syphilis, and in addition many other cases where there were to be recognized marked changes of a more or less definite character. Therefore from these statements

it will be seen that 1.2 per cent. of all cases of syphilis show organic gastric lesions, and further, that these are as likely to occur in congenital as in the acquired form of the disease.

Congenital Syphilis, C. and S. C.	Chiari.	Stolper.	Combined.
Total number of cases autopsied .	145.0	25	170.0
Number of cases of gastric syphilis found	2.0	0	2.0
Percentage of gastric syphilis . .	1.3	0	1.18

Acquired Syphilis, C. and S. C.			
Total cases autopsied	98.0	61.0	150.0
Cases of gastric syphilis. . . .	1.0	1.0	2.0
Percentage of cases of gastric syphilis	1.02	1.64	1.26

Total Cases of Syphilis, C. and S. C.			
Cases autopsied	243.0	86.0	329.0
Cases of gastric syphilis. . . .	3.0	1.0	4.0
Percentage of cases of gastric syphilis	1.2	1.16	1.29

Ewald states broadly that 10 per cent. of all cases of ulcer of the stomach are probably syphilitic in origin. This estimate is, I think, far too high. I have a Wassermann done on all new patients who come presenting pronounced symptoms of disturbed gastric digestion, and judging from our experience in this way I should say that not over 1 per cent. of our ulcer cases show the syphilitic taint. Because of our experience during the past three years we are always on the alert for this disease, regardless of the personal history, and if we have reason to suspect the taint we are not satisfied with one negative Wassermann but have two or even three tests made at intervals during several weeks.

The stomach may be affected in syphilis in two ways: (*a*) functionally or secondarily, and (*b*) organically.

Functional gastric disturbances are common in cases of syphilis in the secondary and tertiary stages as a part of the general systemic disorder. Secondary morbid conditions in the stomach may also occur, as in consequence of lesions of the neighboring viscera, especially in the liver. Thus the circulatory disturbances caused by the syphilitic cirrhosis of the liver may produce congestion, catarrh, ecchymosis, and erosions of the gastric mucous membrane.

Organic syphilis of the stomach occurs in the tertiary stage, and with rare exceptions originates as a more or less circumscribed gummatous deposit or infiltration of the gastric wall. The submucosa is usually primarily and chiefly invaded, the process later extending into the other layers. At a later stage the gummatous mass may break down and ulcerate. Still later the healing of the ulcer may result in the formation of a new fibrous tissue and cicatrices, with possible contraction and stenosis.

In one of Chiari's congenital cases the lesions were not of a gummatous character, but consisted of diffuse syphilitic infiltrations of the mucous membrane. This was the condition of one of our patients who came to operation.

Cases of gastric syphilis may be divided for convenience in their clinical manifestations into four groups, according as the predominating symptoms are of (1) chronic gastritis; (2) ulcer; (3 stenosis. Or as Hausmann suggests, they may be grouped according to a "patho-anatomical" view-point as follows:

1. Syphilitic catarrh, which some clinicians consider is a sequel to syphilitic hepaptitis or myocarditis.

2. Hemorrhagic erosions. These two are sometimes described as secondary to the syphilitic disease of the liver and brought on by stasis.

3. Ulcer. These are due to a syphilitic endarteritis, or from degeneration of the gummata.

4. Gummatous tumors.

5. Cicatrization of a gummatous ulcer, causing deformity of the stomach.

6. Diffuse syphilitic infiltration of the whole or a portion of the gastric walls, causing a more or less marked thickening of these walls. This last group, as Hausmann points out, must be differentiated from (*a*) sclerosing gastritis; (*b*) from Brinton's linitis plastica, which most clinicians now think is syphilitic in origin; (*c*) from diffuse carcinomatosis of the gastric wall; (*d*) from diffuse hypertrophy of the entire organ on a tuberculous basis in individuals affected with pulmonary tuberculosis; and (*e*) from stenosing gastritis.

Manifestations resembling those of chronic gastritis are presented in many cases of gastric syphilis either throughout the case or during the period of development of the lesions. There is nothing distinctive about the symptoms which may consist of dyspeptic conditions, pain and distress, achylia, malnutrition, etc., exactly as in chronic gastritis in general. These symptoms may be protracted over a period of years.

When ulceration develops the symptoms presented are similar to those of ordinary gastric ulcer: pain, vomiting, hemorrhage, anemia, malnutrition, etc. Hemorrhage is likely to be excessive, repeated, and prolonged, making some of the cases very grave. Ulcer is probably the most frequent clinical form in which gastric syphilis occurs, or at least is recognized.

When tumors, thickening of the stomach walls, or cicatricial fibrous contractions are so situated as to cause stenosis or closure of the pylorus the usual consequences of obstruction of this opening result, such as dilatation, stagnation, etc. A considerable portion of cases of tumor are of a pseudo-cancerous type, presenting a course of symptom-complex that may closely resemble those of

gastric carcinoma; dyspeptic symptoms, pain, palpable tumor, emaciation, etc. The cachexia is not so typically manifested as in the true cancerous cases. The course of the disease may be longer protracted (over a period of years) in syphilis than in carcinoma, a point which may aid in diagnosis of the former against the latter condition. And the general physical deterioration is much less marked than in cancer.

Cases of gastric syphilis exhibit various grades of severity, ranging up to cases of the most serious character in which death may result, as from hemorrhage or malnutrition. If recognized in time, however, the prognosis is good. In cases of gastric syphilis there may or may not be a history of known or acknowledged syphilis, and concurrent syphilitic lesions in other organs being absent, the stomach is at the time the only organ affected with tertiary lesions; in others the stomach suffers in company with other organs in some generalized outbreak of the disease.

From the foregoing considerations it will appear that there are no characteristic symptoms in gastric syphilis differing from those of other similar affections of the stomach to attract attention to the syphilitic character of the lesion or to enable a definite diagnosis to be made. The decisive diagnostic criterion is a positive Wassermann or the result of antisyphilitic treatment, under the influence of which the gastric symptoms and lesions disappear. The pathologists sometimes are not inclined to recognize the validity of the therapeutic test, and the macroscopic and microscopic appearance are not always pathognomonic of syphilis, and for practical clinical purposes the disappearance of the morbid conditions as a result of the specific treatment must be regarded as of the highest validity in establishing the diagnosis of syphilis.

As a matter of fact in a large proportion of reported cases the diagnosis of syphilis has been reached in an adventurous and accidental manner. Many of these cases were recognized only at autopsy. In a few cases the appearance at operation undertaken for the relief of ulcer or pyloric stenosis first aroused suspicion of the syphilitic nature of the lesion. Some of the cases were regarded as syphilitic on account of the incidental disappearance of gastric symptoms in the course of treatment of syphilitic lesions elsewhere. In some cases antisyphilitic medication was employed as a result of happy guess, or tried in desperation as a last resource in severe cases that had resisted all other treatment, and the successful result established the diagnosis. It is the exception, therefore, for any of the clinical manifestations of gastric syphilis to attract attention to the nature of the disorder or to suggest to the practitioner's mind the idea of a trial of antisyphilitic treatment. These cases are so common that the diagnosis of syphilis is not likely to occur to the physician, and yet it is essential to the cure of the trouble that the correct diagnosis be made; many of the patients

get into a desperate condition and will die if the disease is not recognized and properly treated; and so effective is the treatment that the gravest cases, and patients almost moribund, may sometimes be saved almost as by a miracle.

From a critical study of the cases that have come under my own observation the following lessons have been learned:

1. That the failure to glean from the individual anything suspicious of a syphilitic taint, or an abortion, or failure to have children, or a negative Wassermann does not prove that syphilis does or does not exist in that patient.

2. A diseased condition of the stomach marked by a long duration, with changeable symptoms, and which do not correspond to one or other of the well-recognized diseases of that organ, and which resist the accepted methods of treatment, should arouse suspicion of lues.

3. Tumors involving the pylorus which do not cause stenosis are more often syphilitic than carcinomatous.

4. Achylia or a low acidity, as occurred in all our cases, is usual in gastric syphilis. And where there is achylia with symptoms of ulcer one is likely to have an ulcerating gumma or a superficial ulcer on a syphilitic infiltration base in the gastric wall.

5. Diffuse syphilitic infiltration is usually easily detected by the palpating fingers because it produces some enlargement of the stomach, which, as happened in some of our cases, may not be readily recognized at operation. This may be true even when the infiltrating mass is to be detected by the roentgen-ray, as was the case of Mrs. S. C. B., reported below.

6. A tumor which does not change its size and shape over long periods of observation may be syphilitic, or a tumor which disappears under antisyphilitic treatment may be presumed to be a gumma.

7. Differential diagnosis may be made, often in a short time, by the use of salvarsan.

8. When the diagnosis of gastric syphilis has been definitely established the patient should not only to put upon appropriate treatment, but should be made to understand the importance of taking a short course of antisyphilitic treatment once a year until late in life.

9. The results of intelligent treatment in gastric syphilis are usually prompt and marked, and at times little short of miraculous.

In my former paper I reported one case of gastric syphilis which I will herewith include because it is so instructive and teaches the necessity for being constantly on the watch for these cases.

The following case reports will illustrate many of the characteristics of gastric syphilis:

In my former paper I reported one case of gastric syphilis which I will herewith include, because it is so instructive and teaches the necessity for being constantly on the watch for these cases.

Case I.—On March 31, 1904, Mr. C. T. consulted me on account of severe gastric symptoms of a progressive nature extending over four years, but which had become worse during the past months. Following my routine custom I asked him specifically if he had suffered from gonorrhea or syphilis, and he denied having had either, declaring that his only illness had been malarial fever four years before, and from which he dated his present illness.

At the time he first came to see me he complained of continuous pain in the epigastrum, uninfluenced by eating or drinking, but always worse at night. He had no appetite, and upon the least exertion was troubled with vertigo. He had a sensation in the stomach as if there was an orange in it, and had aversion to animal food. Thirst was annoying all the time. He experienced no difficulty with deglutition. Eructation of odorless gas was continuous. His tongue was coated down the centre; the tip and edges were clean; fauces in otherwise healthy condition. Breath was not offensive. He suffered from obstinate constipation and distressing flatulence. He had lost thirty-five pounds in weight during the past eighteen months, and felt extremely weak and ill, and looked so. His flesh was flabby and his skin hung in loose folds. He was markedly anemic.

Physical examination showed the heart and lungs to be normal. Reflexes were normal. Liver not enlarged or tender. Spleen apparently normal. Kidneys not palpable. Abdomen somewhat scaphoid; arches and spines prominent. Epigastrium sensitive but without a circumscribed painful area. Splashing sound could be produced from the tip of the ensiform to one and a half inches below the navel. As the abdominal muscles were irritable the examination was somewhat unsatisfactory. When the stomach was inflated the area of gastric tympany was greatly increased downward. At this time no tumor could be palpated. The swallowing sounds were heard normally.

Clinical examination of the gastric contents one hour after an Ewald test breakfast showed the following condition: free and combined HCl absent, the degree of acidity 2; an absence of ferments; an absence of blood, bile, and tissue; the presence of a large amount of mucus. In a fasting condition some of the food eaten the previous day was washed out of the stomach.

At this time I was uncertain whether I had to deal with ischochimia due to markedly weak musculature (quite a rare condition) or to benign or malignant stenosis of the pylorus, but I was inclined to the latter.

On April 14 the patient returned to my office and I was greatly shocked at his loss in weight and the failure in his general condition. At this time, on account of the relaxed and thin abdominal walls, I could easily palpate a somewhat movable tumor occupying the pyloric region. The dilatation of the stomach had increased

considerably. I unhesitatingly pronounced his disease carcinoma of the pylorus, and as he desired to be told the truth so that he could return to a distant city if he was incurably ill, I advised him to lose no time in arranging his departure. A short time thereafter his wife came to see me and said that her husband had just told her that he had denied to me having suffered with syphilis, but that four years ago he had contracted the disease. I asked her to send him to see me at once. Upon questioning him again he gave a typical history of syphilitic invasion with the usual course. He had the initial sore upon the glans penis, followed later on by mucous patches in his mouth and later still by syphilitic eruption on his body. He consulted a physician, who made a correct diagnosis and put him upon a course of mercurial treatment which he followed for a few weeks and then abandoned, because he attributed his digestive disturbances to the medication being given him for the relief of syphilis.

After hearing this syphilitic history I told him that there was a reasonable probability that the tumor was a gumma, and if such was the case he had a fair chance of being relieved of his stomach trouble.

I put him upon antisyphilitic treatment and in a short time his symptoms disappeared; he regained his normal weight and strength and was discharged.

Case II.—Mrs. S. C. B., first consulted me September 13, 1913. Mother died of miscarriage at forty-three. Otherwise family history was negative.

Previous History. Typhoid at six. Pneumonia at thirty-four. One miscarriage. No living children. Married fourteen years.

Duration of symptoms two years. She complained of pain immediately after eating, and lasting as long as food remains in the stomach. The character of the food did not influence the pain. Vomited toward evening each day, affording relief. No hematomesis; marked and continued pyrosis; bowels have a tendency to be loose; headaches nearly all the time.

Physical Examination. Chest organs were normal. Liver and spleen were normal. Both kidneys movable to the second degree. Marked tenderness on pressure over upper right quadrant of epigastrium with slight muscle spasm. Under this area of tenderness is felt an indefinite resistance like a thick anterior gastric wall. The lower border of the stomach comes down to three inches below the navel. The thread test showed the pylorus to be patulous and there was no blood stain. Examination of the feces showed quite strong occult blood at once, on a meat-free diet. The gastric analysis showed a low peptic power, a large amount of mucus, and a trace of blood. Lavage in a fasting state showed food to remain in the stomach hours after it should have passed out. The urine was normal. The blood was markedly anemic. Weight, 103 pounds. My diagnosis was chronic ulcer near the pylorus.

She was put upon ulcer treatment, but after a time showing no improvement, I suggested a roentgen-ray study, which was made by Dr. Christie, with the report that he felt sure she was suffering from a cancer at the pyloric end of the stomach. She was operated upon by Dr. Charles S. White, and at operation no pathological condition was recognized either in the stomach, gall-bladder, or appendix. The patient made an uneventful recovery from the operation, and was entirely relieved of her symptoms for a few weeks, when the same old symptom-complex returned. At this time Dr. Christie made a second roentgen-ray study, with the result that it tallied almost exactly with the first, and brought forth the reiteration that there was an infiltrating growth in the gastric wall in the pyloric end of the stomach. I then referred her to Dr. Vedder for a Wassermann, which was promptly double plus. She was then referred to Dr. Hagner, who gave her a course of antisyphilitic treatment. At the end of four weeks a Wassermann was done and was feebly plus, so that two more injections were given, since which time the Wassermann has been negative. A few days thereafter Dr. Christie made a third roentgen-ray study of this patient and reported that the growth had entirely disappeared and the stomach was normal in appearance. After the first injection of salvarsan she showed distinct improvement and went on to an uninterrupted and complete recovery, gained considerable weight and has remained well.

Case III.—Mr. D. S. M., came to me in November, 1912. Aged fifty-three years. Family history negative. Past history negative. Denies having had any venereal disease. Uses tobacco moderately. No alcohol. Duration of present illness, which he attributes to worry, one and a half years.

Symptoms. Complained of progressive loss of strength and weight. Had lost thirty pounds. Had sense of food lodging in lower part of gullet; the character of the food did not affect this, as he even felt it after drinking water. Had mild nausea and from time to time vomited, but never large quantities. Appetite was always good. Had no severe pain, but said he had a "misery in the pit of the stomach" if he ate a normal quantity of food, the character of which did not influence this. Bowels were costive, requiring use of cascara sagrada.

Physical Examination. Reflexes normal. Chest organs were carefully examined, and were normal except for some dry rales at the bases of both lungs on forced inspiration. Liver, spleen, and kidneys were normal. There was tenderness to pressure over the epigastrium, causing recti to go into spasm. Splashing sound from ensiform to lower border of navel, otherwise abdominal contents were normal. Examination of the blood was interesting in that it, too, pointed to the luetic infection. Hemoglobin was 68 per cent.; red cells, 4,016,000; leukocytes, 5200. Differential count: poly-

morphonuclears, 78 per cent.; small lymphocytes, 7 per cent., large lymphocytes, 3.5 per cent.; eosinophiles, 11.5 per cent. The urine was normal. The feces were normal except that they showed occult blood. Gastric contents one hour after an Ewald test breakfast: free HCl absent; total acidity, 16; benzidine reaction was positive; considerable mucus and many yeast cells were noted.

Thread Test. Duodenal bucket passed the pylorus and was deeply bile-stained, but there was no blood-stain. My diagnosis at that time was severe chronic gastric catarrh. He was put upon a bland but highly nutritious diet and given by mouth six times a day a mixture containing iodine and carbolic acid. In place of cascara he was directed to use enemas and suppositories. He returned at the end of two weeks greatly improved, having gained six pounds in weight and with none of his former symptoms. In two weeks from that time he again came in to see me because of a dusky red swelling on the lower end of his sternum, which he had discovered ten days before and which had increased rapidly. On examination it appeared to be a malignant growth. I referred him to Dr. Wellington, who did a partial resection. The patient made a rather tedious recovery from this operation and the wound would not heal completely. I lost sight of him from that time until about May, 1, when once again he consulted me with another similar growth on the upper third of the sternum. I referred him this time to Dr. John B. Deaver for an opinion. Dr. Deaver said he though it was probably sarcoma involving not only the sternum but the lung as well, and advised against operation. I then had Dr. Christie make a roentgen-ray study. He reported as follows: "Infiltrating growth of middle third of sternum, involving the upper third of the right lung, which is probably malignant in character." Notwithstanding the roentgen-ray confirmed Dr. Deaver's opinion I was not quite satisfied in my own mind in regard to the case and sent him to Dr. Vedder to have a Wassermann test, the result of which was positive. The patient was at once placed under Dr. Hagner's care, with the result that he made a prompt and complete recovery, as the following roentgen-ray report taken at the end of three months shows. "There is no roentgen-ray evidence of the infiltrating growth in the sternum or the lung, which was noted at the first examination."

Case IV.—J. L. L., aged forty-one years; single. Family history negatived. Past history negative except for several attacks of gonorrhea and history of soft chancre fourteen years ago. Denies the knowledge of syphilitic infection. Uses alcohol and tobacco in considerable amounts.

Duration of the present symptoms four years.

Symptoms. Eruption on face with sore feeling in stomach. During the past few days severe pain in stomach two hours after meals, especially after drinking anything alcoholic. Also distended

feeling after meals. Has a full feeling in his stomach from the first few mouthfuls. Bowels are constipated, requiring saline laxative waters.

All reflexes are distinctly sluggish. Motion, sensation, and coördination apparently normal. Chest organs were normal. Liver and spleen were normal. Kidneys not palpable. Examination of the abdomen showed conditions to be normal except that the gall-bladder was somewhat tender to pressure and there was moderate dilatation of the stomach. Examination of the blood showed a moderate anemia with lymphocytosis and a moderate leukocytosis and a slight increase in the eosinophiles. The urine was normal except for a low specific gravity and an increase in the amount of mucus. The feces were normal. The gastric analysis showed a low peptic power with a marked butyric acid fermentation. Roentgen-ray study by Dr. Christie suggested a beginning infiltration in the gastric wall at the pyloric end; possibly malignant. No six-hour residue. No other evidence of stenosis. No evidence of gastric or duodenal ulcer. The first Wassermann was only slightly positive, but after having him abstain from alcohol and tobacco for a week the second Wassermann was promptly double plus. Diagnosis was syphilitic gastritis with syphilitic eruption on the face. He was referred to Dr. Hagner for treatment, with improvement from the start.

A roentgen-ray examination by Dr. Christie nine months later was made with the following report: "The study of the stomach and duodenum at this time shows no sign whatever of abnormality."

Case V.—D. de la F., aged forty-nine years; married; no children.

Family History. Negative.

Past History. Gonorrhea twenty-five years ago. Denies the knowledge of syphilitic taint. Had severe attack of amebic dysentery seven years ago. Otherwise history negative. Uses tobacco in moderation. No alcohol. Has lost twenty-five pounds in four months. Duration of present symptoms four or five months.

Symptoms. Pain in the upper third of the epigastrium, coming on at night, and at the time had pain nearly every night. Skin was jaundiced. Family physician who accompanied him said that the jaundice made its appearance four or five days ago. Nauseated after meals, but did not vomit. Very constipated. Had during the preceding four or five days an itching of the skin on the body, especially where the clothing rubbed. Had marked pyrosis two hours after meals. Was bloated so that he had often to loosen his clothing. Reflexes, motion, and sensation normal. Skin and sclera markedly jaundiced. Chest organs were normal. Spleen normal. Liver dulness appreciably diminished. Kidneys not to be palpated.

Abdomen. Considerable tenderness is elicited on pressure over midepigastrium, beneath which was felt an indefinite resistance which

suggested the thickening of the anterior gastric wall. Marked tenderness over the colon. Recti has a tendency to go into spasm on palpation. There was a moderate chloroanemia, with a moderate lymphocytosis, otherwise the blood picture was normal. Systolic pressure, 120 mm.; diastolic, 80 mm. Examination of the gastric contents after a test breakfast showed the free HCl to be 80; total acidity, 86. The ferments were present and active. Blood was present in the gastric contents macroscopically, microscopically, and chemically. The urine showed the presence of bile, otherwise it was normal. The feces were normal except for a prompt reaction for blood with benzidine. Wassermann was promptly double plus. The diagnosis was syphilitic gastritis with syphilitic hepatitis. He was referred to Dr. Fuller for antisyphilitic treatment, and showed a prompt and gratifying improvement right from the start.

The roentgen-ray examination was made by Dr. Christie, who reported as follows: "There is constant deformity about the duodenal cap and the pylorus, which, taken with the sharply localized tenderness at this region, is excellent evidence of a lesion at this point, the nature of which cannot at this time be stated. No shadow of gall-stones."

Case VI.—Samuel S., clerk, aged forty-one years; married; no living children.

Family History. Negative in so far as present illness was concerned.

Past History. At twenty-two had attack of stomach disorder, at which time he had symptoms similar to those from which he was suffering at the time I saw him. He did not recall the sort of treatment which relieved him. He positively denied having had any venereal disease.

He dated his present illness from the early spring of 1913. It began with pain in his stomach, coming on soon after eating, producing nausea and later on vomiting, which, when it occurred would relieve his pain. The pains were always worse after the night meal. His appetite was keen and he relished his food. The bowels were sluggish, but did not require artificial aid. He had lost twenty-five pounds in the last year.

Physical Examination. The chest organs were normal. The liver and spleen were normal. There was acute tenderness on pressure over the stomach which was found to lie wholly in the umbilical region and to extend to two inches below the navel. No tumor mass was discoverable probably on account of the tenseness of the recti. The gastric contents after a test breakfast showed an achylia with much mucus and a trace of blood. The feces were highly putrefactive and contained a slight excess of mucus and some occult blood. Blood examination was as follows: Hemoglobin,

70 per cent.; red cells, 4,250,000; leukocytes, 13,600. Differential count: polymorphonuclear cells, 53.3 per cent.; small lymphocytes, 24 per cent.; large lymphocytes, 22.7 per cent.

Thread Test. Duodenal bucket passed the pylorus. It was bile-stained, but had no blood-stain. Wassermann by Dr. Vedder was negative. Roentgen-ray by Dr. Christie, a full report of which is given below, seemed to confirm the diagnosis of carcinoma of the stomach. He was put upon a bland nutritious diet and given anesthesin by mouth to relieve the pain. A month later he came to see me, and at this time a definite mass could be palpated in the epigastric area. I referred him to Dr. Howard Kelly, with the hope that he might be benefited by radium, but Dr. Kelly sent him back to me saying that without doubt he had carcinoma of the stomach in a too advanced stage for operation or radium. At this time another roentgen-ray study showed marked increase in the growth. I saw him at intervals throughout the winter, and inasmuch as he seemed to be improving slowly but progressively in strength and had less pain, on February 4, 1914, I ordered another Wassermann done, which proved to be promptly positive. He was then referred to Dr. Hagner for treatment. His improvement was prompt and decided, and continued up to the time when Dr. Hagner gave him salicylate of mercury by hypodermic injection, which caused severe systemic disturbance, with ptyalism, diarrhea, pain in the stomach, bowels, etc. After this he did not do well. In June a Wassermann was positive, so Dr. Hagner gave him another salvarsan injection, from which he appeared to derive great benefit. Soon after this he disappeared and was not seen until November 20, 1914. At this time he was found to be in a precarious condition. Another Wassermann was positive. He is now in a hospital under antisyphilitic treatment.

Roentgen-ray report by Dr. Christie, October 18, 1913: "Stomach below umbilicus in both prone and erect positions; absence of cap; sagged deformity in bismuth shadow along lesser curvatures near the pylorus; constant "cut-out" area along lower part of greater curvature appears in all positions of the patient and remains the same in shape and extent under manipulation in front of the fluoroscope screen; large six-hour residue. The findings indicate the presence of extensive infiltrating growth in the walls of the stomach, probably carcinoma and probably inoperable."

December 29. "Roentgenogram shows further encroachment upon lumen of stomach."

February 7, 1914. "Examination shows practically the same appearance as on December 29, 1913."

February 14. "After salvarsan the defect in the stomach shadow has almost entirely disappeared; the defect in the greater curvature still present."

March 14. "Stomach has almost exactly the same appearance as on February 14."

May 21. "Defect in the stomach shadow has again increased, but has not reached extent shown by the earliest pictures."

November 25. "Marked increase in encroachment upon the gastric lumen over anything seen at any previous examination of this patient."

Case VII.—Mr. S. T., aged forty-two years; married; no living children.

Family History. Negative.

Past History. No history of lues.

Symptoms. Discomfort in the epigastrum coming on at night, waking him and disturbing his sleep. Bowels were constipated.

Physical Examination. Fauces chronically inflamed and injected; skin dry and scaly and covered with an eruption which suggested at once the probability of syphilitic taint. Typical geographical tongue. Pulse, 104, regular and small. Chest organs normal. Liver dulness extended to one inch below the free margin of the ribs. Splashing sound from the ensiform to one inch below the navel. In the upper right quadrant of the epigastrium a soft and definite mass could be felt.

Gastric Analysis. Free HCl, 16; total acidity, 28. Some excess of mucus. Urine and feces were normal. Blood examination was as follows: Hemoglobin, 60 per cent.; red cells, 4,500,000; leukocytes, 14,600. Differential count: Polymorphonuclear, 67 per cent.; small lymphocytes, 13 per cent.; large lymphocytes, 18 per cent.; eosinophiles, 2 per cent.

The Wassermann was double plus. Roentgen-ray showed an infiltrating growth about the pyloric region.

He was referred to Dr. Homer Fuller, and is still under treatment, showing a decided progressive improvement as the following roentgen-ray report by Dr. Christie three months later shows: "Examination of the stomach and duodenum on this date shows the cap to be normal in size but with a few small irregularities on its lower surface."

Case VIII.—Mr. B. G., consulted me December 6, 1914; aged, thirty-eight years; salesman; married; one living healthy child.

Past History. Positively denies having had any venereal disease whatsoever. Says he often had from time to time during past few years a low fever which did not interfere seriously with his work and which would disappear without treatment. No other illness. Used no tobacco and drank only beer. Duration of present illness approximately two years, and he thought worry caused it.

Symptoms. Burning, gnawing sensation in his stomach, which comes on from three to four hours after meals, and is worse after the night meal. Had little nausea, but regurgitated acid contents more or less constantly, and often vomited large quantities of acid

chyme. Bowels were quite constipated, requiring daily artificial aid. Had lost ten or more pounds in weight.

Physical Examination. An undersized, poorly nourished, sallow individual; chest, anteriorly, covered with small scars so symmetrically arranged as to at once excite our suspicions. Except for markedly exaggerated abdominal reflexes there was nothing abnormal in the nervous system. Tongue heavily coated except at the extreme tip, which was unusually red. The chest organs were normal. Pulse, 52, regluar and soft. Radials beady, but soft and pliable. Liver normal. Kidneys not palpable.

Abdomen. Panniculus spare; recti well developed, but go into spasm, upon even light palpation, making examination unsatisfactory. Marked tenderness on pressure over entire epigastrium; succussion splash to navel.

Gastric contents after Ewald test breakfast showed low peptic power and low acidity of 6. Urine was normal except for faint trace of albumin and slight indicanuria. Feces were normal except for a positive benzidine reaction. Blood showed moderate chloroanemia: leukocytes, 14,200; red cells, 5,150,000. Differential count: Polymorphonuclears, 44 per cent.; small lymphocytes, 32.2 per cent.; large lymphocytes, 21.2 per cent.; eosinophiles, 1.6 per cent. Pulse pressure 40 mm.

Wassermann by Dr. Vedder on two occasions proved negative. Because this case pointed so definitely to lues. I had Dr. Vedder make a luetin test, which was strongly positive on about the eighth day.

Roentgen-ray by Dr. Christie, with the following report: "There is a striking deformity of the stomach in this case which seems undoubtedly to be due to an infiltrating tumor mass involving a large part of the pyloric end of the stomach. The shadow does not have the irregular appearance of carcinoma. It may be due to syphilitic infiltration or just possibly to tumor of pancreas adherent to the stomach; the latter does not seem very probable, however."

"There is no evidence of abnoramlity of the colon except atony."

Referred to Dr. Hagner for antisyphilitic treatment.

As I have already pointed out, there is at the present time no recognizable diagnostic symptom-complex or pathognomonic sign of gastric syphilis. Therefore it may be useful to point out a few characteristics common to all of the cases which have come under my personal observation, hoping thereby to establish what may be termed suspicious diagnostic criteria of gastric syphilis, and lead to an earlier recognition of the disease.

In all of these individuals the peptic power of the stomach was lost. The benzidine reaction was positive at one time or another. There was pain in the stomach uninfluenced by the character of the food. This pain was always worse toward night.

There was stagnation of the gastric contents, food remaining for

hours in the viscus, although there was no actual organic stenosis of the pylorus, as the results of the duodenal bucket test showed. In all of the cases the stomach was considerably dilated and atonic.

The duration in each instance was somewhat longer and the degree of physical deterioration was not so marked as is usual in persons suffering with carcinoma of the stomach for the same length of time.

In most of the cases the blood showed a high lymphocyte and eosinophile count, with a moderate degree of chloroanemia.

Notwithstanding the low peptic power, the appetite in all but one case was keen and the food was relished.

Vomiting occurred at some time during the course of the illness in all my cases. There was nothing suggestive in the condition of the bowels. On examination of the abdomen of these cases the recti showed constant tendency to go into marked spasm on palpation. For this reason a tumor mass may not be so easily recognized as it would be in carcinoma of the stomach.

THE VALUE OF TYPHOID VACCINES IN THE TREATMENT OF TYPHOID FEVER.

By E. B. Krumbhaar, M.D.,
PHYSICIAN TO THE OUT-PATIENT DEPARTMENT,
AND
Russell Richardson, A.M., M.D.,
OF THE AYER CLINICAL LABORATORY.

(From the Pennsylvania Hospital, Philadelphia.)

Following such phenomenal success in the prophylactic use of typhoid vaccines it is but natural, with a logical theoretical basis, that they should also be tried for the cure of typhoid fever. The large number of typhoid cases admitted annually to the Pennsylvania Hospital have been utilized by us as a favorable basis for an investigation of the value of such a procedure. While the benefit, of course, is less striking than that following its prophylactic use, we are gratified to be able to report distinctly favorable results from three years' observation on cases at the Pennsylvania Hospital. In the later cases, whether from the larger doses used or the more experience acquired, the results have been so much more favorable that we feel justified in recommending the proper use of typhoid vaccines as a specific and valuable form of treatment of this very important disease.

In 1912 Drs. J. C. Wilson and J. Walker treated 44 cases with a commercial stock antityphoid vaccine, and have been good enough to give us their hitherto unreported material to further this study. Two years ago we began another series, treated with a vaccine prepared by Dr. Richardson from the Rawling's strain, the same as that used by both the English and American armies. In order to give the procedure as critical a test as possible, the vaccine was given only to the severer cases. Our tabulated figures proved but little better for the vaccinated than the unvaccinated. Deceived at first by our method of selection, it was not until we had carefully analyzed the individual cases that we realized how constant the improvement after vaccination had been. Thus stimulated we began again last year with a vaccine differently prepared and in larger doses. Unfortunately we were prevented by extraneous circumstances from applying the excellent results obtained in this series to more than 16 cases, before the epidemic abated, but hope later to supplement this study with other statistics. These three series, aggregating 93 cases, form the basis of this study.

History. The history of the curative use of typhoid vaccines is brief. In 1893, Fraenkel[1] treated 57 severe cases with a vaccine prepared much as are those of today. Typhoid bacilli, grown for three days in thymus bouillon, were killed at 63° C., tested for sterility, and injected subcutaneously (dosage not given). Although he noted a marked improvement and recommended its further use, his work apparently escaped notice, and no further attempts were made on such lines for fifteen years. In 1908 Pescarolo and Quadrone[2] inoculated 20 cases of typhoid fever with living attenuated organisms in small doses and, in spite of a rather severe reaction, reported favorable results.

With an antityphoid serum (prepared from horses immunized with a toxin from typhoid bacilli grown on special media) Chantemesse[3] reduced the mortality from 17 per cent. of untreated cases to 4.3 per cent. in 1000 cases thus treated. According to Semple[4] it is generally accepted that Chantemesse's serum "acts as a typhoid vaccine, owing to the probability that it contains the bacterial elements originally injected into the horses which supplied the serum." In this summary we have not taken account of vaccines prepared by methods differing from Wright's, such as Renaud's irradiated or Besredka's sensibilized vaccines. Results of treatment with these methods are given by Netter.[5]

With the promulgation of Wright's opsonic theory and his treatment by vaccines came a renewed interest in typhoid therapy. In January, 1909, Watters and Eaton[6] reported the results of 30 cases thus treated, the first routine curative use of typhoid vaccine after Fraenkel. The next month Captain Smallman,[7] at Leishman's suggestion, described 36 cases in the Indian army treated with doses ranging from 100,000,000 to 350,000,000 bacteria, prepared according to Wright's method. There were three deaths, no relapses,

and the patients seemed less toxic. With perhaps unconscious humor he says, "It was no uncommon thing to go into the ward when full (sic) and find nearly every patient quietly and comfortably sleeping."

Since then over 1800 cases have been reported by about forty observers, the great majority with favorable results. Generally speaking the larger the dose the better the results obtained. Thus Sadler,[8] using the very small dosage of 1,000,000 and 2,000,000 had fourteen deaths in 92 cases; whereas Meakins and Foster, using one to three doses of 1,000,000,000 to 1,500,000,000, had but one death in 42 cases. The average duration of fever in this series was reduced from thirty-seven to twenty-eight days and complications occurred in 5 per cent. (versus 42 per cent. unvaccinated); relapses in 2.4 per cent. (versus 13 per cent. unvaccinated). To some authors it is doubtful if doses under 50,000,000 produce sufficient effect, and yet Watters and Eaton,[9] with doses averaging 25,000,000 to 30,000,000 reported favorable results in 69 cases (2 deaths, and 6 relapses). In the largest single series reported, Petrowitch,[10] at Uskub, reduced the mortality of 460 cases to 3.2 per cent. as compared with 8 per cent. of 220 unvaccinated cases. He used one to three doses of 20,000,000 each of vaccine supplied from the English army. In Semple's[11] 60 cases there were only 3.3 per cent. each of death and relapses, the dosage being usually four to six doses of 6,000,000 to 50,000,000 in the earlier cases, and of 50,000,000 in the later, and he would now recommend even larger doses.

The latest report by Captain MacArthur[12] emphasizes the importance of early treatment. In 63 cases of his series there were 2 deaths (3.1 per cent.), 2 relapses (3.1 per cent.), and 5 other complications (7.9 per cent.), but all of these occurred in the 29 cases vaccinated in the "unfavorable stage" (after the tenth day).

Less favorable results have been reported by M. W. Richardson,[13] using a dosage of 10,000,000 to 100,000,000 on 28 cases. He found that the results were "not striking," except that there was only one relapse as against 10 relapses in 77 unvaccinated cases. Horner[14] found unsatisfactory results with 40 vaccinated cases and 95 unvaccinated controls. With an average total dosage of 516,000,000 the mortality of the vaccinated was 10 per cent. as opposed to 11.5 per cent. of the unvaccinated. Relapses, 20 per cent.; unvaccinated, 11.5 per cent.; complications, 55 per cent.; unvaccinated, 50.5 per cent. The average duration of fever was twenty-four days; unvaccinated, twenty-three days. Although there were no deaths in Nichols'[15] 11 cases, 2 relapses and 2 prolonged fevers made him feel that "the results were quite inconclusive."

This involves less than 5 per cent. of the total number, however, and in the other 95 per cent. the results have been distinctly favorable. Even such a difficult condition as typhoid osteomyelitis lasting a year has been cured in a few weeks by the use of vaccines

STATISTICS OF VACCINE THERAPY.

Author.	No. Cases.	Deaths.	Relapses.	Dosage.	Remarks.
Anders[19]	8	...	1	25,000,000 to 50,000,000	
Callison[20]	38	5	1	500,000,000 to 600,000,000 (repeated every 4th day)	Few complications.
Carr[21]	2	0	0	25,000,000 to 50,000,000 (2 doses)	
Courmont[22]	39	2	8	....	5 per cent. mortality against 20 per cent. unvaccinated.
Duncan[23]	6	0	0	50,000,000 to 1,000,000,000 (1 to 2 doses)	
Elliott[24]	3	0	0	500,000,000 (1 to 2 doses)	
Fletcher[25]	14	2	1	500,000,000 to 1,000,000,000 (1 to 2 doses)	No bad results; all helped.
Grace[26]	6	...	1	....	Cases made milder.
Gray[27]	126	5			
Hollis[28]	51	2	8	10,000,000 to 250,000,000	Less toxic.
Hornor[29]	40	4	22	Average total, 560,000,000	No beneficial effect.
Jewett[30]	15	2	2	25,000,000 to 400,000,000	No effect in 3; some help in 7; marked in 5.
Krumbhaar Richardson Series 1	44	4	3	Average total, 926,000,000	Mulford's Typhobacterin.
Series 2	33	1 (3)	2	Average total, 720,000,000	"Rawling's" killed at 60°.
Series 3	16	0	0	Average total, 1,640,000,000	"Rawling's" killed at 56°; best.
MacArthur[31]	45	2	7	150,000,000 to 1,500,000,000 (3-day interval)	Improved, especially if early.
McLaughlin[32]	13	0	...	50,000,000 to 500,000,000	Good influence.
Martin[33]	2	1	...	30,000,000 (3 to 5 doses)	One well in 2 weeks, other moribund.
Meakins Foster [34]	41	1	1	1,000,000,000 to 1,500,000,000 (1 to 3 doses)	Less fever, toxemia, and mortality than the unvaccinated.
Nichols[35]	11	0	2	....	Average severity.
Oelsnitz[36]	10	0	0	65,000,000 (several doses)	Did better than the unvaccinated.
Petrowitch[37]	460	15	...	20,000,000 (1 to 3 doses)	3.2 per cent. mortality against 8 per cent. unvaccinated.
Ream[38]	17	0	..	50,000,000 to 250,000,000	14 benefited, 3 no effect.
Richardson[39]	28	...	1	10,000,000 to 100,000,000	Fewer relapses, otherwise not striking.
Sacquepee[40]	28	2	...	100,000,000 to 700,000,000 (1 to 3 doses)	Good effect.
Sadler[41]	92	14	...	1,000,000 to 2,000,000 (several)	Benefited.
Sappington[42]	22	3	...	5,000,000 to 50,000,000 (1 to 9 doses)	75 per cent. benefited.
Semple[43]	60	2	2	8,000,000 to 30,000,000 (4 doses) 100,000,000 to 300,000,000	No risk; benefited.
Simons[44]	6	1	...	....	Less severe.
Smallman[45]	30	0	3	100,000,000 to 350,000,000	Good results.
Watters[46]	158	17	8	2,000,000 to 60,000,000	75 per cent. helped, shorter fever.
Watters (quoted)*[47]	316	14	15		
Wilson[48]	6	0	0	250,000,000 to 500,000,000	Less toxic; shorter fever.
Wolverton[49]	12	0	0	50,000,000 to 300,000,000	Beneficial.
Single reports	6	0	0	50,000,000 to 250,000,000	All benefited (some chronic complications).
Total	1806	99	88		35 out of 39 authors (reporting 93 per cent. of cases) found vaccines useful.

* Loc. cit. For these cases, quoted by Watters, no references were given. None are duplicates from the other authorities quoted by us.

(Rosenberger);[16] and a typhoid periostitis of six years' standing cured in two weeks by vaccines (Sharpless).[17] Two of Meakin's and Foster's[18] series, typhoid carriers of eight and twelve years' duration, were also cured by vaccine therapy. The method, therefore, may be said to have successfully passed the stage of "primary laudation," beyond which Osler says, in *Modern Medicine*, that no specific remedy for typhoid had as yet passed. (See accompanying table of cases thus far vaccinated.)

Theory. The stimulation of antibodies by the injection of dead bacteria in order to lessen the virulence of the attack is theoretically logical, just as is its prophylactic use for the prevention of the disease. A study of the agglutination curve after prophylactic vaccination shows that there is an increase on the fourth or fifth day, which is still further raised on the sixth and eighth day and then slowly drops to normal. Somewhat the same course is followed by the agglutination curve after vaccination during the attack of typhoid fever.[50]* The frequent absence of the Widal reaction until the second or third week shows that the body may take some time to produce the necessary antibodies, and in such cases, if the diagnosis can be made by other means, early vaccination may be of great help in shortening the attack by earlier stimulation to adequate antibody formation. It must be remembered that many strains of typhoid bacilli have very little ability to form agglutinins, while the culture from which our vaccines are made has been picked largely for its value in that direction, and is therefore presumably better than an autogenous vaccine. It is frequently found that a bacillus from a virulent case is poor in agglutination, just as our strain used for vaccination, though strong in agglutinins, is weak in toxic properties.

The natural antibody formation is presumably largely limited to the spleen, lymph nodes, intestines, and places where the typhoid bacilli mainly congregate, and as any body cell may participate in antibody formation it is probable that the subcutaneous injection of the dead bacilli affords new areas for antibody formation, and thus helps to stem the tide of invasion. This appears to be Major Russel's, Leishman's, and Semple's theory of the beneficial action of the curative action of the vaccine in a systemic infection, in spite of Hektoen's[51] experiments on dogs, which tend to show that the tissues at the site of injection of antigen do not take part in the production of antibodies. The "negative phase" of Wright's opsonic work is absent or negligible, according to both Leishman[52] and Russell,[53] and certainly no clinical evidence of its presence is usually seen. In this connection it must be remembered that the rise in temperature that so often follows the injection of adequate amounts of vaccine is no indication of a negative phase, and, fur-

* Recent observations by various authors have lessened the value of this evidence by showing that the agglutination and protection curves do not necessarily run paralle .

ther, that the temperature curve is an index of the degree of intoxication, not of the degree of infection or resistance to it.

According to Theobald Smith,[54] "the effectiveness of vaccines applied in the course of acute febrile diseases, such as typhoid and pneumonia, must be accounted for by principles of which experimental medicine has as yet no definite knowledge," and in this predicament we must fall back on clinical and statistical evidence. The crux of the matter, as Semple puts it, is that "vaccines in quantities sufficient to stimulate increased production of bacteriotropic substances can be injected hypodermically into patients suffering from typhoid fever without adding in the least to their toxic condition." We have increasing evidence that the clinical results of such inoculation are favorable.

Preparation. The vaccine used during the summer of 1913 was prepared after Wright's method. The cultures were grown on plain agar and suspended in sterile normal salt solution. After shaking and counting the suspension, organisms were killed by a temperature of 60° C. for one hour. The vaccine was made with 1,000,000,000 organisms to each cubic centimeter and 0.3 per cent. of lysol added. The only change in making the vaccine for use during the past year was in killing the organisms. This was done at 56° C. for one-half hour.

Analysis of Cases.* *Series I.* Forty-four cases were treated with Mulford's Stock Typhobacterin. In this, as in the other series, the treatment of the vaccinated cases was otherwise identical with the unvaccinated cases. The Widal reaction was positive before inoculation in 24 cases and suggestive in 6. Four of the 14 negative cases gave positive blood cultures, and the other 10 gave sufficient clinical evidence to be considered typhoid by Drs. Wilson and Walker. The total dosage varied from 50,000,000 to 1,650,000,000, given in one to five doses. The average total dosage was 926,000,000 per patient. There were 4 deaths, 3 relapses, and 12 complications (5 hemorrhages, 2 perforations, 2 phlebitis, 1 cystitis, 1 periostitis, 1 abscess).

Case Abstracts. Case 4.—Male, aged twenty-one years, positive Widal, received only one dose of 100,000,000 on the seventeenth day of disease, a hemorrhage occurred eight days later, followed by double otitis media, mastoiditis, meningitis, and death.

Case 11.—Male, aged twenty-two years, negative Widal and blood culture. Received 125,000,000 on the twelfth day and 250,000,000 on the sixteenth day. Was very toxic from the start. Hemorrhages. Death on twentieth day.

Case 32.—Female, aged twenty-one years, positive Widal, 600,000,000 given on twenty-third day; 700,000,000 on twenty-seventh day; 800,000,000 on thirty-first day. Perforated seven

* In order to save space, protocols of individual cases will only be given to bring out special points.

days later. Died twenty-four hours after operation. Second perforation found at autopsy.

CASE 44.—Male, aged thirty-four years, positive Widal, 500,000,000 on fifteenth day; 700,000,000 on nineteenth day. Death three days later, probably from perforation.

Two of these cases, therefore, received very small doses, and on the other two specific treatment was begun at too late a date. Several others, especially where treatment was begun before the tenth day of the disease, showed quick drops of temperature after injection with a short febrile course. (Case 20, nine days fever; Case 24, seventeen days fever; Case 31, fifteen days fever; Case 33, seventeen days fever; Case 41, eleven days fever). Of course it is impossible to predict what the febrile course would have been without vaccination, and it is fair to say that abortive cases appeared among the unvaccinated controls, but not to the extent or degree that was present among the vaccinated. In several unvaccinated cases also these early drops to normal were frequently followed shortly by remissions of temperature.

Series II. The 33 cases in this series were treated with the vaccine prepared by Dr. Richardson from the "Rawling's" strain of typhoid bacilli in total doses varying from 200,000,000 to 1,450,000,000 (one to three doses). The Widal reaction or blood culture was positive one or more times in all cases. In practically all cases a localized redness and soreness of the arm persisted from twenty-four to forty-eight hours. No constitutional aggravation other than a fleeting rise of temperature was noted, and the patients nearly always felt better within a few hours of the injection (Psychic?). There were 3 deaths in this series, but, as the cases abstracts will show, there was only 1 death (3.2 per cent.) (Case No. 66, perforation) in which the vaccine treatment could fairly be considered to have failed, and in this vaccine treatment was not begun until the twenty-sixth day. Of the other two, Case No. 57 had already developed a complicating pneumonia when he was given his first vaccine four days before death, and his death was from pneumonia. The other, Case 59, had recovered from his typhoid, and after ten days' normal temperature, developed lobar pneumonia and died from it. In 170 milder cases of typhoid not getting vaccines, that were treated in the wards during the same period, there were 14 deaths (8.02 per cent.).

In the 33 vaccinated cases there were 2 relapses occurring after vaccination (6 per cent.) (Cases Nos. 65 and 68.) The former is of special interest as the only example in our cases where the vaccine may be accused of having done harm (see Case Abstract). It is of course impossible here to rule out coincidence, and vaccination was begun very late. In the unvaccinated cases there were 16 relapses (9.2 per cent.).

In the vaccinated cases there were 4 complications (12.1 per cent.)

Of these a perforation and a pneumonia have already been considered among the fatal cases. Case No. 52 developed phlebitis and Case No. 67 had a slight hemorrhage, each some days after vaccination. Of the unvaccinated cases 18 were complicated (10.6 per cent.). The average number of days of fever of the vaccinated cases (including relapses and complications) was 36.7 days; of an equal number of lighter unvaccinated cases occurring at the same period 33.7 days. The average temperature of the vaccinated cases, as near as could be determined, was 102.2° F. before vaccination and 101.4° F. after vaccination. The average temperature of the same number of unvaccinated cases was 102.3° F. The temperature variation (taken every fourth hour) was greater in 13 cases after vaccination than before, less in 10 cases, and showed no change in 11 cases. In almost every case a rise in temperature of 1° to 3° was noticed immediately after vaccination. This was followed in 23 out of 33 cases by a distinct fall in temperature that frequently temporarily reached normal. This was nearly always more marked after the second and third doses than after the first. In some cases it fell steadily to normal, where it remained; in others after falling for twenty-four to seventy-two hours it again rose. Of the 10 cases which were not benefited by the vaccines, 5 (Nos. 49, 54, 55, 58, 60) probably did not receive big enough doses (total dosage between 200,000,000 and 850,000,000), 3 (Nos. 52, 59, 66) were all obviously virulent infectious, and 2 (Nos. 53 and 67) showed no benefit, in spite of adequate dosage (850,000,000 and 1,050,000,000) begun on the eleventh and thirteenth days. In spite of special effort to begin vaccine treatment early, the average day of disease of the first dose was the twenty-first. This is due partly to the type of patient in the ward, partly to the delay necessary to make a sure diagnosis. Of 2 who got their first dose before the tenth day of the disease, one (No. 48) had only fourteen days of fever, the other (No. 55) had twenty-nine days of fever. The average days of fever after the first dose was given was 16.3 days after the last dose 11.3 days.

Case Abstracts.—Case 48.—Male, positive Widal. Given 100,000,000 on eighth day of disease (no change); 150,000,000 on twelfth day (temperature rose 1.5°, then dropped steadily until it reached normal in forty-eight hours). Given 400,000,000 on fifteenth day (temperature rose from 98° to 101° for a few hours and returned to normal permanently).

Case 50.—Male, positive Widal. Given 60,000,000 on tenth day of disease (no change); 150,000,000 on fourteenth day (temperature dropped from 102° gradually to normal); 300,000,000 on seventeenth day (temperature reached normal on next day and stayed there permanently).

Case 52.—Male. Positive Widal and blood culture. Given 100,000,000 on eighteenth day of disease; 250,000,000 on twenty-first

day; 500,000,000 on twenty-fourth day. No appreciable change in temperature occurred after any injection, but a new crop of rose spots were noted after the last dose of vaccine. Recovery after forty-eight days of fever due to a complicating pleurisy and phlebitis. (Note: In the light of later cases, further injections would be indicated in such a case, unless the new crop of rose spots were taken, not as a coincidence, but as an index of the liberation of more living organisms, in which case further specific treatment would be doubtful.)

Case 57.—Male. Positive Widal. After twenty-five days of fever, including 2 remissions and relapses, patient developed another rise in temperature. Two days later 100,000,000 were given, but it was found that the increased fever was due to pleurisy and pneumonia. Three days later 100,000,000 were again given and patient died the same day. (Note: This was not a suitable case for vaccine treatment. While it is impossible to form an opinion as to whether the vaccines contributed to the fatal issue, they certainly are not indicated in such a condition.)

Case 59.—Male. Positive Widal. Given 150,000,000 on tenth day of disease, 400,000,000 on thirteenth day, and 700,000,000 on sixteenth day. But little effect from any dose, though the temperature fell gradually soon after last dose. Temperature became normal on forty-second day. After ten days the temperature was normal, a typical lobar pneumonia developed and proved fatal in four days.

Case 65.—Female. Positive Widal. Given 150,000,000 on thirty-third day, and the temperature dropped quickly to normal on the same day. After three days of normal temperature, 400,000,000 were given. This was at once followed by a rise in temperature which ushered in a relapse of considerable severity, lasting twenty-six days. (Note: In this case the vaccine was given to put a stop to a long-continued mild fever. It is doubtful, in the light of this case, whether such procedure is advisable unless there is further evidence of deficient antibody formation.)

Case 66.—Male. Positive Widal. Given 200,000,000 on twenty-fourth day of disease, 450,000,000 on twenty-seventh, and 800,000,000 on thirty-first day. This case was a very toxic one throughout, and although he seemed benefited by each dose (less toxic and lower temperature), he died on the thirty-fourth day from a perforation.

Case 67.—Male. Two positive Widals. Given 150,000,000 on eleventh day of disease, 300,000,000 on fourteenth day, and 600,000,000 on nineteenth day. The temperature went up and stayed up after each dose. A few days after the last dose a mild hemorrhage occurred. Fever continued for seventeen days after the last vaccine was given. (Note: This case may indicate that if no favorable response is made to the first or possibly the second dose the case may be unsuitable, and further specific treatment should be abandoned.)

Case 68.—Male. Two positive Widals. Given 150,000,000 on fourteenth day; 300,000,000 on seventeenth day; 600,000,000 on twenty-second day. Drop of temperature after each, reaching normal after twenty-seven days. Seven days later, following increase in diet and permission to get out of bed, a moderately severe relapse started. (Note: This case should be considered as one in which too early increase in feeding caused a relapse in spite of the administration of vaccines.)

Case 71.—Male. Positive Widal. After forty-three days continuous fever, given 200,000,000 (followed by a quick drop of 3° F.). On forty-seventh day given 400,000,000 (causing greater fluctuations, and drop to normal after several days). On the fifty-seventh day given 600,000,000 (after a temporary rise, temperature became permanently subnormal). (Note: Unless due to coincidence a protracted febrile course was here terminated by vaccines, although the Widal was already positive.) (Compare Case 65.)

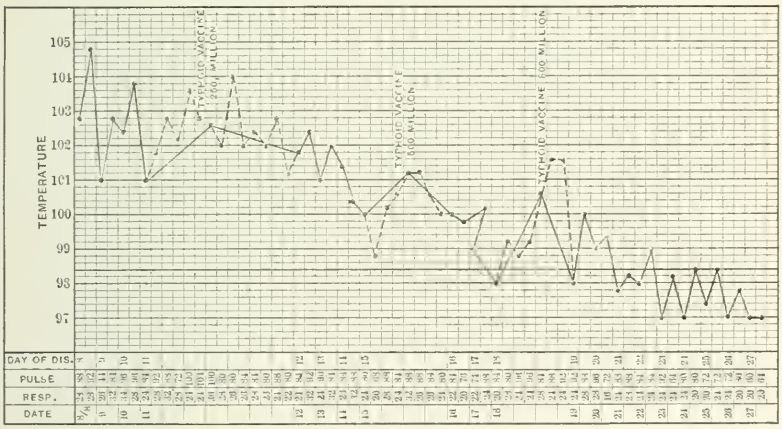

Fig. 1.—Case 83. S. M. Widal positive. Average curative effect of typhoid vaccine. Dotted lines indicate fourth-hour temperature; heavy lines, morning and evening temperature.

Case 77.—Male. Positive Widal. On sixteenth day of disease given 150,000,000. This was followed by a steady drop to normal on the nineteenth day of the disease. (Note: Unless due to coincidence the effect of a single dose of vaccine is here strikingly shown.)

Series III. Owing to the sudden termination of the typhoid epidemic with the colder weather it was not possible to treat more than 16 cases in this manner. The total dosage ranged between 850,000,000 and 3,350,000,000,* (average 1,640,000,000 in one to five doses). There were no deaths, no relapses, and 1 complication. (Case 84 developed bronchopneumonia after

* In three cases where a single dose proved sufficient the amount was naturally smaller.

eighteen days' normal temperature.) The average number of days of fever was 21.6, after the first injection 8.3 days, and after the last injection 3.3 days. The average date of the first injection was on the twelfth day of disease. (The difficulty in securing patients early in the disease has already been commented upon.) In only 2 cases was vaccination begun before the tenth day (Cases 92 and 93), and these two showed only fourteen and sixteen days of fever. Either the Widal reaction or blood culture was positive in all (Widal in 14, blood culture in 3). As usual no aggravation was noted after injection and the fleeting rise of temperature, except in 2 cases (Case 87, diarrhea; Case 91, chilly sensations).

In the 16 control cases (occurring at the same time) there was 1 death, 1 relapse, 2 complications (hemorrhage and perforation); the

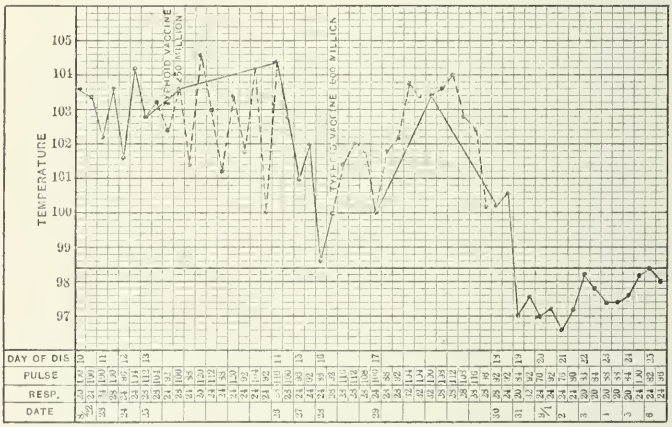

FIG. 2.—Case 85. M. C. Widal positive. More pronounced effect following two injections of vaccine.

average duration of fever was twenty-eight days, and the average date of admission was on the eleventh day of the disease. Thirteen gave positive Widals and 3 suggestive.

CASE ABSTRACTS. CASE 84.—Male, aged forty-five years. Farmer. Positive Widal. Very toxic throughout (stuporous). Was probably sick for two weeks before admission. On nineteenth day (?) received 250,000,000; on twenty-second day, 500,000,000; on twenty-sixth day, 1,000,000,000; on thirty-second day, 800,000,000; on thirty-seventh day, 800,000,000. The last 3 were followed by drops of the temperature to normal, the last time permanently. Patient improved steadily, but still was mentally dull. After sixteen days' normal temperature a relapse began, which ran a mild course lasting eight days.

CASE 87.—Male. Positive Widal. Exhibited a temporary diarrhea and headache after the initial dose of 300,000,000 on the

twelfth day of the disease. Given 700,000,000 on fifteenth day and reached normal on same day. After 1,000,000,000 on nineteenth day the temperature rose to 99.2° for twelve hours.

Case 91.—Male. Positive Widal. Had chilly sensations and a rise of 3° in temperature after his only dose of 600,000,000 on the fourteenth day of the disease. His temperature then fell steadily, reaching normal in thirty-six hours, where it remained.

Case 93.—Male. Positive Widal. Given 600,000,000 on sixth day; 1,000,000,000 on ninth day; 1,000,000,000 on twelfth day. But little change after first two doses. After the third dose there was a steady drop of temperature to normal in forty-eight hours, where it remained.

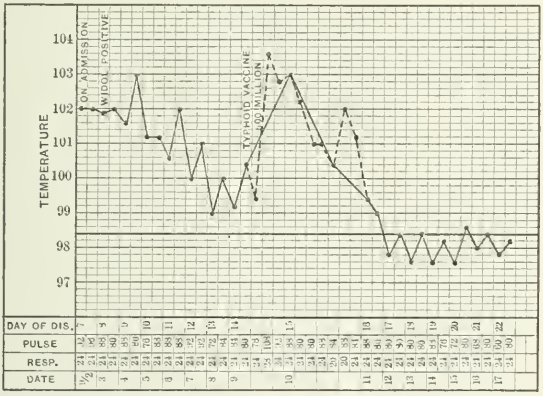

Fig. 3.—Case 91. C. C. Example of occasional curative result following a single injection of vaccine.

Summary

Series.	No. of cases.	No. of deaths.	No. of relapses.	No. of complications.	Average days of fever.	Average days of fever after first dose.	Average days of fever after last dose.	Day of disease when first dose was given.	Average total dose.
1	44	4	3	12	27.4	13.8	6.3	13.0	926,000,000
2	33	3	2	5	36.7	16.3	11.3	21.0	720,000,000
3	16	0	1	0	21.6	8.3	3.3	12.6	1,640,000,000
Total vaccinated	93	7	6	17	25.2	12.8	7.0	15.5	1,095,000,000
Unvaccinated	170	14	6	24	34.7	...	...	...	...

Conclusions. 1. The curative use of typhoid vaccines in the course of typhoid fever in order to stimulate further antibody formation, has a logical theoretical basis, although its mode of action has not as yet been demonstrated experimentally. Practical proof of its value is afforded by the rise in agglutinin curves after such vaccination.

2. The proper use of vaccines in the treatment of typhoid fever has been found clinically to be without harm, and usually to produce beneficial results. It rarely causes any noticeable aggravation of symptoms, beyond a fleeting rise of temperature. Relapses and complications are diminished in frequency, but not prevented. The increase in size of the spleen, noted by others, has not been observed by us.

3. The best results are obtained if the injections are begun early in the disease, especially before the tenth day. A blood culture is more valuable than the Widal test in the early stages. Late in the course of the disease, except in selected cases, the value of vaccines (both theoretically and practically) is more dubious. In the chronic complications of typhoid, such as periostitis and cholecystitis, good results have been obtained from vaccines by other investigators.

4. The contra-indications for vaccine treatment of typhoid are not yet clear. We should hesitate to advocate their use in moribund or very toxic cases, during hemorrhages or suspected perforations, or in such complications as pneumonia or otitis where other microörganisms are involved.

5. The best dosage has also not been determined. Semple, Petrowitch and Watters, and Eaton have had good results with small doses; MacArthur, Fletcher and Meakins and Foster equally good results with much larger doses. While this would indicate to some that the true benefit from vaccines was dubious, we feel that the discordance is due to differences of patients and epidemics, preparation of vaccine, and "personal factors." The dosage must vary within certain limits for each patient, and no cut-and-dried rule should be attempted. The more severe the disease the smaller and more cautious should be the dosage. With our methods of preparation we felt that the best initial dose for average adult was 500,000,000; if this proved to be the proper amount, two or more larger doses were given usually at three-day intervals.

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THE PHYSICAL BASIS OF CHRONIC INFECTIONS AND OF RECOVERY WITHOUT IMMUNITY.[1]

By A. Parker Hitchens, M.D.,
GLENOLDEN, PENNSYLVANIA.

The practical application of bacterial vaccine therapy is generally recognized to fall into two distinct divisions. The first comprises the procedures resulting in the formation of specific antibodies or ferments in the tissues—that is to say, the bacteriological diagnosis and the preparation and proper administration of the vaccine. The second division—I think it may be safely assumed that the tissues always respond to the vaccine by producing corresponding antibodies—deals with the distribution of the newly formed antibodies, especially with regard to their relation to the infecting bacteria.

With few exceptions all studies so far reported in vaccine therapy have been limited to the first division of the subject. These researches have been sufficiently thorough to give us a good working knowledge of methods for the preparation of vaccines and their administration.

For certain infections this knowledge has been entirely adequate, but for other diseases the factors essential to success are still obscure. I believe that many if not all the failures will be accounted for only after the second phase of the subject has been thoroughly investigated. Whether a more intimate knowledge will lead to better therapeutic methods or whether it will reveal merely that we have reached an *impasse* is the problem that stimulates the formulation of the following suggestions.

Practically all our knowledge of the cellular pathology involved in the second phase of this subject is due to the work of Sir Almroth Wright. Nothing of importance has been added to his conception

[1] Read at the first annual meeting of the American Association of Immunologists, held in Atlantic City, June 22, 1914.

of the "conditions which obtain in the foci of bacterial infection." Wright considered that in order to resist an infection and to eliminate it from the tissues, the coöperation of a serum constituent with the phagocytes was necessary. He accounted for the rare occurrence of primary blood infection by calling attention to the unhindered coöperation of the formed and unformed elements in the blood against invading bacteria. Localized infections, on the contrary, are common because the pathogenic bacteria on gaining entrance to the tissues successfully resist the action of the small amount of bacteriotropic substance able to reach them, and the resultant tissue changes make it possible for these bacteria to resist still further the antagonistic forces of the body. This is accomplished sometimes by the barrier of inflammatory tissue which may prevent the entrance of phagocytes to the focus of infection, sometimes by the generation of bacterial products within the nidus, and consequent reduction in potency of the fluid elements which, if they reach the bacteria at all, are then too weakened to be effectual. This is demonstrated by the fact that a focus of infection is an area of low bacteriotropic pressure.

Insofar as the histopathology is concerned, Wright's ideas, founded, of course, upon the teachings of Metschnikoff and others, appear to be final. From the physiological standpoint, however, we have a more lucid and more plausible explanation of the mechanism of infection and immunity in the theory of Professor Victor C. Vaughan. According to the current views of physiologists, proteins, in enteral digestion, are split into peptones and amino-acids in order that they may be absorbed into the blood; according to Vaughan, in the parenteral digestion of bacteria the bacterial proteins are digested by the specific ferments in order that they may be eliminated from the tissues. In this process the bacterial protein molecule is split into two fractions; one of these is a non-specific poison having apparently no relation to the production of immunity within the host; its poisonous action seems to be its sole function. The other part is non-poisonous and highly specific; the formation of specific antibodies depends upon its effects on the tissues. This effect sometimes fails while the poisonous action of the other part is always manifested. This being the case, with the physiology of enteral digestion in mind, the suggestion forces itself upon us that there is a physical basis underlying the action of these two parts. That is to say, the action of the poisonous part never fails because it is diffusible and the tissues offer no barrier to it, while the non-poisonous part is not diffusible and under certain conditions the collection of cells in which it is located do not permit it to reach those cells capable of responding to its action. Accordingly, on the supposition that the molecule of the poisonous part is relatively small and the molecule of the non-poisonous part relatively large, we may divide infections into three classes:

1. Those in which the bacteria are surrounded by a firm wall of inflammatory tissue so dense and so perfect that antibacterial ferments are unable to penetrate to the bacteria. The non-poisonous part liberated by autolysis or by ferments within the focus of infection does not escape through the capsule and the resistance of the host is not increased.

2. Those in which the zone of inflammatory tissue is less dense and less perfect. The non-poisonous part of the protein molecule cannot penetrate the barrier of inflammatory tissue, but specific ferments formed as a result of vaccination or auto-inoculation may penetrate in sufficient quantity to give positive therapeutic results.

3. Those in which the infecting bacteria are not surrounded by a zone of inflammatory tissue which inhibits the activity of the non-poisonous part and the resultant newly formed ferments come in contact with the bacteria without hindrance.

These three classes, of course, merge into one another. Within the same host an organism may be surrounded by a zone of inflammation of one type in one part of the body and of another type in another part of the body. Furthermore, they concern chiefly the cellular pathology of the lesion in its relation to the ferments and the split products of the bacterial protein molecule as described so clearly by Vaughan. The special means by which certain bacteria resist the antagonistic forces of the body are not here taken into consideration, such as, for instance, capsule formation by the *Pneumococcus mucosus* and by the anthrax bacillus.

A typical illustration of the first class of infections is the local lesion formed subcutaneously in guinea-pigs which are immunized with rauschbrand aggressin and afterward injected with virulent black-leg muscle. The immunized guinea-pig withstands many times the fatal infective dose of virus, but at the point of injection a small nodule is formed which gradually breaks down in the centre. From this nodule may be obtained highly virulent rauschbrand bacilli; the animal gradually loses weight and dies in about a month apparently from a chronic intoxication.

Another illustration of this class of infections is the caseous tubercle.

In chronic tonsillar infection we have a prolific source of continuous intoxication without any tendency or any ability on the part of the tissues to overcome the infection. The negative results of vaccine treatment place this type of infection in the first class.

In this connection the carrier state in diseases like typhoid fever is of more than passing interest. It has been suggested that this condition is due to a serum-fast strain. But this does not account for the intermittent appearance of living germs in the feces. May it not be then that the bacilli are growing in a nidus of the first class? In this case their occasional presence is merely

an indication that the germs in a certain nidus have broken their confines. Furthermore, although a few positive results have been reported, treatment by bacterial vaccines is generally unsuccessful, notably in those cases under observation for a long period of time.

The typical illustration of Class II is the staphylococcus furuncle. As treated formerly, patients with chronic furunculosis continued to have one boil after another—it was not uncommon to meet a person who had had more than one hundred. With the application of staphylococcus vaccine, however, I think we have all treated such patients successfully; not only have the boils ceased to appear, but those in course of evolution have receded without "coming to a head." In terms of our hypothesis, then, the non-poisonous part is not permitted to escape the zone of inflammation surrounding the abscess. This zone of inflammation, nevertheless, is not a barrier to specific ferments, because when these are formed as a result of vaccination their specific action is apparent within a very short time.

Examples of the third type of infection are the self-limited infectious diseases, such as typhoid fever. In these the non-poisonous part comes in contact with tissues capable of reacting to it and the specific ferments are free to attack the typhoid bacilli. Such a mechanism results in an infection with a typical evolution, recovery being followed by a period of immunity lasting usually throughout the life of the patient.

The question of the relation of these three classes of infection to treatment is now in order.

For obvious reasons, infections belonging strictly to the first class cannot be benefited by vaccine treatment. If the lesion is located in a part of the body where it can be removed *en masse*, one may administer a few doses of vaccine to prevent the growth of any bacteria which may find their way into the blood stream during the operation, and then to remove the entire focus of infection as, for instance, the tonsils.

Future advances in chemotherapy may give us drugs valuable for treatment of infections in the first class. To be efficient they must be diffusible and possibly bactericidal in themselves. Some of the failures of salvarsan are undoubtedly due to the fact that the complementing action of the body fluids fails to destroy the spirochetes.

In the third class we may confidently expect much benefit from vaccine treatment especially in the early stages of the disease. Later when the number of typhoid bacilli, for example, has reached the maximum and the number being destroyed results in intoxication of the patient up to the limit he is apparently able to withstand, the question as to whether it is safe to risk increased liberation of toxic portion should, theoretically, be considered—actual experience does not seem to warrant this fear. (Whether or not typhoid fever

is a pure infection by the time it has reached its fastigium is not a part of the present discussion, but it is a question which must be considered in drawing deductions from the treatment of typhoid fever with vaccines.)

Typical infections of the second class are no more difficult to treat than those of the third class. The diagnosis is made and the vaccine injected—as soon as the ferments have been produced in sufficient quantity the infection is overcome and the patient recovers. Such simple technique is effective in relatively few diseases—those in which vaccines are at present considered indispensable. But we must not conclude that all other infections belong to the first class; by far the great majority, I think, should be placed in a subvariety of the second class. Although they may react to the mere injection of vaccines with little or no benefit, careful examination of other factors complicating the process will reveal the fact that with accessory methods of treatment, positive results may be obtained.

An interesting illustration of a complicating factor is seen in pyorrhea alveolaris; vaccine treatment alone has little local effect, but when foreign bodies, such as calculi, are removed and the pus pockets carefully cleansed, the results are highly satisfactory. In this case, the complicating factor has been recognized and methods for its successful removal have been elaborated. There are, however, other infections which have not received the careful study devoted to pyorrhea alveolaris. If we are to expect further progress in vaccine therapy, this progress must come chiefly, as I have striven to indicate, through investigation of accessory methods in treatment.[2]

KERATOSIS PILARIS OF THE SCALP.

By Richard L. Sutton, M.D.,
KANSAS CITY, MISSOURI.

In 1869 Hermann Beigel[1] described a peculiar disease of the scalp which was characterized by the presence of small, whitish,

[2] Since the presentation of the above paper the discovery of amebæ in pyorrhea has been announced by Allen J. Smith and M. J. Barrett. This is apparently opening up a new field in etiology, as the work done so far seems to indicate that amebæ constitute a determining cause in pyorrhea and possibly other infections. In its bearing upon the views presented in the above paper this observation is of more than passing interest. In amebic pyorrhea it is entirely possible that the bacteria found in the pockets may be largely enclosed within the amebæ. After digestion of the bacterial proteins within the amebæ the toxic portion alone is thrown off as such, the other fractions being still further degraded in the metabolism of the amebæ before their elimination. If such a condition should exist it would explain one of the factors complicating successful treatment of the disease by bacterial vaccines and call for the accessory use of an amebicide—like emetin.

[1] The Human Hair, Henry Renshaw, publisher, London, 1869.

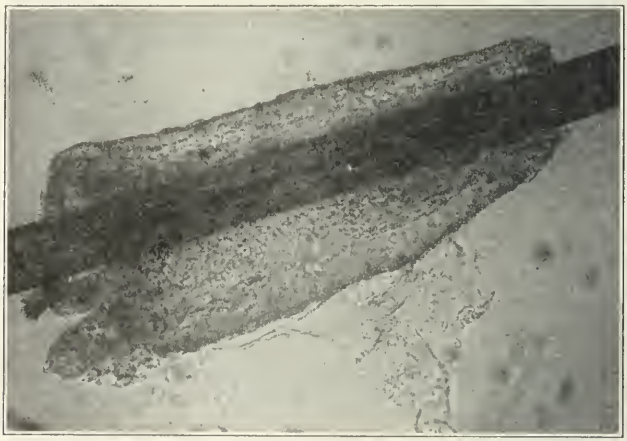
nit-like masses on the shafts of the hairs. Although Beigel's description was written nearly half a century ago, it is so accurate and concise that it may profitably be quoted in full: "The hair appears perfectly intact and normal in texture, but imbedded in a white, transparent, apparently structureless formation of a very peculiar nature. The knots are large enough to be seen by the naked eye, some measuring the tenth of a line in length. They adhere by no means firmly to the hair, but are rather loosely attached to it, and may be stripped off easily. Under the microscope their formation in regular layers, something like the slates of a roof, is very striking. Although some of the divisions are a little narrower than others, yet the whole formation gives the impression of great regularity. There appears to be, as already mentioned, no particular structure, the stratum being only finely dotted and here and there shriveled. This is when the low power is used. But on applying the higher power to one of these knots, prepared for microscopic examination by the application of water or glycerin, and exercising some pressure on the cover-glass in order to produce a thin layer, a structure of a well-known kind becomes visible. The whole knot, thus prepared, is found to consist of cells identical in structure with those of the inner transparent root sheath. . . . There remains no other explanation but one, that a hyperplastic action—perhaps consequent upon irritation or inflammation—exists in the sheaths of the roots of the hair, producing an abnormal number of cells, which are glued together and adhere to the cuticle of the hair while passing through the hair sac."

Grindon[2] described a typical example of the disorder in 1897, and emphasized the differences existing between it and trichorhexis nodosa, monilethrix, the tinea nodosa of Cheadle and Morris,[3] Giovannini's[4] disease, leptothrix, piedra, and the chignon disease of Beigel,[5] which is due to the so-called "chignon" fungus (an organism probably related to, if not identical with, the one found in piedra). In Grindon's case the attack was not preceded or accompanied by seborrheic dermatitis, and there was no history or signs of alopecia pityroides. Grindon suggested the name "ecbolic folliculitis" for the condition, from the fact that the mass of cells was thrust out of the mouth of the follicle.

Recently I had an opportunity to study two cases of this disease, occurring in a mother and her four-year-old daughter. Neither had ever had prolonged arsenical or other treatment. The symptoms were practically identical in the two instances, and one description will suffice for both. The woman was a brunette, a housewife, aged twenty-five years; referred to me by Dr. Howard L. Snyder, of Winfield, Kansas. For several months she had been

[2] Jour. Cutan. Dis., 1897, p. 256.
[3] Lancet, 1879. i, 190.
[4] Arch. f. Derm. u. Syph., 1887, xiv, 1049.
[5] Loc. cit.

troubled by the occurrence of small, white, bead-like masses on the shafts of the hairs of her scalp. The adherent bodies gave rise to no subjective symptoms, but they bore a striking, if superficial, resemblance to the ova of pediculi, and caused the patient much annoyance. A thorough general examination revealed nothing of importance except a slight dryness of the skin. On the external surfaces of both the thighs and the upper arms were considerable numbers of the small, hard, conical papules which are characteristic of keratosis pilaris. The dorsal aspect of the fingers was normal, and there was no suggestion, either here or elsewhere, of pityriasis rubra pilaris or of xeroderma. The patient's hair was long and silky, and there were no signs of seborrheic dermatitis of the scalp. At several points on the scalp there were small, circumscribed, nutmeg grater-like keratotic areas. The hypercornification was



Keratosis pilaris of the scalp, showing epithelial mass on hair shaft (moderate magnification.)

confined to the mouths of the hair follicles, and gave rise to no itching or other disagreeable sensation. There was no alopecia as in Grindon's case. Strung along at irregular intervals on many of the hairs were hard, oval masses of inspissated epithetial cells. So closely compressed were many of the shafts that when the corneous material was forcibly removed the hair was broken off short at the lower margin of the encompassing mass. A number of the affected hairs, together with one diseased follicle and its accompanying horny plug, were secured for laboratory study. Nothing new was discovered concerning the cocoon-like collections of cells on the shafts. Numerous culture experiments with the material proved practically negative, only a few abbreviated chains of streptococci being obtained from one specimen. The piece of tissue was hardened in formalin, mounted in paraffin, and sectioned

serially. The papillary bodies in the vicinity of the follicle were hypertrophied and the interpapillary vessels somewhat increased in size, but there were no signs of the presence of acute inflammation. There was some thickening of the prickle layer, but its relations were unchanged and no inflammatory or degenerative changes were noted. The follicle itself was slightly atrophied at the base, and the hair shaft considerably shrunken. Unfortunately the horny plug at the orifice had become detached at some time during the preparatory process, and its exact relation to the main body of the specimen was more or less a matter of conjecture. The mouth of the follicle was dilated, the walls meeting the hair shaft at a wide V-shaped angle. The corneous layer, which still adhered to the hypertrophied epidermis, was thicker than that usually found in a normal appendage. The contiguous sebaceous glands were much smaller than usual, with apparently some condensation of the surrounding connective tissue. None of the sections were stained for bacteria. From a general view-point the picture was that of a keratosis pilaris lesion which had existed for some time, and in which either as a result of suprafollicular pressure or intrafollicular changes, atrophic changes had occurred.

Treatment. A stimulating antiseptic lotion containing mercuric chloride, chloral hydrate, spirits of formic acid, castor oil, and alcohol, to be applied once daily, at bedtime, and an ointment containing salicylic acid and ammoniated mercury in rose water ointment, to be rubbed into the scalp once each week, were prescribed. The patient was instructed to wash the scalp thoroughly with warm soft water and green soap at intervals of a fortnight. The use of this combination promptly relieved the symptoms, but sufficient time has not elapsed to enable one to judge the permancy of the result.

SERODIAGNOSIS OF RABIES: PRELIMINARY REPORT.[1]

By Michael G. Wohl, M.D.,
PHILADELPHIA.

(From the Neuropathological Laboratory of the Medico-Chirurgical College, Philadelphia.)

The early diagnosis of rabies has been the object of investigation of many an experimenter. Pasteur relied upon rabbit inoculation for diagnosis, but this meant fifteen to twenty days until the patient knew whether to get treatment or not. In some cases, according to Schauder, rabbits inoculated with street virus may

[1] Read before the Pathological Society of Philadelphia, May 14, 1914.

develop hydrophobia two or three months after inoculation, especially is this true where it has been necessary to use emulsion of brain tissue in 1 per cent. phenol such as is the case with brains which have begun to decompose.

Wilson, from the Research Laboratory of New York Department of Health, shortened the period to nine days by inoculating guinea-pigs. Schindler and Fermi have used mice and rats, yet the latter animals are not suitable for diagnostic purposes, for the inoculation period is too short, and hence it is rather difficult to observe upon these animals the development of the symptoms of rabies. The postmortem findings are neither characteristic nor sufficiently constant to warrant a diagnosis.

Thus the hyperemia of the cord and brain and miliary softenings or the leukocytic infiltration described by John and Dexler are likewise found in parenchymatous encephalomyelitis. Babe's rabic tubercles and degeneration of spinal nerve cells, which are accompanied by a disappearance of the chromatin substance, are not found in all cases of rabies so as to be sufficient for diagnosis.

The same holds true of Van Gehuchten's phenomenon, a disappearance of nerve cells and a proliferation of the endothelial capsule with a round-cell infiltration of the sympathetic and peripheral cerebrospinal ganglia.

The negri bodies, first described in 1903, which are found in rabies in the large nerve cells of the central nervous system, are considered today sufficient for diagnosis; yet they were not found before symptoms developed, although the central nervous system was infective at this time. Wilson claims that they are found in rabbits inoculated with street virus on the seventh day and with fixed virus on the fourth day. The complement fixation test tried by Conwall from the Pasteur Institute of Southern India was unsuccessful.

Professor Joseph McFarland, through a personal communication, informed me that he found the complement fixation test unreliable in the diagnosis of rabies, for the reaction proved positive with sera of healthy rabbits.

The discovery of a means of an early diagnosis of rabies is then a desideratum of great importance. It occurred to us that the principle of Abderhalden's serodiagnosis of pregnancy could be applied to rabies as well. As long as there is a virus present which is the causative agent of the disease, then, necessarily, it causes metabolic disturbances of cells with which the virus comes into contact, against these products "protective ferments" are elaborated which rid the body of these foreign elements. To detect these ferments in rabies was the object of our investigation.

At the time of the present writing our work is not completed, yet we feel that we have closed a chapter the records of which we wish to set forth in the present report.

Experiments. We used two series of rabbits.

Series 1. A batch of ten rabbits were inoculated subdurally with fixed virus by Dr. J. Reichel, from Glenolden, Pa., to whom we desire to express our thanks. Ten c.c. of blood were taken from the first rabbit before the inoculation. The same amount was taken from the rest of the rabbits on each successive day and from the first rabbit again on the seventh day. The blood was centrifuged for three minutes, and the serum, drawn off with a sterile, dry pipette, was used for our subsequent tests.

Rabbit.	Tissue used, brain.	Control.		Remarks.
		Serum.	Tissue + saline.	
No. 8269. January 12, 1914. Blood drawn before inoculation.	Faint violet.	—	—	The serum had a slightly reddish tinge.
No. 8270. January 13, 1914. First day after inoculation.	Moderate violet.	—	—	Symptoms on seventh day.
No. 8271. January 14, 1914. Second day.	Deep violet.	—	—	Serum had reddish tinge. Rabbit died four days after inoculation. Autopsy could not be held.
No. 8272. January 15, 1914. Third day.	Blue.	—	—	Placenta plus serum gave a light violet color. Symptoms on seventh day.
No. 8273. January 16, 1914. Fourth day.	Blue.	—	—	Symptoms on seventh day.
No. 8274. January 17, 1914. Fifth day.	Blood completely hemolyzed and dispensed with.			
No. 8275. January 18, 1914. Sixth day.	Blue.	—	—	Blood had red tinge. Rabbit died with symptoms of rabies on tenth day.
No. 8269. January 19, 1914. Seventh day.	Blue.	—	—	Showed symptoms on the same day.
No. 8277. January 19, 1914.	Blue.	—	—	Reddish tinge; symptoms on eighth day.

Brain tissue removed from a rabbit that died of rabies was used as our substrate for two reasons; (1) it was the tissue with which the virus came in contact first, hence if ferments were produced they would naturally cause cleavage of brain tissue first; (2) by using the brain tissue of a rabid rabbit we obtained practically a pure culture of the rabies virus, and if the ferments are specific they would act against the virus grown in the brain tissue of rabbits.

The brain tissue was thoroughly freed of blood. This was accomplished by removing the meninges and allowing water to run over the brain fifteen to twenty minutes. The bloodless tissue was coagulated in the way similar to that used for coagulation of placenta for the diagnosis of pregnancy, *i. e.*, boiled in successive changes of water (to the first boiling a few drops of acetic acid being added) until 10 c.c. from the last boiling with 1 c.c. of 1 per cent. ninhydrin gave a negative reaction. Our thimbles have been tritrated for impermeability of albumin and permeability of pepton and placed in dry beakers.

About 0.5 gm. of brain tissue was put into the thimble and 1.5 c.c. of the serum added. The outside of the thimble being washed off thoroughly; 20 c.c. of water were added to the beaker and distilled toluol to the contents of the thimble and to the beaker.

Controls with serum alone and with tissue plus normal saline were used.

The thimbles were placed into an incubator for sixteen hours and 10 c.c. of the diffusiate boiled for one minute with 0.2 c.c. of 1 per cent. ninhydrin.

The results were as recorded in the table on p. 429.

Series 2. Ten rabbits were inoculated as previously and serum, brain tissue, and spinal cord of a rabbit were prepared as above. Occasionally we used either tissue as indicated below. Results:

Rabbit.	Brain.	Spinal.	Control.		Remarks.
			Serum.	Tissue + saline.	
No. 8228. First day.	Moderate violet.	Faint violet.	—	—	Symptoms on seventh day.
No. 8229. Second day.	Deep violet.	Faint violet.	—	—	Placenta light violet; symptoms on seventh day.
No. 8230. Third day.	Blue.	Violet.	—	—	Rabbit died on fifth day.
No. 8231. Fourth day.	Blue.	Violet.	—	—	Thyroid moderate violet; symptoms on seventh
No. 8232. Fifth day.	Blue.	Blue.	—	—	day.
No. 8233. Seventh day.	...	...	—	—	Thyroid moderate violet. Adrenal moderate violet. Rabbit had symptoms on same day.
No. 8235.	Blood completely hemolyzed.				

No. A. Placenta violet; brain light violet; control rabbit.
No. B. Placenta violet; brain light violet; control rabbit.
No. C. Placenta violet; brain light violet; control rabbit.

From the results obtained in the first series we find that in rabies, brain tissue is broken up as early as the third day after inoculation

if we take the blue color to indicate a positive reaction. The same result was obtained in our second series. The spinal cord was broken up on the fifth day. The blood from No. 8269 gave a faint violet color before inoculation. This was probably due to the hemolysis that occurred in this blood. The result obtained from this rabbit is very interesting. On January 19, 1914, *i. e.*, seven days after inoculation, the reaction was distinctly positive (deep blue).

In our first series placental tissue was broken up in one case; in the second series placental thyroid, adrenal, yet to a very light degree (violet).

The serum of the controls caused cleavage of brain and placental tissue to a light degree.

The distinct blue color obtained with serums from the rabid rabbits indicates that an additional ferment is produced, due to the virus of hydrophobia and upon the intensity of the reaction the diagnosis could be made.

Summary. 1. The Abderhalden reaction might be utilized for diagnostic purposes of rabies.

2. The reaction is positive as early as the third day in rabbits subdurally inoculated with fixed virus.

3. Sera of healthy rabbits cause cleavage of brain and placenta tissue, yet to a very light degree.

REVIEWS

Blood-pressure: Its Clinical Manifestations. By George William Norris, A.B., M.D., Assistant Professor of Medicine, University of Pennsylvania; Visiting Physician to the Pennsylvania Hospital; Assistant Visiting Physician to the University Hospital. Pp. 372; 99 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

In this book of fine appearance and especially readable qualities as to size, paper, and print the author has presented, in its entirety, a subject which is focusing much of medical interest.

The book is more pretentious in size and scope than most of its predecessors, but in his effort to present what is known of blood-pressure, in all its relations, the author has not gone so far as to make the book forbidding by its length. He has made possible the getting at the heart of the subject of blood-pressure, as a whole or in any special connection, with a minimum of reading.

The work possess what is so essential, and the lack of which so often makes books mere compilations of the opinions of others, the personal convictions and beliefs of the author. The value of this is doubly apparent when it is considered how extensive and how often contradictory, the literature on the subject is. Indeed, what a reader seeks in a book is the mature judgment of one specially trained through study and practice in a given subject. This, with due consideration to the clinical and experimental experience of others, the author instinctively gives.

The physiology of the blood-pressure forms the first chapter, and lays a splendid foundation for what is to follow. The second and third chapters deal with instrumental estimations of blood-pressure. Individual instruments are described in detail and criticized and the requirements of instrument and procedure for the obtaining of accurate readings shown.

The newer and less explored field of venous blood-pressure receives a chapter. Perhaps the most engrossing part of the whole book will be met in the chapter on functional efficiency of the circulation as determinable by blood-pressure estimations and allied tests. The man with average facilities has in the past been discouraged in keeping up with advances in this field by the technical knowledge necessary and the intricacy and expense of the instru-

ments involved. How much can be accomplished with the sole aid of a blood-pressure instrument and an understanding of the underlying physical laws is here shown, and well merits close study.

From this point on blood-pressure is considered in its relation to definite clinical conditions. These include essential hypotension, acute infections, intoxications, heart, vascular, and kidney conditions.

The common-sense view which the author takes of arterial hypertension and its treatment is refreshing. One feels that after having been tossed on the troubled sea of conflicting opinion a harbor has been reached where, sheltered by common sense, real progress can be made in handling this troublesome condition.

The closing chapters deal with blood-pressure in the specialties: Nervous Diseases, Surgery, Obstetrics, and Optholmology.

A well-chosen and extensive literature is appended.

A. A. H.

The Backward Baby. A Treatise on Idiocy and the Allied Mental Deficiencies in Infancy and Early Childhood. By Herman B. Sheffield, M.D., formerly Medical Director Beth David Hospital; Instructor in Diseases of Children, New York Post-Graduate School and Hospital and Associate Babies' Hospital (O.P.D.); Visiting Physician to the Philanthropic Hospital and the Northwestern Dispensary, etc. Pp. 184; 22 original illustrations. New York: Rebman Company, 1915.

This essay was awarded the Alvarenga Prize of the College of Physicians of Philadelphia on July 14, 1914. It gives a practical survey of the etiology, pathology, diagnosis and treatment of mental deficiencies of children under five years of age, a period of life in these unfortunates which has not received the attention it undoubtedly deserves. The book gives an excellent and illuminating description not only of the diseases, but especially of the diagnostic aids in recognizing them and practical methods for the relief of many of the minor grades. The chief basis for the work is the author's personal experience. While statistics seem to have fallen under the ban of disapproval, of late years, owing to more or less skilful attempts to create impressions at the will of the statistician, the conclusions would inspire more confidence were the reader given more definite knowledge that the author's experience was large enough to warrant them. Impressions gained from seeing "a fairly large number of cases" gain in value in direct proportion to the number of cases seen. For those who are interested in the psychology of childhood, however, this prize essay is well worth the reading.

J. C. G.

A Manual of Normal Histology and Organography. By Charles Hill, Ph.D., M.D., Professor of Histology and Embryology, Chicago Veterinary College, formerly Assistant Professor of Histology and Embryology, Northwestern University Medical School, Chicago. Third edition. Pp. 483; 312 illustrations. Philadelphia: W. B. Saunders Company, 1914.

This is a reprint, with a few additions, of the second edition published in 1909. Brief descriptions are given of the ruminant stomach and the equine hoof, but otherwise the character of the book is little changed. It remains as before, a simply written and not too condensed account of human histology, drawn chiefly from other text-books, and is a useful and trustworthy book for the student who wishes to learn the main facts of the subject.

W. H. F. A.

Cunningham's Manual of Practical Anatomy. Revised and Edited by Arthur Robison, Professor of Anatomy in the University of Edinburgh. Sixth edition. Pp. 650; 240 illustrations in the text, 22, of which 6 are in colors, in the first volume; pp. 621, 260 illustrations and 11 plates in the second volume. New York: William Wood & Co., 1904.

The term practical anatomy is employed here in a restricted sense. All anatomy is practical to somebody, but, generally, the term applies to that anatomy which is most useful in the daily work of the practising physician, surgeon, or other specialist. But no book can include all that is important on this phase of the subject. The whole subject of anatomy can be most comprehensively treated systematically, or in systems, as the osseous, circulatory, nervous, etc. As soon as one departs from this method and attempts to apply the anatomical facts thus compiled to the needs of the healing art, insurmountable difficulties are encountered in comprehending the whole field. The facts themselves are fairly definite and limited, but the applications that may be made of these facts are without limit. Thus the need of a practical knowledge of anatomy has given rise to a variety of methods of presenting the important facts. Regional, topographical, surface, surgical, and applied anatomy emphasizes various practical phases. Applied anatomy carries anatomy into the discussion of clinical conditions, and must be arbitrarily restricted by the writer or teacher to what he regards as most important.

These two small volumes are practical in the sense that they serve as a guide to the dissection of the cadaver, than which there is no more generally practical method of studying anatomy. It is confined to gross anatomy but covers the whole field for the

dissector. For this purpose we probably have no better work. It is comprehensive and excellently illustrated, many of the illustrations being in colors. Twenty-seven roentgenograms are employed to emphasize certain anatomical facts. The text of this the sixth edition has been altered, some figures changed, others replaced, and new ones introduced. The chief alterations have been made in the section on the brain, which has been rearranged and largely rewritten. The student will make no mistake in purchasing this book, and the practitioner who desires to renew his acquaintance with the details of gross anatomy will find it suited to his purpose. T. T. T.

The Germ-cell Cycle in Animals. By Robert W. Hegner, Ph.D., Assistant Professor of Zoölogy in the University of Michigan. Pp. 346; 84 illustrations. New York: The Macmillan Company, 1914.

Following the publications of Schleiden and Schwann (1838 and 1839) on the cellular structure of plants and animals, Owen (1849), among others, pointed out the existence of the two great groups of cells in the body, viz., germ cells and somatic or body cells. It was his theory that of the progeny of the impregnated ovum, certain cells were early set aside from which the reproductive cells of the matured individual were to be derived, while the remainder of the cells continued to multiply and differentiate to form the various organs of the body. Later, Jäger (1877) and Weismann (1885) stated more emphatically, and with important variations, the idea of continuity of the germ plasm. In the succeeding interval as the result of much intensive study, many of the details in the history of the reproductive cells have been substantiated by actual observation, but for other stages, in many forms of animals, a definite basis for judgment is still lacking and differences of opinion exist. The aim of the present book is to bring together the results of many investigators with the view of correlating them as far as possible into a continuous history of the germ-cell cycle. Much of the book is, therefore, concerned with details of a highly technical cytological character.

Some of the problems dealt with are: how soon can the germ cells be recognized in the early stages of the embryo; where do these cells exist before the definite sexual glands develop; the changes concerned in the final maturation of the sex cells in the mature organism. The part to which the author has given most attention is the segregation of the germ cells in the developing embryo and the visible substances concerned in this process. The most definite results in all these problems have been achieved in the invertebrates,

but information is rapidly increasing with regard to the vertebrates. In the latter it has not yet been possible to distinguish germ cells from other cells in the earliest embryonic stages, but it is probable that the germ cells are set aside before the three definite germ layers are formed, and that they later arrive at the germinal ridge by their own migration. Eigenmann concluded that they were set aside in a teleost fish, which he studied, at the 32-cell stage.

As to the interesting question of chromosomes in the male germ cells of man, reference is made, among others, to Guyer and Montgomery. According to them there are two groups of spermatozoa developed in equal numbers. In one group the number of chromosomes entering into the formation of the sperm is ten and in the other twelve. It seems probable that the former, fertilizing an ovum, is male producing while the latter is female producing. If this is true, sexes in man are determined at the time of fertilization and cannot be influenced by nutritive or other environmental conditions during development.

Among other questions discussed are amitosis and the development of mitachondria in germ cells.

While such a book must find its greatest value in the laboratory of the cytologist, it brings together results of great interest to all students of biology and medicine. W. H. F. A.

A Treatise on Diseases of the Rectum and Anus. By A. B. Cooke, formerly Lecturer on Diseases of the Rectum and Professor of Anatomy in the Medical Department, University of Nashville. Pp. 610; 215 illustrations in the text and 21 full-page plates, 7 in colors. Philadelphia: F. A. Davis, 1914.

The first sixteen chapters are the work of the editor, Dr. Cooke, the remaining fourteen being contributed by several other proctologists of experience and prominence. Cooke's chapters were prepared during the years in which he specialized in this branch of surgery, and have been more recently revised for publication. The book is confined almost exclusively to affections of the rectum and anus. As might be expected from an anatomist, the first chapter, devoted to anatomy and physiology, covers the anatomy thoroughly, only two of the thirty pages in this chapter being given to physiology. Then follows a chapter on general diagnosis, the remaining portion of the book taking up the various affections of this portion of the body. Cooke's sixteen chapters treat of the common affections of the rectum in a lucid and comprehensive manner, and represent a good working guide and a valuable book of reference for the general practitioner.

The other writers contribute as follows: Two chapters on fibrous

strictures of the rectum by Beach; one chapter on benign neoplasms and another on the relation of rectal diseases to the general health by Hanes; two chapters on colotomy and extirpation of the rectum by Evans; one chapter on rectal pathology due to extrarectal causes by Graham; one chapter on local anesthesia by Zobel; two chapters on injuries and foreign bodies in the rectum and sigmoid flexure by Krouse; one chapter on developmental malformations by Yeomans; and one chapter on malignant tumors by Brick.

The book, as a whole, represents a fund of information which is up-to-date, on the affections of the anus and rectum. The illustrations are numerous, illuminating, and, for the most part, diagrammatic. T. T. T.

MANUAL OF THE DISEASES OF THE EYE. FOR STUDENTS AND GENERAL PRACTITIONERS. By CHARLES H. MAY, M.D., Chief of Clinic and Instructor in Ophthalmology, College of Physicians and Surgeons, Medical Department, Columbia University, New York, 1890-1903; Attending Ophthalmic Surgeon to Mt. Sinai Hospital. Eighth edition, revised. Pp. 440; 377 illustrations and 22 plates. New York: William Wood & Company, 1914.

THIS book has been reviewed in its earlier editions twice before in this JOURNAL. What we said of it then remains true today, viz., that the material has been well selected, the style is clear, and that it is probably as good, at least, if not better, for a manual of its class, as any similar work in any language. But it is hardly these qualities, excellent though they be, that make it so remarkable. It is remarkable by reason of its extraordinary success, greater, we believe, than that of any medical work ever written in this country. Since 1900, when it first appeared, there have been eight editions and as many reprints in America, four editions in England; a German, Italian, Dutch, and Japanese translation, each in two editions; and a French and Spanish translation in three editions each. It triumphantly refutes the ancient sneer, "Who ever reads an American book?" Such appreciation is not a source of pride to its author only, but a tribute of which all American ophthalmologists may be proud. It is a model which it will repay manual writers upon other medical specialties also to consider carefully. T. B. S.

TRACHOMA AND ITS COMPLICATIONS IN EGYPT. By A. F. MACCALLAN. Pp. 74. Cambridge University Press.

MACCALLAN divides his monograph into four parts: Part I takes up the history of the disease, its prevalence, mode of infection,

and the various clinical types. Part II deals with the pathology of the disease. In Part III he described the treatment best adapted to the various clinical varieties and briefly discusses ophthalmia neonatorum and gonococcal conjunctivitis, both of which are so prevalent in Egypt. To realize the prevalence of trachoma in Egypt and to appreciate the enormous experience of MacCallan in the treatment of his affection it is only necessary to state that 95 per cent. of the population suffer from this disease and its sequelæ. There are eight permanent hospitals and six travelling hospitals under his supervision, and during 1912 over 28,000 new patients were treated and 21,315 operations performed. Under treatment MacCallan does not describe all the various drugs and methods that have been used or employed against this disease, but he dwells upon those drugs and those operative procedures that his enormous experience has taught him to be of greatest service in the various clinical types encountered. Certainly no one has the privilege to speak with more authority on the clinical manifestations of trachoma than MacCallan, and every ophthalmologist can read his monograph with profit. T. B. H.

Skin Grafting. By Leonard Freeman, B.S., M.A., M.D., Professor of Surgery in the Medical Department of the University of Colorado, Surgeon to St. Joseph's Hospital, The National Jewish Hospital, and the City Hospital, Denver, Colorado. Pp. 139; 24 illustrations. St. Louis: C. V. Mosby Co.

The author has given to his readers a very complete treatise on the subject of skin grafting in all its details. The rather complete historical sketch is very interesting and instructive despite the fact that some of the statements handed down to us appear incredible in the light of our present knowledge. The various known methods of grafting are taken up in detail and the technique described minutely. The questions of transmission of disease, importance of taking the grafts from the patient himself, of absolute surgical cleanliness, gentleness, and accuracy of application, are all referred to as of the utmost value.

Especial emphasis is laid upon the after-treatment as the author thinks that success or failure depends to a large extent upon the proper after-treatment.

The chapter on grafting from animals is very interesting and well worth the time taken in reading it.

The last chapter sums up in an admirable way the salient and important facts which have to be considered in each case of grafting. The advantages and disadvantages of each method are given and the reasons for the choice of a given method in a given case.

The little book is a very interesting and instructive work.

E. L. E.

THE CARE AND TREATMENT OF EUROPEAN CHILDREN IN THE TROPICS. By G. MONTAGU HARSTON, M.D., Examiner in Materia Medica and Therapeutics, Hong Kong College of Medicine. Pp. 232; 47 illustrations. New York: William Wood & Co.

WRITTEN for "newly arrived and junior practitioners in the tropics." this small manual dealing with tropical pediatrics presents in a clear and practical manner, devoid of unnecessary detail or discussion, the opinions of its author, and the results of fifteen years experience with tropical diseases.

The introduction by Sir Patrick Manson states that "the care of the health of the European child in the tropics is yearly becoming of increasing importance," for not only do married men more frequently take their families with them to the tropics than formerly, but children are less frequently, or at least not so early, sent "home" for reasons of health and education as in the past.

The schools of tropical medicine of necessity deal largely with tropical diseases as they affect adults. Consequently, those who upon completing such courses enter active practice in the tropics, are early confronted with practical problems in tropical pediatrics with which they are not at all familiar. For such this little volume will prove most helpful.

The value of modern laboratory methods and the more recent advances in our knowledge of the etiology of certain tropical diseases are given the prominence which they deserve.

The microphotographs of the intestinal parasites by Dr. John Bell, Hong Kong, are a valuable addition to the excellent chapter on diseases due to animal parasites. J. F. S.

OPHTHALMOSCOPIC DIAGNOSIS. By C. ADAM, Berlin. Translated by M. L. FOSTER, New York. Pp. 229; 48 colored plates and 18 illustrations. New York: Rebman Company.

THIS volume is one that will serve well its purpose as a guide to diagnosis for the student in ophthalmology and those in other branches of medicine who desire to avail themselves of the aid offered by the ophthalmoscope and who have not the time for special work along these lines. The plates are excellent, well selected and numerous, and were mostly made with the assistance of the Thorner ophthalmoscope and show the inverted image. The volume is really a combination atlas and diagnosis. The essential changes shown in the plates are fully and yet concisely described. In the text the author has wisely made use of frequent cross references for the plates as well as the text, and in doing so has enhanced the value of his work to those it is intended to serve.

When suitable, the example of Elschnig has been followed, the classification being made according to the ophthalmoscopic signs. The text is subdivided under the following headings: the technique of the examination with the ophthalmoscope; the normal papilla and the normal fundus; conus and staphyloma; atrophy of the optic nerve; neuritis; vessels of the retina; retina; and choroid.

The reviewer cannot endorse the technique described for the so-called direct method of examination of the fundus. It would seem that the method here pictured and described would be inconvenient, if not annoying to the average physician as well as patient. Further, it is practically impossible to use the Loring or similarly constructed ophthalmoscope by the method suggested.

Throughout the volume the text is arranged in a way that will appeal to those endeavoring to study the changes that may be observed in the fundus of the eye, and for those so interested this volume should prove invaluable and will warrant careful study. The author is fortunate in having associated with him in this English translation of his work, one so able as Dr. Foster. T. B. H.

Pathological Inebriety; Its Causes and Treatment. By J. W. Astley Cooper, Medical Superintendent and Licensee of Ghyllwood Sanitarium near Cockermouth, Cumberland. Pp. 151. New York: Paul B. Hoeber.

This small volume is one of the many small books recently published on inebriety. It contains nothing new and is chiefly taken up with the discussion of treatment as practiced in licensed retreats in England. T. H. W.

The Relations of the Lachrymal Organs to the Nose and Nasal Accessory Sinuses. By Professor Dr. A. Onodi, Director of the Rhino-laryngological Clinic in the University of Budapest. With photographic reproductions, in natural size, of 45 Preparations. English Translation by Dr. Dan McKenzie, of London. Pp. 66; 45 illustrations. New York: William Wood & Company.

In many ways this latest work of Onodi's is unique. It consists of 66 pages of text in German, French, and English; one third being devoted to each language. And when one realizes that of the 21 pages in English, about half is taken up with mere preliminary descriptions of the plates in the second portion of the work, a fair idea of the superficiality of the volume may be obtained. Onodi's

photographic reproductions of anatomical specimens are always good and interesting; those in this work, 45 in number, are no exception to the rule, for the good reason that many of them will be found, not once only, but several times, in his earlier publications. To be sure, at the time of their previous appearances, they were not used entirely to show the relationship between the sinuses and the lachrymal organs, but nevertheless, since the text is only explanatory of the pictures, we could wish that he had given us a few more new ones if only for the sake of variety. Several appeared as far back as 1905–06, while the greatest number are found in *Die Nebenhöhlen der Nase beim Kinde* published in 1911 in the same style as the work under discussion. And here, indeed, not only are the illustrations reproduced but the text is frequently word for word in the German and with only slight variations of phraseology in English.

For one who has not Onodi's earlier works it will be of interest and value as the anatomical descriptions of intranasal relationship are well brought out. In the last few plates the newer operations are briefly described although that of Yankauer of New York, the latest one for securing the permanent opening of an occluded lacrimal duct is not mentioned. G. M. C.

Mind and Health. By Edward E. Weaver, Ph. D., Sometime Fellow in Clark University. Pp. 500. New York: The Macmillan Co.

This is a popular work, one of the large number of similar books turned out within the past few years. Its chief value consists in the intelligent quotation of the different cults which have sprung up within the last few years, such as, Christian Science, the Emmaneul Movement, Divine Healing, Dowieism, Metaphysical Healing, etc. The book has nothing original in it and is largely a quotation from other authors. T. H. W.

A Text-book on Gonorrhea and its Complications. By Dr. Georges Luys. Translated and Edited by Arthur Foerster, M.R.C.S., L.R.C.P. (Lond.). Pp. 348; 200 illustrations and 3 colored plates. New York: William Wood & Co.

This is an English translation of an authoritive text-book, two editions of the French work having appeared within a year. This thorough and comprehensive work is of great value, in that it

expresses the views of a recognized authority. It is one of a few good works dealing exclusively with this subject in the English language. The work deals chiefly with gonorrhea in the male, a small chapter of twenty pages is devoted to gonorrhea in women and children. A very entertaining and interesting summary of the history of gonorrhea forms the first chapter, and is followed by a short discourse on the dangers, the social struggle against the disease, and its legal aspect in France. The author devotes particular attention to urethroscopy, and regards the urethroscope of preeminent importance in the diagnosis of the localization and treatment of chronic urethritis. This chapter is profusely illustrated and forms the largest chapter of the book. The portions of the book devoted to the etiology, pathology, diagnosis and symptomatology are brief, but the subjects are well covered. In the treatment of acute gonorrhea, the irrigation method with potassium permanganate is preferred; the treatment of chronic gonorrhea represents the personal experience of the author, and is in keeping with the most recent advances in this line of work. The complications, local and systemic, are briefly considered, but the sequelæ of gonorrhea, notably stricture, impotence, and sterility, are evidently regarded by the author as beyond the scope of the work. In the translator's preface the following significant statement is made: "Some of our readers will regret that the references to vaccine treatment are brief, but as neither Dr. Luys nor myself are greatly impressed by its achievements, we decided not to enlarge the paragraph relative to it." The book is well written, thoroughly illustrated, and is a valuable contribution to the English literature on this subject.

A. A. A.

An Introduction to Experimental Psychology. By C. S. Myers, M.D., Sc.D., Lecturer in Experimental Psychology in the University of Cambridge. Pp. 156. Cambridge; University Press.

This small book is written for the purpose of an introduction to experimental psychology. As such, it serves its purpose. But one wonders why this important subject should have been presented in this manner, for experimental psychology is not a subject for popular reading and for a student one certainly needs a larger work than this.

T. H. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLIFTON SPRINGS SANATORIUM AND HOSPITAL, CLIFTON SPRINGS, NEW YORK.

Xanthochromia in the Cerebrospinal Fluid.—Babes (*Compt. rend. hebdom. des séances de la soc. de biol.*, 1914, lxxvii, 67) has endeavored to discover in what condition xanthochromia may occur aside from those of cerebral hemorrhage, diseases of the nervous system and jaundice. In a series of 50 cases, none showed the phenomenon who were suffering from purely local conditions such as tumors, hernias, etc., but in another group in which the disease process was more general such as pneumonia, phthisis, etc., xanthochromia occurred five times; in none of these five cases was there jaundice or central nervous system disease. In such cases Babes thinks there is an increased permeability of the vessels of the choroid plexus. Examinations were also made in seven cases with icterus; the color intensity of the spinal fluid was compared with solutions of potassium bichromate ranging in strength from 1 to 1000 to 1 to 100,000. The degree of coloring was found to vary between 1 to 5000 and 1 to 50,000. Of numerous tests applied for the detection of bile pigments only that of Jolles was positive in four cases. Babes concludes that the pigments present are really bile pigments, but that most of the usual reactions are not sensitive enough to detect them.

Significance of Meningeal Permeability in General Paralysis.—In some earlier work with Kafka, hemolysins were found in the spinal fluid in two groups of cases: (1) Diseases of the meninges, acute forms as well as those seen in general paralysis. (2) In luetics who show no psychic symptoms, but whose spinal fluid show changes as are found in general paralysis. Weil (*Zeit. f. d. ges. Neurol. u. Psych. Orig.*, 1914. No. 5, xxiv, 501), inclines to regard the finding of hemolysins, in addition to the usual findings, as of great significance in general paralysis. The hemolysin reaction remains constant in general paralysis

contrary to its behavior in the acute cases of meningitis. Only luetics of the above-named kind present difficulties, concerning whom one is not certain whether they will become general paralytics later or not. Hemolysins are present in tabes only when complicated with meningitis or paralysis. Absence of the hemolysin reaction does not necessarily rule out general paralysis. On the basis of this reaction the author inclines to regard general paralysis as arising from an increased permeability of the meninges for substances which otherwise come in contact with the brain either not at all or in exceedingly small amounts.

Studies Concerning the Nature of Complement.—Tissot (*Compt. rend. hebdom. des séances de l'acad. des sciences*, 1914, clviii, 1525) considers that complement is in no sense a ferment, and that the process of inactivation is one of chemical union or dissociation. The acidity of serum as titrated with phenolphthlein is due to the presence of fatty acids. As a result of inactivation at 55° C., the serum acidity decreases, while the alkalinity, as determined with litmus increased. If one adds some sodium or ammonium sulphate to an inactivated serum a marked precipitate forms, quite different from the results if normal sera are used, for in them no precipitate occurs. A similar result obtains if one uses carbonic acid. Dialyzed serum, heated to 55° C. and extracted with ether, gives a much greater precipitate than does unheated serum; and the amount of cholesterin which can be extracted directly with ether is much less in warmed than unwarmed serum. If one adds to serum a substance which tends to prevent the dissociation of soaps—such as an alkali,—then coagulation is hindered even when the temperature reaches 90° to 95° C. Soaps start to separate out after the addition of sodium sulphate to serum in the proportion of 25 to 100, or of sodium chloride to the saturation point. Serum thus treated is protected from inactivation with heat because the altered colloidal state of the soaps prevents the chemical changes which result from heating.

The Oculocardiac Reflex, Especially in Epilepsy.—Lesieur Vernet and Petzetakis (*Bull. et mém. de la soc. méd. des hôp. de Paris*, 1914, xxx, 446), in a study of 33 cases of epilepsy found that in every case pressure upon the eyes caused a much more striking slowing of the pulse than is seen in normal individuals. It was noted that the reflex was much less pronounced in those cases in which epileptic seizures were infrequent than in those having numerous attacks. Stimulated by this finding, Vernet and Petzetakis undertook to study the action of the bromides in cases showing the increased oculocardiac reflex: this underwent a definite decrease during bromide therapy and became hyperactive again as soon as the drugs was discontinued: the strength of the reflex approached the normal more and more as the dose of the bromides was increased, by reason of which this reflex may be of some use in serving as a guide for treatment and an index of its efficiency. The strength of the reflex diminishes markedly immediately after an epileptic seizure. Vernet and Petzetakis also investigated the effect of nicotine and found that in heavy smokers the reflex is always intensified; it approaches the normal as soon as smoking is discontinued.

Clinical Forms of Tuberculous Meningitis in Adults.—Roger (*Montpellier méd.*, 1914 xxxvii and xxxviii), has made a careful study of cases of tuberculous meningitis and has endeavored to group them clinically on the basis of prevalent symptoms, the course of the disease, anatomical changes, etiological peculiarities, and special findings in the cerebrospinal fluid. He makes the following classification: (1) The Symptomatic Group: which he subdivides into (*a*) psychic forms, conditions of hypomania, dementia and coma; (*b*) the motor forms in which paralyses and convulsions dominate the picture; (*c*) cases in which headache is always the prominent feature; (*d*) the typhoid-like cases; (*e*) latent cases occurring chiefly in advanced cases of pulmonary tuberculosis. (2) Group 2 includes only the foudroyant or apoplectiform cases, which may run either a chronic or remittent course. (3) The Anatomical Group is divided according to the location of the disease into the cerebral, spinal, and mixed types: these may show macroscopically as miliary or diffuse exudative forms, or as a "méningite en plaques." (4) In this group Roger calls attention to the relationship between the meningitis and some other primary tuberculous focus and draws a line between the acute and fulminating cases met with generally in the early stages of phthisis or some other tuberculous process, and the variable ones which supervene in advanced cases of phthisis. (5) Cases differ markedly in the findings of the cerebrospinal fluid, such as the pressure, cloudiness, presence of blood, xanthochromia, coagulability, cytological findings, chemical reactions, and the presence of the tubercle bacilli. Upon the findings in the spinal fluid Roger is inclined to place the greatest diagnostic value, but not in any one isolated finding.

Zeinolytic Ferments in the Blood of Pellagrins.—Believing in the undoubted relationship between the use of maize and the disease pellagra, Nitzescu (*Bukarest*, 1914) has endeavored to find some reactions between the proteins of corn and the blood serum of pellagrous patients. As an antigen he used corn which had been prepared according to the method devised by Osborne. Forty-four cases were examined: of these 4 were in early stages and showed only the skin lesions; 8 had been sick for a year or more and showed gastro-intestinal symptoms; the remainder had suffered for variable periods. The Abderhalden reaction was negative in two cases which had been in the hospital over two years and showed only some dementia; in all the other 42 cases it was positive, especially in untreated cases which were still consuming maize. In 12 maize eaters, normal invididuals, the reaction was negative. Numerous cases were tested against wheat and bean proteins and always came out negative. As a result Nitzescu concludes that in certain cases the insufficiently broken down proteins of maize gain access to the blood whereupon the organism responds by the production of zeinolytic ferments: these are in a certain degree specific and tend to disappear from the blood very slowly, as is shown by the presence of positive reactions in individuals who have been on a maize-free diet for months. The reaction possesses distinct diagnostic value and is to be regarded as evidence of a slow, progressive intoxication due to the resorption of a foreign protein.

Characteristics of the Blood and of the Blood Serum Following the Action of the Roentgen Rays.—S. Wermel (*Münch. med. Wchnschr.*, 1914, lxi, 299) reports an experimental study of the effect of exposing blood and serum to the Roentgen rays. To determine whether the blood or serum absorbed Roentgen rays, he placed specimens of each, which had been exposed to the rays, in Petri dishes. Over each dish he then placed a metal disk in which a figure had been cut out. A piece of pasteboard and a photographic plate wrapped in several thicknesses of black paper were then placed on top of the plate. The whole was left in a dark room for two to forty-eight hours. In each instance there was found a figure on the plate corresponding to that in the metal disk. Washed sheep corpuscles and normal horse serum exposed as the blood had been gave similar results. Control experiments with unexposed blood or serum gave negative results. Thus, it seems blood serum and red corpuscles are capable of absorbing Roentgen energy which is manifested in photo-activity. Next, the author examined the blood of a patient whom he had treated with Roentgen rays and found that such bloods exhibited photo-activity as long as three weeks following exposure. Wermel studied the effect of exposed serum (X-serum) on the skin of rabbits and noted lesions which he considered similar to Roentgen-ray dermatitis. X-serum injected subcutaneously or intravenously in rabbits produced a leukopenia in nine to eleven hours, but the blood returned to normal by the following day. Wermel suggests that X-serum may prove useful therapeutically. He has begun its use in cases of tuberculous granuloma and tuberculous adenitis, but has not had sufficient experience to judge of its value.

The Changes in the Leukocytes Following Injections of Tuberculin.—O. Brösamlen (*Deutsch. Arch. f. klin. Med.*, 1914, cxv, 146) has studied the leukocytic formulæ and total leukocyte counts following tuberculin injections in 18 early cases of pulmonary tuberculosis and in 7 non-tuberculous individuals. The tuberculin was injected at 9 A.M. and blood taken for examination at once, at 12 M. and at 6 P.M. and at the same hours on the next day. Similar examinations of the blood were made one or two days prior to the injection of tuberculin. In the non-tuberculous, he found practically no changes in the white cells following injections of as much as 10 mg. of old tuberculin. In tuberculous patients, on the other hand, there was a characteristic reaction. There was usually a rapid, though not great, increase in the total white count, but more important than this, there was a rise in the number of eosinophile cells, which was most striking when the total number of the eosinophile cells per c.mm. were calculated. (The percentage often showed little change.) The eosinophile reaction appeared to be very delicate, as it was frequently present in the absence of clinical signs or symptoms. It appeared usually within three hours of the injection, though often the height of the increase was not reached until nine hours afterward. Following a positive blood reaction, a second injection, if repeated too soon, may fail to elicit a response on the part of these cells; there may even be a decrease. Brösamlen looks upon the reaction, which has also been described by J. M. Swan, as a manifestation of anaphylaxis.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL

Operation for the Removal of Ascites.—Kumaris (*Zentralbl. f. Chir.*, 1914, xli, 1609) in a previous number (No. 43, 1914) of the *Zentralblatt* (for abstract see Amer. Jour. Med. Sci., 1914, cxlvii, 910) recommended the removal of an extensive portion of the parietal peritoneum in order to favor the widest possible adhesions between the intestines and abdominal wall. One patient upon whom this operation was done died of facial erysipelas twenty-two days after the operation and at autopsy a hardly demonstrable quantity of fluid was found in the abdomen. Hans Lorenz did it in combination with Lanz's scrotum operation. A month later the patient was in good health and the ascites was no longer demonstrable. Kumaris operated on a fifty-five-year-old man with ascites. The parietal peritoneum was removed as high as possible, and from the ascending mesocolon on the right side almost to the colon on the left side. A tongue-shaped piece of peritoneum was brought out of the lower angle of the incision in the peritoneum and a piece of omentum was laid on the summit of the bladder and in the depth of the exposed space of Retzius. A considerable portion of the prevertebral peritoneum was also separated. After forty-eight hours, the edema about the ankles had disappeared, the abdomen was completely painless and there was no edema of the abdominal walls. Fluid escaped between the sutures in the upper part of the wound for a few days. After fourteen days puncture of the abdomen for the relief of fluid was no longer necessary and after six months the patient enjoyed complete health, no fluid was demonstrable and there was no edema. There still remains a slight jaundice from the chief liver complaint.

The Treatment of Presternal Dislocation of the Clavicle.—Danielsen (*Zentralbl. f. Chir.*, 1914, xli, 1561) says that this disolocation is rare, is easily recognized and reduced but that the retention of the bone in its normal position has been impossible. Notwithstanding the persistence of the dislocation, the prognosis for good function is generally good. Sometimes the protruding end of the bone causes so severe pain that excision is called for. In other cases the end of the clavicle fails to develop adhesions and the resulting movements give considerable disturbance. In one case reported by Riedinger, because of this mobility,

the patient could not abduct the arm more than 45 degrees. Danielsen says that in assuming that the shoulders should be forced backward to maintain the reduction, we have been wrong. In a recent case he forced the shoulders forward and maintained them in this position by raising the arm upward so that it lay against the cheek and the forearm was over the head. The arm was bandaged in this position and the dislocation remained reduced. Healing occurred without disturbance and the movements became free and painless.

Treatment of Forward Dislocations of the Clavicle.—Braatz (*Zentralbl. f. Chir.*, 1914, xli, 1673) agrees with Danielsen that the generally advised methods of bandaging the arm are wrong, especially the forcing of the shoulders backward, but he obtained complete success by a different method than that employed by Danielsen. He saw the dislocation in a three-year-old boy on the day of the accident. It was easily reduced under narcosis but as soon as the shoulder was pressed backward the dislocation recurred. He placed the arm in the right angled position across the front of the chest without restraint and pressed the shoulder forward. Then over the joint he placed a pad of cotton which was held in place by a strip of adhesive plaster passing obliquely from the back over the shoulder to the left breast. Other adhesive strips were used to reinforce the first and with a bandage the shoulder was fixed in the forward position. A Roentgen ray taken on the following day showed the bones in their normal position. The adhesive was reinforced after fourteen days and a new bandage applied over the whole arm and hand. A Roentgen ray at this time showed the dislocation still completely reduced. The dressing was finally removed at the end of eight weeks and at the end of five months the bones were still in their normal positions. Four weeks retention of the bandage will be sufficient in an adult.

Clinical and Experimental Studies of Hormonal and Neohormonal.—Dencks (*Deut. Zeitschr. f. Chir.*, 1914, cxxxii, 37) studied the effects of these substances on peristalsis in forty animal experiments and about 140 patients observed at the bedside. The claim of Zuelzer, Dohrn, and Marxer that hormonal is a specific in exciting peristalsis has not been sustained. It is a powerful stimulant of peristalsis in animals and men, as well by intravenous as by intramuscular injections. In favorable cases of chronic constipation, the effect of the preparation has been observed to continue for several years. It frequently fails, however, in animals and men. The dangers associated, which are largely due to lowering of the blood-pressure, have been obviated by an improvement of the preparation, neohormonal. This preparation is indicated in all cases of postoperative disturbance of peristalsis and in all forms of chronic constipation. In mild cases of intestinal paresis and those of moderate severity, the neohormonal may be injected into a muscle. At first 20 c.c. should be injected and if a satisfactory effect is not obtained in four to six hours, a second dose should be given and by preference intravenously. At first 20 c.c. should be injected slowly with the usual syringe, and repeated in four to six hours if a satisfactory result is not obtained. In especially severe cases where a very quick effect is necessary, 30 to 40 c.c. should be injected intravenously and

its effect hastened by enemata, applications of heat, etc. In desperately severe cases, the neohormonal should be combined with physostigmin and atropin in large doses. In chronic constipation, 20 c.c. should be injected intravenously, and during the first two to four days should be energetically supported by other purgatives, as castor oil, senna, etc.; if the desired effect is not obtained, in this time, 20 to 40 c.c. more should be injected and this again aided by purgatives. In especially stubborn cases the dose may be increased to 30 c.c. or more. Some of this dose should be given intravenously because the full dose injected into a muscle would cause distressing pain. In children under ten years of age, about half of the above dosage should be tried. The preparation is well borne even in the first year of life. By the employment of sufficiently large doses, according to Denck, failures with postoperative paresis and chronic constipation will be rare.

Intestinal Stasis.—Case (*Surg., Gynec., and Obst.*, 1914, xix, 592) says that while ileal stasis has been definitely shown to exist in connection with marked obstructing adhesions or kinkings of the terminal ileum, and while it is likely that spasm of the ileocecal sphincteric mechanism may be another factor in the production of ileal stasis, it seems demonstrated that incompetency of the ileocolic valve offers a further and more tangible explanation of ileal stasis and that it is probably the essential causative factor in the majority of cases of stasis in the terminal ileum. Ileocecal valve incompetency is almost always associated with the clinical evidences of intestinal stasis. Not all these patients have, as yet, a well developed alimentary toxemia. His experience in the Roentgen study in these cases of intestinal stasis, both before and after operation, leads him to distinctly oppose the tendency toward operative interference for their relief. Surgery should not be seriously considered as the cure for ileal stasis until a most thoroughgoing trial has been made of the various dietetic and mechanical measures at our command. If an operative measure seems advisable, recognition of ileocolic valve incompetence as a potent cause of ileal stasis may present a course of surgical treatment free not only from the dangers associated with short-circuiting with or without colectomy, but actually calculated to restore normal physiological function.

A Contribution to the Surgery of the Lesser Sac of the Peritoneum.—Ziembicki (*Zentralbl. f. Chir.*, 1914, xli, 1489) gives the following *resumé* of the conditions which have been found in the lesser peritoneal cavity: (1) Hernia through the foramen of Winslow, of which Jeanbrau and v. Riche reported about 20 cases; (2) liver abscess from cholelithiasis through the foramen of Winslow (very rare); (3) blood collections from hemorrhagic pancreatitis or the rupture of an aneurysm of the splenic artery; (4) lymph collections from contusions and wounds, or post-traumatic cysts; (5) blood effusions or inflammation in consequence of pancreatic necrosis with perforation into the lesser peritoneal cavity; (6) pseudo-cysts and pancreatic cysts which develop in the lesser peritoneal cavity. Ziembicki reports 2 cases. In one, operation showed the fluid collection in this cavity to consist of bile. The patient recovered from simple drainage, and this with the fact

that the gall-bladder could not be found at the time of operation led to the conclusion that the collection was due to a much dilated gall-bladder. Tumors developing primarily in the lesser peritoneal cavity are exceedingly rare. Only 6 cases were found in the literature, all of which were sarcomata and found at autopsy. The Lembert anatomico-pathological institute possess a specimen, also a sarcoma. Ziembicki had the opportunity of observing an eighth case, which also came to autopsy and was a sarcoma.

Regeneration of Cartilage and Bone, with a Special Study of These Processes as They Occur at the Chondrocostal Junction. — Haas (*Surg., Gynec., and Obst.*, 1914, xix, 604) says that the periosteum is directly and actively concerned in the regeneration of bone. In the very early stages the periosteum proliferates to form cartilaginous tissue, which is later transferred into bone. The exact changes from cartilage to bone cannot be determined. There is considerable evidence in favor of direct change from cartilage to bone. There is at times the appearance of the osteoblasts forming bone and substituting the cartilage. Therefore it seems as though both processes can take place at the same time. The regeneration of bone also takes place from the marrow and cortical bone, but in a more limited degree and at a later period than that from the periosteum. The regeneration of cartilage takes place almost entirely from the perichondrium. It proceeds by a direct proliferation of all the layers of the perichondrium beneath the outer fibrous tissue. There is some evidence in favor of the view that the connective-tissue is also transformed into cartilage under the stimulation of the neighboring cartilage or perichondrium. There is a slight amount of regeneration of cartilage from the original cartilage near the perichondrium, but the remainder of the cut end tends to undergo degenerative changes. The extent of the removed cartilage exerts no influence on the regeneration. There is no evidence of calcareous changes in the regenerated cartilage, even as late as forty-six days.

The Phenolsulphonephthalein Test from the View-point of the Abdominal Surgeon.—Tracy (*Surg., Gynec., and Obst.*, 1914, xix, 734) employed the test in about 300 cases, the material for this paper being based upon the observations of the first 100 cases. He says that it does not seem possible to work out the minimum percentage phthalein output which will be safe to undertake surgical operations, nor is it safe from the phthalein test to determine what cases should or should not be subjected to operation. He believes it will never be possible to determine this point from the phthalein test, as the functional activity of a kidney varies under numerous circumstances and at different times. In determining whether or not a patient should be subjected to operation, the history, clinical symptoms, and physical examination are of much greater value than any renal functional test ever devised. The phthalein test used in conjunction with the clinical symptoms, history, and physical examination is of value. A small percentage output should put the surgeon on his guard and cause him to study the patient most carefully before undertaking an operation. The phthalein test should be used only as one of the many methods of investigation in ascertaining the condition of the patient.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Intrarectal Administration of Sodium Salicylate in Acute Rheumatic Fever.—Heyn (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1004) has had excellent results with the intrarectal administration of sodium salicylate in the treatment of 125 cases of joint affections. The method of administration is as follows: A cleansing soapsuds enema is given and is followed by the salicylate enema given by means of a Davidson syringe and a rectal tube inserted 6 to 8 inches. The dose varies according to the size and sex of the patient and also according to the severity of the case. The first adult dose in men is usually from 8 to 10 gm., in women 6 gm., women being apparently more susceptible to salicylism than men. The amount of salicylate to be given is incorporated in 120 to 180 c.c. of plain or starch water with the addition of 1 to 1.5 c.c. of opium tincture. The dose of salicylate may be repeated in twelve hours when it can be usually determined whether symptoms of salicylism will appear. Usually however, a daily enema suffices with doses increasing perhaps from 30 to 50 per cent. daily until the limit of tolerance is reached. The largest daily dose which has been given has been 24 gm., and the only symptoms of salicylism which usually have appeared have been tinnitus and excessive perspiration. Where salicylism has been excessive, it usually appears within from three to six hours and the remaining unabsorbed portion of salicylate may be washed out of the bowel by rectal irrigation. This has been resorted to very infrequently indeed and it is rare also that the rectum is intolerant of the drug. Heyn found that sodium salicylate given in this way was very promptly absorbed from the rectal mucous membrane usually within fifteen minutes, always within thirty minutes, a strong ferric chlorid reaction appeared in the urine and the reaction usually persisted for from forty-eight to seventy-two hours after the administration of the drug ceased. To show also that complete absorption was usually possible, the stool subsequent to the salicylate enema was examined by acidifying with hydrochloric acid, extraction with ether and testing with ferric chlorid. As a rule usually within from twenty-four to thirty-six hours, depending on the size of the dose, there was complete absorption as shown by a negative reaction. The author cites a few cases which he consideres illustrative of the value of the intrarectal salicylate therapy.

The Present Status of Artificial Pneumothorax Therapy.—Lyon (*Bost. Med. and Surg. Journ.*, 1914, clxxi, 442) reports 74 cases of pulmonary tuberculosis treated by artificial pneumothorax. Of the 74 cases treated, 4 were in the incipient stage of the disease, 38 were moderately advanced, and 32 were in the far-advanced stage. Of the

4 incipient cases, 1 had bilateral disease and 3 had unilateral involvement. In all four instances there was marked improvement following the treatment. Of the 38 moderately advanced cases, 5 had unilateral disease, and in 33 it was bilateral. In the 5 instances where the disease was confined to one lung 3 were benefited by the treatment; and 2, on account of extensive pleural adhesions, failed to show any signs of improvement. Twelve of the 33 patients, whose disease involved both lungs, showed satisfactory improvement, and 21 failed to respond satisfactorily to the treatment. Of 32 patients in the far-advanced stage of the disease, 4 were suffering from unilateral involvement and 28 had the disease in both lungs. The treatment was unsuccessful in all of the unilateral cases, mainly because of extensive pleural adhesions. Three of the 28 patients with bilateral disease were improved by the treatment and 25 failed to improve. Lyon believes that the question of artificial pneumothorax therapy is more complex than is generally supposed. There are many factors essential for success in which error can result in an individual case. Chief among these factors are the maintenance of strict asepsis, the proper temperature of the gas to be introduced, the rapidity of its introduction and the proper dosage. The proper selection of cases is also of vital importance. The author says that artificial pneumothorax is not an infallible remedy applicable to all cases but improvement frequently follows the intelligent, persistent and discriminate use of this method of treatment. He believes that the statement that "artificial pneumothorax can do no harm even though it should fail to benefit" is fallacious. He is convinced that serious damage may result from its careless or ignorant administration.

The Treatment of Phthisis by Pulmonary Compression.—Floyd (*Boston Med. and Surg. Journ.*, clxxi, 440) says that artificial pneumothorax is without doubt a real step in advance in physical therapeutics in the treatment of many pulmonary conditions, and, as it is based upon sound clinical and pathological observations, it is destined to have a permanent place in the treatment of pulmonary tuberculosis. He believes that the proper selection of patients is of prime importance in the successful use of pulmonary compression. This is especially true of pulmonary tuberculosis. It cannot be too often emphasized that this therapeutic method may accomplish one of two things; first prolonged relief of symptoms, or second, the arrest of pathological process. In the latter case the strictly unilateral pulmonary lesion, free from adhesions, is the only one where this can be anticipated. Cures will be secured in bilateral cases, but here the outlook is always one of doubt in the beginning. For the relief of symptoms the range of cases that can be so treated is limited only by the condition of the pleural cavity. The incipient case, which in the judgement of most men should be excluded from the group of cases suitable for artificial pneumothorax, has, nevertheless, frequently shown a rapid recovery. Pleurisy with effusion complicating a moderately active unilateral lesion offers a good field for treatment. Active, rapidly advancing phthisis complicated by secondary infection, is frequently unsuited for this method of treatment. The same is true of long-standing fibroid phthisis accompanied by a weak heart. No case of pulmonary

tuberculosis should be selected for treatment with artificial pneumothorax entirely upon evidence secured from the chest. A high-strung, nervous temperament diminishes the chance of successful treatment. Floyd says that the field of application of artificial pneumothorax has slowly narrowed down. A relatively small number of cases are really suitable for this method of treatment and it is a measure best adapted for patients having institutional care. It is also a procedure which not only demands some skill in its application but most of all, an intimate knowledge of phthisis and the pathological changes which may exist in the pleural cavity.

Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis.—Chadwick (*Boston Med. and Surg. Journ.*, 1914, clxxi, 443) says that the results obtained by this treatment depend upon whether the diseased area of the lung can be partially or wholly collapsed. When there are tough adhesions, a marked thickening of the pleura, or a fibroid lung, effective pneumothorax cannot be produced, and as the respiratory conditions will be very little changed a marked result cannot be expected. Whether suitable conditions exist, only a trial will determine, as some old-standing cases are enexpectedly benefited. A patient in any stage of the disease, of a unilateral case, should have the benefit of an induced artificial pneumothorax if they do not show marked improvement under good sanatorium conditions in a reasonable period of time. Careful selection should be made from the bilateral cases who are not improving, if in one lung the disease is apparently inactive. Chadwick has had no experience in treating first-stage cases with artificial pneumothorax, as Murphy has recommended. Cases of this class usually respond well to sanatorium treatment. If, however, a patient proved to be a progressive case Chadwich would advocate induced pneumothorax without delay. In his opinion artificial pneumothorax is a therapeutic measure of much value in carefully selected cases, but it should be given only to such patients as can be kept under close observation and under sanatorium conditions.

Intramuscular Injections of Blood in the Treatment of Leukemia.—Kiralyfi (*Wien. klin. Woch.*, 1914, xxvii, 1141) says that an acute exacerbation in leukemia is frequently seen during a course of benzol or Roentgen therapy. This exacerbation may occur even when benefit is apparently being derived from the treatment although it is more apt to be a result of overdosage. Kiralyfi recommends the intramuscular injection of defrinated blood in order to combat this. He cites a case in detail where this treatment seemed to have a marked stimulating effect on the bone marrow. This was a patient with myeloid leukemia whose leukocytes after six days of benzol treatment dropped from 31,000 to 13,000. The benzol was discontinued but the white cells continued to drop until they reached 2150 with a drop in the reds to 1,000,000 during the same time. The patient received several intramuscular injections of blood and the blood picture improved so that the red cells now number 2,000,000 and the white cells average from 9000 to 10,000. The swollen glands subsided and there was a corresponding improvement in the patient's general condition.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M D.,
OF PHILADELPHIA.

The Vaccine Treatment of Scarlet Fever. — DONALD MACINTYRE (*British Jour. Child. Dis.*, 1914, xi, 472) mentions the work done by various investigators in immunization against scarlet fever by vaccines. In Russia, Gabritschewsky reports encouraging results by injecting children with prophylactic doses of streptococcic vaccine. An usual moderate reaction was noted and very occasionally a rash and sore throat developed. They record one death in 50,000 cases and the method is said to have proved strikingly effective in controlling the prevalence of scarlet fever. Watters, in America, reported one out of 21 immunized nurses contracting the disease on exposure, whereas 5 out of 14 unprotected nurses were attacked. In England the results of using vaccine in the prevention and treatment of septic complications of the disease have not been encouraging. At Platstow Hospital 100 cases admitted as scarlet fever in children under ten years were treated with a stock vaccine to prevent the onset of septic complications. They were compared with 100 untreated cases and the commercial vaccine had no appreciable effect on the cases treated. Five cases of septic scarlet fever were treated with autogenous vaccines, and while all recovered it could not be said that the vaccine had any definite effect. The success of vaccine treatment of nasal and ear discharge was difficult to prove, but the author concludes from his experience that in regard to nasal discharges cure is obtained more quickly with vaccine treatment. This statement cannot be made, however, in the case of ear discharges.

Status Lymphaticus. — HUGH THURSFIELD (*British Jour. Child. Dis.*, 1914, xi, 465) states that it is exceptional to find a thymus of more than 10 gm. except in the condition known as status lymphaticus. So-called thymic dyspnea is extremely rare and an abscess connected with the deep lymphatic glands or enlargement of these glands themselves is most frequently the cause of the dyspnea and not the pressure of the thymus. Pressure plays no part in the sudden deaths in infants, or in cases under an anesthetic, which are usually attributed to status lymphaticus. The morbid anatomy in infants dying suddenly from no appreciable cause is constant—an enlarged thymus gland, 25 gm. to 30 gm. in weight, hypertrophy of Peyer's patches and enlargement of the mesenteric, bronchial, and cervical glands. But there is no post-mortem proof of pressure on the trachea or the great vessels nor is the theory of pressure on the vagi inhibiting the heart's action borne out by the character of death in these cases. Most of these "anesthetic" deaths, however, are due to status lymphaticus. Other conditions in which an enlarged thymus gland is commonly found are myasthenia gravis and, especially, Graves' disease. Concerning the origin of the

condition Basch and Klose have shown that puppies relieved of the thymus gland grew slowly, their muscles were flabby, their bones soft, their intelligence less, and they died after the fourth month. The bones showed characteristic evidence of rickets and the tissues were deficient in lime salts. They believed the thymus hinders the formation of and neutralizes excess of acids in the system. Status lymphaticus is not merely a disorder of the thymus but a complicated disorder of the whole "ductless gland" system. The diagnosis of the condition is highly important, its chief features being a determination of an enlarged thymus by percussion over the manubrium or by the Roentgen ray, and in addition the history of attacks of dyspnea and a persistently low vitality. These conditions should contra-indicate exposure to an anesthetic. Leonard Williams suggests the exhibition of extract of thyroid gland in the treatment of this condition especially if an anesthetic is imperative and the author suggests the use of pituitrin, since "shock" in a broad sense contributes the fatal results of the lymphatic state.

The Treatment of Infantile Paralysis. — William MacKenzie (*British Med. Jour.*, 1915, No. 2819, 60) gives the results of his work on infantile paralysis during the last eight years. The whole principle of treatment lies around the question of the action of muscles. The basis of scientific treatment is the simple biological point that so-called irreparable damage of the corneal cell must be judged by loss of all the functions of the muscle and not by loss of only one, such as maximum power of a muscle to lift a limb. The conclusion was drawn that the muscle itself could not be considered a primary pathological factor, but that biologically it was all-important for the purposes of treatment. Under the immediate treatment, immediate rest of the muscle is imperative, because muscle adjustments are destroyed and overaction of the opponent muscle occurs. This must be prevented because, otherwise, it does not afford complete rest to the anterior-horn cell and remains a source of irritation; it interferes with its recovery by overstretching the affected muscle, and deformity is produced which interferes with future utility. A muscle is rested only when it is placed in a position where its work is zero and its origin and insertion are nearly on the same horizontal plane. In reëducating a muscle MacKenzie begins each day at zero and works up to and beyond the highest point achieved the day before. Relaxation of the muscles is accomplished by flexing the limb at the joints and applying splints to immobilize it. MacKenzie believes that if these cases were only regarded most seriously at the outset and not left till something developed, the subsequent treatment would be made easier and the splints might act prophylactic ly and actually abort an oncoming paralysis.

The Cause and Significance of Nose-bleed in Childhood.—Heinrich Petry (*Berlin. klin. Woch.*, 1914, li, 1890) reviews the theories and explanations of nose-bleed, especially those of Kresselbach who described histologically an area on the anterior part of the nasal septum which contained an especially large number of capillaries and veins. Several authorities corroborated these findings. Zuckerkandl attributes most

bleedings from the nose to traumatic causes, especially from scratching the nostrils with the finger-nail. A catarrhal inflammation of the anterior part of the septum is undoubtedly an exciting cause, with the formation of small ulcers and scabs which bleed freely on being picked at. These hemorrhages are easily controlled by pressure, small tampons and astringents. Besides chronic nasal catarrh a chronic nasal diphtheria is also a cause of nose-bleed. In infants the two commonest causes of nose-bleed are chronic nasal diphtheria and syphilis and only rarely a chronic dry rhinitis. The nose-bleeds occurring in acute fevers, such as measles and pneumonia rarely assume much significance, although considerable bleeding may occur and the blood swallowed with no external evidence until vomiting of the blood reveals the condition. Septic conditions affecting the mucous membrane of the nose may cause a severe and even fatal hemorrhage. The author cites several cases of pneumonia in anemic children, in whom a hemorrhagic dyscrasia arose with fatal bleeding from the nose. From these considerations it becomes important to inspect carefully the local nasal condition in all cases of nose-bleed. A chronic nasal diphtheria is occasionally found in this way. The diagnosis of septic nose-bleed is unwarranted in septic conditions and infectious fevers without a careful examination of the nostrils. The bleeding from a small ulcer of the septum may gravely complicate the course of a disease and simulate septic infection.

Nervous Disturbance in Children.—Otto Katz (*Berlin. klin. Woch.*, 1914, li, 1835) describes a number of cases of rarely seen, nervous disturbance in children during the past month. The main symptom was a state of anxiety or dread often seen in adults. The cases were all little girls from six to ten years old. In all the cases the condition arose suddenly during good health and showed in pallor, listlessness, anorexia and a tired, melancholic expression of face. From time to time the children stop in their play or occupation and stare fixedly before them into space or walk restlessly to and fro; after from five minutes to half an hour they again assume their former occupation. Two of these cases complained of dizziness. No organic lesions were found in any of the children. From the evidence of the parents and that gleaned from the children themselves the condition developed from hearing gruesome tales about the present European war which acted as the psychic trauma in their condition. Four of the children are offspring of nervous parents. The children described their sensations as being a sudden sense of dread lasting a variable time and recurring. Several mentioned gruesome war tales as starting their sense of dread. Later they could give no reason for their attacks, they simply were afraid. The prognosis is apparently good, excepting in one child whose mother suffered from hallucinations. The treatment is phychic and the condition due to the aforementioned psychical trauma. These cases emphasize the point that children, especially of a nervous type, should be protected from conversation and tales dealing with the gruesome and horrible. The author has lately observed an increase of nocturnal enuresis and polyuria in children of both sexes suffering from milder types of this same nervous condition.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Facial Paralysis after Spontaneous Labor.—Carlsson (*Zentralblatt f. Gynäkologie*, 1912, No. 45) finds that facial paralysis may arise during intra-uterine life and develop during labor, after spontaneous labor, after forceps application, and after other methods of vaginal delivery. His own case was that of a primipara, aged thirty-four years, well developed, previously healthy, who had a somewhat tedious labor. The membranes appeared in the vulva and soon afterward ruptured. The head was then upon the pelvic floor. The child was expelled spontaneously in the first position, vertex presentation, the face being directed toward the right side of the mother. The child was a female, slightly asphyxiated, easily revived, and cried loudly, and on examination a right-sided facial paralysis was present. The child weighed 2710 grams, length 47 cm., and the dimensions of the cranium were not above the average. The placenta was expelled ten minutes after the birth of the child. The examination of the child showed no evidence of adhesions to the amnion. On examining the fetal head carefully, the left posterior parietal bone was pushed beneath the right, at a point 2.5 cm. from the sagittal suture, and 3 cm. from the lambdoid suture there was a pressure-mark 2 cm. long and 0.5 cm. wide in the skin, whose greatest diameter was parallel with the sagittal suture; and at the anterior portion of the skin there was a dark bluish area of small size. There was no impression in the cranial bone, and the caput was upon the right parietal bone and had not extended over the border of the adjacent bone. The forehead was smooth upon both sides, and when the child cried the left side of the face only assumed the usual position. The right eye remained open, the conjunctivæ in both eyes showing small punctiform hemorrhage. On the right side the nasolabial groove could scarcely be discerned. On the left side it was plainly present. The angle of the mouth was drawn toward the left. The uvula was in the middle line, and there was no divergence of the tongue. The child nursed without difficulty. The child gradually improved, so that when it was discharged from the hospital the paralysis was only evident when the child cried. The mother's pelvic measurements were somewhat below the average, the external conjugate being 18.5 cm. The second patient was that of a multipara delivered in spontaneous labor with normal position, presentation, and mechanism. There was no caput succedaneum. The child was a male, weighing 3720 grams. Facial paralysis developed on the left side, but persisted for two days only.

The writer has collected 36 cases in the literture of the subject, in all of whom the conjugata vera was below the normal. He concludes that this paralysis is always peripheral and not central. It is caused by pressure at the stylomastoid foramen upon the nerve trunk during

labor. In the majority of cases this pressure is made by the symphysis pubis, in the lesser number by the promontory of the sacrum. These cases are rarely observed except in moderately contracted pelvis, and the average duration of the lesion is eight days.

Aortitis in a Child Having Congenital Syphilis.—Rebaudi reports from Döderlein's clinic in Munich (*Monatsschrift f. Geburtshülfe und Gynäkologie,* 1912, Band xxxv, Heft 6) 17 cases in which spirochetes were found in the fetal liver, lungs, suprarenals, and other organs. Five of these were prematurely born at seven months, many of them macerated, and seven were prematurely born at five months. One died soon after birth, one was dead born, eight macerated, and three were in the ninth month. Two were dead born and macerated, and one perished three hours after labor; two were fully developed; one at full term was dead born, and another perished five days after labor. Portions were taken from the arch and the ascending and descending aorta, and examined microscopically to determine the existence of spirochetes. Sections were also made and colored by various methods. In addition to the 17 cases, 9 others were obtained from colleagues for purposes of study. In the 13 patients the characteristic lesions of syphilis were found in the portions of the aorta examined, and this was thought to be the cause of fetal death. In 5 of the 13 cases spirochæta were positively present, and in the series of 9 cases also available for examination spirochæta were found in the wall of the aorta in 3. Where the germs were present it was detected in the connective tissue of the adventitia of the aorta and also in the vicinity of the vasa vasorum in the thickened wall between the muscle bundles and elastic fibres. In one case of premature macerated fetus the liver, spleen, kidneys, suprarenals, Fallopian tubes, and uterus, showed abundant spirochæta. The intima of the vessels was enlarged, the hyperplastic and the lumen of the vessels considerably diminished at the point of lesion. Spirochæta were also found in the blood cells in the lumen of the aorta, of the arch, and in the vasa vasorum, either free or surrounded by leukocytes.

Influence of Pituitrin upon the Child. — Spaeth (*Zentralblatt f. Gynäkologie,* 1913, No. 5) cites the case of a primipara with normal pelvis admitted to hospital, the child in breech presentation and in second position. When dilatation was complete the membranes protruded and ruptured during examination, with the discharge of meconium. The child was still high above the pelvic brim. As labor pains were deficient, $\frac{5}{10}$ gram of pituitrin was given subcutaneously, producing vigorous pains which ceased after an hour. A second injection was given, followed by better pains, which brought the breech of the child quickly into the pelvic brim. The mother was then partly anesthetized with ether, the perineum incised in the median line, and the child readily extracted, the cord once about the neck, but apparently not constricted. The child was asphyxiated, the heart beat very slow, and respiratory movements were irregular and infrequent. The child died half an hour after birth. At autopsy there was no injury to the cranium or spinal column, no extravasation of blood in the brain or cord, and no laceration of the tentorium. The thymus was not enlarged, the heart, lungs and kidneys were normal, and the child had not inspired mucus or fluid in the trachea or bronchial

tubes. Labor had proceeded normally, and the median incision of the perineum had permitted prompt birth without pressure, so that it was difficult to find in the labor itself the cause for fetal death. No violence was used in aiding the birth of the child, and uterine contractions excited by pituitrin was the principal factor in bringing about a successful termination of labor. The autopsy gave an entirely negative result. The child's heart sounds were plainly heard half an hour before labor. Although the labor pains produced by pituitrin were strong, they were rhythmical, with the usual pause between the pains, and with no element of tetanus in the muscular contractions of the uterus. In seeking to explain the death of the child, it must be remembered that the different preparations of pituitrin on the market vary greatly in the intensity of their action. Others have noted that the fetal heart became slow after the use of pituitrin. This is thought to be the result of compression of the placenta, and the accumulation of carbon dioxide in the fetal blood. The cardiovascular action of pituitrin is recognized as being similar to digitalis, but is much more rapid, and causes strong contractions of the cardiac ventricle. The drug also exerts an influence upon the cardiac nerves and produces contraction of the coronary arteries.

The Pulmotor in Infantile Asphyxia.—Edgar (*American Journal of Obstetrics*, February, 1913) describes, with an illustration, the Draegen pulmotor, originally for adults, which he has adapted for the treatment of infants. The action of the apparatus is to inflate and deflate the lungs in a regular manner, and by the aid of a certain mechanism controlled by the hand, a given number of respirations per minute can be obtained, The complete apparatus is enclosed in a wooden box, of convenient size, and consists of a small high-pressure cylinder with a capacity of one liter, which contains oxygen or nitrogen and oxygen, under 150 pounds pressure. One cylinder is sufficient to supply the apparatus for one hour, and another can be installed without difficulty. By an automatic reducing valve the high pressure is brought to a constant pressure of about 5 pounds. There is also a gauge which indicates the contents of the cylinder and gives warning when the supply of oxygen or combination is running short. By means of the reduced oxygen pressure there are two nozzles with connecting pipe lines in action—one for suction and one for pressure. The purpose of the apparatus is to force oxygen or atmospheric air into the lungs at any given pressure desired, and then to empty the lungs of the exhausted air which is expelled outside. In the apparatus for use with infants, and filling and emptying of the lungs, or the respiratory rhythm, is under the control of the operator, and by watching the efforts which the child makes at inspiration he can time the action of the apparatus to the greatest advantage. A breathing mask fitting tightly over the mouth and nose, and retained in position by an elastic band, is employed. The control of movements of respiration is secured by moving a lever upon a dial, and beyond the dial are two flexible metal tubes—one for fresh air and one for contaminated air. The claim is made for the apparatus that pure and impure air cannot be mixed. In the newborn it is especially important that inspiration pressure should be obtained, and that suction should be under the control of the operator. This is accomplished by the pulmotor.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Ovarian Transplantation.—This is a subject which has been discussed from time to time in this department, most of the work upon it having been done by French surgeons, of whom Tuffier is perhaps the best known. A rather remarkable case—remarkable chiefly for what was attempted and the manner in which this was undertaken, rather than for any actual accomplishment—has been recently reported from Boston by Storer (*Boston Med. and Surg. Jour.*, 1915, clxxii, 41). The patient was a woman, aged twenty-four years, from whom both tubes and the left ovary had been removed a few years previously, on account of gonorrheal salpingitis. She now wished to marry, this, however, being dependent upon the possibility of conception. Purely for the accomplishment of this end, therefore, the abdomen was opened; the remaining right ovary was found buried in adhesions and riddled with cysts; the tubal stumps were each about a half inch long. The right tubal stump was split open, this incision being continued well into the uterine cornu, so that the cavity was exposed. The ovary was then bisected from above downward, this incision being carried well into the broad ligament, so that each half of the ovary retained at least some of its original blood supply. The cut surface of the distal half was then closed with catgut, leaving that piece to functionate in case the other died. The other segment was then introduced into the cut in the uterine wall, and lightly anchored in place with a fine cat-gut suture in such a way that most of its cortex projected into the uterine cavity. The uterine wall was then brought together over its pedicle, in which there was a fairly good sized artery, with deep and superficial layers of catgut. Six days later a pelvic abscess was drained from below. A month after operation the patient menstruated, as she said, in greater comfort than at any time for three years. Eight months later the patient complained of increasing pain at menstruation, and a mass was palpable to the right of the uterus. The abdomen was therefore opened again, and a "shell representing the degenerated remains of the piece of ovary left *in situ*, together with a peritoneal cyst the size of a child's fist" were removed. Nothing could be seen of the pedicle of the transplanted piece of ovary, though this may have been present somewhere in the many adhesions that filled the pelvis. There was no menstruation for four months after this, when signs of pregnancy began to develop, and three and one-half months later (sixteen months after the transplantation) the patient passed a mass of detritus with some hemorrhage, following which the uterus rapidly decreased in size. The author has no doubt that this was in fact a miscarriage. Following this, the patient had a fourth laparotomy, by another surgeon, for the removal of more peritoneal cysts from the left side of the uterus. Menstruation

then stopped entirely, and in a few months the patient had become a nervous wreck, although in good physical health. This condition continued for two years, when she had a hysterectomy performed in another city, in the hopes of getting some relief, but died from peritonitis. The interesting feature of this case, aside from the rather extraordinary operative procedures employed, is the apparent demonstration of the possibility of pregnancy following the direct discharge of an ovum into the uterine cavity, without the intervention of the tube—providing, of course, we accept the clinical evidence of conception and miscarriage, which seems fairly conclusive. That any real benefit to patients can ever be expected from such procedures seems, however, extremely doubtful.

Spontaneous Amputation of a Myomatous Uterus.—A most remarkable, and probably unique, case of spontaneous amputation of a myomatous uterus due to sudden torsion is reported by Ruppert (*Wiener klin. Woch.*, 1914, xxvii, 270). The patient was a women, aged seventy-two years, brought to the clinic with the diagnosis of intestinal obstruction, as she had had severe abdominal cramps for a week, and no bowel movement for three days. She stated that she had noticed a growing mass in her abdomen for about nine months; she had passed through the menopause twenty-two years previously.

At operation a spherical, bluish-black tumor, larger than a child's head, was found springing from the posterior surface of the uterus; there was no pedicle. In the peritoneal cavity was about a liter of partly coagulated blood. On closer examination it was found that all connection between the corpus uteri and tumor, on the one hand, and the cervix, on the other, had been lost, with the exception of a thin strip of peritoneum, in which there was absolutely no fibrous or muscular tissue. The left round ligament was likewise torn completely in two; at the point of separation of the uterus and cervix the tissue was somewhat ragged, and showed the presence of a few coagula, and a small amount of fresh hemorrhage. The uterus had twisted one and one-half times around its long axis, thus wrapping the round ligaments around the cervix, and tearing one of them in half, as has been said. The uterus was removed after ligating the ligaments, and the small cervical stump covered with peritoneum in the usual way. On examination the tumor was found to be extensively calcified; the uterus and adnexa were intensely congested, and showed extensive hemorrhages throughout. The torsion had evidently not been a very gradual one, but must have occurred fairly rapidly; the cutting through of the cervix was evidently due to the round ligaments which had been wrapped around it. There were no adhesions, and the tumor was of moderate size, with relaxed abdominal walls; there was nothing therefore to hinder the free excursion of the tumor, especially as the senile cervical tissue undoubtedly offered a minimum of resistance to the torsion, all of which conditions the author considers to have been important factors in the occurrence of this truly remarkable case.

Treatment of Anteposed Uteri.—Hutchins (*Boston Med. and Surg. Jour.*, 1915, clxxii, 18) thinks that many cases of backache and pelvic drag are due to uteri which on first examination appear to be in a

normal position, because the fundus is well forward and not retroverted. More careful investigation will show, however, that many of these are in reality what he terms "anteposed uteri in descensus," *i. e.*, the cervix, instead of being held snugly up to the symphysis, with the bladder and anterior wall well supported, is found to have dropped back toward the hollow of the sacrum, the uterus still maintaining its anteposed position. In many of these cases the author has been able to relieve all symptoms by properly placed vaginal tampons, so introduced as to force the uterus as a whole well upward, and thus relieve the drag on the cervix. In all cases when this result is obtained, Hutchins considers it justifiable to open the abdomen and suspend the uterus, even though it appears well forward. When the abdomen of a woman with normal uterine supports is opened, the following conditions will be found, no matter whether the fundus is anteposed or retroposed: (1) There is no fulness or dilatation of the ovarian and anastomosing veins as they run through the infundibulo-pelvic and broad ligaments; (2) there is no drag on the peritoneum covering the lateral walls of the pelvis; (3) there is no tension on either the round or uterosacral ligaments; (4) there is no descent of the bladder or engorgement of the vesical veins. In a patient whose cervical supports have given way, however, Hutchins finds the following variations from the normal: (1) The ovarian and anastomosing vains are full and congested, forming the so-called varicocele of greater or lesser intensity; this congestion ends abruptly above the posterior pelvic brim, from which point upward the veins are normal in size; (2) the infundibulo-pelvic ligaments and parietal peritoneum are put decidedly on the stretch; (3) the round and uterosacral ligaments share in this drag; (4) the bladder has gone down with the descent of the cervix, and the vesical veins have shared in the general pelvic engorgement. If now the anteposed but descended uterus is grasped with forceps and brought vigorously up, the ovarian veins and their branches are seen to empty themselves immediately and become normal in appearance, and the drag on the sensitive parietal peritoneum is completely relaxed. The condition can be permanently cured, the author thinks, by suspending the uterus, provided the conditions named above are found at operation.

Influence of Menstruation on Blood Sugar.—Numerous attempts have been made from time to time to demonstrate some tangible changes in one or other of the bodily processes during menstruation in normal individuals, but for the most part the results obtained have been entirely negative, or have been so irregular and contradictory that no conclusions could be drawn. The majority of these investigations have had to do with such easily measured conditions as temperature, blood-pressure, pulse rate, blood count, etc., comparatively little attention having been paid to the subtler metabolic processes. One of these latter, the carbohydrate metabolism, as indicated by the amount of sugar in the blood, has been the subject of recent investigation by Kahler (*Wiener klin. Woch.*, 1914, xxvii, 417), who says he was led into this study by some remarkable variations he noticed in the blood sugar in a number of women upon whom he was making estimations in connection with an extensive work on carbohydrate metabolism in various diseases. The only explanation he could think

of for these variations was that menstruation might have had some influence, and therefore undertook an independent series of investigations upon the blood of a number of patients suffering from various conditions, taking specimens between, just before, during, and just after the periods. The estimations were all made by the micro-method of Bang, which has apparently established itself as sufficiently accurate for all practical purposes. In most of the cases a distinct rise in the amount of blood sugar was found just before or during menstruation, with a return to normal at its close. Just what this hyperglycemia is due to, or whether, indeed, it is a true hyperglycemia and not merely an apparent increase of sugar due to the presence of other reducing substances in the blood, Kahler has not as yet determined.

Intra-uterine Sterilization with Iodine in Supravaginal Hysterectomy.—Stone (*Amer. Jour. Obst.*, 1915, lxxi, 74) is much impressed with the danger of infection from the cervical canal in supravaginal hysterectomy, and gives the following technique, by which he attempts to render this region sterile at the beginning of operation. The patient is placed in the lithotomy posture and a quarter strength solution of tincture of iodin is applied over the external genitalia and introitus vaginæ. After catheterization the perineum is retracted by means of a speculum and the cervix grasped with a tenaculum. It is then dilated sufficiently to admit the nozzle of a two-ounce glass syringe, by means of which about an ounce of the iodin solution is injected slowly into the uterine cavity, no great amount of force being used. After removing the syringe the cervix is again gently dilated, to make sure that all excess of fluid has escaped. Every part of the vagina is then exposed, and swabbed with the solution. After the hysterectomy has been performed a final application of iodin is made to the stump from the abdomen, before closing over with peritoneum, if there is any suspicion that infectious material has been handled.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

J. SOLIS-COHEN, M.D.,

OF PHILADELPHIA.

A Peculiar Form of Hyperplasia of the Mucous Membrane of the Upper Respiratory Tract.—Under this head, Turner (*Jour. Laryn., Rhinol.*, and *Otol.*, February, 1914) describes 2 cases of his own and 4 from other observers undescribed in any text-book to which he had access. Of these 6 cases, 4 were women and 2 men, and while the age in 1 was not stated, the remaining 5 were aged thirty, thirty-four, forty, forty-four, and fifty-two years, respectively. All of them had apparently enjoyed good health, and with the exception of the throat affection

there was no evidence of disease elsewhere. The outstanding clinical feature was a smooth, uniform, more or less diffuse infiltration of the uvula and soft palate, along with the palatal pillars, the posterior wall of the pharynx, and the structures forming the upper aperture of the larynx. An entire absence of ulceration characterized all the cases and, probably owing to this, pain was not a symptom that was complained of. In a case reported by Brown Kelly the larynx only was unaffected, and a further difference was observed in the fact that the infiltration involved the rhinopharynx. These cases continued for years with little or no change. In the reporter's first patient, seen from time to time during a period of ten years, tracheotomy became necessary twice with an interval of seven years. Distinct evidence of improvement was eventually secured, apparently due to autogenous vaccine treatment from a growth of Streptococcus pyogenes obtained from the patient's throat.

An Anaërobic Organism Associated with Acute Rhinitis.—Tunnicliff (*Jour. Amer. Med. Assoc.*, June 28, 1913) claims to have discovered an anaërobic organism constantly present in the early stage of acute coryza while the discharge is mucoid in character.

Hay Fever.—Morrey (*Jour. Amer. Med. Assoc.*, November 15, 1913) reports a series of 8 cases of hay fever treated successfully by vaccination with mixed cultures from the nose. The theory on which the work was based was the strengthening of the nasal mucosa, so that the irritants, whatever they were, would be without effect.

Mucous Polyp of the Nasal Fossa in an Infant Aged Three Weeks.—Laurens (*Rev. hebd. de laryn., d'otol. et de rhinol.*, February 7, 1914), reports a case of a child, three weeks old, with a mucous polyp attached to the ethmoidal zone, occluding one of the orifices of the nares, and producing grave respiratory trouble; suffocation, dyspnea, cyanosis, and impossibility of alimentation. After hesitation, due to the young age of the subject, operation was decided upon. This consisted of sublabial rhinotomy, enlargement of the pyriform orifices, and resection of the superior hypophysis of the maxilla, after which the tumor was extirpated without hemorrhage and without complications.

A New Modification of an Old Adenotome.—Heath (*Laryngoscope*, February, 1914) describes and pictures his modification to prevent the adenoid mass from escaping, as it often rolls from under the cutting blade of the ordinary adenoid curettes or adenotomes. To overcome this he has added to the La Force adenotome, double tenaculum forceps, each blade of the tenaculum shaped to follow the line of the vault and posterior wall of the rhinopharynx. This tenaculum being situated within the box of the La Force adenotome. This tenaculum forceps when closed grasps the adenoid mass laterally from either side along its entire length, pulling it down and pressing it to the centre of the rhinopharynx, and then the knife is pushed through the adenoid as it is thus firmly held. The adenoid is taken out very completely in this way and with very little difficulty.

Endonasal Radical Treatment of Chronic Suppurative Dacryocystitis.—Taptas (*Annales des mal. de l'oreille, du laryn., du nez et du phar.*, 1re Livraison, 1914), discusses this subject, reports 2 cases upon which he practised the procedure satisfactorily, and described his operative procedures in detail.

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

JOHN F. ANDERSON, M.D.,

DIRECTOR OF THE HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Tetanus and Vaccine Virus.—A recent report from the Hygienic Laboratory, United States Public Health Service, by Surgeon Edward Francis (*Laboratory Studies on Tetanus*, Hygienic Laboratory Bulletin 95, 1914, p. 78), gives valuable data in regard to the biology of the tetanus organism under various conditions. The studies are divided into three sections, the first being the conditions surrounding tetanus spores artificially planted in vaccine virus. The report states that since 1902 there have been examined in the Hygienic Laboratory, in connection with the law regulating the manufacture and sale of vaccine virus, an amount of vaccine representing over 1,500,000 vaccinations. In spite of the fact that this large amount of vaccine virus from all the different manufacturers in the United States has been specifically examined for the presence of tetanus spores, the presence of those organisms has not been demonstrated in a single instance. This is of especial importance in connection with the cases of tetanus that occasionally follow vaccination and which, by some, are attributed to the presence of tetanus spores in the vaccine virus. These extensive studies of Francis, together with his failure to produce tetanus in susceptible animals by vaccination with virus artificially contaminated with tetanus spores, strongly support the belief that the cases of tetanus that occasionally follow vaccination are not due to infection of the vaccine virus, but are due to subsequent infection of the vaccination wound from some outside source. It was found that in guinea-pigs, the germination of tetanus spores in the subcutaneous tissue is favored by staphylococci and in some instances by injections of quinine. The method proposed by Francis for the testing of vaccine virus for the presence of tetanus consists in planting the virus in fermentation tubes of glucose bouillon which have been subsequently heated to 80° for one hour, by planting in fermentation tubes of ordinary bouillon, and by inoculating the virus into guinea-pigs. It was found that the presence of certain

organisms in the virus would, at times, inhibit the growth of the tetanus organism and it was therefore necessary to use the different methods enumerated to cover the different conditions. In one series of experiments it was found that if tetanus spores were injected into one part of the body of a guinea-pig, and quinine and staphylococci were injected into another portion, the animals would usually contract tetanus, and cultures made from the site of the injection of quinine or staphylococci showed the presence of tetanus spores therein. This probably indicates that tetanus spores have been transported from the original site of injection and have become implanted in the tissues in and around the site of the quinine or coccus injection.

A Study of Streptococci Isolated from Certain Presumably Milk-borne Epidemics of Tonsillitis Occurring in Massachusetts in 1913 and 1914.—Theobald Smith and J. Howard Brown (*Jour. Med. Research*, 1915, xxxi, 455-501) have made a careful study of streptococci isolated from milk and from the throats and secondary lesions of a large number of cases in several tonsillitis epidemics, the material being furnished largely by the Massachusetts State Board of Health. A comparative study is made of this material with strains of streptococci from previous well known epidemics—Boston, 1911; Chicago, 1912; Baltimore, 1912). Cultural and morphological characters, fermentation reactions, pathogenicity for rabbits, and agglutination affinities are considered. Equally valuable is a critical discussion of the work of other authors related to the subject of milk-borne epidemics of tonsillitis. From this review and the results of their own work the authors arrive at a number of interesting conclusions of which we quote the following: "The streptococci causing epidemics of tonsillitis are not necessarily the same in different epidemics either in the same or different localities. Spontaneous changes in cultural characters do not proceed rapidly enough if they go on at all, to interfere with current bacteriological methods. There is at present no satisfactory evidence that bovine streptococci associated with mastitis or garget are the agents of tonsillitis in man. Whenever cases of garget are suspected as sources of infection in man, both human and bovine types should be looked for. Mastitis and milk-borne epidemics (of tonsillitis) may, however, be made to coincide in time if the udder be manipulated and the udder ducts infected by a human being suffering with tonsillitis. Under such conditions two types of streptococci may appear in the milk simultaneously, the bovine and the human type. These, being so much alike as regards hemolytic properties, might be regarded as identical by the one studying the milk. Our studies have led us to regard the infection as human and to place the infection, in case of large prolonged outbreaks, back into the udder itself whence the introduced streptococci may be shed in large numbers after multiplying in the udder ducts."

The Plague Eradication Among Ground Squirrels.—In August, 1908, the discovery was made by Officers of the U. S. Public Health Service that plague existed among ground squirrels, which so plentifully infested the land comprised in the rural districts of California. From that time until the latter part of 1914, a total of 1957 plague infected

squirrels have been found scattered over an area of approximately thirteen thousand square miles. Plague infection has been found among ground squirrels over a total of something like 140,000 acres. Since July 1, 1913, practically 3,000,000 acres of land have been subjected to active antirodent measures, and it has been found by a census of the rodent in this area that they have been diminished by about 90 to 95 per cent. On the actually infected and immediately adjoining land a much higher percentage of squirrel destruction has been had, so that they have been reduced to the extent that hunters must cover over twenty-five acres of land in order to obtain one squirrel. As the hunters are able to shoot about 15 per cent. of the squirrels seen, the average squirrel infestation is now about one squirrel to four acres, whereas, prior to the beginning of the antirodent measures the average infestation on the infected land was probably ten or fifteen squirrels per acre, in some cases running as high as fifty to sixty to the acre. Long (*Reprint No. 235 from the Public Health Reports*, November 20, 1914, xxix, No. 47) states in a paper in the Public Health Reports that all discoverable plague has been eradicated from the State of California, and that danger of its further spread has been removed. An important point brought out in Long's paper is that, as a result of the destruction of ground squirrels in the State of California, economic benefits have accrued to land owners far beyond the expectations of any of those interested in the work. Out of 250 replies sent to land owners in the area worked over, it has been noted that the farmers have received in increased crops, in conservation of pasturage, and in reduction of expenditures for repairs to irrigation ditches, canal banks, etc., amounts varying from 100 per cent. to 1000 per cent. of the amounts expended for the destruction of squirrels that infested their lands. Long states that since July 1, 1913, over 20,000,000 squirrels have been destroyed, and the average cost of labor and material used in the anti-squirrel measures has been about 17.4 cents per acre.

The Friedmann Treatment for Tuberculosis.—Probably there has been no announcement of a proposed remedy for a disease which excited more interest in the lay and medical press than did the announcement of Dr. Friedrich F. Friedmann of his treatment for tuberculosis. Dr. Friedmann's claims were investigated by a board of officers of the U. S. Public Health Service composed of Surgeons John F. Anderson and A. M. Stimson, and their report has just been made in Bulletin No. 99 of the Hygienic Laboratory. The board reports that the claims made by Dr. Friedmann for his method of treating tuberculous infections are, in brief, that, by means of injections of a living acid-fast organism, harmless of itself, he is able to cure cases of tuberculosis, pulmonary or otherwise, which have not already advanced to that hopeless stage where death is imminent. From the manner of presenting these claims and from the fact that successes only and not failures are reported, the reader of these claims is bound to assume that such results are the rule; in other words, that a sovereign remedy for tuberculosis has at length been discovered, and incidentally that a method has been devised for the administration of living acid-fast organisms which avoids abscess formation, a complication which has hitherto limited their employment. The results of the investigation

reported by the government investigators do not confirm the claims made by Dr. Friedmann. It was found that the preparation used by Friedmann is not strictly devoid of dangerous properties of itself, still less so when injected into tuberculous subjects; that the favorable influencing of tuberculous processes by his methods is certainly not the rule, and that if we are to ascribe to the Friedmann treatment the improvement noted in a few cases, we are equally bound to impute to it the serious retrogression observed in other cases; and finally that the phenomenon of abscess formation has not been avoided by Dr. Friedmann's methods. It was found that the organism used by Dr. Friedmann differs in important cultural characteristics from any heretofore recognized tubercle bacillus. The subcutaneous and intramuscular inoculation of animals with the Friedmann organism caused the formation of abscess in over 25 per cent. of the animals treated. The treatment of animals with the Friedmann organism—rabbits and guinea-pigs—either before or subsequent to infection with virulent tubercle bacilli, is followed, as a rule, by an increased susceptibility to the disease. Inoculation of monkeys with the Friedmann culture did not show either curative or protective action in those animals against tuberculosis. A report somewhat along the same lines has been made by the U. S. Public Health Service, and published as Senate Document No. 641, on the claims of Drs. Karl and Silvio von Ruck, of a vaccine for the treatment of tuberculosis. The claims for their vaccine as a specific cure for tuberculosis has been subjected to an investigation by the U. S. Public Health Service in accordance with a resolution of the United States Senate. The report gives the results of animal tests with the vaccine and the results of certain serological reactions, claimed by von Ruck to be evidences of immunity following the use of his vaccine. The report states that the claims by the von Ruck's to have developed a specific cure for tuberculosis have not been substantiated, and that the treatment of animals with their vaccine instead of producing an immunity against experimental infection appears to have rendered them more susceptible. The report states, furthermore, that the von Ruck's objected to independent investigations of their vaccine, and for that reason the work was transferred to the Hygienic Laboratory in Washington, where it was completed.

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DR. GEORGE MORRIS PIERSOL, 1913 Spruce St., Philadelphia, Pa., U. S. A.

THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

APRIL, 1915

ORIGINAL ARTICLES

THE HISTOGENESIS OF CANCER OF THE STOMACH.[1]

By William Carpenter MacCarty, M.D.,

MAYO CLINIC, ROCHESTER, MINNESOTA.

It is generally thought that gastric carcinoma arises from postnatal epithelial rests which are supposed to be present either in

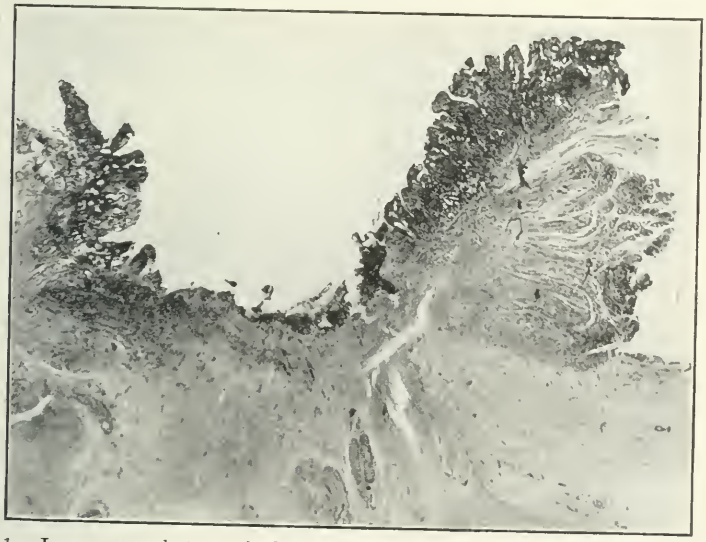


Fig. 1.—Low-power photograph through a section of a simple chronic gastric ulcer.

the scar-tissue bases or the submucosa of gastric ulcers. Since this idea is theoretical, I take the liberty of presenting briefly

[1] Read before the Academy of Medicine, Kansas City, November 20, 1914.

some facts relative to the histogenesis of gastric carcinoma and its relation to gastric ulcer.

Simple chronic gastric ulcers have never, in my experience,

FIG. 2

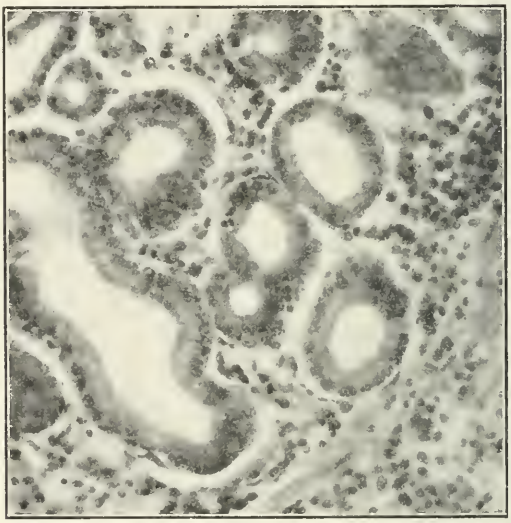
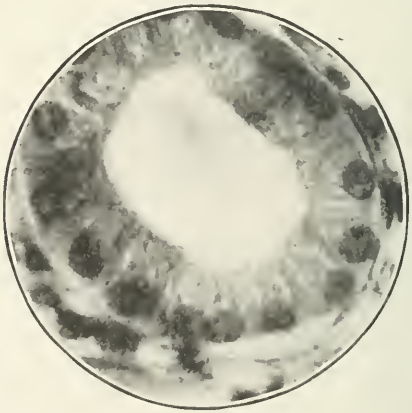


FIG. 3



FIGS. 2 and 3.—Photographs through the border of a simple chronic gastric ulcer. The glands are regular and show little or no distortion. The cells are regularly arranged around the lumen. The nuclei occupy a basal position in the cells.

presented any visible epithelial rests which one could scientificially state were prenatal. Neither have I seen postnatal epithelial rests in the mucosa, submucosa, or ulcer base that were not either com-

posed of atrophic epithelium or real carcinoma, the latter condition being present in the base or submucosa only when there was extensive involvement of the mucosa.

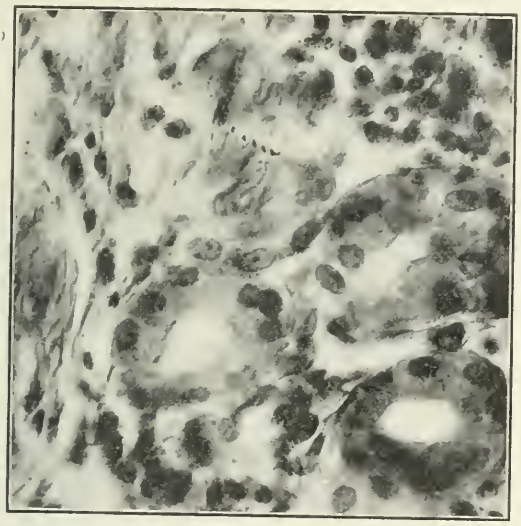


FIG. 4.—Photographs through the same border from which Figs. 2 and 3 were taken. The cells do not present the regularity of arrangement seen in Figs. 2 and 3. The nuclei are not regularly placed at the bases of the cells. They vary in size and shape.

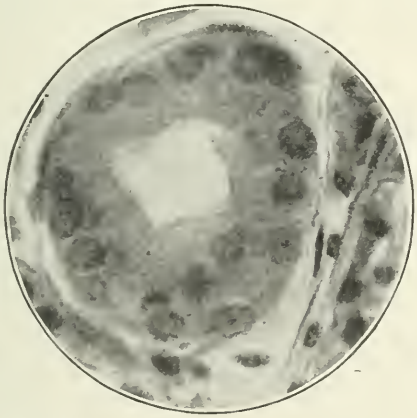


FIG. 5.—Several glands showing the same cytological changes which are seen in Fig. 4. This picture is frequently found in simple chronic gastric ulcers and presents the same cellular appearance which is seen in secondary epithelial hyperplasia in the breast, prostate, skin, and hair follicle.

In the simple chronic ulcer (Fig. 1) one frequently finds the glands composed of columnar or cuboidal cells, regularly arranged with oval or round nuclei, which are almost always of the same

size and are placed near the bases of the cells (Figs. 2 and 3). The cells are sharply demarcated from the stroma, which consists of fibroblasts, differentiated fibroblasts, and some lymphocytes, all of

Fig. 6

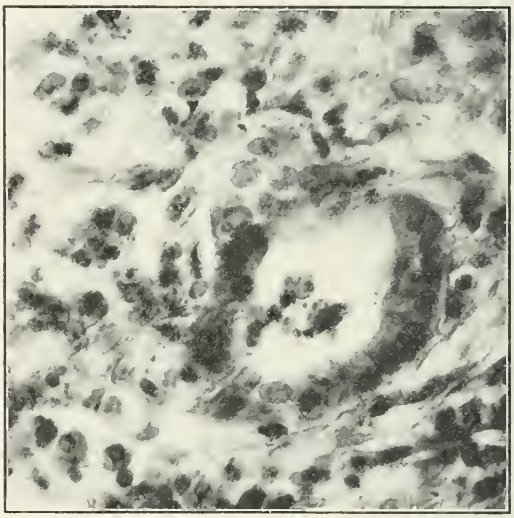
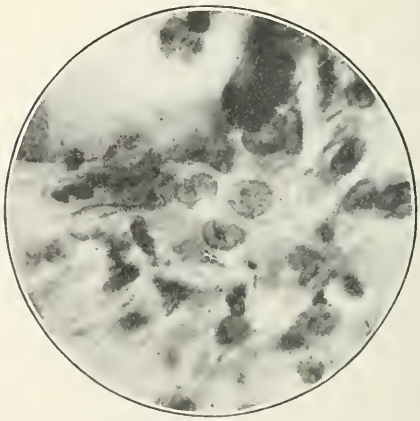


Fig. 7



Figs. 6 and 7.—Intraglandular epithelial hyperplasia similar to that in Figs. 4 and 5 plus extraglandular epithelial cells which are morphologically similar to the intraglandular cells.

which form a histological picture distinguishable from the normal gastric mucosa with great difficulty. From this picture to carcinoma there are transitional apparently intermediary pictures the extremes of which are easily distinguishable.

The epithelial cells of the glands in some ulcers lose their cuboidal or columnar shape and regularity in size and arrangement (Figs. 4, 5, 6). They become oval or round and the nucleoli become larger and more distinct. The exact origin of these cells is at present unknown, since in the gastric gland there are not two distinct rows of cells normally present, as in the breast, prostate, skin, and the accessory epithelial organs of the skin. To my knowledge, a germi-

FIG. 8

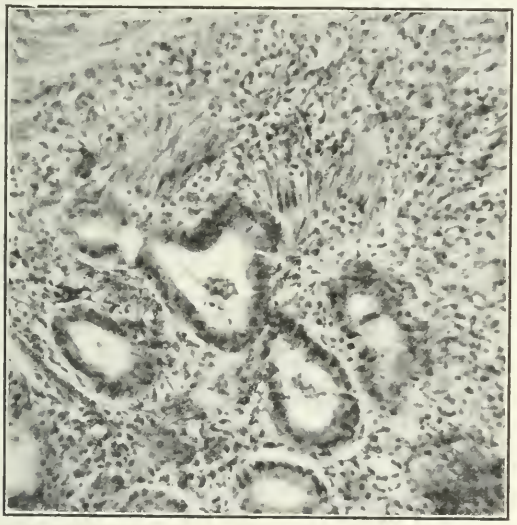


FIG. 9

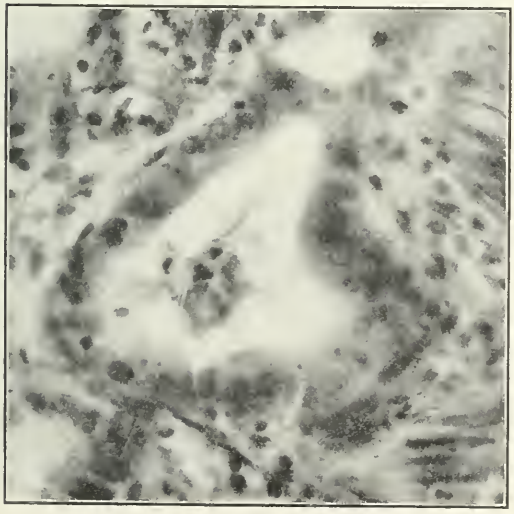
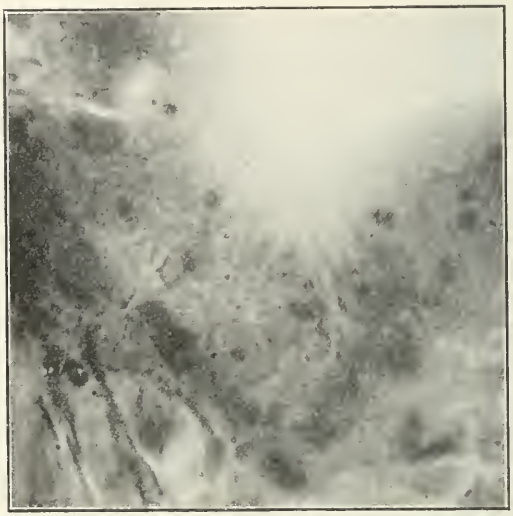


FIG. 10



FIGS. 8, 9, and 10.—Three magnifications of the same gastric gland showing an intraglandular cytoplasia in the mucosa of a chronic gastric ulcer. The cells if compared with those in Figs. 11 and 12 will be found to be indistinguishable.

native layer of cells or a germinative focus of cells has not as yet been satisfactorily demonstrated.

The cells (Figs. 5, 6, 7, 8, 9, 10) which are frequently found, however, present a morphological picture which is indistinguishable from that seen in secondary epithelial hyperplasia in other organs having a germinative layer which is the origin of cancer cells.* Various degrees of intraglandular morphological changes (Figs. 5, 6, 7, 8, 9, 10) are found in the borders until the cells become indistinguishable from cancer cells (Figs. 7, 11, 12, 13). When such a condition is found, careful search frequently demonstrates a lack of demarcation between the gland and the stroma, and epithelial cells may be seen in the stroma, the later condition being accepted by general pathologists to be the histological criterion of cancer. When cancer is definitely present in the mucosa or other coats of the stomach the intraglandular cells always present the condition which has been described as secondary hyperplasia in other organs.

From a cytological standpoint I see no objection to denoting the condition as secondary hyperplasia in the stomach. It is apparent that the histogenesis of cancer in the stomach bears an analogy to that in the breast, prostate, and skin, with the one exception that the germinative stratum or focus has not been demonstrated, a condition which differs from primary epithelial hyperplasia in the organs just mentioned.

* See appended references.

In the production of these apparent stages of epithelial hyperplasia whatever the irritant or irritants are, be they extrinsic or intrinsic, there is an apparent attempt on the part of nature to

FIG. 11

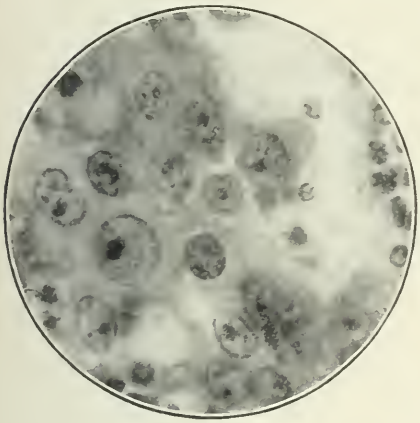


FIG. 12

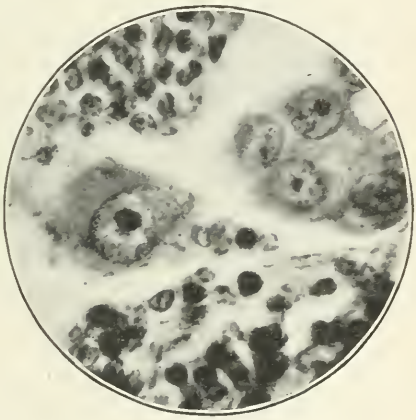
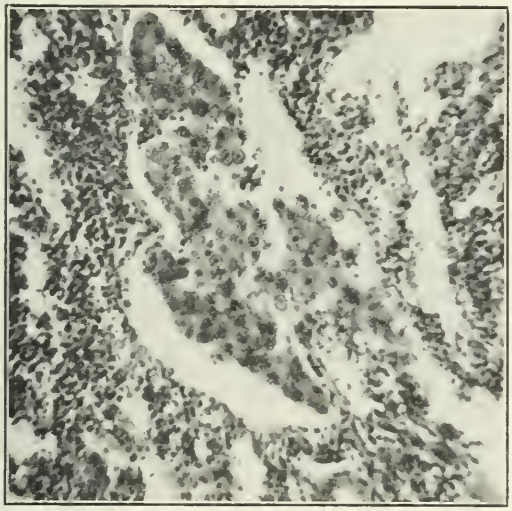


FIG. 13



FIGS. 11, 12, and 13.—Cells from a carcinomatous involvement in a subpyloric lymph gland in a case of gastric carcinoma. The cells are morphologically indistinguishable from the cells of an intraglandular cytoplasia which is frequently seen in simple chronic gastric ulcers.

reproduce the epithelial lining of the glands. In this attempt there is failure to completely differentiate the cells with the coincidental picture of secondary hyperplasia the cells of which differ from cancer cells only in position.

From these facts one may clearly see that the gastric cancer cell arises from intraglandular hyperplastic cells of the mucosa, and represents a malignant end-stage of a process of hyperplasia of normal cells.

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PERFORATED GASTRIC AND DUODENAL ULCER.

By George G. Ross, M.D.,

PHILADELPHIA.

In the whole field of surgery I know of no condition in which more depends upon prompt diagnosis and immediate intervention than in cases of perforated gastric and duodenal ulcers. The treatment of such ulcers in the absence of perforation is still open to discussion—our course when we have to deal with a perforation is plain and we need concern ourselves only with the features of the diagnosis, the operative technique, and the postoperative treatment. I believe also that the symptoms of a perforation of the stomach or duodenum are practically always of such a nature that a diagnosis should be possible without delay, although in a few instances the course of events has been so different from what one might be led to expect that an exact differentiation has been difficult. But in every instance I am certain there is sufficient warrant for the belief that some pathological condition within the abdomen exists which demands prompt operation, unless the case has survived the first few days and the symptoms become masked.

It has been my good fortune lately to see a considerable number of most interesting cases of perforated ulcer, and I cannot do better than to demonstrate the points I wish to make by a direct reference to the case histories. The first case was seen by me in consultation, was referred to the wards of the German Hospital, and operated on by my chief, Dr. John B. Deaver, during his clinic the same afternoon. This was a case of perforated duodenal ulcer. The history is as follows:

H. A. S. was operated on November 15, 1913. His previous history shows that seven or eight years before the present illness he had an attack of indigestion which lasted for several weeks. Three months before his perforation he began to have an uncomfortable feeling of fulness in his stomach, coming on immediately after eating. This condition was relieved by restricted diet. He was never able to belch and never vomited; was constipated and flatulent. Used alcohol moderately. On November 14, 1913, he ate a heavy lunch, and was very uncomfortable during the afternoon. At about 6.30 P.M. on the same day, while sitting at a desk writing, he had a severe attack of epigastric pain, coming on suddenly and radiating up over the chest. The pain was constant, not spasmodic, and was made worse by inspiration. There was no nausea, but the patient tried to induce vomiting in the hope that it might relieve the pain. The pain kept up all night, and was referred also to the back of the neck and right shoulder. The next morning he drank a glass of warm milk and retained it, and his pain was not aggravated by it. I saw the patient the morning after the onset of his acute illness. The abdomen was distended and there was a general board-like rigidity. There was tenderness, its point of greatest intensity being midway between the umbilicus and xiphoid. The liver dulness was diminished. Peristalsis was present. The leukocyte count was 23,500, with 89 per cent. polynuclears. I advised immediate operation upon the diagnosis of perforated ulcer.

At operation an appendectomy was first performed, gas and cloudy serum escaping when the peritoneum was opened, and purulent material appeared when the adhesions about the appendix were broken up. An upper right rectus incision was then made and a perforation of the posterior surface of the duodenum was found. The duodenal opening was closed with linen-thread suture and the gastrohepatic and gastrocolic omentum stitched over it. The duodenum was plicated and a posterior gastro-enterostomy done. The upper abdomen and pelvis were cleaned with gauze pads and a glass tube put in the pelvis for drainage. The patient made an uninterrupted recovery.

This case may be taken as a typical one. Not having seen him earlier, I did not have the clinical picture presented shortly after perforation, but the history approaches a classical one.

First we have a clear history of antecedent trouble, with a long intermission between the two attacks. Next there is the history of a prodromal period of a few hours before the actual perforation. It is true that often a perforation of a gastric or duodenal ulcer comes without any warning, but premonitory signs are not infrequent. In practically every instance we can find, by careful questioning, there is a definite if not typical history of digestive disturbances at some time in the patient's career.

The physical signs on the following day were exactly what one would expect. The patient had evidently suffered some grave accident. The abdomen was rigid. This board-like rigidity is a marked feature of the perforation of upper abdominal ulcers. At first we usually note only a marked rigidity of the upper recti—a sign almost pathognomonic when it is typical.

In the case just described an error in diagnosis would have been difficult. Moreover, in the presence of such a history of digestive disturbances entirely different from that encountered in chronic gastric ulcer we were correct in diagnosing a perforated duodenal ulcer.

Another of my recent cases is even more typical, and was seen earlier in the course of the illness.

E. McC. was admitted to the Germantown Hospital, February 28, 1914, at about 2 A.M., suffering with intense upper abdominal pain. The previous afternoon, while at work lifting a heavy bar, he was taken with a sudden, sharp pain in the epigastrium. After treatment by a druggist with salts and gastric lavage by his doctor —in the course of which much fluid was put into the stomach and but little gotten out—he came to the Germantown Hospital. A diagnosis of perforated gastric ulcer was made on the history, marked abdominal rigidity and distention, rapid pulse, and leukocytosis of 24,000. In this case we could not obtain a history of previous gastric disturbances.

At operation, upon opening the peritoneum, large quantities of gas and stomach contents escaped. It was some time before the perforation could be located, upon the anterior wall about one and one-half inches from the pylorus. It was closed and a gastroenterostomy performed, because the induration to the pylorus and the closure of the ulcer considerably lessened the lumen of the stomach at this point. A pelvic glass drain was inserted and the upper wound closed with cigarette drainage.

Here again we have a typical case of perforated ulcer, but a gastric one. There was, however, absolutely no history of antecedent illness. Mr. Paterson states that it is always easy to distinguish between a perforated duodenal and gastric ulcer, but I have not found it so. In later cases the diagnosis presents an entirely different problem. We do not have the early physical signs to correlate with the history.

Thus a case coming under my care in the Germantown Hospital on January 26, 1914, well illustrates these points:

M. S., female, aged sixty-eight years, gave a history of stomach trouble since childhood, having spells of indigestion coming on three or four hours after eating and causing vomiting. These had been more marked within the past three years, coming on every six or seven weeks. One week before admission such an attack occurred, on Monday, January 19. The following Thursday

she had to go to bed, and on Sunday, January 25, she suffered intense abdominal pain, with vomiting. This continued with little cessation up to the time of admission. The bowels did not move for seven days prior to admission. Physical examination showed the patient to be poorly nourished. The abdomen was tender, but very little distended. There was visible peristalsis, and knuckles of gut could be seen through the relaxed abdominal wall. Vomiting ceased upon absolute starvation. Intestinal obstruction was suggested as a diagnosis, but my diagnosis was a malignant growth of the sigmoid with partial obstruction. After several days' delay I operated and made a rectus incision. There was no evidence of disease in the lower abdomen. A knuckle of ileum was found adherent to the stomach at the pylorus, kinked, and giving rise to mechanical obstruction. This being freed a perforation of the anterior wall large enough to receive a lead pencil was exposed, with no peritonitis about it. It was closed by purse-string suture, etc., and reinforced by an omental graft. The wound was closed without drainage, and the patient made a good recovery.

Here we had a most interesting case from the standpoint of diagnosis. The history of antecedent illness was direct and to the point—a history of ulcer. The onset was subacute, and the progress of the case delayed because a spreading peritonitis was avoided. The second and later pain was that of the obstruction, which also caused the vomiting. Rigidity and marked tenderness were absent because there was no peritonitis.

This really was a case of perforated gastric ulcer in which a diagnosis would have been difficult at any time because of the prompt blocking of the ulcer. At the time of admission an absolutely positive diagnosis could hardly have been made at all, as all symptoms were masked by those of the complicating obstruction.

In instances in which there is but a few days' delay we still have our guiding-points in diagnosis. Another case operated on at the Germantown Hospital, on February 11, 1914, after two days' illness, still showed unmistakable signs of perforated ulcer, and gave an excellent previous history. At operation, however, it was plain why this should be so, as a subdiaphragmatic abscess was found.

On the other hand we may have to deal with an entirely atypical history.

On March 26, 1914, there was admitted to the Germantown Hospital a man, aged twenty-three years, whose history was as follows: The patient was taken sick March 20, 1914, with a feeling of malaise. On March 21 he became worse, had a chill, and went to bed. Later he felt better and got up. The patient had nosebleed the day before admission. He developed abdominal tenderness the day of admission, with pain in the back of the head and

in the neck muscles, and vomited that evening. He had anorexia, but was thirsty. He had a short, dry cough, with tenacious and bloody (?) expectoration. His abdominal pain made breathing painful. His previous history gave us a clue—a history of hunger pain. The patient when I saw him was feverish. On admission he had epigastric tenderness and slight abdominal rigidity. A mass was felt in the upper left abdominal quadrant extending about 6 c.c. below the costal margin.

Three days after admission, and on the tenth day of his illness, he was transferred to my service. A diagnosis of left-sided subphrenic abscess was made, probably due to perforating ulcer. This was confirmed, but a drainage operation only was possible. The ulcer was not found at operation, but various lymph masses about the anterior and posterior stomach walls were not disturbed. The patient died of general peritonitis. A partial autopsy disclosed a perforation on the posterior wall of the stomach and two of the duodenum. There were two small unperforated ulcers of the stomach near the cardiac end. The perforation into the lesser peritoneal cavity and the localization of the abscess above delayed the end in this case, but the whole is a lesson on the consequences of delay in diagnosis and treatment.

It is not impossible to mistake a perforated duodenal or gastric ulcer for a case of appendicitis. This occurred to me in a case operated on five years ago. I do not think, however, that I would make the same mistake now, particularly in a case seen as early as I saw this one. It must be evident then that in perforated gastric and duodenal ulcer we have a problem difficult but not impossible of a proper solution if it engages our attention at the outset of the condition. It is not my purpose to note the pathology of perforations, their site, or to quote statistical facts. These have all been thoroughly investigated and published in papers easily obtainable, notably one by Elliot in 1912. I wish to consider briefly the diagnosis of gastric and duodenal perforations, their surgical treatment and after-treatment.

The history of previous illness is most important. It is but rarely that we cannot elicit a history definitely pointing to a gastric or duodenal lesion. Great care and persistence are often needed, and often the patient before operation is too ill to give us a good account of his past medical history. It is a noticeable fact that in later years we have been more alert to appreciate points in the previous histories of our patients. The situation parallels that seen in cases of gall-stone disease. Formerly we read and heard much of gall-stones without symptoms. The symptoms were merely unrecognized. So it is with ulcer of the stomach and duodenum.

Of the actual diagnostic points when a perforation of a gastric or duodenal ulcer has occurred we have to consider:

1. The history of acute pain.
2. The presence of marked rigidity of the recti, especially above.
3. The evidences in the patient's general condition that he is quite ill.

The pain accompanying acute perforation is generally described by the patient as excruciating, and is referred to the epigastrium. It sometimes comes without warning, although there are frequently premonitory signs, such as gastric heaviness, distress, or malaise after eating. The pain is of such character and so described and localized that I have been inclined to make the diagnosis thereon in the absence of certain of the symptoms. In the spring of this year a man of middle age, who following several severe attacks of epigastric pain and prostration, came to my attention. Abdominal rigidity was absent, but there was a sense of resistance and tenderness particularly noted upon the right side. There was dulness in the flanks. The patient was not, however, shocked. Leukocytes were 11,000. Operation disclosed the abdomen, greater and lesser peritoneal cavities, filled with bright-red blood and clots. The gastrocolic omentum and transverse mesocolon contained hematomata and the posterior wall of the stomach was infiltrated with blood. The source of the hemorrhage was not disclosed. The man temporarily recovered, but a few months later developed an obstruction in which operation was so long delayed that he did not recover. I had concluded that a perforated gastric ulcer must have eroded the wall of the vessel at the greater curvature to have given us such a hemorrhage, but the pathological report on the stomach does not give absolute proof of this upon gross examination, and the microscopic studies fail to show the signs of a healed ulcer.

The abdominal rigidity is intense and characteristic. At first the abdomen may be scaphoid, but later it becomes distended. The rigidity is always more intense in the epigastrium, but when the peritoneal infection spreads we meet with a general abdominal rigidity. Tenderness accompanies the rigidity. It has been stated that the point of maximum tenderness indicates the site of the perforation, but this I am not able to substantiate. Shock was formerly stated to be an important diagnostic point. I do not find it so. The patient suffering from perforated ulcer is evidently ill, is usually prostrated, and may suffer from true surgical shock. Leukocytosis is present in so many conditions that its diagnostic value is slight. When the perforation is protected or already walled off by adhesions or other viscera the rigidity and great tenderness may not supervene—that is, the symptoms of a peritonitis do not become evident.

In cases which survive and suffer from localized collections, such as a subdiaphragmatic abscess or a diffuse peritonitis anywhere within the abdomen, the local symptoms resultant therefrom will be manifest.

The differential diagnosis of perforated ulcer is not, as a rule, difficult. There are many conditions in which errors have occurred, yet I think not often justifiably so. Because of the severe epigastric pain often associated with appendicitis, this is the incorrect diagnosis most often made. Moreover, if fluid drains from a duodenal ulcer into and through the right kidney pouch tenderness and rigidity may be very noticeable in the right iliac fossa. The history and other symptoms, however, should soon make the correct diagnosis.

Intestinal obstruction with sudden onset may simulate the pain of a perforation—the rigidity and inflammatory signs would, however, be absent.

A ruptured gall-bladder would give identical symptoms. The condition is rare and particularly so without a history of trauma or infectious cholecystitis for some time prior to the perforation.

Acute pancreatitis has its onset with pain like that of a perforation. Here the slow pulse, low temperature range, and evidence of involvement of the lesser peritoneal cavity only, without a peritonitis in the greater cavity give us our clue. Subsequent developments are entirely different also, and the symptom-complex of acute pancreatitis is very definite.

When late complications set in after the perforation of an ulcer the symptoms may simulate those of the same complications, due to other causes, and a differentiation may be possible only in the presence of a definite history.

A diagnosis of perforated ulcer having been made surgical intervention is called for at the earliest possible moment. Delay is fatal.

The anesthetic of choice is ether, possibly with nitrous oxide preceding it. A free incision through the upper right rectus exposes the field. The escape of gas, and especially gastric contents, establishes the diagnosis. Rapidly but gently we search for the site of the perforation, bearing in mind that there may be more than one. If there be fluid in the field of operation it should be sponged away, or if there be tissue masses or food particles normal saline may be used to wash it away. Occasionally, as in one of the cases quoted, the presence of an abscess makes it possible to do only a drainage operation, and the perforation is not located. This, however, is fortunately a rare circumstance. The perforation being found it is closed with a purse-string suture of linen thread, if this is possible, reinforced by Lembert sutures. Or it may be merely sewed over. In either case reinforcement by omental grafts is of distinct advantage. If the surrounding induration is such that a closure by suture is impossible we may have to content ourselves with putting drains to the site of perforation. More extensive operations upon the ulcer-bearing area are contraindicated in the presence of perforation.

The possibility of multiple perforations must not be over-looked. In one of my early cases the perforation of a second ulcer was responsible for a postoperative death.

I believe that gastro-enterostomy should be performed only when by induration or suture the lumen of the pyloric end of the stomach or duodenum is encroached upon. Even then, unless it be absolutely essential, it should not be attempted by an inexperienced operator. Such a one should do as little as possible in every case—close the perforation and drain.

It is true that a gastro-enterostomy tends to cure the ulcer, but it is a formidable operative procedure and not to be lightly regarded in the presence of so acute a condition as perforated ulcer. It tends also to prevent secondary perforations, but even herein is not always effective.

The gastric repair being completed and the toilet of the peritoneum finished the abdominal incision is ready for closure. I drain all my cases by a glass tube into the pelvis placed in a lower abdominal stab incision in the median line. The upper wound may be entirely closed in early cases or drained by a cigarette or gauze rubber tube drain where there has been an abscess. Postoperative treatment is simple. The pelvic drain can usually be removed in forty-eight hours and other drainage in four or five days. The patients are kept upright after coming out of the anesthetic, medicated only when necessary, and supplied with saline freely by continuous or intermittent proctoclysis. Morphin is not harmful in these cases when judiciously used. For persistent postoperative vomiting gastric lavage is employed—the operative procedures on the stomach do not contra-indicate it.

I have recently seen a case which is of such unusual interest that I add it to this paper, as I believe it to be a case of perforated gastric ulcer at the cardiac end of the stomach.

J. F., aged forty years; chief complaint was chronic gastric indigestion for many years. His disposition was irritable and unreasonable, due to his continuous discomfort. As a result of his illness he contracted the alcohol habit and had been treated for it in an institution, but had not taken stimulants for five weeks prior to his acute attack. In addition to stomach dyspepsia he suffered from frequent attacks of abdominal pain and diarrhea.

About 10 P.M. on September 6, 1914, he had an attack of nausea, and vomited. The patient stated that the vomitus looked like blood, but this could not be confirmed. Immediately following the vomiting he developed an extremely severe precordial pain, associated with collapse and marked shock. Morphin in large doses failed to relieve the pain, and measures directed against the shock failed. By 2 A.M. on September 7, 1914, the patient developed evidence of acute pneumothorax. A mass could be made out just below the left costal margin, which was very tender, and over

which the rectus muscle was markedly rigid. By 9 A.M. on September 7, when I first saw the patient with his family doctor, Dr. George Cameron, his condition was as above described, only the shock was more intense and the pain unrelieved. His entire abdomen was tender, but was more intense in the left hypochondriac region. The mass in this locality was readily mapped out in spite of the muscular rigidity. The pneumothorax had increased until the apex beat of the heart was to the right of the sternum. Breathing was labored, and he experienced considerable difficulty on inspiration.

Surgery being out of the question a medical consultant was advised, and Dr. George M. Piersol was asked to see the case. He arrived about 11.15 A.M., and while making an examination the patient expired.

In the absence of tuberculosis and traumatism, except the spell of vomiting, and of cough or bloody expectoration, and with the history of prolonged stomach dyspepsia with pain, a diagnosis of perforated gastric ulcer at or near the cardiac end of the stomach was made. The explanation of the pneumothorax was that the ulcer was adherent to the under side of the diaphragm, and when perforation occurred it included the diaphragm and parietal layer of the pleura.

A postmortem was refused, so that this diagnosis must remain unconfirmed and a matter of speculation. However, the evidence seems sufficient to justify the inclusion of the case in this series.

REPORT OF A CASE OF PAROXYSMAL TACHYCARDIA WITH OBSERVATIONS ON TREATMENT.

By Walter L. Niles, M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE, CORNELL UNIVERSITY MEDICAL COLLEGE; ASSISTANT ATTENDING PHYSICIAN TO BELLEVUE HOSPITAL, NEW YORK.

The patient, a married man, aged thirty-seven years, has continuously been under my observation since March 18, 1909. Cardiac valvular disea e was first recognized when he was eighteen years of age, and, according to the family legend, he "strained" his heart at about that time, while rowing. Careful questioning fails to elicit a history of any illness which might be interpreted as acute rheumatic fever or any other infection which would be likely to involve the heart. He was a ways extreme y moderate in the use of alcohol and tobacco, and venereal infections were denied.

The first paroxysm of tachycard a came on in 1905, immediately

after "shooting-the-chutes," and during the next six years he experienced many repetitions. The attacks varied in duration from a minute or two to twenty-eight hours, the average being from four to six hours. Their frequency was also variable, sometimes recurring three or four times a day, while at other times there were intervals of freedom lasting several weeks; the longest was nine weeks. These attacks did not appear to be precipitated by any specific cause, although much exertion would quite surely cause one, as would, apparently, any toxemia.

In 1907 he is said to have had a mild attack of "grip," which was followed by jaundice lasting one week, during which time he had a great number of attacks.

I have frequently noted that a mild coryza, or tracheitis, was likely to be accompanied by paroxysms, and that stasis in the intestinal tract would quite surely precipitate them, often being preceded by a few urticarial spots. I attempted to determine whether any specific protein caused them, but was unable to arrive at such a conclusion. They quite often started at night, and the patient thought they were more apt to occur if he lay on his left side when sleeping, or they began while working at his office, or while eating. He was always immediately aware of the onset of an attack by a sensation of fulness in his chest and throbbing of his heart. He usually went to bed—if not already there—and sat upright with pillows at his back. He had no dyspnea except in long attacks, but was distinctly uncomfortable if he tried to lie down. After about an hour he would complain of "feeling sick all over," having pain in his head, back, and limbs, and constant nausea with frequent vomiting of considerable mucus. He constantly had a mild degree of icterus, and during long attacks this became deeper.

The attacks always ceased abruptly with a "bump" of his heart, and the pulse would then immediately become slow and regular. Within a few minutes he would feel quite well, and could shortly take food. There were no premonitory signs to indicate either the onset or offset of attacks.

Examination between paroxysms showed a man of spare build and poorly developed muscles, with a faint icterus in the skin and scleræ. The pulse was 72 to 80 per minute, regular, and of normal size and force. The vessels were not palpable. Systolic blood-pressure, 110; diastolic, 75. The heart transmitted a diffuse, heaving impulse to the precordium, the point of maximum impulse being in the sixth left interspace, 11 cm. from the median line. The apex beat was in the sixth space, 13.5 cm. to the left of the median line. There was no undue pulsation of the cervical vessels. The upper border of cardiac dulness began at the second rib, the left border was 14.5 cm. to the left and the right border 5 cm. to the right of the median line. Auscultation revealed a long, low, harsh

systolic murmur, best heard at the maximum point of impulse, which could be traced into the left axilla and below the angle of the left scapula, also over the body of the heart and 3 cm. to the right of the midsternal line in the fifth interspace. A long, rumbling, crescendo diastolic murmur, which ceased abruptly with a sharp, loud shock to the first sound, was also heard over a small area just to the right of the apex beat. The pulmonary second sound was much accentuated. Polygraphic tracings showed normal jugular and radial curves. The lungs and abdominal viscera were negative. There was no ascites or edema, and the urine and blood were normal. Wassermann reaction negative.

During attacks the patient was usually found sitting up in bed, looking sick and anxious, but he was not cyanotic. The whole left side of the thorax would be rapidly heaving, and a wavy impulse was seen in the fourth, fifth, and sixth interspaces. The most striking feature of inspection was, however, exceedingly violent throbbing of the jugular bulbs, which was so great that it was impossible to get tracings directly from them. The systolic blood-pressure was 90 to 95. Except in very long attacks, dilatation of the heart could not be demonstrated. The heart sounds, which were perfectly regular, varied from 140 to 190 per minute, usually being about 170. A short, faint, systolic murmur could be heard over the precordium. The pulse was very small, but there was no deficit.

Since the onset of attacks of tachycardia the patient has led a very quiet life, being largely freed from business cares. A great variety of therapeutic measures for stopping the paroxysms were tried, but none, except that noted later, seemed to be of value if the paroxysms lasted more than an hour. They sometimes ceased, with vomiting or defecation. Pressure on the vagi, changes in position, and prolonged holding the breath were without avail, except the latter, which frequently terminated short attacks and was most relied upon by the patient.

It was difficult to get tracings from the jugular bulbs during paroxysms because of their tremendous throbbing, but those obtained show the ventricular form of the venous pulse (Fig. 1). It is quite certain that the auricle was not fibrillating as the heart was always regular, and Lewis has concluded "That auricular fibrillation is never accompanied by regularity of the ventricle except when it is complicated by auricuioventricular heart-block, and it appears reasonable to assume that when the ventricular form of venous pulse is present and the pulse is regular and of normal or increased rate the auricle is not in a state of fibrillation."

During the fall of 1911 the patient was about as usual, having short attacks every few days until November 13, when he had a paroxysm lasting twelve hours. It was accompanied by no unusual features, and on November 14, although he remained in bed, he

felt perfectly well and reported his heart to have been slow and regular all day. However, at 7 P.M. it became rapid (140 to 180 per minute), and so continued, except for short intervals subsequently noted, until 8.30 P.M., November 21, a period of one week. Within forty-eight hours it became extremely dilated. There was congestion of the lungs, with expectoration of bloody sputum, the liver became large, tender, and pulsating, and there was deep icterus and edema of the lower extremities. During the first twenty-four hours he was constantly nauseated, but this subsided later. He felt weak and faint, and much of the time was stuporous, with Cheyne-Stokes respiration. All of the usual measures were tried, but without effect on the heart rate, and the patient was *in extremis*.

The medication and state of the heart can best be followed by daily notes:

November 15. Heart rapid (160 to 180) and regular all day.

November 16. 3 c.c. digalen given hypodermically during the day. Heart regular, 160 to 180.

November 17. *At midnight*, 0.5 mg. crystallin strophanthin given intramuscularly. 3 A.M., strophanthin repeated. 5.30 A.M., heart slow and irregular for two minutes. 6.30 to 9.30 A.M., heart slow and irregular, characteristic of auricular fibrillation (Fig. 2). 11.45 A.M., slow and irregular for two minutes. 12.30 P.M., 0.5 mg. crystallin strophanthin given. 10.20 P.M., heart slow and irregular for five minutes. 11 P.M., 0.5 mg., crystallin strophanthin given, a total of 2 mg. in twenty-four hours.

November 18. Continued rapid and regular until 10.30 A.M., when suddenly became slow (90 to 100) and perfectly regular. Great relief and improvement in patient's condition.

November 19. 6.30 A.M., again rapid, regular. 10.30 A.M., 0.5 mg. crystallin strophanthin given. 11 P.M., heart continues rapid, 160. 0.5 mg. crystallin strophthanthin given.

November 20. 10 A.M., rate 144. 1 mg. amorphous strophanthin given. 9 P.M., slow and very irregular for twenty minutes. In auricular fibrillation. 10.30 P.M., rate 164. 1 mg. amorphous strophanthin given.

November 21. 12.20 A.M. to 6.30 A.M., rate 88 to 96 and absolutely irregular. 9.30 A.M., rapid (150 to 160) and regular. 0.75 mg. amorphous strophanthin given. 10.30 A.M., to 1 P.M., slow (82 to 96) and perfectly regular. 7 P.M., rapid since 1 P.M. 1 mg. amorphous strophanthin given. 8.30 P.M., suddenly became slow (76) and perfectly regular. Tracings showed normal curves without evidence of block, alternation of coupling.

November 23. Continued slow and regular until 10.30 P.M., when suddenly became rapid.

November 24. 10.15 A.M., still rapid. 1 mg. amorphous strophanthin given.

11.30 A M., slow and regular until 3.30 P.M., when became rapid. 9 P.M., rate 170. 1 mg. amorphous strophanthin given.

November 25. 8.30 A.M., continues rapid, regular. 1 mg. amorphous strophanthin given.

November 29. Heart has been slow and perfectly regular until today when it became rapid at 11.40 A.M. 2.30 P.M., 1 mg. amorphous strophanthin given. 3.40 P.M., paroxysm ceased.

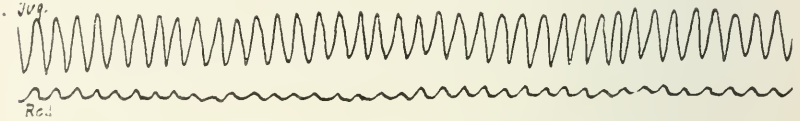

FIG. 1.—Tracing taken during a paroxysm. Pulse rate, 168.

During the next month the heart regained its compensation, though paroxysms recurred every three or four days. Many ceased in an hour or less, but if they lasted more than three hours 1 mg. of amorphous strophanthin was injected into a muscle and

FIG. 2.—Tracing taken November 17, 1911, between paroxysms of regular tachycardia. Rate, 110; auricular fibrillation.

they invariably stopped within three hours and usually in about one hour. The rhythm between attacks was always normal.

From November 29, 1911, to January 20, 1912, strophanthin was administered on thirteen occasions. On the latter date tincture

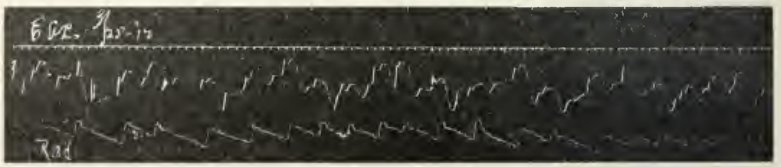

FIG. 3.—Tracing taken after onset of permanent auricular fibrillation. Rate, 70; taking digitalis. Fig. 3 (original) could not be reproduced and was left out.

of digitalis was ordered and continued, with brief interruptions when there was evidence of poisoning. Thereafter, while there were many brief attacks, none lasted more than two hours until March 16, 1912, when a coryza developed with a temperature of 101°. A paroxysm began at 6 A.M. At 9 A.M. 1 mg. amorphous strophanthin was given and the attack ceased at 10 A.M., and the heart remained slow and regular all day. During the night the

patient was very restless and had several short paroxysms. The heart again became rapid at 7 A.M., and at 10.30 A.M. showed some evidences of dilatation. Strophanthin was then given as usual, and the attack suddenly terminated in one hour.

He was not seen again until the next day, when he said that his heart had been irregular since the cessation of the last attack, and

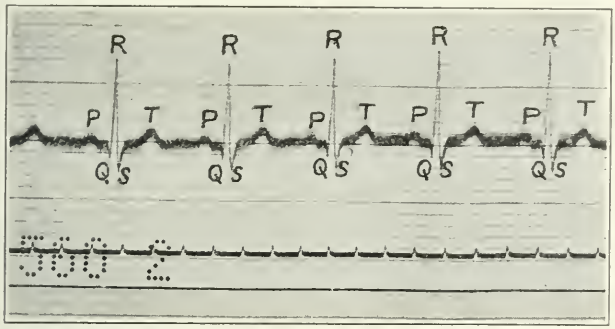

FIG. 4.—Normal electrocardiogram. *P* is due to auricular systole; *Q*, *R*, *S*, *T*, are due to ventricular systole; *P-Q* represents the time consumed in conducting the stimulus from the auricle to the ventricle; *T-P* represents the diastolic period. Time, 0.2 second.

upon examination it showed the characteristics of auricular fibrillation (Fig. 3). This has continued to the present time, and no paroxysms of tachycardia have occurred. While the reserve accommodation force of the heart is slight and there is some pulmonary congestion and a small ascites, the patient is far more comfortable than before and is able to accomplish more work. Digitalis has constantly been necessary, and he is most comfortable

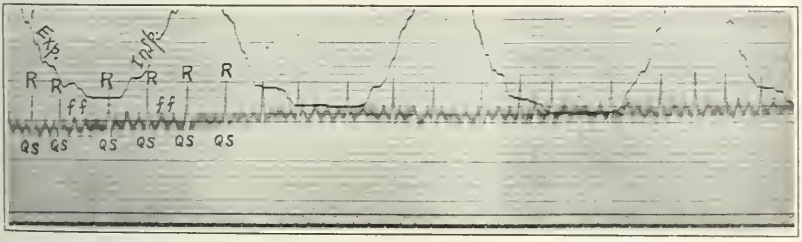

FIG. 5.—Patient's electrocardiogram. Lead II (right arm and left foot). Time, 0.2 second; pulse rate, 108.

when the heart rate is between 60 and 70, a point which I have observed in many instances of auricular fibrillation.

It is unfortunate that no electrocardiograms were obtained from this patient during a paroxysm, but, despite repeated arrangements for them, the attacks never developed at a time and place where they could be taken. However, on April 2, 1912, two weeks

after the onset of permanent auricular fibrillation, electrocardiographs records were taken by Dr. T. Stuart Hart, to whom I am greatly indebted for the ones here reproduced (Fig. 6) and for the interpretation which follows.

(Note. A normal electrocardiogram (Fig. 4) is shown to facilitate comparison with that from the case reported.)

The electrocardiograph records of this case (Fig. 5) show the usual features of auricular fibrillation:

1. Complete irregularity: the ventricular complexes are separated by unequal intervals; long and short diastolic periods follow one another haphazard without any rule or fixed relationship.

2. The *P* wave is absent.

3. There is a series of small waves (*ff*) which continue without interruption throughout the whole of the systole and diastole; these are probably due to the fibrillary activity of the auricle, and occur at a rate of about 375 per minute. The ventricular rate is 108 per minute.

This case presents certain special features. The ventricular complexes, of which the *R* waves are the most evident features, are distorted by the coincident occurrence of the fibrillation waves (*ff*). The *R* waves show a considerable variation in size and are influenced by two factors: they are largest at the end of expiration and smallest in the early part of inspiration, and they vary in height according as they occur coincident with a peak of a fibrillary wave or with a depression between the fibrillary waves. The waves *Q* and *S* are fairly well marked. The *T* waves are small, and for the most part so distorted by the simultaneous occurrence of the fibrillary waves that they can be made out only with great difficulty.

The waves of auricular activity (*ff*) are unusually large and fairly rhythmic. If one disregards the distortion caused by the simultaneous occurrence of the *R* waves of ventricular activity the rhythmic character of the fibrillary waves is seen extending over long periods. The rate of these waves is comparatively slow, for one often sees cases of fibrillation with a fibrillary rate between 500 and 600 per minute. These features—(1) the size, (2) the slowness, and (3) the rhythmicity—suggest that the mechanism of this case is one of auricular fibrillation, which is on the borderline not far removed from the cases of auricular flutter, in which are very rapid (up to 300) coördinated contractions of the auricles with a ventricle which responds to every second or third auricular impulse.

Lewis[1] has shown that the mechanism of auricular fibrillation, auricular flutter, and paroxysmal tachycardia is formation of impulses at an abnormal point (heterogenetic impulse formation)

[1] Mechanism of the Heart Beat, London, 1911, pp. 190–193; Heart, 1912–1913, iv, 171.

in the auricular wall. He concludes that in paroxysmal tachycardia the impulses are generated at a single point, while in auricular fibrillation impulses are generated incoördinately in many foci. In auricular flutter also there is, according to Ritchie,[2] "stimulation, excessive in frequency and intensity, of a localized area in some part of the auricular wall." It is, therefore, evident that, so long as the auricle is in fibrillation, paroxysms of regular tachycardia cannot occur. Hewlett[3] and Mackenzie[4] have also reported cases of paroxysmal tachycardia which under digitalis developed auricular fibrillation, sometimes temporary, with cessation of the attacks.

The only drugs of value in auricular fibrillation are the digitalis bodies, and it is in this condition that their best effects are seen. In auricular flutter, also, Lewis[5] and Ritchie[6] recommend digitalis, each reporting instances in which the normal rhythm has been restored by its use. The return to normal rhythm was often preceded by a short period of auricular fibrillation. Inasmuch as the mechanism of paroxysmal tachycardia is somewhat similar to that of auricular fibrillation, and almost exactly like that of auricular flutter, one might well expect benefit from the use of digitalis in regular tachycardia, such as was obtained by the administration of strophanthin in the case here reported.

The pharmacological action of strophanthin is the same as that of digitalis. It has many advantages in an urgent state, such as prolonged tachycardia with a dilating heart, notably ease of administration by intramuscular injection, which insures rapid absorption and, therefore, prompt effect.

Strophanthin is a powerful, and sometimes dangerous, drug, but it should often be repeated more frequently than is usually done, that is, until a satisfactory effect such as is obtained after several days of digitalis administration by mouth is secured. The patient must be watched carefully for indications of severe poisoning, especially a high grade of heart-block, which can be released by atropin. The induction of auricular fibrillation should not be feared, as, when that occurs, the tachycardia will cease, and it may be transitory, the heart subsequently returning to the normal rhythm. Even if it persists it is often a conservative state and reduces the limits of response very slightly.

I have had only one other opportunity to use strophanthin in prolonged and regular tachycardia as most attacks cease spontaneously or are relieved by vagal pressure. This was in a woman, aged forty-three years, who was brought to Bellevue Hospital with bronchopneumonia. She stated that during the previous four

[2] Auricular Flutter, New York, 1914, p. 28.
[3] Jour. Amer. Med. Assoc., 1908, li, 655.
[4] Heart, 1910–1911, iii, 273.
[5] Loc. cit.
[6] Loc. cit.

years she had suffered from frequent attacks of rapid heart action which began and ended abruptly. The present attack, which began shortly after the onset of the pneumonia, had lasted five days. The rate of the heart was about 200 per minute, and it was extremely dilated. Her feet were swollen and the liver was pulsating. She was given an intramuscular injection of 0.5 mg. crystallin strophanthin, and as no effect was noted this was repeated in three hours. Within a half-hour after the second injection auricular fibrillation developed and her distress was greatly relieved. On the next day the edema was lessened and her liver had ceased to pulsate. Auricular fibrillation continued until her death two days later from vasomotor failure and venous stasis did not recur. An autopsy was unobtainable.

Summary. A case of paroxysmal tachycardia with the ventricular form of the venous pulse is reported. Strophanthin was administered many times during the attacks and they always ceased following it,—usually in about one hour. On several occasions transitory fibrillation of the auricle terminated attacks. Finally under the combined effect of digitalis and strophanthin permanent auricular fibrillation was induced and no more paroxysms have occurred. The case illustrates the close relation between paroxysmal tachycardia, auricular fibrillation, and auricular flutter.

Strophanthin, in repeated doses if necessary, is recommended for prolonged attacks of paroxysmal tachycardia.

THE EFFECTS OF EXERCISE ON THE NORMAL AND PATHOLOGICAL HEART; BASED UPON THE STUDY OF ONE HUNDRED CASES.

By Charles Spencer Williamson, B.S., M.D.,

professor of medicine and clinical medicine, college of medicine, university of illinois.

For a number of years the question of acute dilatation of the heart has been a debated one. Many attempts have been made to settle the question both by clinical observations and direct experiment, but these have led to no generally accepted conclusions. Until about a decade ago there was practically no difference of opinion on the subject. It was conceded that a normal heart when subjected to even relatively slight strains would dilate to a degree dependent upon the severity of the strain. If the heart were normal this dilatation was relatively soon recovered from—a sort of physiological dilatation. In the event of the heart already being weakened from disease this dilatation might become permanent.

This view of acute dilatation of the heart found its best-known exponent, at least in the German-speaking countries, in the Schotts[1] (Aug. and Theo.). These authors took the view that even relatively slight exercise, such as wrestling moderately or bicycle-riding of moderate rapidity and duration, was quite sufficient to produce a perceptible degree of dilatation in a normal heart. In 1890 Theo. Schott undertook to settle the question in a direct, experimental way. He recognized that in the cases reported clinically as instances of acute dilatation of the heart the heart muscle might not have been quite normal, hence such cases were not altogether free from the possibility of error. Schott, therefore, by the accepted methods of percussion, measured the outlines of the heart before and after exercise in wrestlers, and found that the heart outline actually increased, after only a very few minutes of wrestling, from 1 to 2 cm. in transverse diameter.

With the advent of the Moritz orthodiagraph the question was studied by this author along the same lines as Schott had done using, however, the newly invented instrument to determine the size of the heart. Moritz,[2] using four wrestlers and three bicyclists for his subjects, was unable to determine in them, after even very severe exertions, any dilatations such as Schott had found. At first sight it seemed as if the heart were really smaller after exertion, because the left edge of the heart was farther in; but this he considered to be due rather to a lowered condition of the diaphragm, that is, more of an inspiratory condition, allowing the apex to swing downward and inward. Lennhoff and Levy Dorn[3] carried on a similar series of experiments on wrestlers, but could not determine any trace of dilatation.

Aug. Hoffmann,[4] also using the orthodiagraphic method, came to the conclusion that dilatations of any noticeable degree do not occur in normal hearts. He quotes von Leyden in support of his position, inasmuch as the latter author had held that patients with acute dilatation of any considerable degree had but little prospect of recovery. Mendel and Selig[5] conducted tests on two wrestlers who wrestled to the point of exhaustion. One showed no dilatation and the other even showed a certain degree of contraction. Kienbock, Selig, and Beck[6] carried on investigations on the contestants in swimming matches, and found in 11 cases, 10 instances of acute diminution of the heart.

De la Camp,[7] after a series of experiments on both human beings and animals, came to the same conclusions as did Hoffmann.

[1] Verhandlungen d. IX Kongress f. innere Medizin, 1890.
[2] Münch. med. Woch., 1902 and 1905.
[3] Deut. med. Woch., 1905.
[4] Verhandlungen d. Kongress f. innere Medizin, 1902.
[5] Med. Klinik, 1907 and 1908; Wien. Med. Woch., 1907.
[6] Münch. med. Woch., 1907.
[7] Zeitsft. f. k. Med., 1903–1904, Bd. li.

His experiments embraced both normal and pathological cases, using the orthodiagraphic method to determine the size of the heart. In some normal patients who exercised to their limit of endurance on an ergometer he found only slight changes in the cardiac diameters, the largest (in two cases) being only 0.5 cm. in the sense of an increase. In his experiments on pathological cases he found that slightly weakened patients, such as those suffering from moderate tuberculosis, showed relatively little change after exercise. In a few hearts that were seriously damaged, more marked dilatations occurred. His animal experiments led him to the same conclusions. As a result of both human and animal experimentation, de la Camp concludes that acute dilatation of the heart occurs, even after maximal exertions, only when the integrity of the heart muscle is seriously impaired.

In 1908 Moritz,[8] still using the orthodiagraphic method, had arrived at the conclusion that the heart actually does grow smaller after exercise, and that even the pathologically dilated heart might diminish in size. Moritz even suggests that this latter fact might throw some additional light on the question as to whether hypertrophy or dilatation exists in a given case. On the other hand, Schott,[9] in 1897, repeated his previous experiments with wrestlers and bicyclists, using the roentgen-ray picture to determine the size of the heart, and again came to the conclusion that such exercise produces marked dilatation. Judging from the published report, his roentgen technique, even for that day, was not good, and his cases were too few in number to carry conviction as to the correctness of his results. In 1908 Schott[10] investigated the problem for the third time. In this series of experiments he used the orthodiagraph, and his results substantiated his early findings, for he concluded that "bodily exertion which is carried so far as to produce perceptible palpitation and marked dyspnea leads at last to acute dilatation of the heart."

Hornung,[11] who had opportunities of seeing a large number of cases of heart disease in the Sanitorium Schloss Marbach, examined with the orthodiagraph some 1100 patients in the course of seven years. Hornung was already aware of the occurrence of acute dilatation in the acute infections, since in 1900 he had reported cases in pneumonia. He considers acute dilatation in patients with even slight cardiovascular disorders as much more frequent than has hitherto been thought, and states that he has seen many such cases. According to him, very slight exertions or a temporary sojourn at a high altitude or even fright suffices to produce in those with already damaged hearts, acute dilatation. He considers,

[8] Münch. med. Woch., 1908, No. 14; 1908, No. 25.
[9] Deut. med. Woch., 1897, No. 14; 1897, No. 31.
[10] Münch. med. Woch., 1908.
[11] Berlin. klin. Woch., 1908.

however, that in normal individuals the question of acute dilatation is still (1908) *sub judice*. Hornung's results are directly opposed to those of his co-workers, and constitute virtually a return to the view of von Leyden and his school. Indeed, he goes further than von Leyden or even Schott ever did, in that he finds that in many cases merely psychical traumata can produce acute dilatation.

The opinion of Sir Clifford Allbutt,[12] whose essays on cardiac overstress rank among the earliest and most important contributions to this subject, should be of peculiar value, since in 1909 he writes again (in his *System of Medicine*) an extensive article upon this same theme. He says: "After a period of uncritical appreciation of physical signs, especially by the Nauheim school—and for such disorders as these at any rate over wrought therapeutical schemes—a reaction has set in, which, as is usual in the course of opinion where the facts are intricate, is veering to the opposite extreme. The researches of de la Camp and his colleagues, able and important as they are, carry us too far, if they dictate to us that by no voluntary effort are the dimensions of the heart substantially altered. Are not the orthodiagraphists in their turn assuming a somewhat unreasonable dictation which in the Nauheim school we have deprecated? In their valuable method I am personally unskilled, but my not infrequent opportunities of seeing the work of others convince me that as yet there is almost as much uncertainty in the appreciation of magnitudes by orthodiagraphy as by percussion. Of moving objects its pictures are fugacious and the apparent dimensions are still subject to deceptive space—relations." From this and many other similar passages it is evident that this author declines to accept at par the findings of the various workers with the orthodiagraph, and abides substantially by his early conceptions, albeit with a little more reserve as to the limitations of percussion.

The most recent work on the subject is that of Nicolai[13] and Zuntz, published in May, 1914, at a time when practically all of the actual work of this study had been completed. These authors experimented with normal subjects, causing them to work upon an apparatus (Tretbahn) so constructed as to closely imitate mountain-climbing. They strapped the plate holder to the patient's chest and arranged the apparatus so that, without stopping except for the actual exposure time, the subject could lean against a board, and thus a roentgen-ray picture could be taken actually during the exercise as well as before and after. They found the average transverse diameters to be: At rest, 12.8 cm.; during work, 13.2 cm. (increase 0.4 cm.); after work, 12.0 cm. (decrease 1.2 cm.).

According to these authors the diminution in the size of the

[12] System of Medicine, 1909, vi, 196.
[13] Berlin. klin. Woch., May 11, 1914.

heart occurs suddenly, within three seconds after the cessation of exercise, that is, in one or two beats the heart pumps itself empty. They do not lay special stress on the actual figures given, feeling that the margin of error may be considerable, but qualitatively they regard the result as absolutely correct. They adopted an exposure time of one-half second, in criticism of which it should be noted that with a pulse of about 70, such as would probably obtain with their subjects before the beginning of the exercise, this exposure would not include an entire cardiac cycle, hence in these plates they had no way of telling whether the exposure was taken in systole or diastole. Their pictures were taken with a tube distance of one meter, which is not enough to avoid serious distortion, which they attempt to allow for by calculating the enlargement due to the widely divergent rays, and then making the necessary substraction. Their experiments included only four subjects, all presumably normal.

The interpretation which Nicolai and Zuntz put on their work is that during the exercise the right side of the heart is extra well supplied with blood, owing to the activity of the skeletal muscles, and that to this is due the slight increase in the size during work.

This is not, they think, to be interpreted in any way as a sign of cardiac weakness. They believe that instantly after the cessation of exercise this centripetal flow stops in a large measure, and the volume of the heart then rapidly lessens, owing to the increased output of the heart keeping up for some time.

Because of the divergent conclusions arrived at by the authors above mentioned it seemed desirable that the entire question should be investigated afresh. Our work was begun in December, 1913, and finished in May, 1914.

In view of the rather contradictory findings of the investigators who used the orthodiagraphic method it seemed imperative, in any further research on the subject, to use a more objective method.

After careful consideration we believe that the teleroentgen method offers many unquestioned advantages over all other roentgen procedures, and this was, therefore, selected as the method of choice. The usual manner of taking chest exposures gives a considerable degree of distortion due to the nearness of the tube to the object, so that the latter is unduly magnified. As is well known, this false magnification becomes rapidly less with an increase of distance of the tube from the plate, so that with a distance of 200 cm. or even of 150 cm. it becomes a negligible factor. Schmincke[14] has shown that with the former distance the error in taking the silhouette of the heart is only about 1 mm. in each direction. In our experiments the distance of tube from plate was seven feet one inch (or 216 cm.), so that under the conditions of the

[14] Zentbl. f. Herzkrankheiten, 1911

experiment the enlargement due to this cause certainly does not exceed 1 mm. To all intents and purposes the outlines of the heart obtained by the teleroentgen method, with a tube distance of 216 cm., may be regarded as corresponding accurately with the actual anatomic outline of the organ. The most important problem was to be able to secure the outline of the heart during its diastole. Since tonus is a function of diastole, and since the degree of dilatation of the heart is, in last analysis, a question of its tone, that is, its condition in diastole, it follows that all determinations of the size of the heart should be made during its diastole. Manifestly this is impossible by even the most refined methods of percussion, and is exceedingly difficult with the orthodiagraph.

An important point in any method of determining the size of the heart by any of the various roentgen processes is to make the measurement in each case with the diaphragm in the same position, that is, at the same height. The importance of this will be appreciated when we reflect on the position the apex of the heart assumes in deep inspiration and in deep expiration. When the diaphragm is lowered in inspiration the apex swings downward and inward and the reverse in deep expiration, the apex being raised and pushed outward.

Moritz has called special attention to this movement of the apex and to its effect upon the transverse diameter of the cardiac silhouette. Of two measurements of the same heart under the same condition, one taken with the diaphragm in a position of maximum expiration and the other in a condition of maximum inspiration, the latter will be appreciably smaller, owing to the approximation of the apex to the median line. We have made a number of experiments along this line and find that the apparent difference in size due to different heights of the diaphragm may amount to 20 mm. or even more. *Any method of measurement which does not take the position of the diaphragm into accurate consideration cannot be regarded as satisfactory.* In our experiments maximum inspiration was selected as the phase for taking the exposures, since it is the phase of respiration most easy to determine and reproduce with accuracy. One special advantage of the teleroentgen method as used by us is that the position of the diaphragm can be accurately determined on the plate, and any error due to differences in its height may be readily recognized.

This is, of course, a practical impossibility with the orthodiagraphic method. In our work the time of exposure (two seconds) was so short that an appreciable effect on the size of the heart silhouette from the effect of the inspiratory effort would hardly be possible, and inasmuch as the hearts both before and after exercise were always taken while holding the breath in maximum inspiration, any possible change produced by the inspiratory effort itself would be the same in both instances.

Method of Procedure. The details of the method used by us were as follows: The tube distance remained the same throughout all the experiments, namely, 216 cm. (seven feet one inch). After experimentation upon seven people we decided upon the standing position for taking the pictures. In these cases, which were taken with the patient recumbent, the results were not so satisfactory as regards the control of technique, although the variations in size due to exercise were the same. These seven cases have not been, however, included in the tables. A plate holder was arranged so that it could be adjusted to any height by sliding up and down in a rabbeted frame. The patient was made to stand facing the plate holder and with the arms around the frame, so that the chest was held firmly against the plate holder. The chin rested on the upper edge of the holder. With everything in readiness, the patient having previously been stripped to the waist and the tube having been accurately centred beforehand, the patient was caused to take a deep inspiration, and then, while holding this phase, a two-second exposure was made. After the exercise the second exposure was made in precisely the same way, the apparatus remaining set up, just as it was for the first exposure. The patient remained stripped except for a sheet or a loose coat over the upper part of the body, so that it could be instantly removed and the second exposure made immediately after the cessation of the exercise. In this way we sought to avoid the possibility of overlooking any transient change in the heart's outline.

The Roentgen-ray laboratory is immediately adjacent to the stairs on which the patients were exercised, so that the exposure was usually taken before more than twenty seconds had elapsed after the completion of the exercise. The plates were then developed in the usual way. The exercise chosen for the experiments was stair-climbing. The considerations which led to this choice were the following: In order to make even a rough comparison of the energy put forth by different individuals it is highly important that the work they do should be of a nature to which they are accustomed, since, as is well known, a person doing a new and untried kind of work, for example, running a stationary bicycle, may, and usually does, put forth an amount of effort entirely out of proportion to the work actually accomplished. It is quite imperative that the work done shall be of a familiar nature. Stair-climbing meets these requirements, and has the additional advantage that the work done may be readily calculated in terms of the weight of the patient and the vertical height through which the weight is carried. It was, of course, quite impossible to have all the patients climb at the same rate of speed, but this was attempted, in a rough way, in the case of the normal individuals. The tests were so arranged that the subject ran, two steps at a time, at a dog trot, alternately up and down three long double flights of stairs until

he had gone to the limit of his endurance. After repeated preliminary trials it was found approximately how much a young healthy student could do, and it was demanded of each student that he do at least this and more if possible. In a few instances they gave out from exhaustion before doing the stipulated amount of work, and in practically all cases the subjects declared their inability to do more. A study of the pulse rates alone would suffice to show that the amount of effort put forth was in reality quite great. The fact is not lost sight of that athletes, under the stimulus of competition, may put forth much greater efforts than those in our tests, but such men are already trained in wind and limb and do not represent average conditions or subjects.

In the pathological cases the patient was caused to climb the largest number of stairs which seemed safe in his particular case, and at as rapid a rate as he could. In spite of watchful care several patients went beyond their limit and partial syncope developed. In these cases also it is believed that the work done represents about the maximum effort which the patient was capable of putting forth under any ordinary conditions of experiments.

Comparison of the Teleroentgen and Orthodiagraphic Methods. It may be freely granted that theoretically the orthodiagraphic method gives ideal results, but in spite of its theroretical superiority this procedure has serious drawbacks. The first of these is a considerable degree of subjectivity in the interpretation of the findings. Having to work in the dark, with considerable rapidity, on hearts beating at a rate of perhaps 140 to 170 per minute, it is easily comprehensible that, even to the expert, the results cannot always be satisfactory. When we further reflect that the patient after exercise is dyspneic and that the respiratory movements of the diaphragm are necessarily very rapid, it will be seen that this introduces a source of error almost impossible of elimination, since it would be extremely difficult for the patient to hold his breath at any phase of respiration for a sufficient time to permit of the outline to be marked in with a satisfactory degree of accuracy. Perhaps the most serious defect is this inability to be sure as to the position of the diaphragm for any given outline. It is possible that the somewhat greater length of time necessary to outline the heart with the orthodiagraph might be sufficient to allow any evanescent dilatation or contraction to escape. In this respect the method we have employed is vastly superior. A further difficulty with the orthodiagraphic method is that of always obtaining the outline during the same phase of the cardiac cycle, for example, during the diastole. If we consider the diminution in the transverse diameter during systole to amount to 0.5 cm., it will be seen that there is here the possibility of error to that extent. With the method we have employed this possibility of error is eliminated. A little reflection will show that

since, for our purpose, the diastolic outline is desired, that is, the maximum size of the heart, all that is necessary is to be sure that the time of exposure is sufficiently long to include at least one complete cardiac cycle. A two-second exposure time is sufficiently long, assuming even such a slow pulse rate as sixty per minute, to include at least two cardiac cycles, and with the fast pulse rates which obtain after exercise, for example, from 120 to 180, correspondingly more.

The diastolic outline is, therefore, the one obtained under such conditions. As a matter of fact, a double contour was never obtained, since the larger shadow completely encompasses the smaller. One objection which has been raised to the teleroentgen method is that the contours are not so sharp as they might be. Except in the case of exceedingly obese patients this has not proved to be the case, and in such patients it is equally difficult to obtain satisfactory outlines with the orthodiagraphic method. The right border, owing to its smaller range of movement and proximity to the chest wall, is, as a matter of course, always a little sharper and better defined than the rest, as has been found by nearly all observers. In a few cases, owing to extreme obesity or to some movement of the patient or to an imperfect plate, the outlines were not sufficiently clear, and such plates have been of course discarded.

In all our experiments the exercise and second plate were taken immediately after the first, so as to eliminate any possible error due to a different position of the diaphragm, and, therefore, the heart, consequent upon such condition as overfilled stomach, meteorism, etc.

The measurement of the heart's outline was taken in the manner generally recognized as the most reliable. With the plate in the shadow box the median line was drawn in with a T-square, the greatest distance of the heart's outline to the right and left of this median line noted, and the two measurements taken with an accurate millimeter rule. The sum of the two measurements is that given as the transverse diameter.

Classification of Patients. The grouping of the patients was done entirely on the basis of the ordinary methods of examination. For normal subjects, assistants and students were taken who had always been healthy and who were accustomed to engage in ordinary athletics, but no effort was made to pick men of unusual strength or athletic tendencies. In this group also were included patients with minor ailments who were otherwise in good physical condition and in whom the hearts were normal.

The second group consisted of patients with heart lesions in perfect compensation or patients in whom the ordinary examination disclosed no cardiac abnormality, but in whom it was fair to assume some degree of myocardial weakness as a result of severe anemia or

cachexia. The moderately advanced tuberculous cases, nephritis, etc., were also included in this group.

The third group consisted of cardiac cases with frank, but low to moderate grade decompensation, presenting such symptoms as dyspnea on slight exertion, with enlarged and tender liver, edema of the ankles, etc.

In all 125 cases were studied, but 25, for various shortcomings of the negative, such as variable height of the diaphragm, falling of the right cardiac border in the vertebral shadow, etc., were rejected. The results obtained in the remaining 100 cases are given in the following summaries. (N. B.—The detailed results, arranged in tabular form, are omitted here for lack of space, but will be found in full in the reprints.)

Group I: Summary.

Total number of subjects	38
Heart contracted	29
Heart dilated	3
Heart remained of same size	1

Maximum contraction, 23 mm.; average, 6 mm.
Maximum dilatation, 1 mm.; average, 1 mm.

In 29 of 33 cases exercise induced definite contraction of the heart, averaging 6 mm., and in 1 case a young, strong athlete, this contraction reached 23 mm. In only 1 case was the heart unchanged in size, and in only 3 did dilatation occur, and then only 1 mm. It is sufficiently obvious that these last figures are within the limits of error of the method of measurement employed. We may conclude, therefore, *that the normal heart responds to any exercise within its power by contraction.*

Group II: Summary.

Total number of subjects	57
Heart contracted	24
Heart dilated	25
Heart remained of same size	8

Maximum contraction, 14 mm.; average, 4 mm.
Maximum dilatation, 13 mm.; average, 3 mm.

It is evident that a considerable number of pathological cases with damaged hearts respond to exercise in the same manner as the normal heart, that is, by contraction. Of 57 cases, 24 contracted and 8 remained of the same size. On the other hand, about the same number, 25, dilated.

The average contraction was 4 mm., the average dilatation 3 mm. The maximum contraction was 14 mm., the maximum dilatation 13 mm. The relatively insignificant average amount of dilatation, 3 mm., is especially noteworthy. A perusal of the results shows that many hearts, with apparently normal findings,

in patients with various diseases, dilate after exercise, indicating their lessened tonicity.

GROUP III: SUMMARY.

Total number of subjects	10
Heart contracted in	6
Heart dilated in	4

Maximum contraction, 4 mm.; average, 2 mm.
Maximum dilatation, 4 mm.; average, 3 mm.

A study of the results obtained from the patients in the above group, all of them with manifest broken compensation, indicates clearly that there is a distinct tendency to contraction, this occurring in 6 out of 10 cases. The average degree of contraction, as would be expected, was small, 2 mm. On the other hand, in the 4 cases which dilated the average amount was only 3 mm.

Even to one thoroughly familiar with the reaction of the normal heart to exercise the results obtained in Group 3 is more or less of a surprise, since these show in the most striking way the extreme reluctance of the heart to dilate, even when there is already some degree of myocardial insufficieney present.

VALUE OF THE RESULTS FROM THE STAND-POINT OF FUNCTIONAL TESTING OF THE HEART. The writer has elsewhere[15] laid stress upon the value of exercise tests of the heart as supplemental to the routine examination. From these results it seems clear that a heart which dilates under exercise, which should be within its power, is certainly, functionally speaking, below normal. *Vice versa*, a heart, if normal, should contract promptly and definitely to exercise, so proportioned as to be well within its power. To attempt to draw numerical comparisons would be to exceed the limits of justifiable deduction.

Our results justify the statement that, in cases where the condition of the cardiac muscle is doubtful, considerable light may be shed upon its functional efficiency by correctly taken teleroentgen pictures before and after exercise. Bearing in mind the comparatively slight changes in size which occur, the most scrupulous care must be taken to see that the diaphragm height is the same in both negatives, as any material variation in this respect will cause an error so great as to completely vitiate the results.

CONCLUSIONS. 1. Owing to the great apparent variation in the size of the heart due to different heights of the diaphragm, any method which does not enable us to fix its exact position, and thus to be sure that its height before and after exercise is the same, is valueless.

2. The teleroentgen method, as employed by us, offers a highly accurate and perfectly objective method of determining the size of the heart, eliminating completely any possible error due to varying heights of the diaphragm.

[15] The Functional Testing of the Cardiac Powers, Lancet Clinic, 1914.

3. The results of our experiments show that: (*a*) The normal heart responds to any exercise within its power by a diminution in size; (*b*) About one-half of the pathological hearts, which are in good compensation, respond to exercise within their power, with a diminution in size; (*c*) Approximately one-half of the pathological hearts, with manifest, but low-grade broken compensation, respond in the same manner by some degree of diminution in size.

4. In only the most exceptional instances, if ever, are the differences in size due to acute dilatation, sufficient to be determined by even the most refined and subtle percussion.

5. The Roentgen-ray examination of the heart, before and after appropriate exercise, using the technique employed in this research, is capable of rendering valuable assistance in the estimation of the functional efficiency of the heart.

My sincere thanks are due to Dr. Adolph Hartung, instructor in roentgenology, College of Medicine, University of Illinois, for his generous assistance. The negatives of all the cases were made by Dr. Hartung, and to his skill and coöperation much credit is due.

My thanks are also due to Dr. Ernest S. Moore and Dr. Robert Mosser, instructors in the medical clinic, for assistance in the selection and observation of the cases.

DILATATION OF THE ARCH OF THE AORTA IN CHRONIC NEPHRITIS WITH HYPERTENSION.

By William H. Smith, M.D.,

and

Alson R. Kilgore, M.D.,

boston, massachusetts.

(From the West Medical Service of the Massachusetts General Hospital.)

This report is based on Roentgen-ray plates taken in the routine of clinical work at the Massachusetts General Hospital during the last eighteen months by Dr. Walter J. Dodd and Dr. George W. Holmes, to whom we are indebted for permission to use the records of the department. All the plates were taken at a distance of seven feet, that is, with practically parallel rays, thus allowing for quite accurate measurements of the shadows of the heart and great vessels.

With a series of about sixty normal plates available it is not practical to lay down accurate normal limits for the measurements of the transverse diameter of the great vessels, since many of the

plates are slightly distorted on account of not being taken accurately in the frontal plane, etc. The limits of 4.5 and 5.5 cm., however, include by far the largest number of normal measurements (see curve *a*, Fig. 1, of normals). It is fair to state that in no case did the great vessels measure more than 6 cm. in diameter in which there was not evidence of one of the following:

1. Syphilis (*i. e.*, aortitis).
2. Age over fifty years (*i. e.*, probable factor of arteriosclerosis).

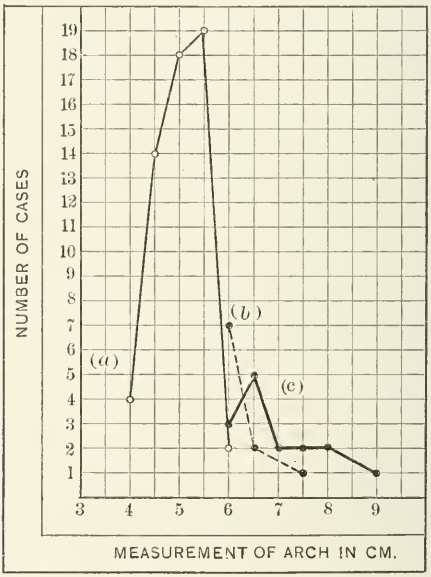

Fig. 1.—To show graphically the limits of arch diameters found in the conditions studied, obtained by plotting the number of cases found at each diameter and including all the cases which had had plates taken at seven feet without selection. *a*, ○——○——○ normal; *b*, ●---●---● cardiac disease with enlargement but without hypertension or syphilis; *c*, ●—●—● chronic nephritis with hypertension.

3. Other serious cardiac disease (*e. g.*, endocarditis or pericarditis with cardiac enlargement).
4. Hypertension (with more or less hypertrophy, *e. g.*, in chronic nephritis).

Therefore, great vessels measuring more than 6 cm. in diameter may usually be considered as dilated.

In this series, cases in which an increase in the diameter of the great vessels could be explained by either (1) syphilis or (2) arteriosclerosis of age have been ruled out, but it is striking to note how many cases of dilated arch remain to be classified under (3) cardiac disease with enlargement and (4) hypertension.

A. Dilatation of the Arch with Other Cardiac Disease.[1] There were ten cases with arches at the upper limit of normal or above (see curve *b*, Fig. 1), in which neither age, syphilis, nor hypertension could be found to explain the dilatation. (As an approximate index of the degree of cardiac enlargement the total transverse diameter of the heart is also given in Table I, *i. e.*, the distance of the right border from the median line plus the distance of the left border from the median line. The maximum normal total transverse diameter of the adult heart is given as 13.2 cm.[2]).

Table I.—Cases of Dilatation of Arch Associated with Other Cardiac Disorders.

Case.	Age.	Diameter of arch.	Total transverse diameter of heart.	Blood-pressure.	Diagnosis.
		Cm.	Cm.		
1	36	6.0	14.0	110	Chronic mitral endocarditis.
2	41	6.0	18.0	110	Chronic mitral endocarditis.
3	28	6.0	15.0	100	Chronic mitral endocarditis.
4	18	6.0	14.0	140	Chronic aortic endocarditis.
5	40	6.0	14.5	120	Hyperthyroidism with hypertrophy.
6	27	6.0	16.0	110	Chronic aortic and mitral endocarditis.
7	24	6.0	12.0	130	Chronic aortic and mitral endocarditis.
8	25	6.5	18.5	120	Chronic aortic and mitral endocarditis.
9	33	6.5	19.0	110	Pericarditis.
10	43	7.5	15.5	100	Adherent pericardium.

All of these cases, therefore, had some other definite cardiac lesion, and most of them had considerable increase in the heart size. Whether the measurements of the Roentgenograms represent the actual degree of dilatation of the arch, or whether some of the increase in diameter may be explained by distortion brought about by the cardiac enlargement, is a question which must be settled by autopsies, by Roentgen rays taken in several planes, etc. The point brought out is that many cases of cardiac disease without syphilis or hypertension show by Roentgen rays, great vessels whose diameter is at the upper limit of normal (6 cm.) or above.

B. Dilatation of the Arch with Hypertension. There were fourteen cases of chronic nephritis in which chest plates had been taken at a distance of seven feet. The blood-pressures ranged from 185 (one case) to 270, taking in each case the highest blood-pressure recorded while in the hospital. The average was 215. The ages were from 29 to 54, averaging 43. The transverse diameters

[1] A well-recognized condition; see McCrae, Dilatation of the Aorta, Amer. Jour. Med. Sci., 1910, cxl, 469.

[2] Groedel, Die Rontgendiagnostik der Herz- und Gefässerkrankungen, Berlin, 1912.

of the hearts varied from 13.5 (one case) to 19 cm., averaging 16 cm. (normal maximum 13.2 cm.).

All but three of these cases had great vessels whose transverse diameters measured over the normal limit of 6 cm., and in one of those measuring 6 cm. the Roentgen-ray diagnosis was "slight dilatation of the arch." In two cases the diameter was 7 cm.; in two cases 7.5 cm.; in two cases 8 cm.; and in one case 9 cm. (See curve *c*, Fig. 1, cases of chronic nephritis.)

TABLE II.—Cases Showing Dilatation of Arch with Chronic Nephritis and Hypertension.

Case.	Blood-pressure.	Diameter of arch.	Transverse diameter of heart.	Age.	Wassermann.
		Cm.	Cm.		
1	240	6.0	16.5	53	Negative.
2	190	6.0	16.5	38	Negative.
3	200	6.0	14.5	49	Negative.
4	230	6.5	14.0	54	Not done.
5	190	6.5	16.0	38	Negative.
6	270	6.5	17.5	45	Negative.
7	200	6.5	15.5	42	Negative.
8	220	7.0	13.5	35	Negative.
9	220	7.0	15.0	35	Negative.
10	185	7.5	18.0	29	Negative.
11	220	7.5	15.0	43	Negative.
12	190	8.0	19.0	43	Negative.
13	250	8.0	14.0	50	Negative.
14	220	9.0	18.5	48	Negative.

In the production of the varying degrees of dilatation of the arch in chronic nephritis four factors must be considered:

1. *Cardiac Hypertrophy*, since it has been shown above (see curve *b*) that (apparent) dilatation of the arch occurs in association with simple cardiac enlargement without hypertension. The diameter of the heart in each case has been plotted as a curve (*d*, Fig. 2), which shows a general but by no means constant increase of the size of the heart with the size of the arch. It will be noted, however, that the degree of dilatation occurring in chronic nephritis is much more than that found associated with simple hypertrophy (curve *c*), so that another factor must evidently be found.

2. *Hypertension* is an obvious factor. The degree of hypertension in each case when plotted as a curve, however (curve *e*, Fig. 2), does not show the greatest hypertensions to be associated constantly with the greatest degrees of dilatation.

3. *Duration of the Hypertension* is undoubtedly an important factor. Chronic nephritis, however, being a disease of notoriously insidious onset, it is almost impossible to determine accurately the duration of any given case from a hospital record, and it was found in this series that no constant relation could be demonstrated between the apparent duration and the size of the arch or

the size of the heart. It is probable that the degree of dilatation of the arch is related to all three factors: the degree and the duration of hypertension and to a small extent associated with the simple cardiac enlargement.

4. *Age.* It was found that the average age of the cases of chronic nephritis with arches measuring from 6 to 7 cm. was 45.5, while the average age of those measuring from 7 to 9 cm. was 40.4. This is contrary to what would be naturally expected, since dilatation of the arch is common, associated solely with the arteriosclerosis of age. It has been suggested as a tentative explanation

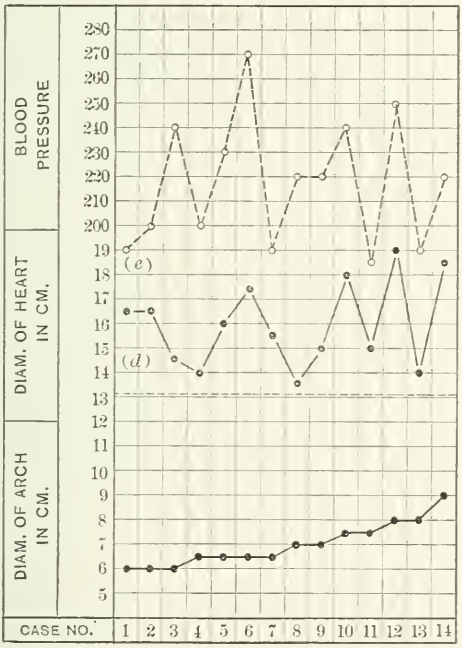

FIG. 2.—Blood-pressure and size of heart in each case of chronic nephritis, arranged in order of increasing diameters of arches. *d*, ●——●——● diameter of heart; *e*, ○---○---○ blood-pressure.

that when hypertension supervenes on an aorta already somewhat stiffened from age it does not stretch as easily as does a young one.

CONCLUSIONS. The point of interest brought out by these cases is the frequency of dilatation of the arch under the age of fifty years in non-syphilitic conditions, especially in chronic nephritis with hypertension. In such cases there were no aortas below the upper limit of normal diameter (6 cm.); three aortas at the upper limit of normal; and eleven aortas definitely dilated. This dilatation may be quite marked—especially in the younger patients—in seven, or 50 per cent., of these cases the diameter measured from 7 to 9 cm., or 1 to 3 cm. above normal.

ACRODERMATITIS CHRONICA ATROPHICANS: ITS SYMPTOMATOLOGY AND DIAGNOSIS.

By Fred Wise, M.D.,
AND
E. J. Snyder, M.D.,
OF NEW YORK.

(From the Dermatological Department of the College of Physicians and Surgeons, Columbia University, New York.)

Although the literature on the subject of acrodermatitis chronica atrophicans is already voluminous and quite comprehensive, more especially in the German language, still the incidence of a case of this type of atrophy of the skin nearly always kindles the interest of him who observes it; besides, rarely is a case presented before a body of dermatologists without exciting more or less controversial discussion as to the nosological position of the disorder. This statement applies chiefly to American dermatologists, for our European confrères seem to have the relationship between this and other types of atrophies pretty well fixed in their minds.

In a previous essay[1] we presented a clinical and histological study of a case of acrodermatitis chronica atrophicans occurring in a woman, aged fifty-eight years, who, aside from her cutaneous disorder, appeared to enjoy normal health. This case (Mrs. B. D.) was peculiar in that it presented an unusual abundance of the soft, doughy, tumor-like masses to which Herxheimer[2] called attention in his second paper on the subject, published in 1905. We attempted to show, in the article dealing with the above-mentioned case, that the clinical features of the dermatosis were sufficiently well-marked and characteristic to uphold the contentions of Herxheimer and Hartmann,[3] who differentiated this form of diffuse idiopathic atrophy of the skin from the clinical types akin to it.

Soon after the publication of this report a second case of the same malady came under the observation of Dr. MacKee and ourselves in the dermatological department of the Vanderbilt clinic. The remarkable and extensive changes which the skin of these patients exhibit, coupled with an etiology as yet shrouded in utter obscurity, incite us to record an additional case in the literature.

[1] Wise, Fred., Acrodermatitis Chronica Atrophicans; the Transition from Infiltration to Atrophy, Jour. Cutan. Dis., April, 1914, xxxii, No. 2.

[2] Further Observations on Acrodermatitis Chronica Atrophicans, Jour. Cutan. Dis., 1905, xxiii, p. 241.

[3] Ueber Acrodermatitis Chronica Atrophicans, Arch. f. Dermat., 1902, lxi, pp. 57 and 255.

The idiopathic progressive atrophies of the skin, while resembling each other in their clinical and histological aspects, have certain distinctive characters for each type. Although it is true that these characters may not always be easily differentiated, inasmuch as one type may appear to merge into another, or two or more types may occur together, it is also true that careful clinical observation and study will reveal certain differences which, though sometimes vague, are at other times quite patent, in various types of cutaneous atrophies which at first glance seem to be almost identical in course, appearance, and evolution.

Finger and Oppenheim,[4] in 1910, published a complete monograph on the subject of the cutaneous atrophies, in which they described, more or less exhaustively, most of the dermatoses in which atrophy plays a part as an essential symptom.

They divided the subject into two main groups, which, for the sake of better orientation, we will note here. The first group comprised all those cutaneous atrophies which are to be differentiated from the true progressive, chronic, atrophying dermatitides, and included:

1. Congenital atrophies.
2. Striæ and maculæ distensiæ.
3. Cutaneous atrophies following nerve lesions.
4. Cutaneous atrophies following chronic infectious diseases of the skin.
5. Senile atrophy and atrophy due to exposure to heat, cold, winds, etc. (element atrophy).
6. Xeroderma pigmentosum, blepharochalasis, kraurosis vulvæ.

The second large group included the idiopathic atrophying dermatitides, with the following sub-groups:

1. Dermatitis atrophicans progressiva idiopathica chronica diffusa.
2. Acrodermatitis chronica atrophicans.
3. Dermatitis atrophicans maculosa.
4. Combinations of dermatitis and acrodermatitis atrophicans chronica idiopathica diffusa, with dermatitis atrophicans maculosa.

It is with the second of these sub-groups, acrodermatitis chronica atrophicans, that this paper is concerned. This type of diffuse progressive atrophy of the skin was first described by Herxheimer and Hartmann[5] in 1902. It is an inflammatory disease, usually beginning on the backs of the fingers and the feet, progressing very slowly and insidiously upward; the inflammation gradually gives place to infiltration and tumor formation, which, in turn, is succeeded by the characteristic atrophy. In addition to the terminal atrophy there may also appear one or more hard, fibrous

[4] Die Hautatrophien, F. Deuticke, Wien und Berlin, 1910, containing most of the literature to date.

[5] Loc. cit.

nodules—"end products" of the disease—usually occurring in the vicinity of the knees and elbows. Pigmentations and depigmentations, telangiectases, desquamation, cutaneous hemorrhages, etc., also play a part in the symptom-complex. The disease is very chronic in its course, and is usually free from subjective symptoms.

The chief diagnostic points to be considered in acrodermatitis chronica atrophicans are the following:

1. The morbid changes usually begin on the backs of the hands and feet and slowly advance upward toward the knees and elbows in a centripetal manner. Hence the name "acrodermatitis," from the Greek "acra," extremity.

2. They are accompanied by well-marked inflammatory and infiltrative formations, which culminate in atrophy. This atrophy is of the peculiar "wrinkled cigarette-paper" type, to which Jadassohn[6] applied the term "anetodermie." The skin appears transparent, loose, wrinkled into fine parallel folds, has lost its elasticity, and can be easily raised from the underlying tissues. It has a silky or velvety feel. The color is rose red or bluish red. The subcutaneous fatty tissue is absent. The underlying veins and tendons shine through the translucent skin.

3. The occurrence of the so-called "ulnar band," to which Herxheimer[7] first called attention. It consists of a strip of inflamed skin, running up the forearm from the wrist to the elbow, usually overlying the ulnar bone. An analogous band may appear on the leg. It occurs as a more or less circumscribed, edematous, or infiltrated band of inflamed skin, varying in length and breadth. In consistency it may be soft and doughy or hard and resistant. The color may be a bright or a dusky red or it may be violaceous. The surface may be tense or wrinkled. It is present during the stage of infiltration and later gives place to the characteristic atrophy. This ulnar band seems to be peculiar to acrodermatitis chronica atrophicans. It is present in the patient who forms the subject of this report, and was described in the case reports of Herxheimer and Hartmann,[8] Bruhns,[9] Lehmann,[10] Baum,[11] Leven,[12] Rusch,[13] Hertmanni,[14] Finger and Oppenheim,[15] Neumann,[16] and others.

4. In the majority of cases of acrodermatitis chronica atrophicans there appears to be an area of skin which seems to be almost

[6] Atrophia maculosa Cutis, Zweiter Kong. Deutsch. dermat. Ges., 1891.
[7] Loc. cit. [8] Loc. cit.
[9] Ueber idiopathische Hautatrophie, Charité Annalen, 1901, xxv.
[10] Ibid., Inaug. Diss., Leipzig, 1902.
[11] Acrodermatitis Chronica Atrophicans, Arch. f. Dermat., 1903, lxiv, p. 446.
[12] Ibid., 1903, lxv, p. 247.
[13] Ueber idiopathische Hautatrophie und Sclerodermie, Dermat. Zeitsch., 1906 xiii, p. 749.
[14] Verh. X Kong. Deutsch. dermat. Ges., 1908, p. 290. [15] Loc. cit.
[16] Lehrbuch der Hautkrankheiten, 1880, 5th ed.

immune from the advances of the malady. It consists, roughly speaking, of a triangle of the integument surrounding the genitals, bounded above by Poupart's ligament and at the sides by the anterior and inner aspects of the upper third of the thighs. Such an area of non-affected skin is illustrated in the photograph accompanying our paper.[17]

These four diagnostic points are by no means constant factors in the symptomatology of the disease; indeed, they rarely occur simultaneously in the same patient. The morbid changes which the integument undergoes are manifested by a slow, but nevertheless constant and progressive alteration in the disease picture; these changes begin with an edema and inflammation, after which follow the infiltration and the terminal atrophy. Each of the various pathological phases of the disease—inflammation, infiltration, atrophy—may involve a period of months or years in their evolution and development. It must be borne in mind that patients have presented themselves for treatment or observation in whom the disease has existed anywhere from a few weeks (Herxheimer and Hartmann) to a great many years (forty years in Wise's case). It is evident, therefore, that a given case may present only one or two of the characteristic points mentioned above, the other features having long since disappeared. The peculiar "ulnar band," for example, may persist for a certain number of weeks, months, or even years without ever having come under the physician's observation. Many of the reported cases have presented themselves long after the subsidence of the active morbid changes, and in whom the terminal atrophy and anetodermia are the only characteristic remaining features of the dermatosis.

On the other hand it may be well-nigh impossible for the most astute diagnostician to recognize the malady in its earlier stages. A chronic edema and inflammation of the backs of the hands, or of the feet, persisting for a number of months without subjective disturbances, may be interpreted in a number of different ways; not until the advent of infiltrative lesions, accompanied by or culminating in atrophy of the affected integument, is there a likelihood that the true nature of the disease would be recognized. Thus, Ehrmann[18] and Weidenfeld[19] have reported instances in which the disease was ushered in by acute swelling and inflammation of the integument, resembling lymphangitis and erysipelas.

It follows, therefore, that in order to formulate a rational symptom-complex of acrodermatitis chronica atrophicans it is necessary to study and compare a number of cases presenting the various evolutionary phases or cycles of the disease, its localization, areas of predilection, mode of progression and termination.

[17] Jour. Cutan. Dis., April, 1914.
[18] Ausgedehnte idiopathische Hautatrophie, Wien. klin. Woch., 1909.
[19] Atrophia cutis idiopathica, Wien. dermat. Ges., November, 1909.

Shortly after the completion of our studies of the case of Mrs. B. D. (*loc. cit.*) there appeared at Professor Fordyce's clinic a second case (Mrs. H. L.) of acrodermatitis chronica atrophicans, also in a middle-aged woman. This patient was presented by Dr. MacKee before the New York Dermatological Society at its October, 1913, meeting.[20] A brief report of the case was subsequently published.[21] The preliminary routine examination of this patient disclosed the interesting fact that her blood showed a positive Wassermann reaction and that a marked glycosuria was present. She had, however, neither cutaneous nor visceral symptoms referable to either syphilis or diabetes at the time she came under our observation.

FIG. 1.—Showing anetodermia of thighs and knees, scleroderma-like appearance of legs and ulceration around ankles. (Patient, Mrs. H. L.)

The marked resemblance in the appearance of this patient to that of our first case was striking: the clinical picture which her skin presented possessed so many points of similarity to that of our first patient that one might be almost justified in saying that the one description may apply to both cases if we except the tumor-like, infiltrative masses which appeared on the thighs of our first patient. In addition, however, the second patient interested us on account of the presence of the "ulnar band," mentioned above as being one of the characteristic features of the dermatosis from which she was suffering.

CASE.—Mrs. H. L., aged fifty-four years; married at nineteen. She was born in Stockholm and came to this country when twenty-five. Her family history was negative. She was the only member of the family afflicted with a skin disease.

Personal History. Her first child was born within a year after marriage. Then followed five successive normal pregnancies; of these, two resulted in the birth of healthy children, while three child-

[20] MacKee, Case Demonstration for Dr. Fordyce, Jour. Cutan. Dis., February, 1914, xxxii, No. 2, p. 143.

[21] Jour. Cutan Dis., February, 1914.

ren were said to have died at birth; the cause of the deaths was not ascertainable. She had had no miscarriages. Three of her offspring are living and said to be healthy. The husband is living and apparently in normal health. Twenty years ago she had an attack of gall-stone colic, accompanied by severe gastro-intestinal disturbances. Fourteen years ago she was treated for a severe attack of jaundice at the Long Island College Hospital. No operation was performed. A little over two years ago she had an attack of pneumonia; since that time she has been afflicted with periodic

Fig. 2.—Showing "immune area" below Poupart's ligament; anetodermia of knees and thighs. (Patient, Mrs. H. L.)

attacks of asthma, bronchitis, and articular rheumatism. Shortly after her recovery from pneumonia examination of the urine revealed the presence of glycosuria. Menstruation ceased at the age of forty-eight.

Physical Examination. The patient is a tall, heavy-framed, obese woman, weighing over 200 pounds. Examination of the thoracic viscera (performed by Dr. Kent) revealed the presence of a rather severe bronchitis and asthma. The abdominal viscera were impalpable, due to the woman's obesity. The blood picture

was normal. The Wassermann test (performed by Dr. Jagle) was positive. The urine, examined on several occasions, presented varying small quantities of albumin and sugar. The patient has a florid complexion and her general health is fair. The hair, teeth, and nails are normal.

The cutaneous changes began about twelve years ago. They were ushered in by the appearance of reddened, inflamed, and edematous, slightly elevated, circular and oval patches of skin over the dorsal surfaces of the feet and on the anterior portions of the lower half of the legs, just above the ankles. There was a moderate amount of scaling. Itching was slight. Similar inflamed areas soon made their appearance on the upper half of the legs and on the thighs; these gradually coalesced and spread upward, toward the groins and buttocks, until practically the entire integument of both lower extremities and buttocks was involved in the process. These areas of inflammation, therefore, began to appear at the distal portions of the extremities and, by their coalescence, spread centripetally toward the trunk. The process seemed to be arrested a few inches below Poupart's ligament, anteriorly, thus leaving a triangular portion of the upper and inner aspects of the thighs free of the disease. After persisting, for an indefinite number of months, in the form of red, swollen, and inflamed patches, these areas would assume a purplish or violaceous hue, becoming more or less resistant to the touch, and somewhat elevated above the as yet unchanged surrounding integument. By the time that fusion of the patches had occurred the affected skin had assumed a dark-red, purplish hue, had become glossy, parchment-like, wrinkled, and dry, especially around the knees and ankles. After a lapse of two or three years (the patient's narrative was very indefinite), the skin around the ankles and

FIG. 3.—Showing anetodermia of thighs and buttocks and tense sclerodermia-like skin of legs. (Patient, Mrs. H. L.)

over the shins changed to a yellowish tint and became hardened and bound down over the underlying tissues, while the skin around the knees, on the contrary, became loose, folded, and flaccid. At the same time the superficial veins and tendons began to shine through the skin. Around the knee-joints, on the calves of the legs and on the thighs and buttocks, the skin became at first reddish pink, then darker red, finally assuming a purplish and violaceous hue; this discoloration and accompanying change in

FIG. 4.—Showing the "ulnar band" of right forearm; atrophy of the skin of the hands. (Patient, Mrs. H. L.)

the texture of the skin gradually extended upward until it reached nearly to the waist line at the sides and on the back. About two years ago an ill-defined patch of inflammatory redness made its appearance on the dorsum of the right hand, followed soon after by a similar patch on the left hand. Since then the same changes appeared on the ulnar aspect of the right forearm, running toward the elbow in the shape of a wide band or strip. This ulnar band seems to have developed during the last few months. On the lower extremities the process appears to have come to a standstill. Now

and then small ulcers would appear on the legs and feet as a result of scratching and infection. The pruritus has always been moderate in severity.

Examination. The affected portions of the integument were distinctly atrophic. The appearance, however, of the various areas of atrophic skin was by no means a uniform one. On the dorsum of the feet, around the ankles and over the tibiæ, the skin was waxy, glistening, smooth, yellowish, and "bound down" over the underlying tissues. To the touch it was hard and resistant, resembling the condition seen in ordinary sclerodermia. Over the

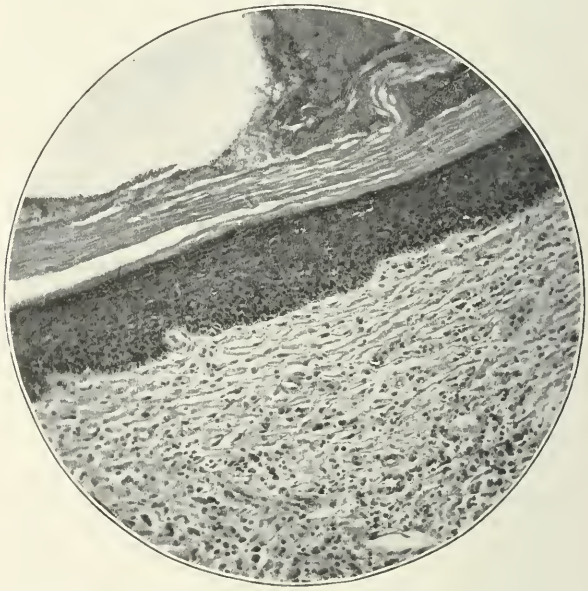

Fig. 5.—Showing hyperkeratosis, loss of interpapillary pegs, absence of papillæ, edema of collagen, lymphocytic infiltration of the corium.

calves of the legs, on the thighs and buttocks, and in the popliteal spaces the integument was thin, more or less wrinkled, flaccid, reddish pink in color and transparent, permitting the underlying veins to shine through as tortuous, blue strands, varying in width and in prominence. Around the knee-joints the skin seemed to be redundant, hanging in loose folds with the patient in the erect position; the surface showed a fine, parallel wrinkling, giving to it a characteristic silky appearance; the color was rose red; to the palpating finger the skin gave a velvety impression, as though it were loosely distended with air or water. When a fold was lifted between the fingers and then released an utter lack of resiliency was manifested. The entire integument of the lower extremities and the buttocks was implicated in this atrophic process, with

the exception of a small triangular area on the inner aspect of the thighs, just below the groins. The upper limiting border of the process showed a somewhat abrupt line of demarcation.

On the buttocks and on the anterior and posterior surfaces of the thighs there were twenty-five to thirty small, rounded, slightly elevated subcutaneous nodules, varying in size from a lentil to that of a pea. They were barely visible, their color differing but little from that of the surrounding integument; but on palpation they could be made out without difficulty, on account of their fleshy, semisolid consistence.

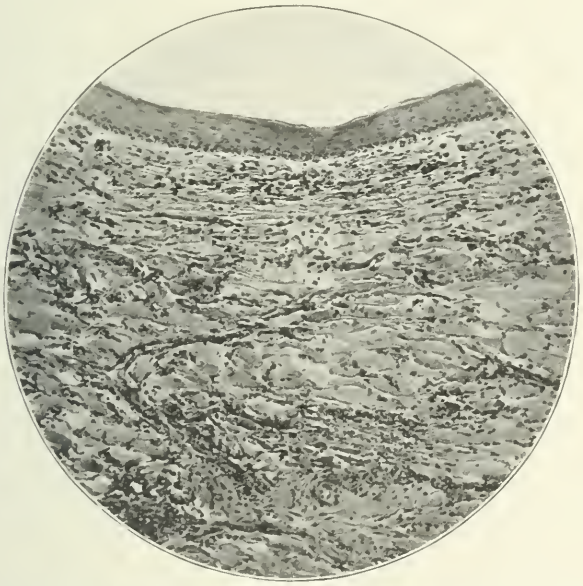

FIG. 6.—Showing similar changes as in Fig. 5, but with advanced atrophy of the epithelium.

The backs of the hands presented a smooth, translucent, atrophic skin, with numerous dark-brown lentigines and tortuous veins underneath, which, together with the tendons, shone through the integument.

Over the ulnar aspect of the right forearm a well-defined, partly erythematous and partly pale, atrophic band of skin was present, extending from the dorsal surface of the wrist to the elbow. With the exception of a small, atrophic patch half-way between the wrist and elbow this area was rose red in color, smooth, glistening, somewhat translucent, and showing a tendency to become bound down to the underlying tissues. There was no palpable infiltration. At the elbow, with the arm fully extended, the characteristic "cigarette-paper wrinkling" was present. Here the skin resembled

the appearances described as being present around the knee-joint: the integument was loose, pink, wrinkled, flaccid, and appeared to be redundant. The edges of this atrophic band merged gradually with the normal skin of the forearm, showing only an indefinite line of demarcation between healthy and diseased skin.

There was complete absence of hair follicles and glandular orifices in the diseased areas, lending to the skin the peculiar "naked" appearance characteristic of diffuse atrophies.

The appendages of the skin were normal, as were also the visible mucous membranes. Dentition was normal. There was no adenopathy.

The patient's urine was examined frequently, and under a moderately restricted diet it remained free from the abnormal constituents which it contained when she first entered the clinic.

Histopathology. Sections for histological study were removed from the skin of the lower third of the flexor surface of the thigh, above the popliteal space. One large piece of skin, together with the subcutaneous tissue, was excised under 1 per cent. cocain solution. It consisted of a small nodule with its surrounding atrophic integument. The tissue was fixed in 10 per cent. formalin solution, dehydrated in alcohol and acetone, imbedded and cut in paraffin. The sections were stained with hematoxylin-eosin, polychrome-methylene blue, Weigert's elastic-tissue stain, Hansen's stain, and hematoxylin-orange G.

Two distinct varieties of pathological changes were readily demonstrable—namely, atrophy and fibrosis. One merged into the other, some areas showing advanced fibrosis, while in others the atrophy was the predominating feature. In the latter there were small areas of round-cell infiltrations, the remnants of the hypertrophic stage of the dermatosis.

In the stratum corneum there was a marked hyperkeratosis, manifesting itself by the laminated arrangement and the distinct separation of the horny layer. The stratum lucidum was poorly defined, being absent in many places. The stratum granulosum consisted of two or three layers of cells, a large number of which showed distinct vacuolization; many nuclei appeared intact, resisting the keratohyalin degeneration. The stratum spinulosum was attenuated, and here, also, many cells showed vacuolization. The intercellular spaces were much narrowed, the cell walls lying almost adjacent to each other. Marked degeneration was manifest, some of the nuclei failing to take the stain. The basal-cell layer, while intact in some places, had in many areas lost its columnar shape and regular arrangement, the protoplasm showing extensive cloudy swelling. There was a total loss of interpapillary pegs, the junction between epithelium and derma appearing almost as a straight line.

In the pars papillaris of the corium there was a total absence of

papillæ and marked degeneration of the collagen, the few remaining degenerated fibers showing a fine fibrillation, the fibers being widely separated and edematous. Scattered throughout this area were seen small mononuclear lymphocytes, together with many plasma cells. The bloodvessels showed distinct endothelial proliferation, the walls of the smaller ones being markedly thickened. The infiltration was not more pronounced in the vicinity of the bloodvessels than elsewhere. There was complete absence of elastic tissue in the upper portion of the pars papillaris; lower down a few fine fibers, showing multiple fractures, were still present.

In the pars reticularis the collagenous material was almost entirely replaced by edematous fibrous tissue, the small-cell infiltration being less pronounced than in the pars papillaris. This region showed areas of fibrous tissue arranged in a roughly stellate manner, around a tiny central fibrous nodule. Here and there were seen a few areas of circumscribed cellular infiltrations, consisting of lymphocytic and plasma cells, together with a few fibroblasts. Marked endothelial and perithelial proliferation was seen in some of the bloodvessels in these infiltrated areas as well as dilatation of the lymph spaces. The walls of the bloodvessels were thickened, some of their lumina being totally obliterated.

There was a total absence of hair follicles and sebaceous glands, while the remaining coil glands showed marked degeneration, the epithelium being absent in a large number of them. A considerable cellular infiltration was present around the coil glands, composed of plasma cells and lymphocytes. The arrectores muscles were few in number and showed extensive cloudy swelling and atrophy. The elastic tissue was markedly reduced throughout, the still remaining fibers being very fine, showing multiple fractures and cloudy swelling. The subcutaneous fat was present in normal amount.

This histological picture is almost the exact counterpart of many, if not most, of the microscopic appearances of the sections obtained from this type of atrophy, as recorded in the literature. It is practically identical with the findings recorded in our first patient, with this exception: In Case 1 we examined sections showing three stages of the disease—namely, hypertrophy, atrophy, fibrosis; in Case 2, the hypertrophic or infiltrative stage of the malady having run its course, we have left only the final atrophy and fibrosis. Evidences of the preëxisting hypertrophic stage were, however, manifested also in our second patient by the presence of the small areas of round-cell infiltrations as described above.

Clinical Considerations. If we compare the dermatoses presented by our two patients from a clinical point of view, we are at once impressed by the fact that the hypertrophic lesions, which comprised the most interesting feature of Case 1, were so few and scattered in our second case that they may have passed

by unnoticed had they not been sought for. Such a circumstance adds added emphasis to what has already been pointed out—namely, that the disease presents totally different types of lesions, depending upon its evolutionary states or cycles of development. In our second patient the transition from hypertrophy to atrophy and anetodermia was probably a much more rapid process than in the patient we described in our first report. The existence of the hypertrophic lesions in Case 2, small and inconspicuous though they may be, again supports the contentions of Herxheimer and Hartmann, who declare that the atrophic phenomena are, at some time or other in the course of the disease, preceded by infiltrative lesions. On section these infiltrations show characteristic cell aggregations of lymphocytes and plasma cells. They must not be confounded with the peculiar fibrous nodules, which occur in the final stages of some cases of acrodermatitis chronica atrophicans (Ketron[22]).

The occurrence of sclerodermia-like areas on the lower extremities of many cases of the disease is a subject which has aroused much interest among those who have studied this dermatosis. Numerous instances have been recorded (Finger and Oppenheim,[23] Herxheimer,[24] Arndt,[25] Heuck,[26] Kingsbury,[27] Kanoky and Sutton,[28] and many others). In nearly all long-standing cases of the disease we are confronted with two types of atrophy, which, clinically, are diametrically opposite in appearance. The skin of the knees, for example, presents the picture of a rose-red, flaccid, wrinkled and folded, translucent and velvety type of atrophy—the anetodermia of Jadassohn. The dorsum of the feet and the lower legs, on the contrary, are covered by an envelope of skin which is hard, tense and drawn, bound down, somewhat opaque, waxy or pale yellow, smooth and glistening—a sclerodermia-like form of atrophy. In the first type the redundant skin may be readily lifted between the fingers; in the second the tense skin cannot even be grasped between the fingers or lifted from the underlying tissues. As Finger has pointed out, the occurrence of these sclerodermia-like areas in acrodermatitis chronica atrophicans has been the cause of frequent errors in diagnosis, many of the cases having been relegated to the sclerodermia group of dermatoses (Jąkobson,[29] for example).

"With regard to the relationship existing between anetodermia

[22] Dermatitis Atrophicans, with Report of a Case showing Fibroid Formations, Urol. and Cutan. Rev., 1913, i, p. 286.

[23] Loc. cit.

[24] Loc. cit.

[25] Verh. d. X Kong. deutsch. Dermat. Ges., 1908, p. 351.

[26] Acrodermatitis Chronica Atrophicans cum Sclerodermia, Ikon. Dermat., 1907, ii, plate x.

[27] Acrodermatitis Chronica Atrophicans with Sclerodermia, Jour. Cutan. Dis., September, 1907.

[28] Jour. Cutan. Dis., 1909, xxvii, 556.

[29] Berlin. dermat. Ges., 1906, v; Dermat. Zeitsch., 1906, xiii, p. 873.

and sclerodermia," says Finger,[30] "we have already called attention to the fact that a certain group of cases, the so-called morphea of French and English authors, give the impression of being transitional stages between the two diseases. It would be necessary to demonstrate a more intimate relationship between these two processes to convince me that anetodermia and sclerodermia may exist conjointly in the same individual. Their simultaneous occurrence would point to a common etiology. Such, however, is not the case. We have mentioned the fact that the diagnosis of sclerodermia has been made erroneously with reference to the infiltrated lesions of acrodermatitis chronica atrophicans as well as the tense forms of atrophy which occur in the course of diffuse anetodermia in those areas in thich the skin is naturally ("physiologically") more or less tense and drawn—namely, the dorsum of the foot and the lower leg, anteriorly. After a thorough perusal of the literature, I am unable to convince myself that a combination of the two forms of tissue changes may coexist; and if such a case does occur, it is an open question whether an etiological factor is common to both, or whether we are dealing merely with a coincidental appearance of two unrelated dermatoses . . . Taking into consideration the fact that all of the so-called atrophies begin with inflammatory phenomena, it would seem wiser not to employ the term "atrophies," but rather "atrophying dermatitides," to designate the two groups—namely, (1) anetodermias; dermatitides culminating in flaccid atrophy; (2) dermatitides culminating in tense atrophy."

Róna,[31] on the contrary, seemed to look upon the tense, bound-down, atrophic areas in acrodermatitis chronica atrophicans as being a true sclerodermia. In a discussion on the chronic atrophying dermatitides, he states: "To what extent sclerodermia and acrodermatitis atrophicans are inter-related, is a question which can be decided only after much further study, especially with relation to etiology. There seems to be little doubt, however, that the same pathogenic factor may give rise to the cutaneous changes resulting in typical sclerodermia, as well as typical acrodermatitis, for twelve cases have already (1908) been recorded in which the two diseases occurred simultaneously in the same individual."

Oppenheim[32] presented a patient with the sclerodermia-like areas on the lower legs, before the Xth Congress of the German Dermatological Society. He excised a piece of skin from the dorsum of the foot, in an area which presented the transition from the dense, yellowish to the soft, wrinkled and reddish integument;

[30] Die Hautatrophien (Atrophia diffusa, Anetodermie, Atrophia maculosa) und deren Verhaeltnis zur Sklerodermie, XVI Internat. Cong. Med., Budapest, 1910.

[31] Acrodermatitis Chronica Atrophicans, Verh. d. X Kong. Deutsch. dermat. Ges., 1908.

[32] Vehr. d. X Kong. Deutsch. dermat. Ges., 1908.

that is, a section in which two coexisting morbid processes were manifest to the naked eye.

The histological examination of the transitional portion of this section presented the following changes: absence of papillæ; attenuation of the epithelium over the atrophic area; almost normal epithelium over the thickened area. The connective tissue of the cutis was rather dense in the upper portions; the bloodvessels in the atrophic area were dilated, showed only moderate infiltration, their walls being but slightly altered; in the thickened portion there was much greater infiltration and no dilatation of the bloodvessels.

The chief changes affected the elastic tissue. In the atrophic portion this was totally absent in the upper layers of the cutis, but in other areas there were small islands of elastic fibers which showed structural changes; they were thickened, clumped, failed to take the elacin stain, but in the deeper layers of the cutis, they appeared to be normal. In the thickened portion the elastic fibers in the cutis were preserved up to the epithelial border; they were delicate, tortuous and wavy, and took the stain in a normal manner; there was a sharp line of demarcation between the areas in which the elastic fibers were present and in which they were absent.

"The significance of these histological findings point to the existence of a scar-like tissue, which may develop, as the result of secondary influences, from the atrophic tissue. We cannot regard these areas in the light of a sclerodermia on account of the absence of increase in collagen, absence of papillæ, and lack of bloodvessel changes; nor can we regard it as an atrophic stage, on account of the preservation of the elastica and because the clinical picture is strongly against such an assumption."

Evidently the question as to the true nature of the sclerodermia-like areas in acrodermatitis atrophicans will eventually be determined by further laboratory investigation. For it must be admitted that those observers who look upon them as being ordinary sclerodermia, base their opinion on clinical grounds alone.

The "ulnar band" and its analogue on the calf of the leg is so characteristic of the disease that it must be considered an important diagnostic factor in the differentiation of acrodermatitis atrophicans from other forms of diffuse cutaneous atrophies. Its absence, as has already been pointed out, is of little diagnostic significance, while its presence is a strongly corroborative symptom of the disease. Hertmanni[33] alone presented a series of seven consecutive cases from his clinic, in each of which the ulnar band was a prominent symptom.

As to the etiology of the disease, nothing is known definitely.

[33] Acrodermatitis Chronica Atrophicans, Verh. d. X Kong. Deutsch. dermat. Ges., 1908.

Oppenheim[34] thinks it may be partly due to intra-uterine pressure. A nervous origin, a tuberculous origin, and disturbances of internal secretions have all been considered by many authors. The existence of a transient glycosuria in our patient is probably an unrelated phenomenon, as the cutaneous changes began about ten years before any abnormal constituents in the urine were discovered. The patient gave a positive Wassermann test, but no other evidences of syphilis were discoverable. The coexistence of the disease with syphilis has been recorded on several occasions (Fordyce,[35] Grosz[36]). No definite conclusions can, of course, be drawn from such isolated instances.

The prognosis as to life is good. The disease is usually free of all subjective sensations, barring occasional itching, which is readily relieved by ordinary antipruritic applications. The majority of the patients seem to enjoy ordinary good health. The disease does not seem to shorten life, nor does it seem to make its victim more susceptible to intercurrent affections.

The treatment is purely palliative. In the early stages the application of dry heat, combined with injections of fibrolysin, are said to have given promising results. Patients suffering with pruritus and ulcerations on the legs, occurring as the result of malnutrition of the tissues, are treated by ordinary remedies, with good results. Arsenic and thyroid gland have been employed empirically.

Conclusion. We have, in acrodermatitis chronica atrophicans a distinct clinical variety of diffuse, progressive, atrophying dermatitis, possessing certain characteristic and more or less constant features, by means of which it may be differentiated from similar cutaneous pictures. These features are: (1) The presence of early inflammatory and infiltrating lesions, preceding or occurring together with atrophic changes; (2) the first evidences of the malady appearing usually on the hands and feet and progressing centripetally toward the trunk in an exceedingly slow and insidious manner; (3) the occurrence of the ulnar band or its analogue on the calf of the leg; (4) the relatively "immune area" below Poupart's ligament; (5) the anetodermia, most pronounced around the knees and elbows.

We extend our thanks to the staff of the dermatological clinic for its kindness in preparing sections, photographs, and photomicrographs of our case; and for the privelege of making use of the material from his clinic, we are greatly indebted to Prof. J. A. Fordyce.

[34] Etiology of Acrodermatitis Chronica Atrophicans, Wien. klin. Woch., 1912, xxv, p. 367.

[35] Symmetrical Cutaneous Atrophy with the Coincident Development of Syphilis, Jour. Cutan. Dis., 1904, xxii, p. 155.

[36] Atrophia maculosa auf dem Boden luetischer Effloreszensen, Wien. dermat. Ges., February, 1908.

THE SEQUENCE OF THE PATHOLOGICAL CHANGES IN ACUTE APPENDICITIS AND APPENDICULAR PERITONITIS.

By E. MacD. Stanton, M.D., F.A.C.S.,
SCHENECTADY, N. Y.

The study upon which this paper is based was originally undertaken with the idea of tracing the progress of the processes of inflammation and repair in cases of acute appendicitis both as regards the primary appendicular inflammation and the complicating peritonitis. During the course of the study I have examined microscopically 539 appendices removed during or within ten days following an acute attack, and I have studied the gross pathology as found at operation in more than fifteen hundred cases of appendicitis. In every instance the pathological data has been classified especially with reference to the duration of the symptoms previous to the time of the observation of the pathological conditions. As regards the appendicitis itself, the time was figured from the first onset of symptoms while as regards the more extensive peritoneal involvements it was found necessary to determine not only the time of the beginning of the attack but also approximately the time of occurrance of any exacerbations of peritoneal symptoms.

When the lesions are studied in this way in a sufficiently large series of cases the progress of the processes of inflammation and repair can be readily traced. Furthermore, it is apparent that most of the so-called varieties of acute appendicitis represent only different stages of development of the inflammatory process, and in spite of minor variations in the intensity and extent of the destructive process there is found to exist a striking general similarity in the fundamental pathological changes as they occur at each of the succeeding periods following the onset of symptoms.[1] In fact, if we stop viewing the appendices removed at operation as museum curiosities and study them as examples of a disease process, grouping them according to the day of the disease in which they are removed, it is surprising how fundamentally alike are the specimens removed during each succeeding day of the attack.

[1] We frequently hear statements to the effect that in appendicitis it is often impossible to predict with any degree of accuracy from the clinical symptoms the pathology existing in the abdomen. This is true as regards diagnoses based on the physical findings alone, but it should not be true as regards diagnoses based on the physical findings plus a good working knowledge of the pathology of each day of the disease. Given the date of the onset of attack, the time of any acute exacerbation of peritoneal symptoms, if such there has been, and the physicial findings as regards the extent of abdominal rigidity, and one should be able to predict the pathology with an accuracy not surpassed in any other intra-abdominal condition with which I am familiar.

Even more uniform is the sequence of changes in the complicating peritonitis, for if peritonitis be studied as a disease process it will be found that as regards any given area of involvement the lesions, of say eighteen hours' duration, present certain fundamental features which are essentially similar in each case. Likewise forty-eight hour cases present features typically characteristic of the forty-eight hour stage of the infection, and so on from day to day throughout the course of the disease.[2]

In this paper I shall not attempt to detail the occasional, and for practical purposes unimportant, variations from the usual progress of the disease. Those interested in this phase of the subject I would refer to Aschoff's monograph[3] on the pathology of appendicitis and to my paper published in 1905.[4]

It is interesting to note, however, that in the later cases studied by me the variations from the average have been much less noticeable than in the earlier cases, probably in part because of more accurate histories, but very largely because in most of the later cases the appendix and surrounding organs had been kept at rest by therapeutic means during the time between the onset of symptoms and the operation.

First Day. The pathological changes found during the first twenty-four hours of an attack of appendicitis are essentially similar in nearly all cases. I have never seen a real case of acute appendicitis operated at this stage of the disease in which a definite obstruction of the lumen of the appendix was not demonstrable. Proximal to this point of obstruction the appendices show little, if any, noteworthy pathological changes. Distal to the point of obstruction, the appendices are constantly distended to a point approximating the maximum distensibility of the organ. After the first eight or ten hours of the attack, fibrin is usually found on the peritoneal surface, and toward the close of the first twenty-four hours a considerable proportion of the appendices show macroscopic evidences of beginning gangrene. The true gross pathology of the first day of appendicitis can only be observed at the operating table because the loosening of peritoneal tissue bands incident to removal of the appendix, removes the causal obstruction or, if the obstruction is due to impacted fecolithes, these are often displaced

[2] This statement as regards the changes occurring in any given area of involved peritoneum is based not alone on the observations made in cases of appendicular peritonitis, but has been checked by observations made at operation and postmortem in peritonitis of widely different origins such as perforating gastric ulcer and ruptured pyosalpinx. The question as to the frequency with which these lesions under favorable conditions will progress to resolution or local abscess formation must be determined from actual experience. That it is the rule in cases of pelvic peritonitis is well known to all, but there is as yet a difference of opinion as to how frequently it actually does occur in unoperated cases of appendicular peritonitis.

[3] Die Wurmfortsatzentzundung, Jena, 1908.

[4] Stanton, E. MacD., The Sequence of Pathological Changes in Appendicitis, Jour. Amer. Med. Assoc., June 10, 1905.

during the manipulations so that by the time the appendix reaches the laboratory the complete picture of the gross pathology is usually lost.

The microscopic changes of the first day consist of an intense diffuse, polynuclear leukocytic infiltration with in all but the milder cases, focal areas of hemorrhages and necrosis involving all coats with a more or less extensive destruction of mucosa, and in many cases a fibrinous or fibrino-purulent exudate on the peritoneal surface. One of the most striking features in these early cases is the presence throughout the majority of the sections of numerous focal areas of necrosis. These areas are larger but are not as a rule more numerous in those cases which show macroscopic evidences of gangrene.

Many writers on the pathology of appendicitis would have us believe that acute appendicitis begins as a catarrhal inflammation of the mucosa, extending to the lymphoid tissue of the submucosa and finally through the muscular coats to the peritoneum, thus inferring that so-called catarrhal appendicitis is an early stage of the acute process. In ten years' time, in which I have made a microscopic examination of practically every first-day appendix that I could lay my hands on, I have never found a single instance of catarrhal appendicitis in a specimen removed during the acute stage of the attack. The diffuse infiltration of all coats is demonstrable even in cases operated within five or six hours of the onset of the first symptoms. Moreover, I have never seen an example of so-called catarrhal appendicitis diagnosed as such by other pathologists which, on referring back to the clinical history, did not prove to be either an appendix removed at an interval operation or a symptomless appendix removed incidental to other intra-abdominal surgery.[5] I believe this question of catarrhal appendicitis is worthy of emphasis for I am certain that the acceptance on the part of general practitioners and surgeons of the belief that catarrhal appendicitis is really a clinically important pathological entity has led to many grave errors in the field of appendiceal surgery.

The peritoneal lesion of this first day is essentially a fibrinous or serofibrinous exudate. On the surface of and in the immediate neighborhood of the appendix the primary exudate seems always to be of a dry, fibrinous character. In the cases studied by me extensive serous exudates have been found only toward the close of the first twenty-four hours of the attack, and then only in cases which had been given strong cathartics soon after the onset of the symptoms.

Even in the presence of a fluid exudate of greater or less extent

[5] Kocher (Cor. Bl. f. Schweize Aerzte Basel, 1913, xliii, 1633) in a recent discussion of this subject says, "I see appendicitis catarrhalis only as a chronic form and as a residue after earlier acute attacks."

at this stage of the disease the general peritoneum is smooth, and aside from a more or less intense congestion of the subendothelial bloodvessels there is little evidence of a true peritonitis.

From a surgical view-point I believe that the peritoneal involvement of the first day may in nearly all cases be ignored and the abdomen closed without drainage. This assertion is, I am certain, borne out by clinical experience, and bacteriological studies (Kelly,[6] Watzold,[7] Cohn,[8] Aschoff,[9] DeQuervain[10]) show that in the majority of cases this first-day exudate is free from bacteria.

I have dealt somewhat at length on the first day's pathology in acute appendicitis because it is the foundation upon which the subsequent course of the disease is based.[11]

Second Day. Beginning with the second day of the attack, the peritoneal involvement, which is present to a greater or less extent in over half of the cases, assumes great practical importance and from now on we are really dealing in the majority of cases with two pathological conditions which must be described separately. First the inflammed appendix, and second the associated peritoneal infection.

In the appendix itself we find a continuation of the inflammatory process begun on the first day. Owing to a coalescence of the microscopic areas of necrosis seen in the first day cases there is by the second day a decided increase in the frequency of macroscopic areas of gangrene. Gross perforation of the appendix itself, with or without gangrene, if it is going to occur at all usually takes place before the end of the second day.[12]

Microscopically, second-day appendices show an intense leukocytic infiltration involving all coats together with a more or less extensive ulceration of the mucosa, while over 70 per cent. show

[6] The Vermiform Appendix, 1905.
[7] Quoted by Aschoff.
[8] Arch. f. klin. Chir., Bd. 85, Heft 3.
[9] Loc. cit.
[10] Cor.-Bl. f. Schweize Aerzte, 1913, xliii.

[11] I believe that the pathology of this first day corresponds closely with the clinical symptoms. First, we have the obstruction causing the primary colic which, like all other colics originating in the gastro-intestinal tract, is, as a rule, referred by the patient to the pit of the stomach or mid-abdominal region. As in gall-stones, strangulated hernia and other obstructive lesions in the gastro-intestinal tract this colic is usually accompanied by nausea and vomiting. It is interesting to note that pressure over the appendix at this very early stage often causes an increase in the pain referred to the umbilical region. A few hours later, with the development of the inflammatory reaction in the appendix, we have a new subjective pain due to the inflammation itself and referred by the patient to the region of the appendix. Local tenderness and rigidity apparently develop with the first involvement of the peritoneal covering of the appendix.

[12] The term perforation as applied clinically and meaning a sudden increase in peritoneal involvement has, I believe, little definite relationship to gross perforations of the appendix itself but rather to the sudden giving away of adhesions limiting a peri-appendicular infection. Histological studies would seem to show that the great majority of appendices are bacteriologically perforated early in the attack, and that protection of the general peritoneal cavity against the infection depends far more upon the maintainance of the integrity of the fibrinous protecting adhesions surrounding the appendix than upon the bacterial impermeability of the inflammed wall of the appendix itself.

a well-marked fibrinopurulent exudate on the peritoneal surface. In those cases which presented macroscopic evidences of gangrene the areas of necrosis as seen microscopically are decidedly more extensive than in the similar cases of the first day group, while in those cases which did not present microscopic evidences of gangrene the focal areas of necrosis, so prominent in the first day cases, are still evident in the majority of sections, but are often obscured by the leukocytic infiltration.

Third Day. By the third day the destructive process in the appendix itself has, in the majority of cases, reached its maximum both as regards the macroscopic and microscopic evidences of disease.

Histologically, the third-day appendices show a diffuse inflammation of the same character as that seen in earlier groups. In the macroscopically gangrenous cases the necrosis is prominent, while in the non-gangrenous cases focal areas of necrosis are seen only in the mucosa. The most striking histological feature which distinguishes this group from the earlier groups is the evidence of beginning repair as seen by the presence of fibroblasts in all sections. These new-formed connective-tissue cells are especially numerous in the region of the peritoneum, although present in other areas, particularly in those cases showing the least marked leukocytic infiltration.

From the third day on changes in the appendix itself have chiefly to do with the process of repair which proceeds with surprising rapidity, the histological picture varying from day to day in the same manner as in any other inflammatory process undergoing repair by organization. However, the rapidity of the repair varies considerably in different cases, being slowest in those cases accompanied by extensive gangrene and most rapid in those cases accompanied by the least primary destruction.

Fourth Day. The fourth day is characterized chiefly by an increase in the evidences of repair. Microscopically the gangrenous cases show large areas of complete necrosis, the histologic picture differing but little from that seen in the gangrenous cases of the third-day group. In sections of the non-gangrenous cases and in sections taken at some distance from the necrotic areas in the gangrenous appendices, the most noticable histologic feature which distinguishes this group from the preceding one is a decided increase in the relative number of fibroblasts and the presence of numerous lymphocytes, and in many cases plasma cells. In those cases accompanied by a peri-appendicular exudate a few fibroblasts and many new-formed bloodvessels can be seen extending into the exudate from the peritoneal surface. Focal areas of hemorrhage into the exudate occurring from these new-formed bloodvessels and frequently seen in the sections.

Fifth Day. The microscopic lesions of the fifth day may be classified into two rather sharply defined groups. In the cases presenting macroscopic evidences of gangrene, the necrosis and polynuclear leukocytic infiltration is still the predominating characteristic, although the repair process is well advanced in some instances. In the non-gangrenous cases the polynuclear leukocytes have practically disappeared except at the surfaces of the ulcerations in the mucosa and of the peri-appendicular exudates. Throughout the coats of the appendix there is a marked increase in the number of fibroblasts and often an intense lymphocytic infiltration. In the peri-appendicular exudates the new-formed bloodvessels penetrate to a greater distance than in the fourth-day group, and this granulation tissue is decidedly richer in fibroblasts.

Sixth and Seventh Days. Histologically, the repair processes are seen on the sixth and seventh days are decidedly more advanced than in the fifth-day group. The gangrenous cases show well-marked evidences of repair, the histological picture of which is similar to that seen in the non-gangrenous cases of the preceding group. The non-gangrenous cases now show areas in which the fibroblasts are massed together and elongated so as to resemble young connective tissue cells. Small ulcers in the mucosa have apparently been largely repaired.

Second Week. After the first six or seven days the repair processes in all but the most extensively damaged organs are so far advanced as to present microscopic pictures of a subacute or chronic character. Even in the more severely damaged appendices the repair proceeds rapidly, and as a rule results ultimately in a surprisingly complete restitution of the organ.

Acute recurrences following dietary or other causes if they occur at this stage result in the engrafting of a new acute lesion upon the histological picture of partial repair. Evidences of this type of acute recurrence were rather common in my earlier cases, but while I suspect the too free use of cathartics and dietary errors as the cause I have not been able to collect any really trustworthy evidence on this point. The fact remains, however, that in more recent years I have not observed more than three or four appendices showing an acute lesion engrafted upon a subacute process.

Appendicular Peritonitis. Before describing the progress of the pathological changes associated with the complicating peritoneal infection I would emphasize the fact that the distribution of this infection in the peritoneal cavity seems to be dependent very largely upon purely mechanical factors.

It is a popular assumption that the extent and seriousness of the peritoneal infection bears a rather definite relation to the extent of the destructive lesion in the appendix itself, but fluid exudates frequently occur without gangrene or actual perforation, and cases are frequently observed with extensive gangrene which must have

existed for several days without the presence of peri-appendicular pus, showing that other factors, such as the resistance of the patient, peristalic movements, and the virulence of the infecting organisms must play an important part in determining the character of the lesion during the early stages of the inflammation. Instead of finding gangrenous and perforated appendices associated with an extensive and severe peri-appendicular peritonitis it is the rule to find very limited peritoneal involvement, in spite of the most estensive destructive lesions of the appendix itself, in all of those cases referred by physicians who have from the first directed their treatment toward the prevention of the mechanical spread of the infection.

Surgeons may honestly differ as to the advisability of immediate operation in certain stages of the disease, but there can be no question as to the advisability of treating every case of even suspected appendicitis by the so-called Ochsner treatment until the diagnosis is possible, and the services of the surgeon procured.

In this connection I cannot do better than quote from Mr. Moynihan,[13] of Leeds, who says: "It is now about seven years since I was first brought firmly to the conviction that in cases of appendicitis it is the administration of an aperient that is responsible for the acute castastrophe of gangrene and perforation which ends in an acute peritonitis. I do not remember one single case that I have operated upon since in which it was not perfectly clear that the same sequence of events—pain, aperient, perforation—had occurred, and I therefore do not hesitate to say that in almost every instance of acute peritonitis due to the perforation of an appendix it is the treatment directed to the relief of the condition that is the cause of the serious and so often fatal catastrophe. The taking of a purgative medicine is something more than an impressive antecedent —it is, in my judgment, a definite cause. The only possible exceptions occur in those rare cases where direct violence gives rise to a rupture of the appendix or the laceration of the adhesions which enwrap it. In cases of appendicitis, however acute their origin may be, perforation followed by an acute general peritonitis does not seem to occur if no aperient is given and if absolute starvation is adopted from the first. The acute spreading or general peritonitis which occurs in this disease is due to treatment; it is a 'therapeutic peritonitis.' I am quite prepared to learn that this emphatic statement is received with a shrug of doubt and the tolerant smile of disbelief, but if strict inquiry is made into the intimate details of the history of the cases I cannot think that my experience of this disease will prove to be singular. In appendicitis, *perforation spells purgation.*"

[13] Acute Emergencies of Abdominal Disease, British Med. Jour., April 1, 1911.

Deaver[14] emphasizes this same point as follows: "Perhaps the most important question that concerns the internist and practitioner, as well as the surgeon, is the use of purgatives during the acute stage of the disease. It is not long since we all thought that a purge should be administered in the initial stages of the disease, but we have come to realize that the contents of the bowel play practically no part in the continuation of the disease, while the peristalsis induced by purgation has proved to be a most unfavorable factor, defeating the end and principle upon which our treatment is based—namely, anatomical and physiological rest. The purgative is more deadly than the scalpel. Of this I have long been convinced, but with a view to obtaining exact figures to support my contention, I have had the year's work analyzed with respect to this point. Among 259 adults there were 79 that had a history of being purged before admission. Of these 79 cases all save 2, at the time of operation, showed appendices that were either perforated, gangrenous, acutely ulcerated, or surrounded by an abscess. The remaining 2 only were simple catarrhal inflammation. Of the 7 deaths occurring in the series 5 were purged before admission. Of those drastically purged, 97.5 per cent. showed the severest kinds of appendicular disease. The exact figures are here given:

"Pathological lesion of appendix: perforation, 30; gangrene, 9; acute ulcerative and suppurative, 23; peri-appendicular abscess, 15; acute catarrhal, 2.

"Among 100 children the same rule holds. There were 56 that had been vigorously purged. Of these, 86 per cent. showed the more serious lesions, such as gangrene, perforation, abscess, etc. Twelve cases had diffuse peritonitis, all of which had been purged before admission. The table is as follows:

"Pathological lesion: perforation, 22; gangrene, 15; acute ulcerative, 6; peri-appendicular abscess, 4; acute catarrhal, 8; indefinite, 1.

"In this series there were 44 acute cases that were not purged, and in this group there was but one case of perforation, 8 cases of gangrene, and no peri-appendicular abscesses."

My own conception based on pathological and clinical studies is that the great majority of appendices are bacteriologically perforated after the first few hours of the attack irrespective of whether or not there is a gross perforation or gangrene evident to the naked eye, and that the protection of the general peritoneal cavity from infection depends upon the maintainance of the integrity of the fibrinous peri-appendicular protecting adhesions rather than upon the bacterial impermeability of the wall of the appendix itself.

As stated above the peritoneal lesion of the first day of the attack is essentially a fibrinous or serofibrinous exudate. On the surface of and in the immediate neighborhood of the appendix the primary

[14] A Year's Work in Appendicitis, Trans. Coll. of Phys. of Philadelphia, 1912, xxxiv, 227.

exudate seems always to be essentially of a dry, fibrinous character. In cases studied by me extensive serous or seropurulent exudates have been found only toward the close of the first twenty-four hours of the attack, and then only in cases which had been given strong cathartics soon after the onset symptoms.

The peritoneal lesions encountered after the first day of an attack of appendicitis may be divided into two sharply defined groups: (1) those cases in which the inflammed appendix is protected from the general peritoneal cavity by a zone of fibrinous exudate massing together continguous intraperitoneal structures, usually the omentum, the head of the cecum, a portion of the parietal peritoneum, and one or two loops of small intestines, with or without a localized collection of pus in the immediate vicinity of the appendix, and (2) cases with more or less diffuse peritoneal involvement. It is this latter class of cases which gives to appendicitis its mortality, and it is of the greatest practical importance for us to have a clear conception of the sequence of the pathological changes as they occur in this complication of appendicitis.

The time of onset of the more diffuse peritoneal involvement can nearly always be determined from the clinical history. Usually the onset of well marked peritoneal symptoms follows a few hours after the giving of a cathartic on the first or second day of the disease, although, we not infrequently find that the acute exacerbation of peritoneal symptoms occurs on the third or some subsequent day—a so-called late perforation. Such acute exacerbations are almost invariably the result of giving food or cathartics by mouth or of active muscular movements on the part of the patient. At operation these cases of late "perforation" show peritoneal lesions of different ages, almost invariably a lesion of limited extent in the region of the appendix with a pathological picture corresponding to the day of the disease and a more or less diffuse lesion with a pathology dating from the time of the acute exacerbation.

Cases operated during the first twenty-four hours following a so-called perforation show that the first exudate thrown out by the peritoneum under these conditions is essentially a fluid exudate, and at first of a distinctly serous or sero-purulent character.[15] The

[15] A. V. and E. Moscheowitz (Arch. f. klin. Chir., 1907, Bd. lxxxii, 707), in reporting the pathological findings in 313 cases of appendicitis accompanied by peritonitis, deny that they found any evidence that serous, seropurulent and purulent peritonitis represent different stages of the same process because figuring from onset of the attack of appendicitis there was only a slight difference in the time at which these three forms of peritonitis were encountered at operation. They believe that it is far more probable that the three forms represent differences in the virulence of the infection, and differences in reaction on the part of individual patients. Similar observations were made by me in my earlier studies when my data was limited to that found in hospital histories but this apparent contradiction to the usual phenomena of inflammation promptly disappeared when I began to study cases coming under my personal observation, and was able to determine not only the time of the onset of the primary appendicitis but approximately the time of onset of the complicating peritonitis.

peritoneal surfaces during the first few hours are still smooth, and aside from a moderate congestion of the subendothelial vessels, there is little change in the peritoneum itself. In fact, except for the extent of the distribution of the fluid exudate, it is usually difficult to say just how far the peritonitis really does extend.

Following the first outpouring of serum, which gives to the first day its predominating characteristic, we have a continued migration of leukocytes and production of fibrin so that by the second day the intraperitoneal exudate, which is usually of considerable extent, is found to be distinctly seropurulent or purulent in character. The peritoneal surfaces now show more or less loss of lustre with here and there adherent flakes of fibrin, but they do not as yet show the marked roughening seen after the beginning of organization on the third day, and the absence of well-defined limiting adhesions is still a noticeable feature of the pathology.

It is during this second day of the peritoneal involvement that the serous surfaces continue to lose their lustre and that the relatively harmless exudate of the first day changes to the distinctly purulent exudate so characteristic of the third day and later cases. Likewise it is at this period that the mortality in operative cases begins to rise very rapidly.

It is well to note here that Murphy[16] in his reports of so-called diffuse peritonitis deals entirely with peritoneal lesions of under forty-eight hours' duration. As far as I know, Murphy does not report a single case of over forty hours' duration, and in a discussion before the Chicago Medical Society he referred to the third and fourth day lesions as cases of "pocketed" peritonitis which corresponds to my own observations concerning the sequence of changes in peritonitis. In other words, we must remember that the "diffuse" lesion described by Murphy by the onward march of the pathological process ends about the close of the second day of a peritoneal infection.

By the third day the continued fibrin production, together with the leukocytic migration, has resulted in transforming our previously diffuse fluid exudate into irregularly pocketed collections of pus. Limiting adhesions are now fairly well developed in most instances, but the lesions are as yet of a decidedly diffuse character, the area involved being much more extensive than at a later period, and there is as yet little or no evidence of the formation of sharply defined abscess cavities. The gross changes in the involved peritoneum, especially in the immediate neighborhood of the appendix, are now very noticeable, due in part to the more abundant fibrin, but chiefly to the changes in the peritoneum incident to the beginning organization which seems in all cases first to become noticeable on the third day following the involvement of any given area of peritoneum.

[16] Perforative Peritonitis, Surg., Gyn., and O 1st., June, 1908.

I believe that the subsequent course of the disease depends largely on whether or not the inflamed peritoneal surfaces are allowed to remain in the same relative position one to another. Certain it is if at this stage, or earlier, we put our peritoneum at rest by withholding food and cathartics and administering opiates in suitable quantities, we find that by the fourth or fifth day all fibrinous adhesions are being replaced by organizing granulation tissue which is also noticeable over the surfaces of the peritoneum in direct contact with the purulent fluid exudate. This granulation tissue serves not only to limit but to encapsulate the pus, and it is from this time on that the formation of definitely defined abscess cavities is observed. These abscesses are at first usually more or less multilocular but later become more localized to form, usually one well-defined cavity. The first evidences of the formation of a true abscess cavity are observed on the fifth or sixth day following the onset of the infection, although it is not until the seventh or eight day that the cavities become sharply defined with limiting adhesions firm enough to permit such manipulations as the packing away of the non-involved intestines without great danger of accidentally opening the abscess at some undesired point.

After the process of organization is well established on the fourth or fifth day there is every evidence of a progressive diminution in the extent of the peritoneal involvement which becomes less extensive as the abscess cavity becomes more sharply localized by the organizing adhesions.

This phase of the repair process which results in the more or less complete resolution of the peritoneal lesion beyond the immediate wall of the abscess has been well shown in a number of cases coming to operation on the tenth and eleventh days, the clinical picture in each having been on admission that of a severe diffuse peritonitis. In these cases the abscess cavities were surrounded by a narrow zone of organizing adhesions, while the peritoneum of the ascending colon and nearby loops of small intestines beyond the wall of the abscess cavity, although non-adherent, was thickened, reddish, and distinctly granular without fibrin or other evidences of an acute lesion. The clinical picture was on the third and fourth days undoubtedly that of a diffuse peritonitis, and this view is confirmed by the pathological findings as observed later at operation, although by the tenth or eleventh day the diffuse lesion had so far cleared up as to leave but slight, though unmistakable, evidences of its having existed.

Summary and Conclusions. In conclusion I would emphasize the following points:

1. Acute appendicitis is even during the first day of the attack a diffuse inflammatory process involving all coats of the appendix.

2. The destructive process in the appendix reaches its height on the second and third days of the disease. From the third day

on the subsequent changes occurring in the appendix itself have chiefly to do with the repair of the damage done during the earlier periods of the attack.

3. The diffuse inflammatory process involving the walls of the appendix is of such character that even without gross evidences of perforation the protection of the general peritoneal cavity from infection depends upon the maintainance of the integrity of the fibrinous periappendicular adhesions rather than upon the bacterial impermeability of the walls of the appendix itself.

4. My observations lead me to agree with Deaver, Moynihan, Ochsner and others when they state that clinical perforation would almost never occur if the general practitioner and the laity would appreciate the fact that in appendicitis "perforation spells purgation" and withhold cathartics during the early stages of suspected cases.

5. If in cases of diffuse peritonitis the peritoneal surfaces are put at rest by withholding food and cathartics by mouth the sequence of subsequent changes occurring in the involved area represents a definite and essentially uniform process tending to the resolution of the lesion or the formation of definitely circumscribed abscesses.

6. After the first thirty-six to forty-eight hours of a diffuse peritoneal infection the lesions encountered are of such a character as to be essentially undrainable and not well suited to surgical interference, a condition which continues until the period of localized abscess formation.

TUBERCULOSIS OF THE VULVA.

By Kenneth Bulkley, M.D.,
NEW YORK CITY.

Since Koch,[59] in 1882, published his paper, there has grown up an enormous literature on the subject of tuberculosis. Among this can be found in nearly every language excellent and complete descriptions of the disease in its various forms. But although the process in the more common locations has been frequently described, some of the rarer manifestations have received but meager attention. It is the object of this paper to report a new case of tuberculosis of the vulva and to collate the scattered literature on the subject.

The following case has recently come under my observation. Mrs. G. M., aged forty-one years, was first seen in October, 1913. Her history at that time was as follows: Married, husband suffering from pulmonary tuberculosis, but as far as could be ascertained

had no genital lesions. One normal delivery with healthy child twenty-two years previously. About seven years ago patient miscarried at five months. Five years ago she first noted a small raw area on the inner surface of the labia minora. This lesion has been progressive since that time. It has given no discomfort other than occasional moderate burning, but coitus has been painful. It has discharged moderately but persistently. There has been absolutely no history of hypertrophy. During the past five years a large number of non-operative attempts at healing have been made, without effect. Her genital history is otherwise negative. Menstruation regular, painless, and normal. In 1911 patient

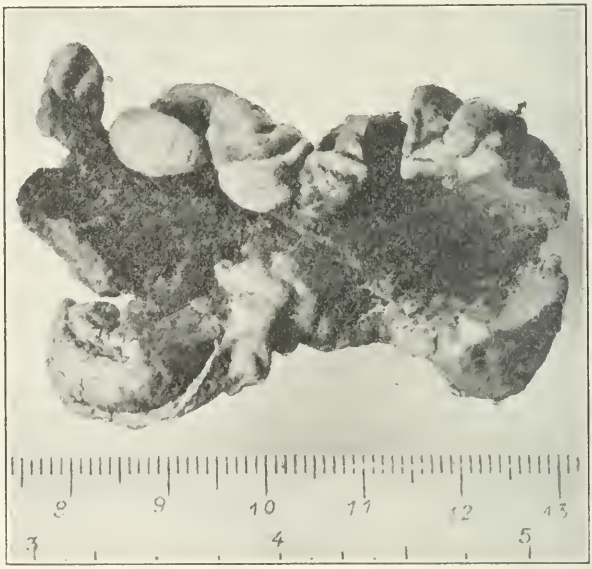

Fig. 1.—Excised specimen from author's case. Scale reads in centimeters and inches. View looking at ulcer surface. On the right the deep excavation anterior to the rectum; to the left the more shallow ulcer extending up the anterior vaginal wall. Between the two a narrower ulcer surface.

developed a pulmonary tuberculosis, for which she was treated in a sanitorium and finally discharged as cured. For the past year she has had no symptoms referable to the lungs.

Physical examination when first seen was as follows: A rather small-framed, wiry, thin woman, not anemic, and apparently in good general condition. Repeated examination of the chest failed to elicit any signs of active tuberculosis, nothing but relative dulness and some increased voice and fremitus remaining at both apices as evidence of her previous trouble. No enlargement of inguinal or other superficial lymph nodes. Abdomen and extremities apparently normal. Wassermann reaction negative.

Local examination disclosed the following: Uterus readily felt, retroflexed but freely movable without pain, fornices clear, no tenderness, no masses. Cervix shows old bilateral tear but is otherwise normal. Vaginal mucosa without lesion. Rectal examination negative, no stricture, fistula, or abscess. The left labia minora is replaced by an ulcer, the general shape of which is that of a dumb-bell, its long axis extending anteroposteriorly. It encroaches to a slight extent on the lateral vaginal wall above and on the inner surface of the labia majora below. Anteriorly its superficial diameter increases and reaches the vestibule and the edge of the urethra. Here it dips sharply upward along the anterior vaginal wall and parallel to the urethra to the depth of an inch.

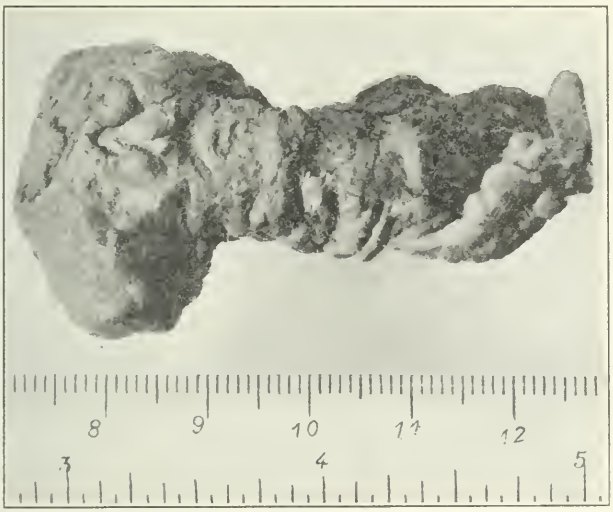

FIG. 2.—Excised specimen from author's case. Scale reads in centimeters and inches. Lateral view showing the general dumb-bell shape of the lesion (somewhat distorted in fixation).

Posteriorly it shows a similar extension beneath the posterior vaginal and anterior rectal walls. There is no hypertrophy and no induration about the ulcer base or edge. The latter is a little irregular, well defined, rather poorly nourished, precipitous, and not undermined. The base of the ulcer is formed of irregularly disposed granulation tissue, grayish, edematous, not readily bleeding, not sensitive. Its surface is covered with a slimy mucus admixed with a moderate amount of pus.

In view of the tuberculous history, the duration of the lesion, the absence of anything suggestive of epithelioma, and the negative Wassermann reaction the case was considered as a tuberculous ulcer and excision advised. Under gas and ether anesthesia this was done on October 24, 1913. The entire labium majus, the region

of the labium minor, and a portion of the left lateral vaginal wall were excised *en masse*, together with the extensions along the urethra and rectum. Both these latter structures were preserved and the wound repaired by a modified perineorrhaphy. The immediate convalescence was smooth and, except for a small hematoma at the posterior portion of the wound, due to insufficient hemostasis at time of operation, the healing was by primary union.

A month later examination showed a small recurrence in the form of an ulcer at the urethral edge in the line of suture. As this lesion improved with the application of 10 per cent. silver nitrate, and as the patient gained twenty pounds in the two months following operation, it received no further treatment until February

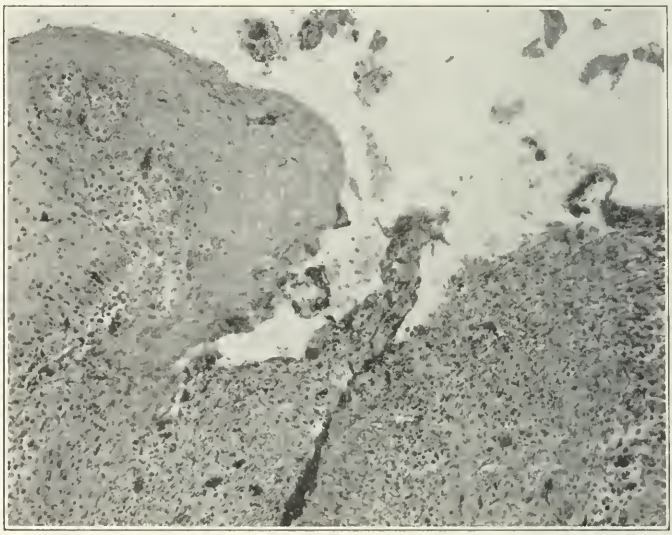

FIG. 3 (× 175).—Author's case. Low-power photograph showing the slightly overhanging epithelium at the ulcer edge and the general character of the ulcer base.

24, 1914, four months after the initial operation. It was then thoroughly cauterized with the Paquelin cautery, and in two days the patient returned to her home out of the city.

Unfortunately the patient was not seen after this date. According to her own statements and those of her husband the area cauterized became smaller and was apparently in process of healing until the time of death. About two weeks after cauterization the patient began to run an irregularly intermittent and finally a continuous temperature. No definite physical signs to account for this temperature could be found by several physicians who examined her, but the prevailing opinion was that death, which occurred on April 8, 1914, was due to an acute general miliary tuberculosis. No autopsy was made. Locally healing continued until time of death.

Microscopic section shows an ulcer whose base is formed of granulation tissue everywhere infiltrated with small round cells and polymorphonuclear leukocytes. In the deep subcutaneous tissue beneath the ulcer base and also beneath the overlying epithelial edges surrounding the ulcer are found typical miliary tubercles. In the centres of the majority of these are collections of multinu-

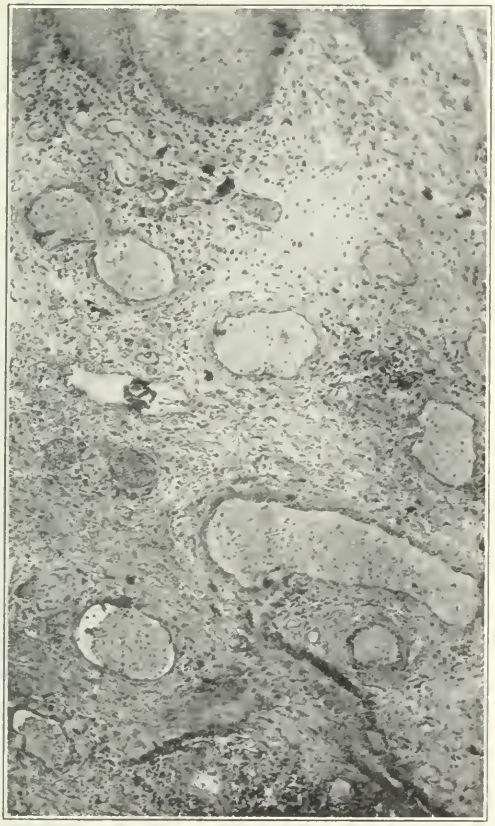

FIG. 4 (× 100).—Author's case. Section taken a short distance from ulcer edge to show the great vascularity. To the left can be seen the deeper layers of the epithelium. Note the dilated and engorged bloodvessels and the beginning round-celled infiltration in the deeper layers of the section.

clear giant cells whose nuclei are arranged peripherally. About the ulcer margin some of these tubercles are found nearly reaching the deep layers of the epithelium. This latter is of normal thickness, and in some areas slightly cornified. There is a great increase in the number and size of the bloodvessels of the subcutaneous and submucous tissue about the ulcer edge. No tubercle bacilli can

be anywhere found. This is probably due to the fact that the specimen has been preserved for six months in alcohol.

Historical Note. Tuberculosis of the female genitalia was practically unknown until Morgagni,[75] in 1771, discovered at autopsy and described a case of tuberculosis of the tubes and uterus. This finding created at the time but little comment, for although there are scattered through the literature of the following years occasional references to the subject, no further contribution of note appears until a description by Raynaud,[84] in 1831, of a case of pulmonary tuberculosis in which there was an associated tuberculosis of the

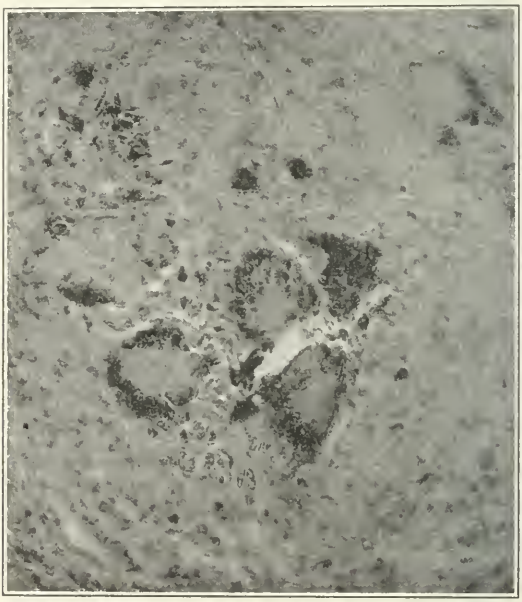

Fig. 5 (× 300).—Author's case. Section taken through the centre of a tubercle situated deeply in the connective tissue beneath the mucosa, to show the character of the giant cells.

uterus, tubes, and vagina. This is the first vaginal case reported. In 1849 Huguier[52] coined the unprecise term "esthiomene," and suggested that some of the cases might be due to tuberculosis. Interest in the subject increased rapidly from that date and numerous important and interesting observations were made. Bernutz,[7] in 1874, and Martineau,[71] in 1883, each reported cases of esthiomene, supposedly tuberculous. In the same year Babes[2] found tubercle bacilli in the vaginal secretion, and in the following year Mandach[67] reported the operative removal of tuberculous tubes and ovaries. It remained for Hegar,[50] in 1886, to thoroughly popu-

larize the subject clinically among the profession. Among the more recent articles in English dealing with the general subject of female genital tuberculosis should be mentioned the papers of Williams,[108] Senn,[93] and Murphy.[77]

Tuberculosis of the vulva as such has received far less attention. The first undoubted cases were reported independently, in 1881, by Cayla[13] and by Winckel,[109] although the cases of Bernutz,[7] in 1873, Cornil and Rigal,[18] in 1879, and others should, without question, be included in this class. Since 1881 many cases have been reported and not a few notable monographs placed on record. Among these should be especially mentioned articles by Bonnin,[9] in 1904, Bender,[4] in 1906, Combeléran,[17] in 1906, Daniel and Jianu,[21] in 1907, Stoica,[100] in 1907, Forgue and Massabuau,[36] in 1909, and Daniel,[20] in 1913.

Frequency. While statistics on the frequency of genital tuberculosis in women are readily obtainable, we have been unable to find any definite statistics relative to the frequency of involvement of the vulva in the tuberculous process. Its rarity is apparent not only from the fact that since 1881 only 71 cases have been reported, but also from the following statistics:

Geil[42] in 45 cases of tuberculosis of the uterus found no cases involving the vulva.

Mosler[76] in 47 cases of female genital tuberculosis found no cases involving the vulva.

Daurios[23] in 166 cases of female genital tuberculosis found no cases involving the vulva.

Beyca[8] collected 69 cases of cervical tuberculosis and found no cases involving the vulva.

Berkeley[6] among 8000 autopsies found genital tuberculosis 62 times and no cases involving the vulva.

Schiler[90] in 68 cases of genital tuberculosis found no cases involving the vulva.

Martin[70] in 53 cases of genital tuberculosis found no cases involving the vulva.

Simmonds[95] among 600 autopsies found genital tuberculosis 80 times and no cases involving the vulva.

Schlimpert[91] in 3514 autopsies found genital tuberculosis 73 times and no cases involving the vulva.

It is thus impossible to say in what percentage of cases of pulmonary, general miliary, or genital tuberculosis a localization in the vulva can be expected. Considering the fact that tuberculosis of the genitals is found in about 2 per cent. of cases coming to autopsy, showing other lesions of tuberculosis, and recalling the above figures, we must admit that the possibilty of vulva involvement is exceedingly small. That it occurs in animals as well as humans is shown by the report of Joest,[55] who describes a case of primary tuberculosis of the vulva in a cow.

Age. Bonnin[9] calls attention to the relative frequency of tuberculosis of the vulva in children. Table I (compiled from 72 cases) not only sustains this view, but shows that the disease is more common during the years of greatest sexual activity. A study of this table brings out the following points: Over 12 per cent. of the total number of cases occur during the first five years of life and nearly 17 per cent. before the tenth year. After that age there is a rapid fall in incidence, and no cases have been reported between the ages of ten and fifteen. As sexual life develops we see the possiblity of involvement increasing to such an extent that between the ages of twenty-five and forty one-third of the cases are found. With the subsidence of sexual activity comes a decline in incidence, so that after the age of fifty-five cases are but rarely seen. The youngest case in this series was seven months and the oldest eighty-eight years.

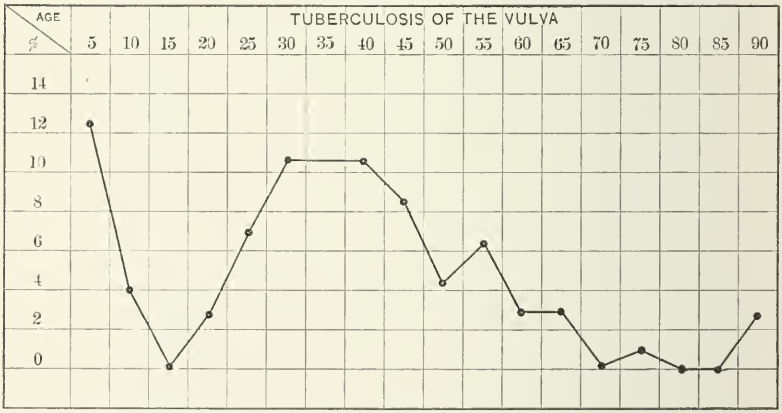

Fig. 6.—Table of age incidence compiled from sixty-two cases in the literature in which the age is given.

Pathogenesis. "As in all tuberculosis the bacillus of Koch is the condition *sine qua non* of the lesion." For infection to occur there must be not only local but also general causes. These latter do not concern us here, as they are of the same nature as those partially responsible for the development of tuberculosis elsewhere in the economy.

The local causes are, however, of importance, for in an individual predisposed to tuberculosis or already harboring a tuberculous focus elsewhere in the body these causes must operate for the localization of the infection at the vulva, whether it be primary or secondary. They may be grouped as inflammatory and traumatic.

Trauma is probably a factor tending to a certain extent to favor the localization of the infection. Experimentally, Popoff[80] was unable to produce genital tuberculosis in pigs or in rabbits

without traumatism. Gorowitz,[44] working independently, obtained similar results. In the 59 cases here reported above the age of fifteen years traumatism seems to have played some role. In 4 of these there was a definite history of injury either by a fall or by violent coitus; 23 cases are definitely stated to have had previous pregnancies, some of them going to full term, a number being instrumental, and a few terminating in abortion. In 32 cases the data is incomplete, but when we consider that these were all adults it is reasonable to suppose that some, at any rate, had borne children. It is worthy of notice that trauma is not mentioned in any of the 12 cases occurring before the age of ten years, but the source of infection can be reasonably traced in the majority of these children, and the trauma of handling and washing may have been sufficient not only for the *locus minoris resistensiæ*, but for the direct implantation of the bacilli. As Bonnin[9] says, "Traumatism, great or small, evident or unknown, appears after all as necessary for the development of tuberculous lesions in the region of the vulva."

Inflammation is also considered by some writers as playing a prominent role in the local predisposition to infection. Deschamps,[29] Jorfida,[56] and Combeléran[17] all lay emphasis on this, and point to acute simple vaginitis, gonorrheal vulvovaginitis, local manifestations of syphilis, simple ulceration, and excessive coitus as agents resulting in inflammatory processes predisposing to later tuberculous infection. In this connection it should be pointed out that a fair proportion of the cases in this series have been prostitutes.

Mode of Infection. The majority of authors in describing the mode of infection in vulvar tuberculosis have divided the cases into three groups, as follows: Primary vulvar tuberculosis, primary vulvar tuberculosis by auto-inoculation, and secondary vulvar tuberculosis. In the first group are placed those cases having no other focus of tuberculosis in the body. The second group comprises those cases in which the individual already harbors a tuberculous focus and infects herself by fingers, sputum, etc. The third group includes cases found in tuberculous subjects in which the vulva is infected by transmission of the bacillus within the body. This classification has seemed to us unnecessary. We will retain the first group as correct. The two following groups we will include under the heading of "secondary vulvar tuberculosis."

Primary Vulvar Tuberculosis. This is the most uncommon of the three forms, but that it does and can occur is indubitably proved by reported cases and experimental work. Popoff[80] and Gorowitz[44] have each been able to produce tuberculosis of the vulvovaginal mucosa in pigs and rabbits by the local deposit of tubercle bacilli after suitable traumatism. Among 47 cases of female genital tuberculosis Mosler[76] found 9 cases (19.5 per cent.) which he considered as primary. Among 119 cases Spaeth[97] considered 27

TABLE I.—CHRONOLOGICAL TABLE OF REPORTED CASES OF TUBERCULOSIS OF THE VULVA.

o	Year.	Reporter.	Age.	Type.	Parts involved.	Trauma.	Associated tuberculous lesions.	Treatment.	Results.	Remarks.
1	1881	Cayla[13]	42	Ulcer with hypertrophy	Entire introitus	1 child	Advanced pulmonary tuberculosis	None	Died	Anus and vulva a "cloaca" at time of death. Child died of tuberculosis.
2	1881	Winckel[109]	28	Ulcer with hypertrophy	Both labia minora	Miscarriage	None found	None	Died	Autopsy case.
3	1881	Winckel[109]	26	Ulcer with hypertrophy	One labia majora and minora	?	Tuberculous inguinal adenitis	None	Died	Autopsy case.
4	1884	MacDonald[66]	40	Ulcer	Entire vulva and perineum	Children	None found	None	Died after 2½ years	Lupus type.
5	1884	MacDonald[66]	33	Ulcer with hypertrophy	Right labia majora and minora	Injury by fall 2 years previous	None found	Curette and cautery	Well 1 year later	One child.
6	1884	MacDonald[66]	46	Ulcer with hypertrophy	Both labia majora	8 children	None found	Curette and cautery	"Cured;" end result ?	
7	1885	Deschamps[29]	25	Ulcer with hypertrophy	Labia minora and posterior commissure	Injury by fall 4 months previous	Advanced pulmonary tuberculosis and lupus of face and hand	Palliative	Died in 3 months	Prostitute. Autopsy showed other genitals normal.
8	?	DeFontaine[25]	40	Fistula	Labia majora	?	Tuberculous wrist and lungs	Cautery	Healed in 6 months	Fistula also communicating with rectum.
9	1886	Chiari[16]	30	Ulcer with hypertrophy	Clitoris, labia majora and minora	Injured during coitus 2 years previous	Tuberculous ulcers rectum. Autopsy showed general tuberculosis	None	Died	Autopsy case
0	1887	Demme[26]	13 mos.	Ulcer with hypertrophy	Labia minora	None	Tuberculous inguinal adenitis; tuberculous meningitis	Curette and cautery	Healed locally	Mother had pulmonary tuberculosis. Child died at 16 months of tuberculous meningitis.
1	1887	Demme[26]	7 mos.	Ulcer	Vulva	None	?	Curette and AgNO. No healing Healed after HNO	Well 2 years later	Father tuberculous.
2	1887	Demme[26]	15 mos.	Ulcer	Vulva	None	Tuberculous inguinal adenitis; pulmonary tuberculosis	None	Died	
3	1888	Zweigbaum[112]	32	Ulcer	Both labia minora and majora	?	Tuberculous lungs, vagina, and cervix; tuberculous rectovaginal fistula	Local	Died	Primary in cervix, then vagina infected, and then vulva.
4	1889	Weinlechner[107]	38	Ulcer	Entire side of introitus	3 children	None found	Cautery excision	Recurrence in 18 months; end result not given	Tuberculous ulcer developing on luetic base.
5	1890	Haeberlin[45]	27	Ulcer with hypertrophy	Both labia, majora, and minora and clitoris	1 child	None found	Excision	?	Father died of tuberculosis.

1891	Viatte[106]	32	Ulcer with hypertrophy	Left labia, majora, and minora	Married	None found	2 excisions; tuberculin	Cured	Recurrence after each incision; finally healed with Koch's tuberculin; lupus type.
1894	Emanuel[32]	?	Ulcer with hypertrophy	Posterior fourchette	No children	Tuberculous cervix and vagina	Hysterectomy	Died	Operative death following panhysterectomy. Autopsy showed generalized miliary tuberculosis. Vulva secondary to cervix.
1895	Martin[58]	23	Ulcer with hypertrophy	Left labia minora	?	Tuberculous lungs and rectum and rectovaginal fistula	None	Died	Vulva and rectum a veritable cloaca at time of death.
1895	Montgomery[74]	30	Ulcer with hypertrophy	Both labia majora	4 children	None found	None at time of report	?	Case demonstrated. Advised treatment with iodoform in collodion.
1896	Hintze[51]	?	Ulcer	Mons veneris, both labia and perineum	3 children	None found	Excision	?	Possibly a primary case.
1896	Kuttner[61]	6	Ulcer with hypertrophy	Right labia majora; mons veneris	?	Tuberculous lungs and inguinal glands	Excision	Well in 3 months	End result not given.
1896	Schenk[89]	4½	Ulcer	Both labia minora, clitoris and urethra	?	Tuberculous inguinal adenitis	Excision	Recovery; end result unknown	Possible primary case. Infection from tuberculous playmates by fingers.
1897	Karajan[57]	2	Ulcer with hypertrophy	Clitoris and labia majora	?	Secondary tuberculous ulcer of vagina	Excision	Recurrence	Possible primary case. No sign of tuberculosis elsewhere in body. Vaginal ulcer developed as recurrence after first operation.
1898	Havas[49]	21	Ulcer	Entire vaginal orifice	?	Pulmonary tuberculosis	?	?	
1896	Winter[110]	?	Ulcer	Labia minora	?	?	?	?	Pathologic specimen. Practically no data given.
1899	Brosin[12]	Old	Ulcer	Vulva	?	?	?	?	
1899	Davidsohn[24]	?	Ulcer	Vulva	Following severe labor	Generalized miliary tuberculosis	None	Died	Autopsy case; also tuberculous vagina.
1899	Fiocco and Levi[34]	52	Ulcer with hypertrophy	Vulva	?	?	Curette and cautery	Rapid healing	End result not given.
1899	Gebhard[41]	?	Ulcer with hypertrophy	Urethral edge	?	?	?	?	
1899	Gebhard[41]	?	Ulcer	Labia minora	?	?	?	?	
1899	Hansen[47]	4	Miliary tubercles	Vulva	?	Tuberculosis of kidneys, tubes, uterus, vagina.	None	Died	Autopsy case; supposedly primarily renal and involving other structures secondarily.
1899	Rieck[87]	39	Ulcer with hypertrophy	Labia minora	Married; children	None found	Excision	Cured	Husband had pulmonary tuberculosis; possible primary case.
1901	Ehrmann[30]	32	Ulcer	Urethral orifice	Prostitute	Pulmonary tuberculosis	Iodoform	Healed in 6 months	Prostitute.
1901	Ehrmann[30]	50	Ulcer	Labia majora and posterior commissure	?	?	Iodoform	?	Old case of s
1901	Ehrmann[30]	56	Ulcer with hypertrophy	Labia majora and posterior commissure	?	No sign of pulmonary tuberculosis	Excision		

TABLE I.—CHRONOLOGICAL TABLE OF REPORTED CASES OF TUBERCULOSIS OF THE VULVA—(Continued).

o	Year.	Reporter.	Age.	Type.	Parts involved.	Trauma.	Associated tuberculous lesions.	Treatment.	Results.	Remarks.
5	1901	Jorfida[56]	23	Ulcer with hypertrophy	Labia majora and posterior commissure	After delivery	Tuberculous vaginal ulcers; tuberculous inguinal adenitis	Excision	Cured	Supposedly infected by tuberculous friend.
	1901	Martin[69]	32	Ulcer with hypertrophy	Labia majora	3 children	Pulmonary tuberculosis	Excised	"Primary cure"	End result not given; two sisters had tuberculosis.
5	1901	Rechenbach[85]	33	Ulcer with hypertrophy	Labia minora, clitoris, edge of urethra	4 children	No sign of tuberculosis elsewhere	Cautery and curette	?	
9	?	DePaoli[27]	?	Ulcer with hypertrophy	Both labia	?	?	?	?	
0	?	DePaoli[27]	?	Ulcer with hypertrophy	Both labia		Tuberculous intestine and peritonitis	?	?	
1	1902	Poeverlein[79]	49	Hypertrophy only	Labia majora	1 child	?	Excision	Recurrence in 4 weeks	End result not given. Diagnosis before operation "sarcoma."
2	1903	Petit and Bender[78]	33	Hypertrophy only	Both labia majora	Forceps delivery	No sign of tuberculosis elsewhere	Excision	Recurrence in 2 months	End result not given.
3	1904	Bender and Nandrot[5]	39	Ulcer with hypertrophy and fistula	Both labia majora	Local injury from fall	No sign of tuberculosis elsewhere	Excision and cautery	Remained cured	
4	1904	Chiarabba[15]	?	Ulcer with hypertrophy	Labia majora and minora	?	Tuberculous peritoneum, uterus, tubes, and cervix	?	?	
5	1904	Frattali[38]	19	Ulcer	Labia majora	?	Tuberculous inguinal adenitis; tuberculous ulcer vagina	?	?	Lupus type.
6	1904	Renaud[86]	4	Ulcer with hypertrophy	Left labia minora	None	No sign of tuberculosis elsewhere	Iodine and iodoform	Healed in 15 days	End result not given; supposedly a primary case of vulva infection.
7	1906	Audry and Combeléran[1]	1	Ulcer	Right labia minora	?	Tuberculous inguinal adenitis	Excision	?	Mother had pulmonary tuberculosis.
8	1906	Bender[4]	26	Hypertrophy only	Both labia minora	?	?	?	?	
9	1906	Combeléran[17]	50	Lupus	Right labia majora	?	None found	Excision	?	Lupus type.
0	1906	Dambrin and Clermont[19]	88	Abscess	Right vulva	?	Tuberculous osteitis of pubis	Incision	?	Secondary to tuberculosis of bone. Only case on record.
1	1906	Danlos, Pathaut and Gaston[22]	55	Ulcer with hypertrophy	Clitoris and labia minora	?	?	Excision	Recurrence in 6 months	End result not given.
2	1906	Hamburger[46]	3	Ulcer	Posterior commissure and labia minora	?	Tuberculous cervical and inguinal adenitis	Hygienic	Healed	Mother had pulmonary tuberculosis; sister died of tuberculous meningitis.
3	1906	Logothetopoulos[65]	75	Ulcer with hypertrophy	Urethral edge	No children	Pulmonary tuberculosis	Excision	Died	Operative death in 6 days.

1907	Daniel and Jiaut[21]	15	Ulcer with hypertrophy	Both labia minora and clitoris	3 children	Tuberculous rectum	Excision	Healed	End result not given.
1907	Daniel and Jiaut[21]	45	Ulcer with hypertrophy	Labia majora	?	No sign of tuberculosis elsewhere	Excision	Healed	End result not given.
1907	Meriel[73]	20	Hypertrophy only	Left labia minora	?	Pulmonary tuberculosis	Excision	Cured	Well locally 7 years later, but pulmonary condition slowly progressive.
1907	Meriel[73]	26	Ulcer	Labia minora	?	?	Excision	Healed	End result not given.
1907	Wolff[93]	51	Ulcer	Vulva	?	Pulmonary tuberculosis	Excision	?	End result not given.
1908	Boursier[10]	63	Hypertrophy only	Right labia majora	Children	Pulmonary tuberculosis	Excision	Healed	But, 2 years later, lesion of left labia minora.
1909	Forgue and Massabuau[36]	35	Hypertrophy only	Right labia majora	?	Tuberculous cervical and axillary adenitis; pulmonary tuberculosis	Excision	Recurrence	Recurrence in 10 months before death due to pulmonary tuberculosis.
1909	Kelly[58]	55	Ulcer	Anterior commissure	?	?	Excision	?	
1909	Lecène[64]	40	Bartholin's gland	Bartholin's gland	?	Possible tuberculous cervix	Excision	?	
1909	Lecène[64]	23	Ulcer and Bartholin's gland	Labia minora and Bartholin's gland	?	Pulmonary tuberculosis; tuberculous fistula in ano; tuberculous inguinal adenitis	Excision	Recovery	End result not given. Considered by author a blood infection.
1910	Kroemer[60]	44	Ulcer with hypertrophy	Vulva	5 children	?	Excision	?	
1910	Lagane[62]	6	Ulcer	Entire introitus	?	Pulmonary tuberculosis; tuberculous kidney and bladder	?	Died	Father had tuberculosis. Four brothers and sisters died of tuberculous meningitis. Case of probable secondary infection from kidney.
1910	Mauler[72]	37	Ulcers	Introitus		Tuberculous lungs, uterus, tubes, vagina, peritoneum, intestine, spine	None	Died	Autopsy case.
1910	Mauler[72]	41	Ulcers	Introitus	?	Tuberculous lungs, multiple joints, intestine, kidney, suprarenal, uterus, tubes, vagina, spine	None	Died	Autopsy case. Introitus involved by direct extension from vagina.
1910	Stoeckel[99]	28	Ulcer	Anterior commissure	Married	Miliary tuberculous intestine	Excision and cautery	Recovery	End result not given.
1911	Rossle[88]	87	Ulcer	Anterior commissure	?	Tuberculous lungs, uterus, cervix	None	Died	Autopsy case. Urinary passages normal.
1912	Brault[11]	7	Ulcer	Clitoris, labia majora and minora	?	No sign of tuberculosis elsewhere	Excision	Died	Early attempts at healing with chemical and thermal caustics without avail.
1913	Daniel[20]	36	Hypertrophy only	Right vulva and prepuce of clitoris	Miscarriages	Tuberculous inguinal adenitis	Excision	Recovery	End result not given. Husband had pulmonary and genital tuberculosis.
1914	Bulkley	41	Ulcer	Labia majora and minora	1 child; 1 miscarriage	Pulmonary tuberculosis	Excision	Recurrence; died	Died 6 months after operation with signs of an acute general miliary tuberculosis.

(24.5 per cent.) as primary. Numerous modes of infection have been suggested. Among them can be mentioned coitus, masturbation, clothing, pessaries, douche tips, wash-cloths, baths, toilets, the presence of tubercle bacilli in wash water, and air infection. Senn[93] considered most of the cases of all types infected by tuberculous sputum. Probably in the majority of cases, certainly of primary vulvar tuberculosis, infection occurs either by sputum or coitus. While it may be admitted that in any given case it is wellnigh impossible to point out with certainty the mode of infection, yet in a certain number of the cases in this series it seems fairly evident. We shall make no attempt to divide our cases into the two classes which we are now describing because of the manifest difficulty of doing so with any degree of accuracy. Nothing short of a complete postmortem on every case could make such a classification reasonably accurate. A few can be pointed out as examples of the probable mode of infection. In the two following cases the bacilli were probably derived from sputum. Schenk[89] describes a case involving the labia minora, clitoris, and urethra in a child four and one-half years old. This patient showed no other signs of tuberculosis, and repeated examinations of the chest were normal. It was later discovered that this child had a playmate with pulmonary tuberculosis, and the supposition is that the vulva was infected from tuberculous sputum probably transmitted by the fingers. Audry and Combeléran[1] describe a child of one year showing no other lesion of tuberculosis, who was probably infected from the soiled linen of the mother, who was tuberculous.

Much experimental and clinical evidence has accumulated in favor of the view that tuberculosis, local or generalized, can be transmitted from the male by coitus even in the absence of male genital tuberculosis. But here as before the local or general predisposition to infection plays its part, for when we consider the large number of cases of tuberculosis of the epididymis and prostate in married men, and the fact that very few of the wives of these men develop a tuberculous vulva, it at once becomes evident that coitus cannot always be incriminated. Some writers from this fact have argued that tuberculosis of the vulva is usually a descending infection, but Murphy suggests that the semen is usually transmitted beyond the vulva, into the vagina, and so the former escapes. Colnheim,[14] in 1879, first suggested that genital tuberculosis might be transmitted by coitus. Corroborating this, Fernet[33] reported the cases of two women who after intercourse with tuberculous men developed local genital lesions. Glockner[43] has described a case of tuberculosis of the cervix due to coitus, and Verchère[104] has published similar cases. Straton[101] narrated an instance of a tuberculous growth in the vaginal wall of a previously healthy woman after marriage with a tuberculous husband. And finally Gaertner[40] inoculated the testes of rabbits and guinea-

pigs with tubercle bacilli and found that females fecundated by these developed tuberculosis and showed lesions of the vagina and uterus.

Verneuil[105] was the first to maintain that a tuberculous individual *without* genital lesions could transmit the bacillus by coitus, and the observations of others corroborate his view. Thus Spano[98] studied microscopically and by means of cultures the sperm of a patient dead of tuberculosis and found no bacilli. This same sperm, however, when inoculated into the peritoneal cavity of a guinea-pig gave positive results two out of three times. Sirene and Pernice[96] report amost identical experiments with the same outcome. Landouzy and Martin[63] using the sperm from a living patient obtained similar findings. Foa[35] succeeded in finding the bacillus in the sperm of men dead of tuberculosis but without genital lesions, while Jani[54] in 8 cases of phthisis found the bacilli five times in the testes and four times in the prostate, but was unable to find them in the sperm. And finally the work of Derville[25] is of interest. In 8 cases of genital tuberculosis in women he found the bacilli in the secretions of 5, and in examining the husbands and lovers of these women found that all had a tuberculous epididymitis.

Among the cases in the series here reported there are a number in which it is reasonable to suppose that the infection was by coitus. Thus in the case of Montgomery[74] there was no sign of tuberculosis elsewhere and no evident source of infection other than a husband probably tuberculous. In Rieck's[87] case also no other lesion could be found, and the husband was proved to be tuberculous. In our case also coitus may have been responsible, as the husband had an active pulmonary tuberculosis, but as far as could be ascertained no genital lesion.

Secondary Vulvar Tuberculosis. Secondary vulvar tuberculosis can occur from the transmission of the bacillus either without or within the body. It is then known respectively as primary vulvar tuberculosis by auto-inoculation (primary secondary tuberculosis [Pozzi[82]]) or as secondary vulvar tuberculosis. The first group includes all cases occurring in individuals having a focus of tuberculosis in the body from the discharge of which the tubercle bacilli are transmitted locally to the vulva outside of the body. Thus tuberculous sputum or tubercle bacilli from a discharging tuberculous bone sinus might be transmitted by means of fingers, clothing, wash-cloths, etc., to the vulva. Many authors consider that the majority of reported cases should be placed in this class.

The second group includes all cases in which there is a previous focus of tuberculosis in the individual and in which the path of infection lies within the body. In this type of lesion there are four possible routes of infection.

They are:

(*a*) Hematogenous.
(*b*) Lymphatic.
(*c*) Contiguity of tissue.
(*d*) Continuity of surface.

(*a*) *Hematogenous.* Although this path of infection is generally admitted there is very little conclusive evidence in the literature showing that it occurs with any regularity. Fiocco and Levi[34] believe that it is a common way for the distribution of bacilli, particularly in cases of tuberculous enteritis. Here they consider that the bacilli reach the mesenteric lymph nodes, then the thoracic duct, and in that way the blood current, and so are distributed to the vulva as well as elsewhere. The evidence is rather scanty, and in view of the more plausible and more nearly proved modes of infection the hematogenous route can safely be discarded except in theory. The only case in our series in which this path of infection seems fairly certain is that described by Hansen[47] in a child of four years, who at autopsy showed signs of a generalized miliary tuberculosis involving also the vulva, and even here the infection might have been from the urinary tract.

(*b*) *Lymphatic.* For anatomical reasons this mode of infection must be infrequent. The lymphatics of the vulva drain into the superior internal glands of the groin, and into these same glands drain the lymphatics from the lower central portion of the abdominal wall, the region of the anus and perineum, and the median surfaces of the buttocks. These channels all freely intercommunicate, and it is conceivable that a superficial tuberculous lesion of any of these regions might travel by way of the lymphatics and so reach the vulva. Practically this mode of infection is most difficult to differentiate from infection by contiguity of tissue. Thus in Martin's[69] case there was not only a tuberculosis of the vulva but a series of ulcerative lesions on the buttocks and upper inner thighs which was thought to be lupus. This is the only case in the series in which lymphatic infection seems even possible, but there are a number of cases in which ulcers of the lower rectum or anal canal might have infected the vulva by the lymphatic channels.*

(*c*) *Contiguity of Tissue.* It is possible to include more cases in this than in either of the two preceding classes, and in studying our material some unusual possibilities have presented themselves. Direct extension of tuberculous vaginal ulcers so as to include the vulva in the ulceration is the most common form encountered. After this we find direct extension from tuberculous lesions of the rectum. Here the vulvar lesion may present itself either as an

* The question has been raised as to whether a tuberculous infection can travel by the lymphatic channels against the normal direction of lymphatic flow. In this connection a case of tuberculosis of the breast reported by Power[81] is of interest. This was in a girl, aged fifteen years, in whom there was extensive axillary involvement and relatively little breast involvement. Powers believes that the axillary glands were the seat of infection and that the breast involvement was secondary.

ulcer or as a fistula. It is safe to say that direct extension by contiguity of tissue is most frequently from one of these two sources. Occasionally it may take place from tuberculous lesions of the skin, as already mentioned in the case described by Martin.[69] A most unusual case, and the only one of the sort we have been able to find in literature, has been described by Dambrin and Clermont[19] in a patient eighty-eight years of age. This patient, otherwise in good health, complained of a tumor of the right vulva. It was incised and found to be a cold abscess, originating in a tubercuous osteitis of the os pubis. Lecène[64] has published reports of two cases of tuberculosis of the vulva, both by direct extension of tuberculosis of Bartholin's glands. This is a unique observation, and is only paralleled in medical literature by the report of a case of tuberculous infection of Cowper's gland, the male analogue (Hartman and Lecène[48]).

(*d*) *Continuity of Surface.* The infection taking place under this head is believed to be derived from tubercle bacilli in the discharge either from the urinary system, genital system above the vulva, or from the feces from cases of tuberculous enteritis, etc. Examples of all of these three types of infection can be found in this series, and it might at first be thought that the constant passage of tubercle bacilli from one of these sources would lead to a frequent vulvar involvement. The fact is, however, that this does not occur with any great frequency, as can be readily judged from the figures already quoted as to the frequency of tuberculosis of the internal genitals and also from the frequency with which tuberculosis of the kidney and bladder is seen. In the 72 cases of vulvar tuberculosis here analyzed, lesions of the internal genitals are mentioned in only 9 patients who showed tuberculosis of the uterus five times, cervix five times, tubes four times, and vagina eight times. In only 3 cases is a tuberculosis of the kidney described, and only once tuberculosis of the bladder. The intestine has been involved but four times and the rectum but five times. We believe that too much stress has been laid by previous authors on this mode of infection.

Symptoms and Clinical Forms. Tuberculosis of the vulva clinically presents itself in a number of forms, some of which are more or less characteristic of the disease itself, while others are of such a nature as to rather mask the diagnosis. It has been the custom in the past to recognize three main forms of the disease. They are as follows:

(*a*) Hypertrophy with ulceration (*forme ulcereuse, forme ulcerogommeuse, chancre tuberculeuz*).

(*b*) Lupus type (*forme lupique*).

(*c*) Hypertrophy without ulceration.

In studying our collected cases it has seemed to us that this classification is either not comprehensive or is too sweeping. There

are undoubted cases reported which cannot be reasonably included under any of the above headings. Some of the cases which this paper considers are but scantily described, and we shall make no attempt to place each case in its class. We would, however, venture to suggest the following classification, into the divisions of which can be readily placed any given case in which sufficient data is reported.

1. Hypertrophy with ulceration.
2. Hypertrophy without ulceration.
3. Ulceration without hypertrophy.
4. Lupus type.
5. Fistulas and abscesses.

We will presently take up in detail the local findings in each of these five types, but before doing so it will be well to consider briefly the signs and symptoms common to them all.

The general symptoms are relatively slight and in primary vulvar tuberculosis comparatively negligible. In other cases they are in direct proportion to the amount of involvement of other organs. Here we see the general symptoms which may accompany tuberculosis of any part of the body, fever, increased pulse rate, loss of weight, anemia, etc.

Locally the subjective symptoms are often very slight until the disease is fairly well advanced. Burning or smarting, pruritus, or a vulvar enlargement may be the first symptom noted. With ulceration, especially if extending into the vagina, leucorrhea may be the first symptom, or possibly a burning urination, due to the passage of urine over a raw surface. Pain is usually not marked, except possibly during coitus. Functional symptoms are lacking in the absence of involvement of the internal genitals or urinary system. We cannot agree with the statement that hypertrophy is invariably present. Our case, as well as many in the literature, totally lacked this feature. The local findings in the various forms can be best described according to types.

1. *Hypertrophy with Ulceration.* This is the most common of all forms, and into this class the majority of cases can be placed. It is a disputed point as to whether the hypertrophy precedes the ulceration, or *vice versa*, or whether they develop hand in hand, but when first seen both processes are usually already evident. The hypertrophy may include the labia majora, minora, or the prepuce of the clitoris, or any of these parts may be involved singly or in combination with others. One side or both may be hypertrophied. The increase in size varies from small areas of leukoplakia of the mucous surface of the labia minora to tumor masses larger than two fists involving all the parts. This apparent hypertrophy may be an edema or a definite hyperplasia. Possibly it starts as the former, and continuing over a period of time gradually becomes transformed into the latter. When due to an edema the

surface appears smooth, tense, and uniform. There may or may not be discoloration. The margins are ill-defined and fade gradually into surrounding healthy tissue. The consistency is soft and depressions can readily be made with pressure of the examining finger. When due to hyperplasia the surface is of a rougher appearance, in color a little darker red, more nodular, its borders more precisely defined. The consistency is firm, brawny, and pitting is slight or absent. It corresponds more to the "elephantiatische tuberculose" of the Germans. There is seldom, if ever, any tenderness. It is questionable whether there are ever seen in this type the minute "apple-jelly" tubercles of true lupus.

Associated with this hypertrophy is ulceration, which varies in extent from minute areas the size of a pin-head to losses of tissue so great that the entire vulva, perineum, and anal region may be transformed into a veritable cloaca. These ulcerations occur with great frequency on the inner surface of the labia majora and minora, but may be found elsewhere. A quite frequent site is near the urethral edge or near the clitoris. At times they are a continuation of a vaginal ulceration. As already stated they frequently result in much loss of structure, so that it is not unusual to find an entire labia minora replaced by one of these ulcers. They may be single or multiple. Probably the larger single lesions represent the fusion of previous multiple ulcerations. Their irregular, indented borders are well defined, poorly nourished, seldom excavated, usually precipitous. Commonly superficial and not of greater depth than a quarter inch, these ulcers at times extend far into the subcutaneous or submucous surfaces. We have seen them extend in this manner to the depth of an inch. The base of the ulcer is formed of unhealthy granulation tissue, which shows its poor quality not only by its grayish, edematous appearance but also by the difficulty with which it can be induced to bleed. The surfaces of the lesions are covered with a rather profuse grayish, seropurulent discharge. They are seldom tender to the touch. The inguinal lymph nodes are often enlarged, at times due to definite tuberculous infection and at times due to a suppurative adenitis from absorption of the common pyogenic bacteria from the raw surface. Induration about or beneath the ulcer is usually absent.

2. *Hypertrophy without Ulceration.* This is an exceedingly rare form of which only 7 cases have been reported. Locally the findings are much the same as those already described in the previous section, lacking, of course the ulceration. The hypertrophy in these cases is usually due to hyperplasia and not to edema. Of the 7 reported cases 2 had an associated pulmonary tuberculosis and 3 a tuberculous inguinal adenitis. All occurred in adults.

3. *Ulceration without Hypertrophy.* In this group are placed all cases in which hypertrophy is not evident either from the history or examination of the patient. Many writers believe that such a

grouping is impossible because hypertrophy is always present, but our study of the collected cases has not convinced us on this point, and we believe that in a certain proportion of the patients, especially children, this hypertrophy is not found during any stage of the disease. In seven of twelve children under the age of ten years it was absent. The local examination of cases coming under this grouping shows ulcers similar in all respects to those already described, and needs no further comment. It is possible that some of the cases should be placed under the lupus type as late ulcerating lesions.

4. *Lupus Type.* That the vulva is a rare location for the development of lupus vulgaris so commonly seen about the face is shown by the statistics of Bender,[3] who among 380 cases of lupus found the vulva involved only once. The appearance, however, about the vulva differs but little from that of lupus elsewhere, except possibly for the fact of rather more frequent and early ulceration, due no doubt to the location upon a mucous membrane and the constant presence of moisture. There are the same brownish, rather deeply situated tubercles, fading on pressure to a yellowish color, giving the "apple-jelly" appearance, and being either single or multiple, with the tendency to grouping and confluence of multiple lesions to form a single lesion which early ulcerates. In some cases, as in one reported by Combeléran, the lesion may present itself as an apparent simple leucoplakia. Practically all of these lesions develop on the inner surface of the labia. It may be the development of these lesions, undetected until well advanced which contributes the majority of cases to the group we have called "ulceration without hypertrophy." Probably in this class should also be placed the occasional case in which there is a generalized miliary tuberculosis, including the vulva.

5. *Fistulas and Abscesses.* At certain times tuberculous lesions develop in the neighborhood of the vulva, caseate or become secondarily infected, and in seeking an exit for their contents, either distend one labia into a pus socket or perforate it, leaving through it a sinus which in course of time becomes lined with tuberculous granulation tissue. It is needless to point out that these must all of necessity be secondary tuberculous vulvar lesions. Thus a tuberculous osteitis of the os pubis has pointed at the vulva, a tuberculosis of Bartholin's gland has infected it, and tuberculous rectovulvar fistulas have been described. In all these cases, no matter what the point of origin, there will be present either an abscess or a fistula. The former can be identified as tuberculous only by a recognition of the primary focus, the latter in the same way or by the nature of the granulations lining the sinus, or by the recovery of tubercle bacilli in the discharge from it.

Pathology. While it is unnecessary to describe further the gross appearance of tuberculous lesions of the vulva as they occur

locally, it will be of interest to refer to the relative frequency of involvement of different portions of the vulva and to note the associated tuberculous lesions which in this series have been found in other parts of the body.

From the following brief tabulation it will be seen that the labia majora and minora are most frequently involved:

	Cases.
"Vulva"	10
Labia majora	29
Labia minora	30
Clitoris	8
Entire introitus	7
Posterior commissure	6
Anterior commissure	3
Mons Veneris	2
Edge of urethra	5
Bartholin's gland	2
Prepuce	1

The condition is more frequently unilateral than bilateral, and involvement of the labia majora and minora is the most frequent association.

Looking over our cases with a view to ascertaining what other portions of the body can be expected to show most frequently an associated tuberculosis, we obtain the statistics tabulated below. These must be judged only relatively, for their accuracy is marred not only by lack of complete reports but also by the fact that in the majority of cases the observations were clinical only, and not confirmed by autopsy record. The parts involved were as follows:

	Cases.
No associated tuberculosis mentioned or found in	31
Tuberculosis of lungs	21
" inguinal lymph nodes	11
" cervical lymph nodes	2
" axillary lymph nodes	1
General miliary tuberculosis	4
Tuberculosis of joints	2
" spine	2
" os pubis	1
" kidneys	3
" bladder	1
" suprarenal glands	1
" uterus, body	5
" uterus, cervix	5
" tubes	4
" vagina	8
" peritoneum	3
" intestine	4
" rectum	5
" meninges	1
" skin (lupus vulgaris)	1

It is thus seen that an associated pulmonary lesion is most frequently found and next in order a tuberculous lesion of some higher portion of the genital tract.

In describing the microscopic picture we can conveniently divide the lesions into two types, deep and superficial. To the former belong the four following clinical groups: hypertrophy with ulceration, hypertrophy without ulceration, ulceration without hypertrophy, fistulas and abscesses. To the latter belongs the lupus group. In the former the lesions are deep and involve not only the epidermis and derma or the mucosa and tissue immediately beneath it, as the case may be, but also the subcutaneous or submucous tissue. In the latter the superficial structures only are involved.

In the deep form the variation from the normal is as follows: The epithelium is at times perfectly normal and without noticeable alteration except, of course, where there is loss of surface. At times it is thickened and cornified. There is sometimes, but not always, seen in the derma an infiltration of plasma cells clustered together in masses in the centres of which may or may not be found giant cells. The lesions are especially marked and at times only seen in the subcutaneous or submucous tissue. This infiltration may be diffuse and lacking in giant-cell formation, due, as Unna[102] has shown, to lack of pressure and the elasticity of the parts involved. The white and elastic fibers are increased in size and swollen with a clear fluid. They present the appearance of a chronic edema. Many dilated bloodvessels and lymphatic spaces are seen. In the centres of and about the giant cells and diffusely scattered in the areas of diffuse plasma-cell infiltration tubercle bacilli can be found.

As they progress these lesions reach the surface and ulceration ensues. This process may take place only in parts of the lesion, usually the centre. The extent of the diseased area cannot therefore be judged alone by the extent of the ulceration. In some cases, as in the one described by Bender and Nandrot,[5] we find lesions on the point of involving the epidermis or mucous membrane, but the latter still preserved. Such findings substantiate the view held by some writers that the hypertrophic form of tuberculosis of the vulva represents delayed ulceration and is in reality the preulcerative stage of hypertrophy with ulceration. This delay in ulceration may possibly be due to the thickening and cornification of the epidermis which is more marked in the pure hypertrophic form than in the type with ulceration, where it is practically wholly lacking.

In the superficial form (lupus type) the lesions are confined to the surface layers and do not differ from the well-known picture of lupus as seen on the more common locations. They need not here be described other than to again emphasize the fact that the subcutaneous tissue is not involved.

Differential Diagnosis. The lesions which simulate tuberculosis of the vulva may be either acute or chronic.

Among the acute non-tuberculous lesions which may show ulcerations are gonorrheal vulvovaginitis, anogenital diphtheria, the ulcerations occasionally seen in the acute exanthemata, gangrene of the vulva in the eruptive fevers, acute Bartholinitis, and acute phagedenic and round ulcers (Vautrin[103]). In all of these the acuteness of onset, the presence of other local or general phenomena, and the bacteriological examination of the secretions are of essential diagnostic importance and need only be mentioned.

Greater difficulty in diagnosis will be encountered among the subacute and chronic lesions, as is shown by the use of the word "esthiomene." This term has been used to describe a chronic vulvar ulceration with or without hypertrophy, in the production of which a chronic lymph stasis plays an important role. Various lesions which should have received more accurate diagnoses have been described under this term. We agree with Bonnin,[9] who condemns the use of the word, and with Combeléran,[17] who points out that many cases described as "esthiomene" are true cases of tuberculosis of the vulva. Biopsy only will prove this point.

Syphilis of the vulva is encountered in a number of forms. The initial chancre is of more acute onset, the surrounding edema is of greater extent, the induration of the base more marked, the ulceration not so deep, the borders less excavated, and the granulations of a brighter red, than seen in tuberculosis. There is greater enlargement of the inguinal lymph glands than in tuberculosis. Microscopic examination of smears from the ulcer base will show the Treponema pallidum. In the mixed chancre the inflammatiory character of the lesion will be even more marked, and the bacillus of Ducrey will also be found. Syphilitic mucous patches of the inner surfaces of the labia can be differentiated from a tuberculous leucoplakia only by a search for the Treponema pallidum. *Late secondary* and *tertiary* syphilitic lesions of the vulva usually ulcerate and closely simulate tuberculosis. The ulcerations are, however, more acutely inflammatory and their granulations brighter. Microscopic examination of smears serve to differentiate them. Papulohypertrophic lesions of syphilis occasionally are confused with the hypertrophic form of tuberculosis. But in syphilis, fissures are usually present and the papillomatous character of the lesion is more marked. In all the various manifestations of syphilis about the vulva (except the early chancre) the presence of a positive Wassermann reaction establishes the diagnosis. Other evidences of the disease may be present. Rapid healing under specific treatment proves the luetic nature.

Simple chancre (chancroid) is frequently seen about the vulva. Here the acute onset, the greater pain and inflammation, the tendency for development of new lesions on coapted surfaces, the frequency of suppurative inguinal adenitis, and the microscopic finding of the bacillus of Ducrey should differentiate it from tuberculosis.

In *epithelioma of the vulva* the raised edges and hard nodular borders should identify the character of the lesion. They are not seen in tuberculosis. (Biopsy is conclusive.)

Sarcoma of the vulva is an exceedingly rare lesion, hard, firm, not ulcerating until a late stage, when metastatic lesions are already evident. In its early stages it is distinguished from the hypertrophic form of tuberculosis by its local character, involving one portion only of the vulva.

In *kraurosis vulvæ* the lesions are generalized and the skin and mucous membranes are grayish. Atrophy takes place to so great an extent that the labia majora and minora are much distorted and may be fused. This atrophy is not seen in tuberculosis.

Various *miscellaneous lesions* which may simulate tuberculosis have been mentioned in literature. None of them are of great importance and few of them should give rise to difficulty in diagnosis. Bonnin[9] refers to actinomycosis and molluscum contagiosum, both of which can be recognized microscopically. Combelèran[17] speaks of acne, furuncles, suppurative vulvar folliculitis, and herpes of the vulva. Froelich[39] has described a diabetic vulvar ulcer.

It is thus seen that there are many conditions from which tuberculosis of the vulva must be differentiated. In most of them a clinical diagnosis is possible, but the ultimate diagnosis must rest upon microscopic examination either of smears or of biopsy specimens.

Prognosis. We have reviewed the cases here collected to study the results of treatments used and to determine the prognosis. This latter is not good. In 23 cases the data as to immediate or late result is too meager for use in our study. In 49 cases such data is partially or wholly given. Of these 49 cases, 21 or nearly 43 per cent. died, while 28, or about 47 per cent., recovered. One case was reported well locally seven years after treatment, but when last seen had a steadily progressive pulmonary tuberculosis. Of the other cases reported "recovered" many were lost sight of shortly after treatment and some few have had recurrences. The true end-result was given in so few cases that the prognosis is probably even worse than the above figures indicate. An associated tuberculosis was found elsewhere in the body in all cases which died. There were two operative deaths recorded. One occurred from shock following a panhysterectomy for an associated tuberculosis of the body and cervix of the uterus; the cause of death in the second case was not given. Prognosis is no more favorable in one type of the disease than in another. The lupic type is considered by some writers more benign.

Table II shows briefly the results in this series of various forms of treatment. "Healed" and "recurrence" refer to the local condition for various intervals of time during which each case has been under observation. "Healed" cannot therefore be inter-

preted as an end-result, although for any individual case it may be such.

TABLE II.

	No. of cases.	Healed.	Recurrence.	Per cent. healed.
Excision	20	13	7	65
Curette and cautery	6	5	1	83
Excision with cautery	1	0	1	0
Cautery	1	1	0	100
Nitric acid	1	1	0	100
Iodoform	2	2	0	100
Tuberculin	1	1	0	100
General hygiene	1	1	0	100

TREATMENT. While the form of local treatment must vary with the individual case, the necessity of careful general management of the patient, rather than the disease, must not be lost sight of. It is unnecessary for us to here enter upon a discussion of the general treatment of tuberculosis. To suitable changes in diet, environment, and mode of life can be added, we believe with advantage, tuberculin. The details of technique, selection of patient and preparation, and dosage must be governed by those same rules which have given such excellent results in surgical tuberculosis elsewhere in the body. General miliary or active pulmonary tuberculosis contra-indicate the use of tuberculin.

The local treatment may be palliative or radical. Reference to Table II shows the results in this series of the different forms of treatment. Palliative measures vary in severity from the use of simple dusting powders or ointments to cauterization by mineral acids or heat. The value of local antiseptics is questionable and empirical. Iodoform, which is most frequently used, can be taken as an example. Fränkel[37] has shown that bacteriologically it is not antiseptic, and that after sterilization at high temperatures the iodin is driven off. Its chief value seems to be in its fibroplastic power. Because of this it may be useful in the treatment of localized tuberculosis. Fränkel,[37] however, prefers pure sterile bone carbon for this purpose. The pathology of the disease proves the uselessness of local applications which do not destroy. They cannot penetrate to the necessary depth.

The various caustics are also insufficient because of their lack of depth of action. Silver nitrate is worthless. The action of lactic and the mineral acids cannot be controlled. Thermal cauterization should be classed among radical measures.

Radical local measures include curettage, cauterization by heat, excision of the lesion with the thermocautery, and dissection excision. While each of these methods of treatment has its advocates it is difficult to decide among them.

Remembering that tubercles may be found at some distance from the apparent edge of the lesion, we can mention curettage only to condemn it. The procedure should never be used. It is more apt to spread than to cure the lesion.

Theoretically, dissection excision should give the best results, provided, of course, that the dissection can be carried on entirely in healthy tissue. This is often difficult. The depth of the lesions is at times considerable and the anatomical arrangement of the parts makes a wide excision often impossible without serious mutilation of surrounding structures. It is this limited operative field which has been responsible for the dissection in so many cases passing through active infective tuberculous material. That such material has been entered is shown by the local recurrence and the frequency with which an operative interference has been followed by a diffuse general miliary tuberculosis. Operation upon tuberculosis of this region of the body (perineum) seems particularly prone to disseminate the disease. This may be due to the close proximity and almost invariable simultaneous involvement of mucous membrane in the tuberculous process. Elting[31] has reported 9 cases of tuberculous fistula in ano, 4 of whom died subsequent to operation from a progression of their pulmonary tuberculosis. Similar untoward results are at times seen in tuberculosis of other mucous membranes. Thus Shepherd[94] has reported a case of tuberculosis of the tongue which after removal developed an acute general miliary tuberculosis rapidly terminating in death. Quénu and Hartman,[83] however, prefer dissection excision to cautery excision in tuberculosis about the perineum.*

Thermocauterization if carried sufficiently deeply should not only eradicate the lesion, but also seal off the lymphatics so that dissemination cannot occur. Its use is, however, limited by the proximity of surrounding important structures. Superficial cauterization is valueless. Only deep and thorough cauterization is sufficient. This will, unfortunately, leave a large area to heal by granulation.

Excision with the cautery knife seems to be the method of choice, even though destruction of tissue be large. By this method the exact limit of the areas to be excised can be determined and adhered to. Less destruction of contiguous parts will take place with a thin cautery blade than with a blunt cautery point.

If inguinal lymph glands are evidently infected, they should be removed. Dissection *en bloc,* as for an epithelioma of the vulva, is unnecessary. In the absence of evident involvement the lymph glands need not be removed. This is in accordance with the current view of the analogous problem in tuberculosis of the mammary gland.

* It is never certain that any operative procedure on an apparently local tuberculous focus will not activate some other known or unknown tuberculous lesion in the body. This is not only true of tuberculosis involving mucous membranes as above mentioned but also of other parts of the body. Powers[81] has reported a case of tuberculosis of the breast which after operation died of a pulmonary tuberculosis. Ill[53] and others have reported similar results in dealing with tuberculous kidneys, etc., and the list might be indefinitely multiplied.

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THE OPERATION OF CRANIAL DECOMPRESSION.

By William Sharpe, M.D.,

HEAD OF THE DEPARTMENT OF NEUROLOGICAL SURGERY, NEW YORK POLYCLINIC MEDICAL SCHOOL AND HOSPITAL, NEW YORK CITY.

There are few operations in surgery having the wide application and immediate beneficial results as cranial decompression, particularly the subtemporal method. It is an operation that has been much neglected in the past, and one that is capable of still greater usefulness in the future. It is a comparatively simple operation, requiring no special technique and no special training other than a thorough knowledge of the anatomy of the temporal region and the avoidance of operative complications; if, however, difficulties are encountered then the use of the best methods for controlling them must be known. Naturally, careful hemostasis is a most important factor in obtaining good results in all cranial operations as well as due respect and regard for the delicate nerve cells of the cerebral cortex by the avoidance of unecessary and rough manipulation and digital examination; and, also, of the greatest importance, a strict asepsis.

Cranial decompressions have been limited in the past chiefly to the relief of intracranial pressure in cases of unlocalized cerebral tumor and in cases of fracture of the skull showing signs of medullary compression; the operation was performed not only to lessen the danger of a medullary edema but to avoid a secondary optic atrophy—so commonly observed in tumors of the brain. In these latter cases the site of the decompression was most frequently over the parietal area or the upper temporal region, and thus, as the tumor enlarged, the increasing intracranial pressure forced the underlying cerebral tissue through the bony opening, producing herniæ cerebri of tremendous sizes—the bane of cranial surgery. Fungi cerebri were also a common result of such protrusions. Not only was this complication to be feared, but operative damage to the underlying motor area with resulting paralysis of the opposite side of the body was always risked; besides, the intracranial pressure in cases of fracture of the skull as well as in tumors of the brain frequently produced a motor impairment by forcing the motor area upward through the bony ring of this decompression.

The reason for these complications is obvious. To remove an area of either parietal bone, not only may the underlying motor cortex be impaired at the time of the operation, but also subsequently by its protrusion upward through the bony opening. This is made possible by the extremely weak protection afforded by the scalp overlying the parietal bone; other than the cutaneous tissues in this area there is only the epicranial aponeurosis, so that

even a moderate degree of intracranial pressure is sufficient to cause a hernial protrusion. If the decompression is performed in the parietotemporal area the cranial origin of the temporal muscle to the parietal crest must be destroyed, and thus the possible protection of the temporal muscle is lost.

In contrast to these methods of cranial decompression the subtemporal route offers an almost ideal operation for intracranial conditions, requiring either a relief of the increased pressure or an exploratory procedure; not only is the underlying cortex a part of the temporosphenoidal lobe (which is a comparatively "silent" area of the brain), but the removal of the squamous bone is technically less difficult, in that it is the thinnest part of the vault of the

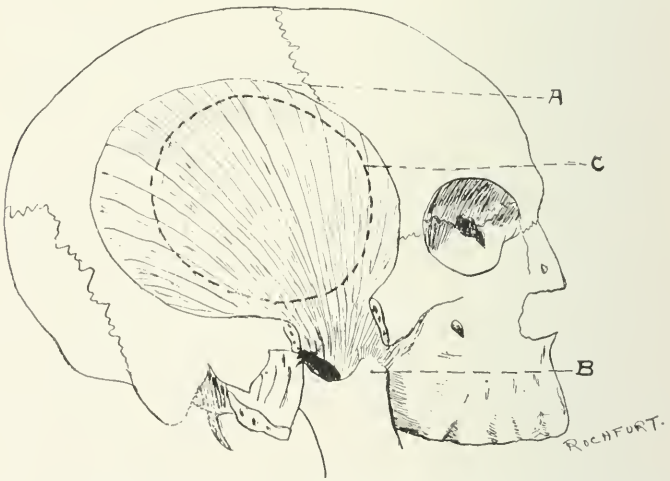

Fig. 1.—Anatomical relations of the subtemporal decompression. The temporal muscle: *A*, its origin along the parietal crest; *B*, its insertion at the coronoid process (the zygoma having been removed). The dotted line *C* shows the extent of the bony decompression opening protected by the overlying temporal muscle. The direction of the muscle fibers illustrates how easy it is to separate them longitudinally.

skull; again, the decompression opening is amply protected by the overlying temporal muscle, so that it is a rare occurrence to have a hernia cerebri following this method of cranial decompression; if the attachment of the temporal muscle to the parietal crest is carefully preserved, then it is practically impossible for a marked protrusion to occur (Fig. 1). In my opinion this method of cranial decompression should be the one always to be employed, and in this article when the word "decompression" is used it is the subtemporal decompression that is meant. In subtentorial lesions affecting the cerebellum, naturally a suboccipital decompression is to be preferred; especially is this true of tumor and abscess formations in it. As the tentorium strongly separates the cerebrum from

the cerebellum, any increase of the subtentorial pressure is more effectively relieved by a suboccipital decompression than by a supratentorial operation; besides, not only may the lesion be removed at the same time, but the bony opening will be protected by a thick layer of occipital muscles, and thus a large hernia be prevented.

The purpose of the subtemporal decompression has been much enlarged during the past few years, and it seems that its usefulness is to be developed still more in the future. Although its chief function is the relief of intracranial pressure, yet it is a most valuable method of exploration. In these two divisions, practically all of the intracranial conditions for which the operation may be advisable can be classified, and the following is a brief consideration of them:

I. The Relief of Intracranial Pressure.

A. *Tumors of the Brain.*

1. Localized Tumors of the Brain.

(*a*) Large cerebral tumors: For fear the cerebral cortex would be much more extensively damaged by opening the skull directly over the tumor, it is frequently advisable in cases of high intracranial pressure first to make a subtemporal decompression on the side of the head opposite to the tumor and then to perform the osteoplastic "flap" operation to remove the tumor. In this manner not only may the tumor be enucleated with little impairment of the surrounding cortex, but in cases where the tumor is not found as localized clinically (an occurrence of only too great frequency), then the brain may be "dislocated," as it were, toward the opposite side of the head, as made possible by the decompression opening on that side, and in this manner an exploration can be conducted with but little or no injury to the surrounding cortex. This is a most important function of the decompression in facilitating the removal of large cerebral tumors; within the past year I have removed large cerebral tumors in three cases by this method, and I am confident the operation would have ended fatally if this procedure had not been used.

(*b*) Irremovable tumors of the base and of the mid-brain: Frequently these tumors are non-malignant, the most common one being the tuberculoma; my series contains four of them. It is of the greatest importance to prevent secondary optic atrophy and its resulting blindness by an early relief of the intracranial pressure. These tumors may enlarge to a certain size, then remain stationary, become smaller, and even disappear clinically, so that if blindness is prevented during their stage of active growth, then an excellent result may be obtained. If the tumor should continue to grow, then the headaches and blindness may be delayed for months until the last stage of the condition.

2. *Unlocalized Tumors.* In the hope that the tumor may localize itself clinically and thus permit of its removal, and yet to prevent the secondary optic atrophy resulting from the increased pressure

of its growth, it is advisable to perform an early decompression and, if necessary, a bilateral decompression. During the past year I have treated five cases in this manner; it is surprising to observe the improvement in such cases; a cessation of headache, nausea and vomiting, the rapid subsidence of the beginning "choked disk" —the forerunner of secondary optic atrophy and blindness. No case of high intracranial pressure producing "choked disks" should be permitted to remain weeks while a definite diagnosis is being made without a relief of that pressure by a decompression; only too frequently such cases are brought to the surgeon after blindness has occurred, and once an advanced degree of secondary optic atrophy has supervened there is little if any recovery of sight. Not only will an early decompression delay and even prevent blindness in these cases, but in will prolong the life of the patient by lessening the medullary compression, and thus the unlocalizable tumor may extend into a part of the brain producing unmistakable signs of its situation, so that the tumor can be successfully removed. This is the common history of tumors of the frontal and temporosphenoidal lobes, especially of the right cerebral hemisphere; as tumors of the frontal lobe extend posteriorly to the motor area then a motor impairment of the opposite side of the body appears, and if downward upon the optic nerve, then an ipsolateral primary optic atrophy results; motor aphasia frequently appears as tumors of the left frontal lobe extend backward into the motor speech area; in tumors of the temporosphenoidal lobe a similar motor impairment occurs if the lesion extends upward into the motor tracts or forward into the motor speech area.

In similar cases of suspected tumors of the frontal or parietal lobes, and if the intracranial pressure is not extremely high, it is advisable to perform an osteoplastic "flap" operation first, and if the tumor is not found or after its removal the brain is still under marked tension, then a subtemporal decompression can be performed by rongeuring away the squamous portion of the temporal bone and the lower portion of the bone flap itself; in this manner another scalp incision is avoided.

B. *Fractures of the Skull.* Whether the fracture is of the vault or of the base a decompression is advisable only when the fracture is associated with high intracranial pressure; naturally the palliative expectant treatment of absolute rest and quiet, an ice-bag to the head, catharsis and liquid diet, are usually sufficient for those cases of fracture of the skull showing no marked signs of intracranial pressure; that is, a fracture of the skull is not an indication for an operation unless there are definite signs of an increase in the intracranial pressure. An ophthalmoscopical examination of the fundi of the eyes is the most reliable and accurate means of determining an increase of the intracranial pressure, whether this increase is due to a swollen edematous brain, a depressed fracture of the

vault, or to an intracranial hemorrhage of extradural, subdural or intracerebral origin with cerebral lacerations. It is not so essential to remove the depressed area of bone or the intracranial clot as it is to offset the pressure effects of the depression or clot upon the cerebral cortex; naturally, in depressed fractures of the vault, the depressed area should be elevated or even rongeured away, and in cases of intracranial hemorrhage, the clot should be removed, but in many cases, even when their removal is possible, the intracranial pressure still remains high and it is this continued increase of intracranial pressure which damages the cerebral cortex and produces the impairment—both physical and mental. It is not so much a question of fracture of the skull as the effects upon the brain of the injury producing the fracture; in many cases a fracture of the skull is not present and yet a cortical hemorrhage and even cerebral lacerations may have resulted from the injury. It is in these cases of intracranial lesions resulting from injuries to the head and showing definite signs of increased intracranial pressure that an early relief of this pressure is advisable—not only to avoid the danger of a medullary compression and its possible collapse, and therefore the death of the patient, but to lessen the percentage of the post-traumatic conditions so common in these cases, such as persistent headaches, dizziness, changed personalities varying from the depressed state to a highly irritable condition, generally nervous instability, and even epilepsy in its different forms. A decompression should only be advised when there are marked signs of intracranial pressure as revealed by the ophthalmoscope. Signs of medullary compression, such as a retarded pulse, a slow and irregular respiration of the Cheyne-Stokes type, and a high blood-pressure are rather late signs of intracranial pressure, and if the patient is allowed to reach this dangerous condition, then it is doubtful if the patient will recover—operation or no operation; a medullary edema and collapse of the patient may occur at any moment.

1. Fractures of the Vault.

(*a*) Linear fractures with no depression of the fragments: In these cases a decompression should be performed if the intracranial pressure is high. It has been rare in my experience for fractures of the vault, unless small locally depressed ones, to be limited to the vault alone; usually the "crack" extends downward to the base—the thinnest and weakest part of the skull. However, this type of fracture, as revealed by the Roentgen-ray, frequently shows no sign of intracranial pressure, and therefore an operation should not be considered.

(*b*) Depressed fractures of the vault should always be elevated. If this is impossible, then it is usually wiser to remove the depressed fragments, whether the intracranial pressure is high or not. The danger of local damage to the underlying cortex with the subsequent

formation of adhesions, etc., rendering the cerebral cortex unstable and thus subjecting the patient to the frightful risk of epilepsy, is a calamity always to be feared, and especially in depressed fractures of the vault. If the intracranial pressure is high, then it is wiser to perform a subtemporal decompression on the same side of the head as the depressed area, and in this manner the general intracranial pressure is relieved. If the depressed area overlies either motor tract of the cerebral cortex, and the intracranial pressure is very high, causing a double papilledema, then it is advisable to perform the subtemporal decompression first and thus relieve the pressure, so that there will be less danger of injury to the motor tract when the depressed area is elevated or removed; otherwise the intracranial pressure may be so extreme as to force cerebral tissue through the fractured opening of the vault and a motor impairment of the other side of the body result.

2. Fractures of the Base. These cases should be treated by the expectant palliative method; however, if the signs of high intracranial pressure appear then an early decompression will not only save a larger percentage of patients than the other method of treatment, but it will lessen the number of post-traumatic conditions. In this connection it may be interesting to note that of the total number of 77 cases of fracture of the skull which were admitted during the year ending June 1, 1914, to the department of neurological surgery of the New York Polyclinic Hospital, 27 of them died; that is, a mortality of 35.06 per cent. Of these 27 cases, however, 20 of them were moribund upon admission—11 of them dying within a few minutes to two hours after admission, and the remaining 9 dying within six to twelve hours after admission; 36 cases of the 77 admitted were operated upon, with a mortality of 9 cases following operation; that is, an operative mortality of 25 per cent.; however, 4 of them revealed at autopsy subtentorial fractures with hemorrhage—a most dangerous condition, as it causes direct pressure upon the medulla; 2 died, nine and sixteen days respectively following the operation, from meningitis due to infected hematomata of the scalp; 1 died on the twelfth day postoperative from pneumonia—the patient being seventy-five years of age—and the ninth case died on the sixth day postoperative from a meningitis, probably due to a "slip" in the operative technique. Naturally the cases operated upon were the severe cases showing signs of high intracranial pressure. It is a mistake to operate upon these cases when in a condition of severe shock; it is better to wait several hours until the shock has been overcome, otherwise the operation is but an added shock.

C. *Brain Abscess, Particularly of Either Temporosphenoidal Lobe.* The accurate diagnosis of brain abscess is a most difficult one, and any operative procedure should always be conducted as an exploratory operation. As a rule, abscess of the cerebellum is

diagnosed with less difficulty than abscess of either temporosphenoidal lobe or of either frontal lobe; therefore if an abscess of the cerebellum can be excluded in a case with the usual history of previous otitis media it is much wiser to perform a subtemporal decompression over the suspected temporosphenoidal lobe and thus be enabled not only to relieve the intracranial pressure (if present), due to the abscess, but to permit a careful exploration of the entire temporosphenoidal lobe through a non-infected area; if the abscess is found, then free drainage is afforded through the lower angle of the split temporal muscle, and the decompression will offset the pressure effects of the swollen edematous brain resulting from the exploratory punctures and the presence of the abscess itself; again a meningitis is much less liable to occur with free drainage and a lowered intracranial pressure than if the intracranial pressure were high enough to lessen the resistance of the tissues to an infective meningo-encephalitis; if the abscess should not be found then a relief of the intracranial pressure has been obtained and no harm done; the abscess may localize itself later. It is a dangerous procedure to puncture the dura blindly or open it through an infected area such as the mastoid; if the abscess is not found the danger of infection is great indeed; and if it is found the resulting cerebral edema can not be lessened by the small operative opening, so that the danger of a medullary compression is a serious menace; in my opinion, patients die not so much from the presence of the abscess, but rather from the cerebral edema with its resulting medullary compression.

Within the past year I have operated upon two cases of abscess situated in the anterior median portion of the left temporosphenoidal lobe, and if I had not used the subtemporal decompression I am confident I should have overlooked them. Again, in cases of suspected brain abscess it is much better to perform an early exploratory operation than to wait until the patient shows marked signs of medullary compression; the danger of the abscess rupturing into either the subdural space or the ventricle is then much greater.

My own series of operated cases of brain abscess is limited to 10. Of these 4 died: 2 from medullary edema resulting from a too small opening of the occiput in cerebellar abscess; 1 from a meningitis following the drainage of a left frontal abscess through a small opening—no decompression having been performed; and the fourth one died from a large temporosphenoidal abscess—three to three and a half inches in diameter—which gnawed its way into the ventricle after a decompression with free drainage had been established. The remaining 6 cases recovered; 4 were situated in the temporosphenoidal lobes, and each one was drained through a subtemporal decompression; 1 a cerebellar and 1 a right frontal abscess—the latter case having a decompression performed until the abscess located itself clinically seven weeks later.

D. *Cerebral Spastic Paralysis.* Selected cases due to an intracranial hemorrhage at birth. Attention has been centred in the past upon the correction of deformities and the lessening of spasticity; the improvement following these operations has been only temporary in all but the mild cases. Naturally the cases of spastic paralysis due to a lack of development or malformation of the brain and its pyramidal tracts are not operated upon and could not be benefited by any cranial operation, but only those cases of cerebral spastic paralysis having a history of difficult labor with or without instruments, and upon ophthalmoscopical examination of the fundi, the definite signs of intracranial pressure are to be observed in the dilated retinal veins, edematous blurring, and haziness of the nasal halves of the optic disks and the more marked signs of old intracranial pressure—these are the cases that can be improved by merely a relief of the intracranial pressure; the local pressure effects of a hemorrhage or of its resulting cystic formation are offset by the decompression, and if the intracranial pressure is high then a bilateral decompression may be performed. If the hemorrhagic clot or its subsequent cyst can be removed, so much the better; but this is not possible in many cases. Naturally the longer the clot and its cystic formation are allowed to exert pressure upon the cortex the more impaired do the nerve cells of the cortex become; in my experience of 65 operated cases, however, only 5 of them revealed the hemorrhagic cyst in or beneath the cortex; that is, the cortical nerve cells were not primarily destroyed but merely impaired by the pressure of the clot and its cyst upon them, as was the condition in 45 cases observed at the operation; thus the longer the condition of intracranial pressure is allowed to continue, just so much more will be the impairment of the cortical nerve cells, resulting in a persistent and even increasing stiffness and spasticity, and a steady mental deterioration in the majority of cases. Most of my cases have been from five to eight years of age—the youngest six months and the oldest twenty-one years of age; the older the patient above twelve years of age the less was the improvement; but even the older ones are improving. The operative mortality has been 6 cases; 4 of these, however, were extreme cases of spastic diplegia under two years of age, very much emaciated and having great difficulty to breathe or to swallow; this type of case should not be operated upon, as the anesthetization alone is too great a risk. However, no case of spastic paralysis, no matter how extreme, should ever be operated upon unless there are definite signs of intracranial pressure as shown by a careful ophthalmoscopical examination; in this manner the spastic cases due to a lack of development and malformation of the brain and its tracts are easily excluded and should never be operated upon, as their condition could not possibly be improved by a cranial operation. Naturally, sufficient time has not yet elapsed since the first operation

(June, 1913) to establish the permanency of the improvement in these selected cases of spastic paralysis, but from pathology of the condition we see no reason why the children should not continue to improve as they are doing. A report in detail is to be published soon.

II. As an Exploratory Procedure.

This is particularly true of suspected lesions of either temporosphenoidal lobe, the lower portion of either motor area, the posterior lower portion of either frontal lobe, and the motor speech areas. It is a much more simple operation technically than the osteoplastic "flap" operation, requiring half the time, and the bony opening can be firmly covered by the temporal muscle so that no deformity results. Again, if an increase of the intracranial pressure is found at operation then the decompression will relieve it.

Besides the cranial conditions selected above as being benefited by the operation of subtemporal decompression, there are other intracranial lesions for which the decompression may be used; but this work is now in its experimental stage, and will be discussed later.

Not only will a decompression itself relieve the increased pressure, but a tapping of the lateral ventricle may be easily performed through the decompression opening by means of a small blunt cannula, and in this manner the presence or the absence of a dilatation of the ventricles is ascertained—a most important aid in ascertaining the location of the intracranial lesion; besides, the ventricular tapping will greatly relieve the intracranial pressure—at least temporarily.

The Technique of the Subtemporal Decompression. There should be the usual preparation of the patient for an operation. The side of the head selected for operation is carefully shaved, either on the preceding night and a green soap poultice applied, or in emergency cases the operative site is closely shaved just before the operation. Unless there are clinical signs indicating a lesion of the left hemisphere the decompression is always performed on the right side in order to avoid the motor speech area, which is situated in right-handed persons in the posterior portion of the third left frontal convolution, and *vice versa* in left-handed patients. The patient is placed upon his back with his right shoulder elevated by a sand-bag, so that the right side of the head can be more easily made parallel to the table; in this manner the operative site is well exposed and it does not compel the operator, standing at the head of the table, and his assistants to assume tiring positions. The anesthetist is seated under a sheet at the waist of the patient, and in this way he is entirely excluded from the field of operation. The anesthesia in these cases requires the most skilful administration; especially is this true to avoid an extreme cyanosis and congestion not only during the induction of narcosis, but after the

dura has been incised and the cerebral cortex exposed; coughing or even labored respirations at this stage of the operation may result disastrously by forcing the cortex through the bony opening; the cortex may be ruptured and serious hemorrhage occur. Dr. Charles S. Hunt, who has administered the anesthetic in all of my cases, uses a mixture of ether and oxygen most successfully; he has found it necessary to deepen the narcosis just before the dura is incised, otherwise the sudden relief of intracranial pressure will allow the patient to show signs of consciousness by coughing, etc.—a complication to be feared at this stage of the operation.

The side of the head and face are now carefully "scrubbed" with green soap and water for five minutes, and then alcohol is sponged over the operative area. Iodin is only used in emergency cases when the scalp can not be thoroughly prepared; it tends to irritate the skin in many cases and thus render a secondary infection possible. A superficial incision in the skin is now made to indicate the area of the operation, and then towels wet in a 1 to 3000 solution of bichloride are clipped to the scalp at each side of this incision; in this manner the head is completely covered and the towels can not become disarranged, so that there is little danger of infection.

By using the method of pressure-traction at each side of the incision and the forefinger of the assistant to compress the temporal artery as it passes over the zygoma, the incision can be made with little loss of blood—a most important factor in all cranial operations; a cranial tourniquet cannot be used in this operation, and the other methods for controlling hemorrhage of the scalp, such as deep sutures, clipping of the scalp, etc., are time-consuming, troublesome, and even dangerous by increasing the risk of infection; besides they are ineffective in many cases.

The incision itself is made vertically upward through the scalp from a point just above the zygoma and one-half inch anterior to the external auditory meatus to the middle of the parietal crest, and thus overlying the origin of the temporal muscle; it is about three to three and a half inches in length, and is parallel to the fibers of the underlying temporal muscle (Fig. 2). Small curved hemostats are used to compress the branches of the temporal artery, and then the temporal fascia is incised vertically and the fibers of the temporal muscle are split longitudinally and retracted, exposing the squamous portion of the temporal bone. A sharp periosteal elevator is used to separate the muscle from the underlying bone; great care should be taken not to destroy the attachment of the muscle and its fascia to the parietal crest—otherwise the closure of the temporal muscle will be greatly weakened.

The Doyen perforator and burr are now employed to make a small opening at the lower angle of the operative area—that is, the thinnest portion of the squamous bone (Fig. 3). Small rongeurs enlarge the opening until it is possible to use a larger rongeur having

one blade bevelled and flattened so that it can be easily inserted between the dura and bone; frequent explorations and removal of adhesions between dura and bone with the dural separator will prevent the dura from being torn. In this manner a circular opening as large as possible under the temporal muscle is made—extending from the base of the skull up to the parietal crest and having a diameter of two and a half to three inches.

Before opening the dura it is important that all oozing from the bony margins should be stopped; the best method for controlling this bleeding from the diplöe and its sinuses is the rubbing of a

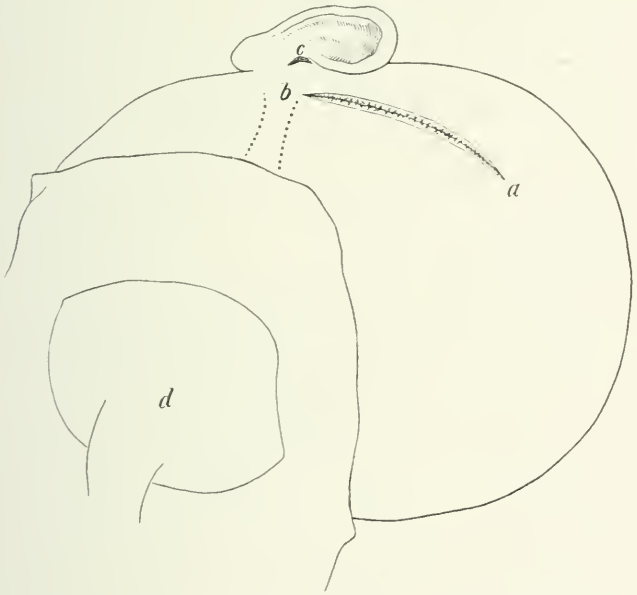

FIG. 2.—The superficial incision *a–b* shows the vertical extent of the operation—two and one-half to three inches; *a*, the middle of the parietal crest; *b*, the zygomatic arch; *c*, the external auditory meatus; *d*, the ether-oxygen apparatus in position.

bone-wax into the edge of the bone, and it is surprising how quickly this troublesome complication is overcome. Dr. Norman Sharpe has formulated a bone-wax which is most effective; its composition is as follows: white wax, 7 parts; almond oil, 2 parts; salicylic acid, 1 part. It should be kept in a 5 per cent. solution of carbolic acid. This wax may be sterilized before each operation and then allowed to cool so that it hardens and is easily moulded; small pellets, the size of peas, are then applied to the oozing bone. It is an effective method of plugging the middle meningeal artery when it channels the bone; it seems to me that it might be used in operations upon bone elsewhere—such as the mastoid, resections

of bone, etc. It is far superior to the old method of using wooden pegs in cranial surgery. In fractures of the skull the middle meningeal artery is frequently torn in the subtemporal area, so that it is a simple matter to remove the clot and then plug the bleeding point with the wax.

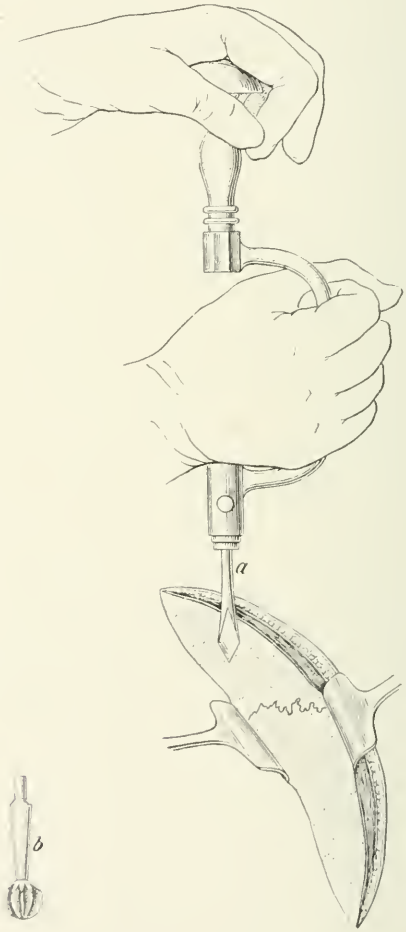

FIG. 3.—The temporal muscle retracted. Using the Doyen perforator *a* to open the skull at the lower angle of the incision, that is, at the thinnest part of the squamous portion of the temporal bone. The Doyen burr *b* is next used to enlarge this opening so that rongeurs may be employed.

The dura is now incised by carefully cutting through its outer layer first with a sharp knife; elevating the dura from the underlying cortex by means of the small dural hook inserted into its outer layer, the inner layer can now be safely incised until a small pinpoint opening is made; a grooved director bent at right angles may

now be carefully inserted and the dural opening enlarged by cutting the dura upon the director (Fig. 4). When the dural incision is about one inch in length, I have found it easier and quicker to insert a spoon-shaped spatula and then cut the dura with a sharp pair of scissors; this method is not only safer, but it allows the incision to approach the dural vessels as closely as possible, so that these vessels may be clamped before being cut. Not only is it time-consuming and troublesome to ligate the dural vessels with silk or catgut, but it is dangerous to insert a needle beneath the vessels

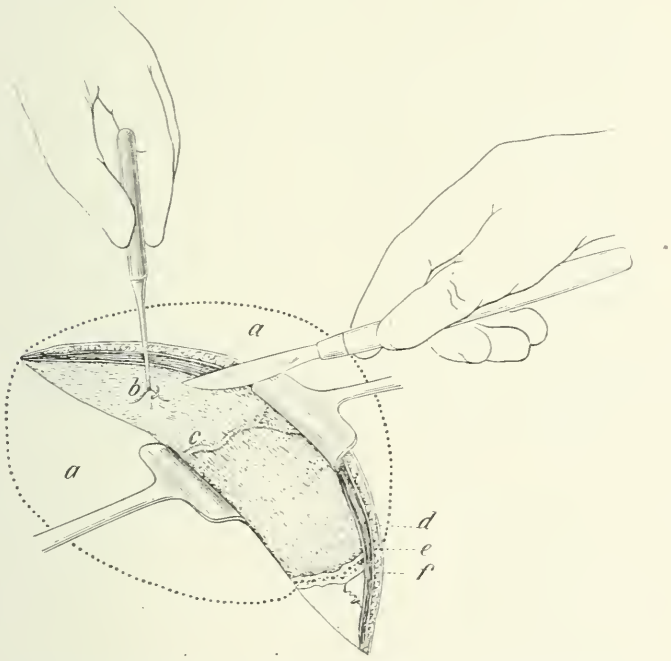

FIG. 4.—Dotted lines *a* show area of bone (two and one-half by three inches) removed. Incising the dura which is elevated from the underlying cortex by the dural hook *b*; *c*, middle meningeal artery; *d*, skin; *e*, temporal fascia; *f*, temporal muscle.

before the dura has been incised for fear of puncturing one of the many cortical vessels lying beneath and thus complicating the operation; if the decompression is to be performed it should at least not injure the brain. An excellent method of dealing with the dural vessels is the application to them of the small silver V-shaped clips used by Dr. Harvey Cushing, and then the dura and its vessel may be safely cut between each pair of clips and no bleeding result; these clips may be left on the vessels, and I have never seen any ill-effects occur; in three cases at autopsy within two years after

operation, the clips were found *in situ;* no tissue reaction had occurred, so that they are apparently not irritating foreign bodies; in some cases where the dura was very vascular I have used as many as eight clips. The clips are made by snugly wrapping German silver wire No. 24 around a rectangular rod and then bisecting the roll; V-shaped clips are thus formed, and after sterilization these can be put in a clip holder (similar to a hemostat with a grooved end) and slipped upon the dural vessel. This method saves much time and entails no risks.

The dural opening is thus enlarged in a crucial or stellate manner until the bony margins of the decompression are reached. It is important to incise the dura downward to the base of the skull so that the middle fossa of the skull can be easily and freely drained—so essential in all fractures of the skull with edematous, swollen brains with or without hemorrhage. Through this opening any underlying pathological lesion can be dealt with freely and safely; subdural clots may be removed in fractures of the skull; tumors enucleated and abscesses drained. Aided by the spoon-shaped spatula and a good electric head-light, the neighboring areas of the frontal lobe, the parietal lobe, and the posterior portion of the temporal lobe may be accurately explored for any cortical lesion. If the cerebral tension is high then the ipsolateral ventricle may be drained by the ventricle puncture needle; all parts of the temporosphenoidal lobe and even the posterior portion of the frontal lobe and the lower portion of the parietal lobe can be accurately explored in this manner in cases of suspected sub-cortical lesions, as tumors and abscess.

After the cerebral lesion has been removed or drained, or if merely the relief of intracranial pressure is desired, then a rubber tissue one-quarter inch in width and several layers in thickness is inserted at the lower angle of the wound and inside the dura beneath the temporosphenoidal lobe as far as possible; in this manner excellent drainage is afforded the middle cranial fossa. Before closure of the opening it is important that there should not remain any bleeding-points—no matter how small; small cotton pledgets wet in warm saline solution are frequently sufficient in many cases of cortical oozing, or a small piece of the temporal muscle applied to the bleeding point and then compressed for a few seconds will stop a most troublesome oozing. When tumors are removed, then packs of cotton wet in warm saline solution and pressed for a few moments into the cavity of the enucleated tumor mass will quickly prevent a large hemorrhage; it is rarely necessary to leave packing intracranially.

The drain having been inserted beneath the temporosphenoidal lobe the temporal muscle is now sutured with interrupted fine black silk—usually in two layers (Fig. 5); then the temporal fascia and finally the subcutaneous tissues; the vessels of the scalp are not

ligated as the mere suturing of the subcutaneous tissue is sufficient to compress their vessels; at times, however, the temporal artery

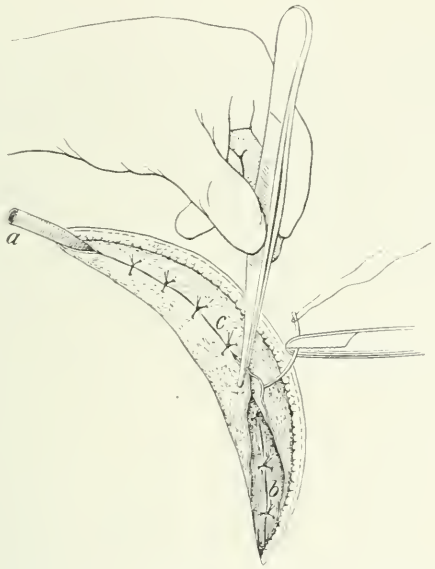

FIG. 5.—Rubber tissue drain *a* inserted into middle fossa beneath the temporosphenoidal lobe and passing out at lower angle of incision; *b*, fibers of temporal muscle reunited by layers of interrupted fine silk sutures; *c*, temporal fascia being sutured by interrupted fine silk.

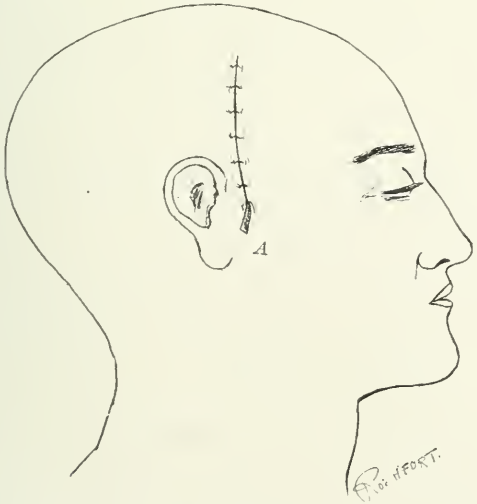

FIG. 6.—Skin sutured with fine silk. All towels removed. *A*, drain of rubber tissue.

itself is ligated. The skin is carefully approximated by fine black silk (Fig. 6). Dry gauze pads are now applied to the operative

area, and after a cotton pad well covered with sterile vaselin is placed behind the lobe of the ear to prevent its being pressed against the skull and causing severe pain, the usual bandage of roller gauze is used and held in place by several strips of adhesive plaster (Fig. 7).

In operations of subtemporal decompression the dural opening is never sutured together; in the first place, if there is much intradural pressure, it would be impossible to approximate its edges, and secondly, to suture the dura would be to destroy the object of the decompression—the relief of intracranial pressure; for in adults the dura is inelastic, so that there can be no real decompression if the dura is unopened or sutured after being opened. There

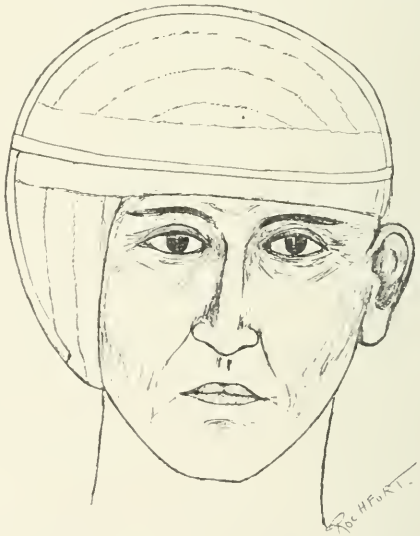

Fig. 7.—Dressings applied and held by bandage of roller gauze. A small pad of cotton and sterile vaseline is placed behind the lobe of the ear to prevent pain from its pressure against the bony skull; opposite ear left uncovered. Small strips of adhesive plaster used to hold bandage firmly.

is no danger apparently in leaving the dura opened; adhesions do not form, and in three cases at autopsy, two of them revealed the formation of an entirely new dura. The overlying temporal muscle forms a safe protecting covering.

The postoperative treatment consists of a moderate elevation of the head and shoulders, with the administration of hot saline solution per rectum every four hours for the first day; if much operative shock is present, then hot black coffee per rectum may be given immediately after the operation. The patient should be quiet—morphin or codein being used if necessary. Water may be given by mouth as soon as the nausea ceases, and liquids on the following day; soft diet on the fourth day.

At the first dressing on the second day, the drain is removed and possibly one-third of the skin sutures. At the second dressing on the fifth or sixth day postoperative, all sutures are removed and the patient may now have a light diet. In uncomplicated cases the patient may leave the hospital on the tenth day postoperative. It is surprising how quickly patients recuperate from the operation—there being, as a rule, little if any shock.

The advantages of the subtemporal route over other methods of cranial decompression are chiefly due to its anatomical relations. Not only is the squamous bone underlying the temporal muscle the thinnest part of the vault of the skull and therefore less difficult to remove, but it exposes a part of the brain most frequently involved in cases of fracture of the skull where the middle meningeal artery is torn or the temporosphenoidal lobe is lacerated; in cases of abscess of the temporosphenoidal lobe following its usual cause an otitis media. With little difficulty the lower portion of the motor tract may be explored as well as the posterior portion of the frontal lobe, and on the left side the motor speech area is easily observed. Another important advantage is the fact that the part of the brain lying directly beneath the decompression opening is the cortex of the temporosphenoidal lobe—a comparatively silent area of the brain; for this reason any possible operative damage is not revealed clinically, and in cases of high intracranial pressure the protrusion of this part of the brain into the decompression opening does not produce paralysis, etc.—a frightful result of decompressions performed in the parietal area. That is, a subtemporal decompression relieves increased intracranial pressure without cerebral impairment. Besides it affords excellent drainage for the middle fossa of the skull at its lowest point—an important consideration in cases of fracture of the skull.

Again, the thick overlying temporal muscle not only makes possible a firm closure but also allows the underlying bone to be removed so that a permanent decompression results with no danger of a hernia cerebri. The scalp is not weakened by draining through the split temporal muscle and no unsightly protrusion occurs; the scar is always inside the hair-line. In men the rim of the derby or straw hat affords some protection to the area of the decompression, although no protection is really necessary, as the temporal muscle is thick and thus the underlying cortex is well protected; besides the cortex itself is comparatively a silent area of the brain, so that even if it were injured by an object being thrust into the opening, no clinical signs would appear unless a large cortical vessel were torn.

The vertical incision of the scalp in this operation is far superior to the older method of a curvilinear incision over the parietal crest. Not only may the pressure-traction method of hemostasis be used much more effectively with the vertical incision, but the

temporal artery is clamped at its lowest point and before it ramifies into numerous smaller vessels, whereas in the curved incision the many branches of the temporal artery are severed individually and each one must be clamped separately; again, it is easier to enlarge the bony opening downward to the base of the skull when the vertical incision is used—an important point for drainage in cases of fracture of the skull. To preserve the strong attachment of the temporal muscle to the parietal crest is difficult and even impossible when the usual curved incision is used; in this manner the decompression may so weaken the side of the head that a hernia cerebri appears as the intracranial pressure increases; especially is this true in irremovable tumors of the brain; this complication is a most rare occurrence following a decompression performed with the vertical incision and a careful regard for the attachment of the temporal muscle.

Conclusions. The operation of cranial decompression is one that should be used much more frequently than it is at present; especially is this true in the conditions of brain tumor, fracture of the skull, brain abscess, and selected cases of spastic paralysis due to an intracranial hemorrhage at birth.

The subtemporal method of cranial decompression is the ideal route; besides being less difficult technically it exposes an area of the brain most frequently involved. This permanent decompression opening does not weaken the skull in that the thick overlying temporal muscle protects it most adequately, so that herniæ cerebri are not to be feared.

The operative mortality is low. Patients with intracranial conditions should not be permitted to become blind or to reach the dangerous stage of medullary compression without a subtemporal decompression being performed early.

FRACTURE OF THE BASE OF THE SKULL WITH ESCAPE OF CEREBROSPINAL FLUID FROM THE EAR. THE EFFECT OF ATROPINE AND EPINEPHRIN UPON THE SECRETION.[1]

By J. Walker Moore, M.D.,
LOUISVILLE, KENTUCKY.

The purpose of this paper is threefold:

1. To report a case of fracture of the base of the skull with the escape of an unusual amount of cerebrospinal fluid from the ear.

[1] I have to thank Dr. Charles H. Frazier most cordially in making it possible for me to carry out the work presented in this paper, and freely placing at my disposal valuable unpublished data concerning the effects of the injection of certain saline extracts of the body organs upon the secretion of cerebrospinal fluid in dogs.

2. To outline briefly the evolution of the hypothesis that the cerebrospinal fluid is a true secretion.

3. To present the effect both chemically and clinically of the hypodermic injection of atropin and epinephrin upon the secretion of cerebrospinal fluid.

Fracture of the base of the skull with the escape of cerebrospinal fluid from the cranium has been observed for centuries. Bidloo the elder (quoted by St. Clair Thomson), writing in the latter half of the seventeenth century, reported a case of a patient who had a fracture of the bridge of the nose followed by a continuous flow of clear watery fluid from the right nostril; twenty ounces of this fluid escaped in twenty-four hours. Stalpartius von der Wiel, in 1725, published a case in which a large quantity of clear watery fluid escaped from the ear after a severe injury to the head. Matthein and others have collected a number of such cases. Indeed, judging from the recent literature, surgeons do not look upon this as a matter of rare occurrence.

The case which we have to report is not a unique one by any means, however, judging from his age, weight, and stature; the amount of cerebrospinal fluid that escaped from the ear at regular intervals is rather remarkable.

Case I.—W. R., Episcopal Hospital, aged six years, male; weight thirty-five pounds.

Eighteen hours before admission into the hospital the child fell down a flight of stairs backward while attempting to catch a ball that he had thrown upward. The screams attracted the mother's attention. She found the child lying on the floor, in an unconscious condition, bleeding from the left ear. Within a few minutes blood and clear colored fluid flowed alternately from the left ear. Later (about twenty minutes) the blood ceased entirely, but the clear colored fluid continued to flow, with occasional momentary stoppage up to the time of admission into the hospital. The child remained unconscious for six hours after the accident; thereafter was conscious of things around him. He vomited just after the fall and again six hours later.

The child was of instrumental delivery. Since the age of eight months the patient has had frequent epileptic seizures, the attacks occurring at irregular intervals. The child may go as long as three days without a seizure, on the other hand the attacks may occur daily, or several times during the day, and continue in this manner for two or three days. The oncoming attack is usually ushered in by the child being peevish, fretful, restless, spitting, etc. Then comes the seizure which manifests itself by a rapid contraction of arms and legs, a sudden scream and a falling to the floor, rapidly becoming cyanotic and blue in the face. At times the child froths at the mouth but never bites his tongue. The attack is usually three minutes in duration. The child, acccording to the parents,

is bright and has a wonderful memory. No history of mental deterioration. Had a discharging right ear two weeks ago which rapidly cleared up under treatment. Mother states that the child did not have an epileptic seizure before the fall, nor were there any symptoms of an attack following the accident.

On admission to the hospital, eighteen hours after the accident, the examination revealed a fairly well-nourished child of six years, somewhat restless, but nothing more than one would expect of a child in a strange place. The child would heed immediately when his name was called, and would protrude the tongue or raise the arm when asked to; we were unable to draw the patient into a conversation, but he would at intervals articulate words, as water, mother, and the like. However, he would never utter a complete sentence.

Aside from the discharging left ear the physical examination was essentially negative. There were no signs of injury to the scalp. Eyes reacted promptly to light, pupils were equal. Ocular movements normal. Cardiac action was rapid, pulse of good tension and volume. Lungs, abdomen, and extremities were negative.

The patella, achilles, biceps, and triceps reflexes reacted promptly but were not increased. There were no palsies, no ankle-clonus. Skin reflexes and sensation normal.

Temperature, 97°; pulse, 130; respiration, 24.

From the left ear could be seen a continuous flow of clear watery fluid. The flow was so rapid that within a short time the pillow-cover in the region of the head would be soaked with the fluid. The fluid reduced Fehling's solution. Specific gravity, 1007. One c.mm. showed 1730 red blood corpuscles, 49 polymorphonuclear leukocytes, and 39 lymphocytes.

March 16. The child is quiet, lies with the right side of the head on the pillow. The left ear continues to discharge a clear watery fluid at irregular intervals; that is to say, the flow ceases an hour or more, two or three times in the twenty-four hours.

The child had a convulsion which lasted two minutes; during the convulsion the lips became cyanosed, face pinched, upper and lower extremities contracted rapidly. There was no frothing at the mouth nor biting of the tongue. Had to be catheterized. Temperature, 103; pulse, 135; respiration, 24.

March 17. Very little change in condition. The child drinks a great deal of water and takes liquid diet well.

The ear continues to discharge at irregular intervals. Had a convulsion, similar to the one on the previous day. No record was made of the amount of secretion during the convulsion, but the attending nurse states that there was not a noticeable increase during the convulsion, judging from the wet spot on the pillow cover.

March 18. The ear ceased secreting only once during the twenty-four hours, and that was for about three hours, while

the child was asleep. There is a suggestive Kernig and reflex resistance of the neck muscles to flexion of head. The right ear began to discharge mucopurulent material Secretion collected from the left ear by means of an eye dropper in sixty minutes was 15 c.c.

The eye-grounds were examined by Dr. Bromley. The report was as follows:

O. D. Nerve circumscribed and flat; very little venous congestion. Media clear.

O. S. Slight engorgement of veins, nerve perfectly flat and circumscribed. No edema of retina. Media clear.

March 19. Patient takes water and liquid nourishment freely. The fluid collected from the ear in sixty minutes amounted to 21 c.c. The child dropped off to sleep and the ear stopped secreting for hours. On awakening the ear began secreting again.

Ten grains of urotropin were given, and fluid collected every five minutes for two hours and placed in separate test-tubes. We were unable to demonstrate the presence of urotropin with the bromine water test in the fluid collected.

Blood Count. White blood corpuscles, 17,200; polynuclears, $66\frac{2}{5}$ per cent., mononuclears, 3 per cent.; transitionals, $7\frac{2}{5}$ per cent.; lymphocytes, $22\frac{1}{5}$ per cent.; eosinophiles, 1 per cent.

March 21. Very little change in condition of patient. Kernig's sign suggestive. No rigidity of neck.

March 23. Child is quiet most of the time, occasionally becoming restless. Kernig is positive. No rigidity of neck; no bowing of back.

March 24. The child is quite restless at times. There is rigidity of the neck muscles, with slight retraction of the head. Kernig's sign is positive. No bowing of the back. Pulse is rapid; secretion from left ear is scanty.

Blood Count. White blood corpuscles, 25,350; polynuclears, 79 per cent.; transitionals, 3 per cent.; lymphocytes, 18 per cent.

March 25. The patient appears to be in great agony, crying out at frequent intervals; retraction of neck is marked; there is also bowing of the back, with drawing up of lower extremities. The left ear has ceased secreting entirely. Skin is dry; eyes sunken; tongue parched; radial pulse scarcely perceptible.

From this point the patient rapidly went downward, and died March 28.

The autopsy was performed by Dr. C. Y. White, director of the pathological laboratory of the Episcopal Hospital. He reports as follows:

The dura is transparent, the inner surface being smooth and glistening. The vessels of the pia mater are only slightly congested. No macroscopic evidence of a meningitis. No edema beneath the pia.

On severing the brain from the cord an excessive amount of cerebrospinal fluid escaped into the base of the skull.

The dura is entirely stripped for the purpose of examining the skull, and there is found a fracture involving the squamous and anterior surface of the petrous portion of the left temporal bone. That part of the fracture involving the petrous portion is Y-shape, and extends into the internal auditory meatus. One limb of the Y begins with the depression for the Gasserian ganglion; the other with the opening for the small petrosal nerve. The two uniting just external to the Hiatus Fallopii and running outward parallel with and $\frac{1}{8}$ of an inch beneath the superior border to the squamous portion, where it continues directly upward in that bone for one inch.

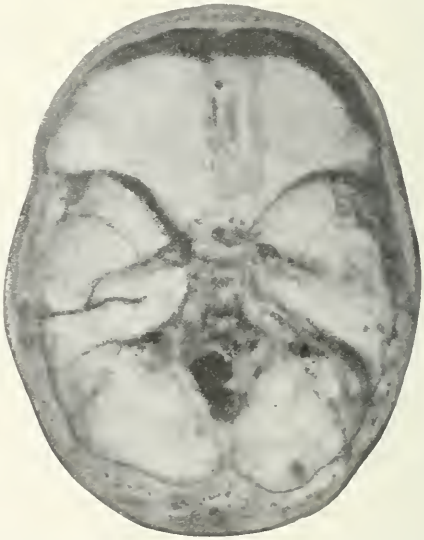

Figure showing the Y-shaped fracture involving the petrous portion of the left temoral bone. The fracture was outlined with lead pencil and a photograph taken of the bone of skull.

Dr. W. B. Cadwalader made numerous sections of the brain and choroid plexus, and submits the following report:

Sections were made from various parts of the cerebral cortex and the cerebellum. For the most part they were entirely negative, but here and there in some sections a few polymorphonuclear leukocytes could be seen infiltrating the pia, and grouped about some of the smaller bloodvessels within the fissures of the cortex. This was a real meningitis, yet it was so slight that it would require more than a superficial examination to find it. Sections from the basal ganglia, internal capsule, pons cerebellum, and different levels of the spinal cord appear to be entirely normal. There were no evidences of meningitis in these parts and the tissue stained

normally with the Weigert stain. Sections of the choroid plexus were made and were stained by a number of different methods. All the cells appeared entirely normal. I could not demonstrate some of the granules which are thought to react differently to stains, and which have been supposed to have some relationship to secretory functions. Comparing the sections taken from this case with similar sections of two other brains which ought not to have had any disease of the choroid plexus, I could not really find any difference. On the whole it is just to conclude that this specimen, brain and cord, shows absolutely nothing abnormal except a very mild and diffuse infiltration of the pia which was probable of recent origin.

The Evolution of the Hypothesis that the Cerebrospinal Fluid is a True Secretion. The hypothesis that the cerebrospinal fluid is a secretory product of the choroid plexus has been the source of infinite research for a number of decades. Leonard Hill,[2] in the early 90's, advocated the hypothesis that the fluid is a serous transudation from the capillaries of the vascular choroid. He regards the cerebrospinal fluid as the lymph of the brain, its secretion and resorption being explained on the same lines as other lymphatic exudate. He contends that the secretion of the fluid increases with the rise in cerebral capillary pressure and the latter varies directly and absolutely with vena cava pressure. He cites a case of St. Clair Thomson's in which there was a continuous flow of cerebrospinal fluid from the left nostril. At the invitation of St. Clair Thomson[3] he made the following observations:

I.

1. Patient sitting quietly, and in five minutes 23 m. were collected.
2. Patient sitting and straining, and in five minutes 35 m. were collected.
3. Patient sitting quietly, and in five minutes 19 m. were collected.
4. Patient sitting and straining, and in five minutes 33 m. were collected.
5. Patient lying—lying down and not straining, 27 m. were collected.
6. Patient sitting with head overhanging in five minutes, 28 m. were collected.
7. Patient sitting with head forward, and in five minutes 15 m. were collected.

II.

1. Abdomen compressed, and in five minutes 27 m. were collected.
2. Sitting quietly, and in five minutes 14 m. were collected.

[2] The Cerebrospinal Fluid, Allbutt's System of Medicine, 1899, vii, 239.
[3] Ibid., New York, 1899.

3. Abdomen compressed, and in five minutes 24 m. were collected.

4. Sitting quietly, and in five minutes 23 m. were collected.

The experiments carried out by Hill are valueless, owing to the short space of time given to each procedure.

It is stated that the normal amount of cerebrospinal fluid present in the subarachnoid space is about 100 c.c. That this fluid is rapidly formed is shown by the enormous amount of fluid escaping from the ear of my patient. It is clear that any condition which would cause congestion of the cerebral vessels would mechanically encroach upon the subarachnoid space, thereby increasing intracranial pressure. A sudden increase of flow after straining or compressing the abdomen, and a decrease in flow when the mechanical pressure is released, is to be expected. Suffice it to say, if the straining or compression of the abdomen had been kept up for twenty to thirty minutes, Hill's observations would have been different, as will be shown later. Furthermore, Sabin has shown that the subarachnoid space is fully developed, long before the lymphatics have budded out from the subclavian and iliac veins.

Mott[1] is credited with giving the following compositions of the fluid, which he considered to be against its being a transudation from the blood or a lymphatic secretion.

1. It contains 0.02 per cent. of proteins against 7 per cent. in blood plasma and 4.5 per cent. in body lymph.

2. There is an absence of lipochroma.

3. There are no leukocytes in normal cerebrospinal fluid.

4. In enteric fever there is an absence of agglutination.

5. It has no hemolytic action on the blood corpuscles of other animals.

6. It contains no alexins.

Willis, in 1664, first mentioned the glandular appearance of what is now called the choroid plexus. Faivre, in 1853, maintained that the cuboidal cells which cover the choroid plexuses are secreting cells concerned in the formation of cerebrospinal fluid. Mott examined histologically the choroid plexus of a human subject. He reports that the sections under high power reveal tufts of vessels surrounded by a loose connective tissue covered by a single layer of cubical, spheroidal or polyhedral cells lying on a basement membrane. Around the arteries and arterioles and lying in the loose connective tissue numerous nerve fibers are seen in a form of a plexus. In the sections he also observed vacuoles in the cells, and cup-like cavities in others, as one would expect if fluid had escaped from the vacuole. He concludes, therefore, from the histological evidence that the choroid plexus is a gland with an external secretion, but with an internal destination. Being a mixed gland, he suggests

[1] The Physical and Chemical Properties of the Cerebrospinal Fluid, Oliver Sharpey's Lectures, Lancet, July 2 and 9, 1910.

that its mode of formation is in an inverse manner to those formed by epithelial invagination of glands with an excretory duct. Ependymal invagination occurs for the choroid plexus.

Kramer[5] describes the histological appearance of the choroid plexus as highly vascular projections of the pia mater into the ventricle, covered with villous-like projections about 1 to 2 mm. in diameter, under the microscope these villi are seen to be made up of a number of secondary villi about 25 mm. in diameter, which again show grape-like projections. Through the centre of the villi run comparatively thick-walled bloodvessels, giving the organ a highly vascular appearance. The connective tissue of the villi is that of the pia mater. Covering the villi of the plexus is a layer of spheroidal cells in each of which may be seen in addition to the nucleus, yellowish granules. These cells are probably the secreting cells of the organ. These cells are without ducts, pouring their secretions directly into the ventricular system of the brain.

Carl Schmidt, in 1850, advanced the chemical evidence in favor of a true secretion. Petit and Girard,[6] in 1902, demonstrated the secretory functions of the choroid plexus in different classes of vertebrates. They found that administration of substances endowed with hypersecreting action caused histological changes in the cells covering the plexus. Dixon and Halliburton have experimental proof that an intravenous injection of an extract of choroid plexus produces an increased secretion of the cerebrospinal fluid. The injections of extracts of the brain produces the same effect upon the respiration, blood-pressure and flow of the cerebrospinal fluid, as does the injection of extract of choroid plexus. So also in cases of general paralysis and brain softening, where destructive processes are actively taking place, the cerebrospinal fluid when injected, produces identical effects. They suggest, therefore, that the increase in output of fluid is due to the stimulating action of some chemical substance (harmone) in the extract on the secreting cells of the gland, and that the harmone is a product of the brain's metabolism which passes to the choroid plexus and stimulates the secreting cells of the plexus.[7]

Writers as Levy, Cushing, Obersteiner, Cavaggani, Frazier, and others likewise maintain the secretory activity of the choroid plexus as the formation of cerebrospinal fluid.

The following observations were made in the case of the patient herein reported:

[5] Fall of Pressure Produced by Choroid Extract, Jour. Amer. Med. Assoc., 1911, lvi, 265.

[6] Smith, E., The Cerebrospinal Fuild, Guy's Hosp. Gaz., London, 1911, xxv, 141.

[7] W. Mestregat, in a recent publication, expresses his belief that the cerebrospinal fluid is neither a transudation nor a secretion, but is a product of dialysis from the blood plasma.

TABLE I.

Time	Amount collected in five minutes approximate in c.c.	State of patient.	Hear rate	Analyses of cerebrospinal fluid.					Expressed as grams per 100 c.c. fluid.		
				Duration, minutes.	Actual am't, c.c.	Solids, gm.	Ash gm.	K_2O gm.	Solids.	Ash.	K_2O.
	Period I— Control										
11.05	.73 c.c. (12 m.)	Apparently asleep	126								
11.10	1.54 c.c. (25 m.)	Apparently asleep	130								
11.15	1.23 c.c. (20 m.)	Apparently asleep	128								
				30	5.4	0.0720	0.0494	0.0008	1.35	0.91	0.015
11.20	.48 c.c. (8 m.)	Apparently asleep	130								
11.25	.49 c.c. (8 m.)	Apparently asleep	128								
11.30	.86 c.c. (14 m.)	Apparently asleep	126								
A.M.	Period II[8]										
5	.73 c.c. (12 m.)	Restless and quiet	170								
10	.37 c.c. (6 m.)	Restless and quiet	140								
15	.30 c.c. (5 m.)	Restless and quiet	163								
20	.37 c.c. (6 m.)	Restless and quiet	134								
				40	4.4	0.0676	0.0476	0.0009	1.54	1.08	0.017
25	.73 c.c. (12 m.)	Restless	170								
30	.55 c.c. (9 m.)	Restless and quiet	147								
35	.37 c.c. (6 m.)	Quiet	136								
40	.86 c.c. (14 m.)	Quiet	140								
	Period III										
45	.96 c.c. (16 m.)	Quiet	140								
50	1.50 c.c. (25 m.)	Restless and quiet	136								
55	1.38 c.c. (23 m.)	Quiet	136	25	7.2	0.0751	0.0501	0.0009	1.04	0.70	0.013
60	1.68 c.c. (28 m.)	Restless and quiet	168								
65	1.38 c.c. (23 m.)	Restless	168								
	Period IV										
70	1.20 c.c. (20 m.)	Restless	164								
75	1.14 c.c. (19 m.)	Restless	164								
				20	4.75	0.0587	0.0379	0.0006	1.24	0.80	0.013
80	1.02 c.c. (17 m.)	Restless	164								
85	1.20 c.c. (20 m.)	Restless	166								
	Period V										
P.M.	Not measured		...	90	Not measured	0.0614	0.0392	0.0007			
2.35	Period VI										
5	1.14 c.c. (19 m.)	Quiet	140								
10	1.14 c.c. (19 m.)	Quiet	138								
15	1.20 c.c. (20 m.)	Quiet and restless	145								
				30	7.0	0.0648	0.0414	0.0006	0.92	0.59	0.009
20	.96 c.c. (16 m.)	Quiet	138								
25	1.02 c.c. (17 m.)	Quiet	140								
30	1.20 c.c. (20 m.)	Quiet	140								
	Period VII										
35	1.08 c.c. (18 m.)	Apparently asleep	140								
40	.96 c.c. (16 m.)	Apparently asleep	138								
45	1.14 c.c. (19 m.)	Quiet	140								
				30	7.1	0.0930	0.0624	0.0011	1.31	0.88	0.016
50	1.14 c.c. (19 m.)	Quiet	138								
55	1.38 c.c. (23 m.)	Restless	144								
60	1.14 c.c. (19 m.)	Restless	144								
	Period VIII										
	Not measured		...	65	13	0.1530	0.1022	0.0014	2.73	1.82	0.025
P.M.	Period IX										
5	.30 c.c. (5 m.)	Restless	150								
10	.12 c.c. (2 m.)	Apparently asleep	140								
15	0.0	Apparently asleep	138								
20	0.0	Apparently asleep	136	110	6.9	0.1096	0.0632	0.010	1.59	0.92	0.011
25	0.0	Apparently asleep	136								
30	1.02 c.c. (17 m.)	Restless	140								
110	5.76 c.c. (96 m.)										
	Period X										
5	.96 c.c. (16 m.)	Apparently asleep	150								
10	1.20 c.c. (20 m.)	Apparently asleep	140								
15	1.14 c.c. (19 m.)	Apparently asleep	136								
20	1.32 c.c. (22 m.)	Apparently asleep	138								
25	2.40 c.c. (40 m.)	Apparently asleep	138	45	13.4	0.1612	0.1065	0.0015	1.20	0.80	0.011
30	1.38 c.c. (23 m.)	Restless	140								
35	1.80 c.c. (30 m.)	Apparently asleep	140								
40	1.38 c.c. (23 m.)	Apparently asleep	140								
45	1.32 c.c. (22 m.)	Restless	150								

[8] Epinephrin (1 to 1000) 5 m. injected subcutaneously. A blanching appeared at point of injection.

TABLE I—Continued.

Time	Amount collected in five minutes approximate in c.c.	State of patient.	Heart rate.	Analyses of cerebrospinal fluid. Duration, minutes.	Actual am't, c.c.	Solids gm.	Ash gm.	K_2O gm.	Expressed as grams per 100 c.c. fluid. Solids.	Ash.	K_2O.
	Period XI										
5	.80 c.c. (15 m.)	Quiet	144								
10	1.20 c.c. (20 m.)	Restless	150								
15	1.14 c.c. (19 m.)	Quiet	142								
20	1.14 c.c. (19 m.)	Quiet	140								
25	1.02 c.c. (17 m.)	Quiet	138								
30	.96 c.c. (16 m.)	Quiet	150								
35	1.14 c.c. (19 m.)	Restless	154								
40	.90 c.c. (15 m.)	Quiet	150	75	14.5	0.1607	0.0934	0.0013	1.10	0.62	0.009
45	.84 c.c. (14 m.)	Quiet	157								
50	.96 c.c. (16 m.)	Restless	170								
55	.84 c.c. (14 m.)	Restless	168								
60	.60 c.c. (10 m.)	Restless	168								
65	.60 c.c. (10 m.)	Restless	166								
		Was given water									
70	.84 c.c. (14 m.)	Quiet	150								
75	.84 c.c. (14 m.)	Apparently asleep	140								
	Period XII										
80	1.80 c.c. (30 m.)	Apparently asleep	140								
85	2.10 c.c. (35 m.)	Apparently asleep	138								
90	.84 c.c. (14 m.)	Apparently asleep	140								
95	1.20 c.c. (20 m.)	Restless	140								
100	.90 c.c. (15 m.)	Restless	144	45	12.4	0.1131	0.645	0.0008	0.91	0.52	0.006
105	.84 c.c. (14 m.)	Quiet	150								
110	1.14 c.c. (19 m.)	Restless	154								
115	1.50 c.c. (25 m.)	Quiet and restless	145								
120	1.50 c.c. (25 m.)	Quiet and restless	148								

AVERAGE OF PERIOD.

	Solids.	Ash.	K_2O
I	1.35	0.91	0.015
II to X (except V)	1.38	0.91	0.014
XI and XII	1.02	0.59	0.008

PERCENTAGE OF ASH IN TERMS OF TOTAL SOLIDS.

I	68.6	V	63.9	IX	57.8
II	71.9	VI	63.9	X	66.1
III	66.7	VII	67.3	XI	58.1
IV	64.6	VIII	66.8	XII	57.0

AVERAGE.

I	68.6	II to X (inc. V)	65.3	XI to XII	57.7

The table summarizes the amount of fluid excreted in five consecutive minutes, the state of the patient, whether quiet, restless or apparently asleep and the heart rate. (The heart rate was taken twice in each five minute period, with a stethoscope, and the average recorded.) The fluid was collected in sterile glass test-tubes, labeled periods I, II, III, IV, V, VI, VII, VIII, IX, X, XI, XII. The tubes were given to Dr. Charles H. Frazier, who in turn secured the valuable service of Dr. A. E. Taylor, professor of physiological chemistry in the University of Pennsylvania, for chemical analysis.

March 20. Epinephrin (1 to 1000) 5 m. injected subcutaneously into the arm. Eight hours and forty minutes later atropin sulphate, gr. $\frac{1}{250}$, was injected hypodermically. Experiment begun at 11 A.M.

TABLE II.

At 3.35 water, ʒiv, given by mouth, and twenty-five minutes later atropin sulphate, gr. $\frac{1}{200}$, hypodermically.

Time.	Approximate amount in c.c.	State of patient.	Heart rate.
2:35			
5	2.70 c.c. (45 m.)	Quiet	134
10	2.70 c.c. (45 m.)	Quiet	130
15	2.40 c.c. (40 m.)	Quiet	134
20	2.70 c.c. (45 m.)	Quiet	132
3:00	Atropin, 0.05 gr. hypodermically.		
5	2.40 c.c. (40 m.)	Restless	140
10	1.50 c.c. (25 m.)	Restless	145
15	1.50 c.c. (25 m.)	Quiet	138
20	1.50 c.c. (25 m.)	Quiet	136
25	.96 c.c. (16 m.)	Quiet and restless	138
30	1.14 c.c. (19 m.)	Quiet and restless	136
35	1.32 c.c. (22 m.)	Quiet and restless	138
40	1.08 c.c. (18 m.)	Apparently asleep	138
45	1.26 c.c. (21 m.)	Apparently asleep	140
50	1.14 c.c. (19 m.)	Apparently asleep	138
55	.90 c.c. (15 m.)	Apparently asleep	140
60	.90 c.c. (15 m.)	Apparently asleep	138
65	.96 c.c. (16 m.)	Apparently asleep	144
70	.60 c.c. (10 m.)	Apparently asleep	140
75	.90 c.c. (15 m.)	Apparently asleep and restless	144
80	1.02 c.c. (17 m.)	Apparently asleep	138
85	.90 c.c. (15 m.)	Apparently asleep	138
Milk is given.			
90	.66 c.c. (11 m.)	Restless	145
95	1.38 c.c. (23 m.)	Restless	146
100	1.32 c.c. (22 m.)	Restless	144
105	——	Exceedingly restless	...
110	.96 c.c. (16 m.)	Restless	146
115	.96 c.c. (16 m.)	Restless	144
120	.90 c.c. (15 m.)	Restless	150

TABLE III.—TO SHOW THE INFLUENCE OF SLEEP, QUIET, AND RESTLESSNESS UPON THE SECRETION OF CEREBROSPINAL FLUID, MARCH 22.

Time.	Approximate amount collected in 5 minutes in c.c.	State of patient.	Heart rate.
11:00	.30 c.c. (5 m.)	Quiet	134
5	1.08 c.c. (18 m.)	Quiet and restless	134
10	1.08 c.c. (18 m.)	Quiet	135
15	.60 c.c. (10 m.)	Restless and Quiet	145
20	.90 c.c. (15 m.)	Quiet	134
25	.90 c.c. (15 m.)	Quiet	140
30	.96 c.c. (16 m.)	Quiet	140
35	1.14 c.c. (19 m.)	Quiet	138
40	1.38 c.c. (23 m.)	Quiet and restless	144
45	1.14 c.c. (19 m.)	Quiet and restless	142
50	1.08 c.c. (18 m.)	Quiet	134
55	1.50 c.c. (25 m.)	Quiet	136
60	1.14 c.c. (19 m.)	Quiet and restless	140
65	1.08 c.c. (18 m.)	Quiet and restless	144
	COLLECTED THE FOLLOWING DAY, MARCH 23.		
11:00 A.M.			
5	.90 c.c. (15 m.)	Quiet and restless	140
10	.84 c.c. (14 m.)	Quiet and restless	138
15	1.02 c.c. (17 m.)	Quiet and restless	140
20	2.28 c.c. (38 m.)	Quiet	138
25	1.38 c.c. (23 m.)	Quiet and restless	142
30	.90 c.c. (15 m.)	Restless	150
35	.96 c.c. (16 m.)	Restless	144

A Summary of the Effect of Atropin on Cerebrospinal Flow.—Table I. The normal secretion during one hour amounted to 17.7 c.c., average heart rate was equal to 139 beats per minute. After the injection of atropin, gr. $\frac{1}{250}$ hypodermically, the amount of secretion during one hour amounted to 11.8 c.c., a decrease of 5.9 c.c. in one hour. Average heart beat 153 per minute, an increase of 14 beats to the minute.

Table II. The normal secretion for twenty minutes amounted to 10.8 c.c., or at the rate of one hour, 32.3 c.c.; average heart beat per minute 132. After injection of atropin, gr. $\frac{1}{200}$ hypodermically, the amount secreted in the first twenty minutes amounted to 7.1 c.c. a decrease of 3.7 c.c. in twenty minutes. Average heart rate 138 per minute, an increase of 6 heart beats. The amount secreted in one hour was 16.1 c.c. a decrease of 16 c.c. for one hour. Average heart beat 141 per minute, an increase of 9 heart beats per minute. The amount secreted the following thirty minutes at the rate of one hour was 14.1 c.c. The chemical analysis of Table I shows a diminished solid, ash and potassium[9] content with an increased volume of fluid per time unit after injection of atropin. From the above observations it would undoubtedly follow that atropin exerts a partial inhibitory influence upon the secretion of cerebrospinal fluid; that is to say, atropin depresses the nervous stimuli of certain secretory cells of the choroid plexus in the same manner as it does other glands of the body dependent upon nervous stimuli for their secretion. Capelleti has shown that on dogs, atropin and hyoscyamin diminished the flow of cerebrospinal fluid, while pilocarpin increased it. Yoshimura states that atropin produces microscopical changes which are a manifestation of the inhibitory influence brought to bear on the secretory activity of the cells. Dixon and Halliburton[10] have found that after the administration of atropin, subsequent injection of choroid extract produces an increase of cerebrospinal flow.

The decrease in secretion of cerebrospinal fluid can be explained by one of two ways: (1) By granting that there is only one type of secretory nerves in the choroid plexus, and that the activity of the nerve endings depends entirely upon the presence of a chemical substance or harmone, and that the harmone is produced by the choroid cells themselves, atropin[11] would decrease the flow then, by depressing the cells which give rise to the formation of the harmone. The increase in flow following the injection of choroid extract, after the animal has been atropinized would be due to the mechanical replacing of a substance necessary for the stimulation

[9] The potassium was determined by the volumetric method of Drushel (cobaltinitrite method), and was not done in duplicate, as the amount of fluid was too small.

[10] Jour. of Physiol., 1913, xlvii.

[11] These secretions dependent upon nervous stimuli are depressed; those dependent upon chemical stimuli are unaffected by the action of atropin.

of the cells to secretion. It is not likely that this gland produces its own harmone. We know of no other gland in the body where such a mechanism occurs. It has been shown further that the extract of the brain and cerebrospinal fluid in general paralysis contains a harmone similar to that found in the choroid plexus. (2) It is more plausible to speculate that the gland is supplied with two sets of secretory nerves, namely: those dependent upon nervous stimuli for their action, the remaining ones dependent on chemical stimuli for their activity. The former would explain the diminution in flow after the injection of atropin. The latter would explain the increase after the injection of choroid or brain extract. Dixon and Halliburton suggest that the chemical stimuli or harmone are some part of the product of the brain's metabolism.

Summary of the Effect of Epinephrin on Flow of Cerebrospinal Flow. Table I. The normal secretion for thirty minutes amounted to 5.4 c.c. or in terms of sixty minutes 10.8 c.c. Average heart rate 128 beats per minute. After the injection of adrenalin (1 to 1000) ℿv subcutaneously, the amount secreted in the first thirty minutes amounted to 3.1 c.c., or in terms of one hour, 6.1 c.c., a decrease of 2.3 c.c. in thirty minutes, or in terms of sixty minutes a decrease of 4.7 c.c. Average heart rate for thirty-five minutes after injection of adrenalin was 150.

The following fifty minutes the secretion at the rate of an hour was 15.2 c.c. Three hours after the injection, the blanching upon the arm becoming smaller, the secretion amounted to 14 c.c. per hour. Five hours after the injection the secretion amounted to 13 c.c. per hour. Six hours later the blanching on the arm had entirely disappeared. The secretion gradually diminished and ceased entirely for fifteen minutes, the child apparently being asleep. The child became restless and the secretion began to flow again. The first five minutes amounted to 1.06 c.c. The collection for the following eighty minutes was 5.9 c.c. Seven hours after the injection the secretion collected in sixty minutes amounted to 17.7 c.c.

The chemical analysis of the fluid following the injection of epinephrin shows such marked variations that it would be stretching a point to attempt an interpretation.

We notice, then, that after the injection of epinephrin the secretion is diminished a little more than one-half in the first thirty minutes. Frazier has likewise reported a marked diminution in his experiments on dogs. What is the explanation? Does epinephrin constrict the cerebral vessels, and by decreasing the blood supply to the choroid plexus diminish the cerebrospinal flow?

The increase in pressure in the circle of Willis after the injection of epinephrin, as is found by Biedl and Reiner, and the decrease in flow from the external jugular vein, reported by Pick, point to a local constriction in the cerebral arterials. In experiments made

upon an isolated brain (in the skull) perfused with an artificial circulation, Wiggers[12] states that the addition of epinephrin causes a diminution in outflow from the organ. He believes the drug constricts the cerebral vessels in the same manner as it does vessels of other organs, and therefore suggests the existence of cerebral vasoconstriction nerves. On the other hand, Bayliss and Hill experimentally could discover no constricting effect of epinephrin on the cerebral vessels. Gerhardt concludes that nothing more than a passive dilatation occurs within the cranium. Dixon and Halliburton, as a result of their experiments on dogs, state that they have never observed constriction of the cerebral vessels from the use of epinephrin, and they challenge the technique as carried out by Wiggers.

Guillard, Huber, and Hunter have demonstrated that the vessels of the brain are provided with perivascular nerve plexuses. But writers as Roy and Gherrington, Hill Wagner[13] and others from their experimental studies conclude that the cerebral vessels do not possess vasomotor nerves. Masso,[14] as quoted by Howell, has shown by observation upon men with trephine holes in the skull that the constriction of the limbs is always accompanied by dilatation of cerebral vessels. Cushing[15] states that only those vessels of the body that receive nerve fibers from the thoracicolumbar cord are constricted by epinephrin. The blood is, therefore, diverted from the organs supplied by the thoracicolumbar segment, and as a result the cerebral vessels become passively dilated. Suffice it to say, experimental evidence points to the non-constricting action of epinephrine on the cerebral vessels. Further, Frazier[16] has shown experimentally that ligation of both carotids in dogs, thereby decreasing the blood-supply to the choroid plexus has no retarding influence on the rate of the secretion of cerebrospinal fluid. He has also demonstrated that the injection of saline extracts of certain organs, especially of the liver, kidney, spleen and pancreas, caused a fall in blood-pressure, and at the same time a marked increase in flow of cerebrospinal fluid. Likewise amyl nitrate produced an increase in flow of the fluid. On the other hand, he has shown that the injection of epinephrin caused a rise of blood-pressure, and coincident with this a marked decrease in flow of cerebrospinal fluid. That is to say the general rise in blood-pressure accompanied by an increased flow of blood through the brain, and increased intracranial pressure, is followed by a diminution of cerebrospinal secretion, and the fall in blood-pressure which is accompanied by a decrease in flow of blood through the brain and decreased intra-

[12] Am. Jour. Physiol., 1905, xiv, p. 452.
[13] Howell, W. H., Text-book of Physiology, Philadelphia, 1907, p. 580.
[14] Ibid., p. 579.
[15] Text-book of Pharmacology and Therapeutics, Philadelphia, 1910, p. 334.
[16] The Cerebrospinal Fluid as a Problem in Intracranial Surgery, Jour. Amer. Med. Assoc., 1914, lxiii, 287.

cranial pressure results in an increased secretion of cerebrospinal fluid.

It would appear that the cerebrospinal fluid which fills the space of the cranial cavity not occupied by vessels and nerves adjusts the mechanism of the circulation of the brain tissue by equalizing pressure. So nature has adjusted, so to speak, through its nervous mechanism, the secretion of the choroid plexus in such a way, that the activities of the cells are diminished when there is a rise in blood-pressure (increased intracranial pressure) and an increase in the activities occurs when the blood-pressure falls (decreased intracranial pressure). There is then a certain inverse relationship between the blood-pressure (intracranial pressure) on the one hand and the secretory activities of the choroid plexus on the other, and this relationship has the characteristics of a purposeful adaptation. Therefore, the diminution of flow which occurs after the injection of epinephrin is to be explained by the inverse relationship between blood-pressure and the secretory activity of the choroid plexus.

The fact that a marked increase of secretion occurred forty minutes after the injection of epinephrin is to be explained on the ground that the action of the drug had been spent[17] by this time and as a result the blood-pressure fell with a corresponding incresae in flow of cerebrospinal fluid. I was particularly attracted while making my observations and perplexed at the time to find, when collecting my controls, or when urotropin was given, that the secretion invariably decreased when the child was restless, and increased when asleep. At times the patient would be in a violent anger, striking as I would attempt to collect the fluid, and if the hands were held, would toss, scream, and contract violently every muscle. During the entire procedure we were amazed to find the secretion markedly decreased. At other times, after the child had been asleep for some time, restlessness would cause a momentary increase in flow, which is to be explained upon a mechanical basis. However, if the restlessness existed any length of time the momentary increase would be followed by a decrease in flow for the entire time of restlessness. (See Table III). This likewise carries out the inverse relationship between the blood-pressure which rises during restlessness, and falls during quietude and sleep, and the secretory activity of the choroid plexus, and further substantiates the purposeful adaptation theory. In pathological cases, however, this does not hold good. Here we are dealing with a degenerative process which is taking place in the brain tissue, causing an increase in brain metabolism. Thus there is added to the blood stream a superabundance of harmones, which in turn stimulates those cells

[17] The action of epinephrin when injected intravenously is of short duration. When injected subcutaneously it causes a blanching at the point of injection and in large doses the blanching acts as a reservoir, so to speak, for renewed supply.

of the gland dependent upon a chemical stimulus for their activity to hyper-secretion.

We also noticed that there was a marked increase in secretion ten to fifteen minutes after the intake of water; and a very slight change, if any, after the intake of milk. Throughout the entire observations, the pulse rate bore absolutely no relationship to the amount of secretion.

The child was given, on different occasions, large doses of urotropin by mouth, and the cerebrospinal fluid collected in sterile glass tubes at five-minutes intervals for several hours after the intake of the drug. We hope within the near future to publish the results of the appearance and disappearance of urotropin in cerebrospinal fluid, as is found in the case of the patient herein reported.

We wish to express our great indebtedness to Dr. Louis Mutschler, under whose service the child was treated, for kindly permitting us to publish full observations of the case.

REVIEWS

Diseases of the Bronchi, Lungs, and Pleura. By Frederick T. Lord, M.D., Visiting Physician, Massachusetts General Hospital, etc.; Instructor in Clinical Medicine, Harvard Medical School. Pp. 605; 93 engravings and 3 colored plates. Philadelphia and New York: Lea & Febiger, 1915.

The book itself is an exhaustive and altogether satisfactory grouping of the diseases of the respiratory tract with the exception of tuberculosis, which, on account of its length, is necessarily excluded. It is divided into three sections, as indicated by the title, and, as would be expected, more than half of the volume is devoted to diseases of the lungs. The chapter on bronchial asthma devotes considerable space to the theories of its causation, but does not attempt to decide the matter. He suggests that whether the immediate cause lies in the bronchial mucous membrane or in the bronchial muscles or both, some internal or external underlying factor must be assumed to exist. The infectiousness of the condition of acute tracheobronchitis is regarded as settled and the influenza bacillus receives most of the blame. Chronic bronchitis, he rightly argues, is usually to be regarded as merely a symptom of some more important basal process.

The chapter on lobar pneumonia is the longest in the book and deals very completely with the subject. The bacteriology and the questions of animal experimentation and immunity receive considerable space, and the symptoms, physical signs, and treatment are given ample attention. Very little mention, however, is made of the out-of-door treatment, of which the author apparently does not approve.

He states that hemoptysis may occur more or less frequently in fifteen different conditions, but tuberculosis must be considered guilty until proved innocent. He regards pulmonary syphilis as a rare condition and hard to diagnose. Other clinicians, however, claim to have observed it more frequently.

He believes that tuberculosis is also the cause of the majority of the cases of acute serofibrinous pleuritis. He does not place himself among the extreme radicals who believe there is no exception to this rule, but he argues that while all cases cannot be so classed, it is best for purposes of treatment to assume it in every case unless there is good reason to believe otherwise. Thoracentesis is given

a detailed description, including the indications, the technique, and the difficulties likely to be encountered.

A number of the less commonly met diseases of the lungs, such as actinomycosis, streptothricosis, blastomycosis, and aspergillosis, are presented along with a chapter on animal parasites and tumors.

It can safely be recommended as a reliable and handy reference work, in the preparation of which the author has drawn largely on his own researches and clinical experience and on clinical and pathological data which has accumulated in the Massachusetts General Hospital. S. J. R.

A Text-book of Diseases of the Nose and Throat. By D. Braden Kyle, A.M., M.D., Professor of Laryngology and Rhinology, Jefferson Medical College. Philadelphia. Fifth edition, thoroughly revised and enlarged. Octavo, 856 pages; 272 illustrations, 27 in colors. Philadelphia and London: W. B. Saunders Company, 1914.

The fifth edition of this already well-known work has been brought up to date in all essentials. The following new articles have been added: vaccine therapy; lactic bacteriotherapy in atrophic rhinitis; salvarsan in the treatment of syphilis of the upper respiratory tract; sphenopalatine ganglia neuralgia; negative air pressure in accessory sinus diseases; chronic hyperplastic ethmoiditis; congenital insufficiency of the palate. The chapter on tonsils has been revised, with the addition of the Sluder operation and technique brought up to date.

In many of the chapters additional information has been incorporated; such as the ocular symptoms in diseases of the nasal cavities; correction of septal deformities (various methods); thymic asthma, and many other subjects. A number of new illustrations have been added, and many of the older ones have been replaced by new.

As in former editions the striking feature of the book is the descriptive pathology brought out in connection with each subject, Dr. Kyle for many years being an authority on the pathology of the upper respiratory tract.

Though at times there is some repetition in the text, it is apparent that the author is desirous to make each subject concise and complete, and to save the reader the unnecessary obligation to refer elsewhere.

Dr. Kyle's book is as much for the student and general practitioner as for the specialist; the subject matter going into the many elementary details may be easily found by reference to the very voluminous and well-arranged index, which covers fifty-one pages. B. D. P.

Obstetrical Nursing. A Manual for Nurses and Students and Practitioners of Medicine. By Charles Sumner Bacon, Ph.B., M.D., Professor of Obstetrics, University of Illinois, and Chicago Polyclinic; Medical Director, Chicago Lying-in Hospital, etc. Pp. 355; 123 illustrations. Philadelphia and New York: Lea & Febiger, 1915.

The book opens with a short introductory chapter on the ethics concerned in obstetrical nursing. The second chapter deals with anatomy, physiology, and embryology in such a manner as to simplify to the nurse their relation to a study of pregnancy and labor. Pregnancy is considered in the second chapter in both its normal and abnormal aspects. The sections on the management of pregnancy and the pathological changes of pregnancy may well be commended to the careful study of the prenatal visiting nurse.

A full third of the book is devoted to labor. Thorough instructions are given for the guidance of the nurse often in sole charge of the patient for the greater part of this period. The chapter is replete with practical expedients. The object and general character of obstetrical operations are included. The care of the puerperal woman is discussed at length in Chapter V. The care of the infant forms the subject of the concluding chapter which gives an excellent outline for the care of the premature infant.

The principles governing this particular and important department of nursing are admirably presented, and the book may be heartily recommended as an aid in the practice of obstetrical nursing. P. F. W.

The Clinics of John B. Murphy, M.D., at Mercy Hospital, Chicago. Vol. III, No. 5 and No. 6, October and December, 1914. Pp. 190 and 175; 113 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

These numbers conclude the third volume of Murphy's *Clinics*. Each contains one or more "Clinical Talks on Diagnosis," besides the usual variety of case reports, with Dr. Murphy's incisive, caustic, but withal entertaining and instructive comments. In addition, the last number contains a splendid advertisement of Dr. Murphy's new offices, showing a ground plan of the arrangement of the apartments assigned to himself and to various members of his staff, and numerous photographs of interiors and exteriors, bringing forcibly to the attention of the reader what great facilities are

afforded for the diagnosis and treatment of all the surgical ills to which poor human nature is heir. We are informed, moreover, that "The building is situated on Calumet Avenue, between Twenty-fifth and Twenty-sixth Streets, next door to the Calumet Avenue entrance to Mercy Hospital. It is, of course," the advertisement continues to read, "at Mercy Hospital that Dr. Murphy and his staff do all their work."

To enhance the interest of the volume, there is included an admirable full-length portrait of Dr. Murphy, seated in his boudoir, and with the "counterfeit presentment" of his countenance skilfully reflected in a mirror.

> "Upon what meat doth this our Murphy feed,
> That he is grown so great? Age, thou art sham'd!
> Chicago has lost the breed of noble bloods!
> When went there by an age, since the great fire,
> But it was fam'd with more than with one man?"
>
> *παντὰ κόνις καὶ παντὰ γέλως καὶ παντὰ τὸ μηδέν.*

A. P. C. A.

Abdominal Operations. By Sir Berkeley Moynihan, M.S. (London), F.R.C.S., Leeds, England. Third edition; two volumes. Pp. 488 and 492; 371 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

Moynihan's *Abdominal Operations* well deserves the popular esteem it has won with the profession in America, the author's indebtedness to many members of which is handsomely acknowledged in the preface to the newest edition. Though this preface also tells us that a considerable revision has been required, and that certain chapters have been entirely rewritten, it is apparent even from a cursory survey of the volumes that a more extensive revision and rewriting would have been required to make them represent contemporary knowledge in all the subjects included.

Though Moynihan employs, and describes with adequate illustrations, Crile's methods of "anoci-association technique" in making the abdominal incision (which is an evidence of modernity), he yet persists in employing irrigation in acute peritonitis, and advises making in such cases from three to five counter-incisions for purposes of drainage. He also recommends that a glass tube be run up the lumen of the bowels to secure their evacuation, during operations for acute peritonitis; this, he adds, should be "considered an almost routine practice."

There is nothing about "Lane's kink," nor about "cecum mobile," and not enough about visceroptosis. The statistics of the operation for intestinal perforation in typhoid fever have not been brought

up to date; indeed, it does not appear that any changes in this chapter have been made since the publication of the first edition of the work.

In performing gastrectomy, Moynihan first ligates the pyloric artery and severs the pylorus; then turns the stomach far to the patient's left, divides the coronary artery, and completes the gastro-enterostomy before detaching the diseased portion of the stomach. He still credits E. J. Senn with Stamm's method of gastrostomy. *Capitonnage* is confused with marsupialization of hydatid cysts of the liver.

A frequent error is repeated in describing Kocher's gall-bladder incision: It is described and illustrated not as either described or illustrated by Kocher himself, but as lying chiefly to the outside of the semilunar line, instead of almost entirely over the rectus muscle. The fact that Kehr has abandoned (since 1912) the lower limb of his "Wellenschnitt" is ignored, and Czerny's incision is not mentioned, though incisions recently described by Don and by Perthes, and which are virtually modifications of Czerny's, are noted. Nor is Sprengel's transverse incision mentioned; it appears to be gaining in favor in many quarters.

Moynihan strongly favors cholecystectomy. He writes: "During the last eight years I have inclined more and more to the performance of cholecystectomy, and after some hesitation and some trepidation, which experience has removed, I am strongly disposed to advocate the frequent, though certainly not the invariable, adoption of this operation in preference to cholecystotomy in view of the character of the cases that submit themselves to surgical treatment."

Though the beauty of the illustrations and the charming simplicity of the description of the steps of the operations remain, yet we are forced to acknowledge, and we do it with sincere regret, that the present edition is less representative of contemporary abdominal surgery than were either of the editions which have preceded it.

A. P. C. A.

On Dreams. By Prof. Dr. Sigm. Freud. English Translation by M. D. Eder from the second edition. Pp. 110. New York: Rebman Company, 1914.

This is a popular edition of Freud's work on dreams, and is an English translation of a German work by M. D. Eder. The introduction is by the well-known English alienist W. Leslie McKinsey. Dr. McKinsey, like other English neurologists, is gradually beginning to appreciate the psychological value of some of Freud's work. It is questionable whether in this small volume of 110 pages one can

get more than an impression of the subject matter, but perhaps this is all that is intended. If one is interested more seriously the larger work, of which there is an English translation, should be consulted. T. H. W.

Orthopädische Chirurgie. By Dr. Gust. Albert Wollenberg. Pp. 258; 147 illustrations. Klinkhardt: Leipsic.

This hand-book, which is about to be discussed, is in German, which fact diminishes largely its value in the hands of the average American orthopedist. The order of this book is practically the same as that which is followed by most orthopedists. There is nothing specially original in the illustrations and they are of no special value. The methods advocated herein are the usual methods which are found in the practice of the average orthopedist. There is a moderate claim to originality in certain of the methods advised, but close comparison with the work of other men shows that the underlying principles of the methods in question are a common commodity. In the treatment of scoliosis there is a rather general collection of the various methods used by the leading orthopedists in the treatment of the various stages of this affection. It omits, however, an intelligent discussion of the latest methods employed for the correction of spinal curvature and certain other orthopedic procedures. To the person who reads German fluently this book would be valuable from the point of view of interest in the work of the author, but as a scientific addition to the orthopedist's library the reviewer can lay no special stress upon this work.

W. J. M.

The Evolution of Anatomy. By J. Ewing Mears, M.D., LL.D. Pp. 26; 6 illustrations. Philadelphia: Wm. J. Dornan, 1914.

This book of about seven thousand words contains briefly the history of evolution in the study of anatomy. The average student of anatomy as he enters this field of science has no conception of the hardships through which the earlier investigators passed unless he has acquainted himself with some of the facts which this little volume contains. The names of investigators from Hippocrates down to the present time are given, with a brief *resume* of their achievements. The different epochs in the development of knowledge of human anatomy are clearly defined, and the work accomplished during this

time is presented in an attractive manner. The value of this work is especially historical, and the facts which is contains should be a ready asset in the knowledge of a present-day anatomist.

W. J. M.

The Intervertebral Foramen. By Harold Swanberg, A.M., Ph.D., M.D. Pp. 101; 16 plates. Chicago Scientific Press, 1914.

This book is given somewhat in a tabular form. The anatomical relationships under normal conditions are accurately described and the book bears evidence of careful research. It is a well-known fact that a large group of symptoms originating in the spinal structures are due to mechanical defects in the complex structure of this part of the human anatomy. How much slight defects in this mechanical arrangement may be the cause of vasomotor and nerve disturbances is not absolutely known. Investigations of Swanberg emphasize the fact that slight changes in relationships in the spinal structures may give rise to varied symptoms. The work here presented is highly commendable, and bears evidence of a thorough and careful investigation. To persons interested in nervous diseases and also in mechanical disturbances of the spine this book should be of unusual interest and value.

W. J. M.

Nervous and Mental Diseases. By Joseph Darwin Nagel, Consulting Physician to the French Hospital of New York; Member of the New York Academy of Medicine. Second edition. Pp. 293; 51 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

This is the second edition of this manual. The reviewer who has taught neurology for over ten years in medical schools, has come to the conclusion that manuals and primers of any specialty are of necessity of limited value. How can a large subject like nervous and mental diseases be presented in 280 short pages in which about one-third the space is covered by diagrams? For example, the subject of cerebral localization, to which the reviewer in his third-year class gives ten hours, is covered in about six pages, most of these being made up of diagrams, and in one diagram of "the lateral aspect of the left hemicerebrum, showing the cortical centres," the motor centres are placed on either side of the central fissure. However, considered as a manual, the book is not without merit, and as a supplementary text-book will prove helpful to students.

T. H. W.

Medical Laboratory Methods and Tests. By Herbert French, M.A., M.D. (Oxon.), F.R.C.R. (Lond.). Third edition. Pp. 202; 88 illustrations. Chicago: Chicago Medical Book Co.

The third edition of this excellent handbook, introducing new methods and tests and modifying old ones, will be welcomed by those who have used it in the past and will prove a valuable addition to the armamentarium of the general practitioner or student who is, as yet, unfamiliar with it.

In addition to the more or less limited number of tests, applicable in the past as routine measures, in the work of the general practitioner this little work has made others, such as the quantitative estimation of urea, uric acid, chlorides, sulphates and ammonia in the urine, tests for occult blood in the stools and reactions for the more common poisons and drugs, available at but little outlay of time and money. A. A. H.

Urgent Surgery. By Felix Lejars, Professeur Agrégé a la Faculté de Medicine de Paris; Cherurgien de l'Hospital Saint Antoine; Membre de la Saciete Cherurgie. Vol. I, seventh edition. Pp. 614; 1086 illustrations and 20 plates. New York: Wm. Wood & Co., 1914.

This volume covers Head, Neck, Chest, Spine, and Aldomen. It is the third translation into English of the seventh French edition. In this last edition the work has been enlarged, revised, and remodeled. Chapters have been added on acute dilatation of the stomach, acute pancreatitis, obstruction of the mesenteric vessels, sigmoiditis, perisigmoiditis, and dislocations of the pelvis, and 92 more figures.

The author has taken up the matter of urgent surgery from the practical standpoint. There exists no theoretical discussions, no complex descriptions of untried methods or tiresome bibliography. In the introduction is outlined preparations and equipment, anesthesia and minor surgery in detail. Thereafter the book is arranged in chapters according to the region affected thus enabling the reader to refer to his subject readily without even the help of the index.

Throughout the work the author has made numerous fine print footnotes on subjects and facts that although not of primary importance, nevertheless, are well worth giving restricted space. The text is well presented, clear, concise, and reads easily and entertainingly, and frequently shows its French origin although translated into English.

The book is a good one and should be in every active practitioner's library. E. L. E.

Manual of Surgery. By Rose and Carless. Revised by Albert Carless; M.B., M.S., (Lond.) F.R.C.S. Professor of Surgery in, and Surgeon to, King's College Hospital; Consulting Surgeon to King Edward's Memorial Hospital, etc. Ninth edition. Pp. 1408; 609 illustrations and colored plates. London: Wm. Wood & Co., 1914.

This manual endeavors to meet and judging by the number of editions has met the present day needs of the body of its readers. It was written for students and general practitioners. It is in no sense a system on the subject, but does cover fully all the points that a student should know and further fulfils to a great extent the role of a working book for the practitioner. Facts are presented in a concise and clear manner. Theories and bibliographical references are relegated to a minor position. Subjects which are rarely met with or which bear only a slight relation to surgery are fine typed and presented in compact form. The special branches of surgery: eye, ear, etc., are touched upon and considered as fully as may be needful to the general worker. In fact, for its size the book furnishes a wonderful amount of detailed consideration of its many subjects.

This, the ninth and latest edition has added many new illustrations and a few colored plates, and a new chapter on heat, light, electricity, anoci-association, etc., without adding additional pages and hence bulk to the book. E. L. E.

Elementary Biology, Animal and Human. By James Edward Peabody, Head of the Department of Biology, Morris High School, Bronx, and Arthur Ellsworth Hunt, Head of the Department of Biology, Manual Training High School, Brooklyn, New York City. Pp. 212; 228 illustrations. New York: MacMillan & Co.

This is an elementary text-book embracing those subjects in general biology which lead up to human biology. Insects, fishes, protozoa and bacteria are emphasized in their economic and hygienic relations for obvious reasons. The effect of the book is to give the principles upon which the human body is constructed and upon the physiology which keeps it healthy; in other words the basic principles of hygiene. The book further aims to interest the young student in natural history and to teach him the conservation of animals. There are outlines of study, laboratory exercises and a bibliography. H. F.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLIFTON SPRINGS SANATORIUM AND HOSPITAL, CLIFTON SPRINGS, NEW YORK.

The Specificity of Cholesterin Antigens in the Wassermann Reaction.—Walker (*Arch. Int. Med.*, 1914, xiv, 563) bases this report upon the examination of 1000 Wassermann reactions performed on the blood and spinal fluids of 800 different individuals. As a knowledge of the technique used is necessary for the intelligent interpretation of results, Walker describes his method in some detail, and special emphasis is put upon the antigen used, an alcoholic extract of human heart reinforced with 0.4 per cent. cholesterin. This antigen has the advantage of being easily made from any human heart; its antigenic properties are quite constant; and it is sensitive, but not in a non-specific way with the luetic sera from patients in the late stages of the disease. The antigen must simply be accurately controlled to eliminate the disadvantages which have been advanced against it. In the series, 667 gave a negative reaction, and in none of these was lues suspected. Of the 110 who gave complete fixation there was no evidence of a false reaction; 24 sera showed incomplete hemolysis, and in all of these there was evidence of lues which had been favorably modified by treatment. Even when the antigen was used 1 to 6, a dilution near the anticomplementary dose, no false complete inhibitions were noted in 400 instances. A second part of the article deals with Walker's titration methods; the amount of serum necessary to give fixation varies in different people, even in the same stage of the disease, but if the amount of serum necessary is determined, then it can be shown that the amount of antigen necessary is a constant in different individuals in the same stage of the disease. By this method Walker claims to be able to tell an early from a late rash, and to distinguish an aneurysm from a slight aortic

dilatation. Using the least amount of serum necessary to give fixation and then determining the minimal amount of antigen required to bind with the serum, he was able to show by increasing the amount of serum that it became possible to use a proportionately smaller amount of antigen to give fixation. By these and other experiments it became clear that cholesterin is the specific agent which, in the presence of complement, binds with a syphilitic serum.

The Normal Diastase-content of the Urine.—Brown and Smith (*Johns Hopkins Hosp. Bull.*, 1914, xxv, 213) have studied the diastase content of the urine, with a view to finding out a normal value, hoping that variations might prove of value in the diagnosis of pancreatin disease, and that the test might further serve as a reliable test of renal function. The twenty-four hour specimens of urine of normal adults were diluted to 3000 c.c., and decreasing amounts were added to a series of tubes, the amounts decreasing by mathematical progression; each tube further received 2 c.c. of H_2O and 2 c.c. of a 0.1 per cent. solution of soluble starch; after incubation at 38° C. for half an hour the tubes were rapidly cooled and tested by adding a few drops of $\frac{n}{50}$ iodin solution; the limit taken was the tube just before the first tube in which blue is seen. Brown and Smith, as a result of their observations, conclude that the diastase content of normal adults falls within quite definite limits; marked decrease in the amount, in the absence of renal diseases, is strongly suggestive of some pancreatic disturbance, but such a finding is not diagnostic *per se*. The chief value of knowing normal values will be in furnishing criteria for testing renal function.

Functional Diagnosis of the Spleen with Adrenalin.—In some previous work Frey (*Zeit. f. d. ges. exp. Med.*, 1914, iii, 416) was able to demonstrate a definite marked lymphocytosis, coming on within a certain period of time after the injection of adrenalin. The present work attempts to determine where the adrenalin makes its point of attack, and whether, as was assumed, the increase in the lymphocytes is due to a mere mechanical heaping up of the cells. The effect of adrenalin injections was noted in animals before and after extirpation of the spleen in humans suffering from diseases of the lymphocyte-producing organs and after splenectomy. In puppies adrenalin apparently acts upon the smooth muscle of the spleen and causes a squeezing out of lymphocytes into the blood; in dogs, similar injections seemed to exert no influence upon the blood-picture; and in guinea-pigs, the resulting lymphocytosis stands in no relation to the spleen. In human beings suffering from lymphosarcoma and allied diseases, adrenalin causes a rise in lymphocytes equally as marked as in normals; in these cases where lymphatic destruction is going on, Frey asserts that the lymph glands cannot be the seat of production. In diseases of the spleen its cellular content is of much significance for the occurrence of adrenalin reactions; thus in Banti's disease practically no lymphocytosis occurs; on the other hand a good reaction occurs in cases of chronic hemolytic jaundice in which the structure of the splenic follicles is normal. Adrenalin causes a pronounced rise in cases of leukemia, lymphocytes almost exclusively of the lymphatic types, but myelocytes as well in the spleno-

medullary forms. The spleen was removed in a case of congenital hemolytic jaundice, which previously had shown a positive adrenalin reaction. For a time after splenectomy no reactions were induced but untimately they recurred. Frey inclines then to the view that adrenalin lymphocytosis is essentially a splenic reaction possessing considerable diagnostic importance.

Pancreatitis not Biliary in Origin.—In reviewing the literature of 250 cases of chronic pancreatitis SALLIS (*Rev. de chirurg.*, 1914, xxxiv–xxxv) was able to find only 50 which were not of biliary origin. The present paper is an analysis of these cases which occur usually in the female sex. They are caused, so far as is known, by no particular organism, but may occur in the course of most any general disease, and especially during pregnancy or secondary to trauma. Infection, contrary to the biliary cases which are usually lymphatic in origin, occurs through an ascending process in the ducts or by way of the blood-stream. Atrophy or hypertrophy may result, but in either case the gland becomes unusually hard. The disease generally commences with mild symptoms which invariably become worse or occur in attacks of increasing frequency. In either case the symptoms ultimately become continuous and lead sooner or later to death. Several clinical forms may be recognized. When the entire gland is affected, as was the case in 27 out of the 50, the prominent feature is attributable to the lack of the pancreatic digestive juices; when only the head of the gland is involved, jaundice and severe digestive upsets are common. The most valuable symptoms are pain, which is variable in intensity and location, emaciation, vomiting, and jaundice, and finally evidences of the disfunction of the gland, which is generally early in appearance. Glycosuria is but rarely present, and the Cammidge reaction is useless. The stools contain much fat in various forms, undigested muscle fibers, and cell nuclei. The diagnosis from carcinoma is made only with much difficulty and uncertainty. The most frequent complications are inflammation of adjacent viscera, portal thrombosis, cystic or malignant degeneration of the gland itself. Surgical treatment is the only one, and if instituted early, gives good results; symptoms vanish almost immediately, but in many instances healing of the wound is a matter of considerable time.

On the Finding of Diphtheria Bacilli in the Internal Organs in Fatal Cases of Diphtheria.—LIEDTKE and VOELCKEL (*Deutsch. med. Wochenschr.*, 1914, xl, 594) have examined the internal organs of seven children dying of diphtheria for diphtheria bacilli. In their cultural studies they have employed Conradi's medium. The results in all cases were the same. Diphtheria bacilli were abundant in the heart, lungs, liver, spleen, kidneys and bone marrow. In two cases they were able to examine the brain and in each they obtained positive cultures. The organisms recovered were typical morphologically and tinctorially. They were virulent, killing guinea-pigs in ten to forty-eight hours. In the experimental animals the characteristic changes were found postmortem, that is, redness and swelling of the adrenals, hemorrhages into the fat of the pancreas, infiltration at the site of inoculation and punctate hemorrhages in the intestine. Confirming the findings of Conradi and Beirast, the authors report that of thirty urines from diphtheria

patients, they found diphtheria bacilli in six instances. These cultural studies show that in severe "septic" cases of diphtheria it is not only the intoxication, but also the actual invasion of the body with the organisms that one has to deal with.

The Abderhalden Test in Infectious Diseases.—E. Voelkel (*München. med. Wchnschr.*, 1914, lxi, 349) has applied the Abderhalden test to the study of diphtheria, anthrax, and typhoid infections, as well as to infections with trypanosames and spirochetes. Substrata of the bacilli were prepared by suspending the organisms in water, boiling and then testing the filtrate until no color reaction occurred with ninhydrin. Trypanosomes were obtained by infecting guinea-pigs with nagana, bleeding the animals, and collecting the blood in normal salt solution, to which 1.5 per cent. sodium citrate was added. On centrifuging, the trypanosomes collected above the red corpuscles and were removed. Spirocheta pallida could not be obtained entirely from culture medium. The organism was grown on horse serum. In the experiments with the Spirocheta pallida controls were used by boiling up the medium alone and using this as an additional substratum. The sera for study were obtained from experimental and human infections. All the luetic sera were human. In all of the infections studied the Abderhalden reaction appeared to be entirely specific.

Experimental Purpura Caused in Animals by the Introduction of Anti-blood Plate Sera—Ledingham (*Lancet*, 1914, clxxxvi, 1673) found that it is possible to produce in guinea-pigs by the introduction of anti-blood-plate serum a disease similar to purpura. The serum is obtained by immunizing a dog against guinea-pigs' blood platelets, since it has been found difficult to secure platelets in sufficient amounts from human beings. Some 20 to 30 guinea-pigs are bled for a total of 150 to 250 c.c. of blood, and this is placed in two or three volumes of sodium citrate solution in normal saline. This is centrifuged and the cloudy supernatant fluid is obtained, which contains the platelets and a few erythrocytes. After centrifuging a few more times a serum free from corpuscles is secured and this is used for immunization. In all seven to eight injections are given at intervals of six to eight days, and the dosage used is 0.5 c.c. of platelets in normal saline. The immune serum always agglutinates guinea-pig platelets in the test-tube. When injected into guinea-pigs (1.5 c.c.) collapse and death occur in about one and one-half hours; autopsy reveals the presence of free blood in the peritoneal and pleural cavities, and the heart's blood contains completely agglutinated red corpuscles. After two intraperitoneal injections an animal of 500 grams died in four days. Section showed many subcutaneous hemorrhages in the intestinal mucosa, free blood in the peritoneum. Subcutaneous injections likewise cause death in three or four days, at which time there are numerous petechiæ in the skin, lungs, diaphragm, epicardium, and serous coats of the intestines.

The Dual Source of Cerebrospinal Fluid.—Weed (*Jour. Med. Research*, 1914, xxxi, 21, 51, 93) concludes from previous observations, recorded in the same journal that there are several pathways of escape for the spinal fluid: (1) it may reach the major circulation by passage

into the sinuses from the arachnoidal villi; (2) there probably is some drainage by way of lymphatic channels; (3) there may be some retrograde passage from the venous system into the subarachnoid space. No evidence was obtained of the escape of spinal fluid into the cerebral veins or capillaries. During the work upon which these observations were made, studies were carried on in the hope of producing genuine evidence for the growing idea that spinal fluid is a product of the choroid plexus and of the nervous tissue itself. Evidence of a convincing nature was obtained as to the choroid origin of spinal fluid. A new technique was devised whereby ventricular catheterization could be carried out without there being any admixture of the products of the perivascular system. Moreover, the operative procedure was so improved that the usual condition of low arterial blood-pressure at the time of catheterization was eliminated. A new detail was the standardization of the resistance to flow in the catheters employed. When such a catheter is in place, fluid continues to flow for several hours, cessation being due presumably to an exhaustion of the choroid plexus. The second phase of the problem was attacked by means of a new method of the subarachnoid injection of ferrocyanide solution. Provided such injections are made under suitable pressure conditions, the perivascular spaces around the veins and arteries are heaped up with Prussian-blue granules. This along with other evidence leads the authors to conclude that the fluid obtained by lumbar puncture represents not only the secretion of the choroid plexus, but also the fluid waste products of nerve-cell activity, poured into the subarachnoid space by way of the perivascular channel.

The Cultivation of the Causative Agent of Rabies—H. Noguchi (*Berlin. klin. Woch.*, xli, 1931) reports the successful cultivation of the causative agent of rabies. The culture medium employed was that which he had used successfully in the cultivation of the spirochete of relapsing fever. Some of the inoculated tubes remained sterile, others were contaminated, but in many the organism grew in pure culture. It has been possible to carry it through as many as twenty-one generations. Microscopic examination of the virulent cultures showed nothing; microscopic examination, however, revealed the presence of numerous granular chromatin bodies of varying size. Some were scarcely visible; the larger bodies measured 0.2 to 0.3μ. Groups of very small pleomorphic chromatin bodies, measuring 0.2μ to 0.4μ wide and 0.5 to 4.0μ long, were also noted. They stained red or bluish with Giemsa's stain. On four occasions Noguchi observed the development of bodies with a single round or oval nucleus surrounded by a membrane; these arose in cultures which originally contained only the granular or pleomorphic bodies. The nucleated bodies were numerous and of varying size (1 to 12μ), and were observed singly or in groups of two, three, four or more cells. The nuclei were stained dark blue or violet with Giesma's stain, the cytoplasm azure, and the membrane reddish. Certain of these bodies were in every particular identical with Negri bodies. Inoculations of rabbits, guinea-pigs, and dogs with cultures which contained granular bodies or granular and nucleated forms produced typical rabies.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The Abbott Treatment of Rigid Scoliosis with a Report of Sixty Cases.—Kleinberg (*Amer. Jour. Orthop. Surg.*, 1914, xii, 134) says that 18 cases gave up the treatment during the first six months; seven of this number discarded the jacket during the first few days while the rest were observed from three to six months. In all instances it was the discomfort, restlessness, and pain incident to the treatment that caused the patients to discontinue it, although these patients were willing to undergo a great deal of inconvenience for the hope of improvement. The remaining 42 cases are divided into five groups. The first includes 8 cases, all of the severest type, presenting without exception "razor backs." In none of these did the treatment produce any appreciable improvement. The second group, including 10 cases, had all very advanced and rigid deformities, the curve of the spine being S-shaped in every instance with the two parts of the curve almost equal. When the treatment was interrupted every patient was satisfied and there was improvement, in some very marked, in the external appearance. However, the conditions of deviation and rotation of the vertebræ, as judged from the Roentgen-rays, either remained unaltered or in some cases seemed to change for the better while the patient was in the jacket, but relapsed a short time after it was removed. One cannot, therefore, predict whether the improvement noted will be permanent. The third group, including 8 cases, all had severe deformities with marked rotation and deviation of the spine, but the dorsal curve was either the only one or was the more prominent with a slight compensatory curve. In this group there has been no complete correction of the deformity but there has been an unusual and very decided improvement in the external appearance and in most instances an actual partial reduction of the deformity of the spine, as shown by the Roentgen-ray. In the fourth group, of 10 cases, the deformity was rigid and varied from mild to severe types. In every instance there was marked improvement in the external appearance but especially in the Roentgen-ray findings. As most of these patients are still wearing supports and under active corrective treatment, a final report is impossible. The fifth group, of 6 cases, all had mild curves of moderate degree. Of these, two were greatly improved, two apparently corrected, and two apparently overcorrected, but all of them have relapsed to

their original condition. Kleinberg reached the following conclusions: The Abbott jacket from its weight and shape and the pressure exerted on the body is at all times a severe tax to the patient. Aside from temporary indisposition and the discomfort of the pressure on the chest, anorexia, etc., incident to the treatment, no untoward results have been experienced excepting the hollowing of the chest which has remained permanent only in one instance. As might have been expected, it was found that the deformity even in its mildest form, did not yield rapidly to the Abbott treatment, and that it took many months to effect any real radical change. Of the 60 cases, 18, some of which offered hope of improvement, gave up the treatment; 8 were not improved at all, and 34 were definitely made better in external appearance with or without a definite change in the spine itself. Of this latter number, 6 cases relapsed. This method, therefore, is applicable to the milder degrees of rigid scoliosis, most of which the writer has seen improved, though he has not yet seen any case, no matter how mild, cured, *i. e.*, transformed into one with a perfectly symmetrical back.

Observations on Myeloid Sarcoma with an Analysis of Fifty Cases.—Stewart (*Lancet*, November 28, 1914, 1236) says that myeloid sarcoma is locally malignant and does not undergo dissemination. It is to be clearly distinguished, both clinically and pathologically, from malignant giant-celled sarcoma, in which death with visceral dissemination is the rule, even after the most radical treatment. The histological diagnosis it based on the morphological characters of the giant cells, especially as regards their nuclei. In myeloid sarcoma the latter are numerous, uniform, small, and without mitoses; in malignant giant-celled sarcoma they are few, sometimes single, irregular, and often very large, while mitotic figures are frequent. After investigating this comparatively large series of cases, and from study of the literature Stewart feels bound to advance a strong plea for the conservative treatment of myeloid sarcoma. Especially would he advocate thorough curettage as the operation of choice in the first instance in suitable cases; failing this, a local resection of the growth. Amputation should be the last resort, and only after the failure of less radical measures. An accurate histological investigation of the tumor in all cases is essential.

Operative Treatment of Acute Epididymitis.—Smith and Frayser (*Annals of Surgery*, 1914, lx, 719) report their observations after reviewing over 300 cases in Ancon Hospital since 1908, in which operative treatment gave most gratifying results. They describe the operation at follows: After shaving the parts thoroughly they use a 3 per cent. alcoholic solution of iodine. External and parallel with the epididymis, an incision is made into the tunica vaginalis which should be large enough to deliver the testicle. Examine the epididymis and multiple punctures with a blunt probe in that portion which is inflamed. Gently massage the part, wash with warm salt solution and return testicle to scrotum. Close the tunica with catgut and insert a narrow iodoform gauze drain. The external wound is closed with silk-worm gut, using the subcuticular stitch—the drain passing out at the lower

angle. After operation apply a sterile gauze dressing and use a suspensory bandage to support the scrotum. On the second day the wound is inspected and the iodoform drain removed. Daily dressings are not necessary. Usually on the fourth day the patients are up and allowed the freedom of the wards. On the fifth day a 2 per cent. alcoholic solution of iodine is applied over the line of incision and the sutures removed, if silk-worm gut has been used. In the majority of cases patients return to work on the sixth day. Epididymoty is the rational thing to do because it shortens the duration of the disease; relieves the severe, weakening, sickening pain at once, causes the temperature to fall and induration to disappear rapidly. What is radical today is conservative tomorrow.

Genital Symptoms in the Diagnosis of Appendicitis.—Lanz (*Zentralbl. f. Chir.*, 1914, xlvi, 1705), after referring to the suggestion of Horn that the pain produced by dragging on the spermatic cord was a valuable sign, sometimes, in appendicitis, says that he found this symptom constant in four cases operated on. He also observed, from observations on a dozen cases, that the cremaster reflex was weakened or absent, and that frequently the right spermatic cord was thickened from collatereal edema in acute cases and exquisitely tender when it was rolled under the examining finger just after it emerged from the external inguinal ring, at the internal attachment of Poupart's ligament and external to the spine of the pubis. While the tip or end of the finger can be introduced into the external ring on the left side without trouble or pain, on the right side it detects the rigid lower border of the internal oblique and transversalis muscles which prevent further penetration into the canal. This rigidity is due to the same muscular defence which we recognize in the right rectus muscle in appendicitis. Lanx advises examination of the genital symptoms in the following order, a comparison being made with the left side: (1) Canal symptoms: (*a*) tension of the pillars of the external ring (*b*) muscular resistance on pressing the finger into the inguinal canal, (*c*) pain produced by coughing while the finger is in the canal; (2) Spermatic cord symptoms: (*a*) pain on pulling the cord, (*b*) pain from pressing on the cord, (*c*) Swelling of the cord at the external ring; (3) Testicular symptoms: (*a*) cremaster reflex. Systematic comparison of these findings with those at operation will help us in deciding before operation the severity of the attack, the localization of the focus, its relation and its eventual extension to the peritoneum.

An Experimental Study of Osteogenesis.—Mayer and Wehner (*Amer. Jour. Orthoped. Surg.*, 1914, xii, 213) say that all four series of their experiments—transplants of periosteum, subperiosteal resections, cap implantations, and bone transplants—combined to emphasize the osteogenetic function of the specific-osteoblastic cells of the periosteum and the inability of the adult bone cell to form new osseous growth. Bone growth occurred in all the transplants of periosteum after subperiosteal resection; it was, however, absent in the cap experiments where the ingrowth of periosteum had been excluded. In the bone transplants, the adult bone cells of the grafts gave no evidence

of activity whereas the periosteum showed marked osteoblastic properties. Similar osteogenetic power was manifested by the transplanted endosteal cells lining the marrow cavity and the Haversian canals, provided their vitality was maintained by intimate union with the tissues of the environment. Bone macroscopically bare of periosteum can be successfully transplanted into the soft parts, not because the bone cells give rise to new bone formation, nor because of a metaplasia of the surrounding connective tissue cells into connective tissue osteoblasts, but because of adherent periosteal cells, and of living endosteal cells. The practical conclusions for the surgery of bone transplants are self-evident: bone should be transplanted with the periosteum; if feasible it should be split lengthwise, so at to insure an intimate union of the endostium with the surrounding tissue uses. Bone macroscopically bare of periosteum can, however, be transplanted with good hope of success if care be taken not to scrape away the adherent cells of the osteogenetic layer of the periosteum. The classical conception of the complete necrosis of the bony portion of the transplant must be modified, since, though the majority of the transplanted bone cells necrose, numerous cells can maintain their vitality until the graft has become vascularized. These cells, however, give no evidence of osteogenesis. The process by which the necrotic bone of the transplant is replaced by living bone consists not only in the usual sequence of lacunar absorption and subsequent bone apposition, but in a "creeping replacement." In this process the young bone cells, before they have assumed the adult form and before the bone has become lamellar in structure, show evidence of direct cell division, and of power to absorb necrotic bone and form new bone. The living osseous tissue advances into the old by the intercellular deposit of bone, also probably by a direct advance of the young bone cells in the old lacunæ.

Pott's Disease; Albee's Bone-grafting Operation; Results in a Series of Twenty-six Cases Operated More Than Six Months Ago.—Ryerson (*Amer. Jour. Orthoped. Surg.*, 1914, xii, 259) says that 21 of these 26 cases are apparently well in a minimum time of six months after operation. Five are at least distinctly improved and may possibly make complete recovery. Eleven more cases were operated on less than six months before the reading of the paper. In all of the 37 cases there was no mortality whatever. He thinks these results will bear comparison with those obtained under any other form of treatment as yet devised, especially when it is remembered that a majority of these patients had been long and patiently treated by consecutive orthopedic measures, and were operated on as a last resort. It is Ryerson's belief that the work must be done rapidly to be safe, rapidly but not hastily. A motor saw is a practical necessity for the saving of time and for the accurate cutting of the splint. The splitting of the spinout process must be carefully done and can be done with a narrow chisel better than with the broad ones which are now in fashion. No attempt need be made to split the shafts of the spinous processes in children, for they are too thin to be split by any operator. The most that one can do is to split the tips and strip off the periosteum along one side of the shafts. The muscle and periosteum should not be stripped from the opposite

side of the spinous processes, as the bone needs all the blood supply it can get. The splint should be sewed in with heavy braided silk sutures, boiled in bichloride and then in paraffin. These sutures should be strongly placed in the deep tissues or in the tips of the processes themselves, if it is desired to make any correction in the deformity. In three of his cases one or two of these sutures came out a few monthf after operation, without marring the result in any way. Kangaroo tendon is unreliable under the tension which he uses. A needle-holder is a necessity in placing the sutures sufficiently strongly. In most cases a considerable correction of the deformity can be and should be obtained. The point of greatest importance is to make a splint that will extend well above and below the diseased vertebræ. It is not too much to have it go at least three vertebræ above and below the limits of the disease, if this is possible to accomplish. It is far better to immobilize several vertebræ too many than one vertebra too few.

Some Practical Considerations in the Diagnosis and Treatment of Abscess of the Cerebellum.—Milligan (*British Med. Jour.*, November 14, 1914, 833) says that the decades from 10 to 20 and from 20 to 30 provide the greatest number of cases of abscess of the cerebellum. Males are affected twice as frequently as females, and abscess on the left side is twice at frequent as abscess on the right side. The great majority of chronic cases are secondary to labyrinthine suppuration, the aqueductus vestibuli being the actual route of infection in 30 per cent. Of the clinical indications of cerebellar disease, nystagmus is one of the most important. In labyrinthine suppuration it is first directed toward the affected side and subsequently toward the sound side. It remains toward the sound side throughout the course of the disease and decreases *pari passu* with the destruction of the labyrinth. Cerebellar nystagmus is directed first towards the sound side and subsequently toward the affected side. It increases with the progress of the suppuration within the cerebellum. To test the function of the labyrinth the caloric test is the most convenient and can be applied with the patient sitting up or lying in bed. To fix the position of the eyes a geniometer it useful. Speaking generally, exploration of a cerebellar abscess should be made through the posterior antral wall in the space between the interauditory meatus and the sigmoid sinus groove. Counter drainage behind the "groove" is a valuable measure and much facilitates after-treatment. Prior to operation the withdrawal of a small quantity of cerebrospinal fluid is advisable to lessen existing intracranial tension and to prevent sudden respiratory or cardiac failure. For the drainage of chronic abscesses the author uses a special form of drainage tube, a tube within a tube, so that the inner tube may be removed without disturbing the position of the outer tube. He operated on 27 cases in the past ten years, 17 being in males and 10 in females. Seven were on the right side and 20 on the left side. Seventeen were cured and ten died.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Use of a Series of Vaccines in the Prophylaxis and Treatment of an Epidemic of Pertussis.—Hess (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1007) reports on the use of a series of vaccines in an epidemic of pertussis occurring in an institution for young children. He found that none of the four vaccines, including an autogenous strain, was of value in curing or tempering the disease. That this failure was not due to tardy inoculations is emphasized by the fact that many of the severest cases received not only early active treatment but also prophylactic vaccination. No other conclusion seems possible from a review of the epidemic of 85 cases and a comparison of the severity of the disease among the vaccinated and the unvaccinated. This opinion is based solely on his experience in this epidemic and does not preclude the possibility that a different dosage of vaccine or treatment with a modified vaccine, may not prove to possess curative properties. The use of the vaccines in prophylaxis seemed to offer greater promise in view of the established fact that other vaccines, for example the typhoid vaccine, possess prophylactic although no curative power. This seems to some extent, although to a far less degree to be true of pertussis vaccine. In view of the fact that twenty children developed pertussis in spite of the prophylactic treatment, we cannot compare its protective value to that of typhoid vaccine. However, the proportion of unvaccinated children who developed pertussis so greatly exceeded the number of the vaccinated who developed the disease, that we conclude that the vaccine has protective value in a certain percentage of cases, and that it should be employed in institutions and in families to prevent the spread of this infection.

The Action of Potassium and Sodium Iodid and of the Iodin Ion on the Heart and Bloodvessels.—Macht (*Johns Hopkins Hosp. Bull.*, 1914, xxv, 278) says that the rationale and the scientific basis for the use of the iodids are very inadequate and he endeavored to obtain more exact knowledge of their action by experimental work. His work was chiefly directed to the effect of the iodids upon the circulatory apparatus. His experiments indicated that the potassium ion produces a relaxation of the bloodvessels and a marked depression of the heart; that the sodium ion has a slightly stimulating action on the bloodvessels and also stimulates the heart, and the iodin ion is a powerful stimulant to both the heart and bloodvessels, as shown by its action in experiments on isolated organs. The stimulating effect of the iodin ions however is greatly inhibited in the intact animal by their chemical combination with the protieds of the blood. Whether the chemical compound thus produced in a stable

one or whether it is a loose one and slowly breaks up, setting iodin free, remains an open question. If iodin is set free a stimulating effect is to be expected. The action of sodium and potassium iodid on the heart and vessels can be best understood from the action of their component factors. Sodium iodid possesses no depressing property for the sodium ion is a vascular constrictor and a cardiac stimulant, and the iodin ion insofar as it is free to act has the same action. Potassium iodid on the other hand, clearly shows the depressing of the potassium ion on the heart and vessels, especially of mammals, not only on isolated organs, but also in the living animals. It is therefore no a matter of indifference which of the iodids is to be chosen for the purpose of depressing the circulation as, for instance, in the case of an aneurysm. Macht says that so far as experimental evidence goes the iodids possess no special virtue of lowering the blood-pressure, but that effect is really due entirely to the potassium and could be produced even more efficiently by other potassium salts.

Active Immunization in Diphtheria and Treatment by Toxin-Antitoxin.—Park, Zingher, and Serota (*Jour. Amer. Med. Assoc.*, 1914, lxii, 859) say that the property of toxin-antitoxin mixtures to produce immunity in animals has long been known. In 1913, Behring published the results obtained in human beings. The combined substances were either neutral or slightly toxic to the guinea-pig. Individuals were injected with small doses (from $\frac{1}{20}$ to $\frac{1}{10}$ c.c.) which were repeated in from seven to ten days. The first injections were made subcutaneously or intramuscularly, while later the intracutaneous administration was favored, since the more distinct local reaction was believed to induce a greater efficiency of vaccination. The results as reported from different observers have not been uniform, and as a rule are not distinctly stated. Hahn reports antitoxin production in 36 out of 40 treated, but the fact that 25 of the 40 had natural antitoxin already present modifies greatly the favorable nature of this result. The immunizing response to vaccine varies widely. It seems greatest in young adults and Zangmeister reports the interesting fact that the newborn are nearly a hundred times less susceptible to vaccine than adults. Kissling reports results in the immunization of 310 patients who were exposed to infection. In the 111 who were injected twice no diphtheria developed. In the 109 cases injected once, 8 patients developed clinical diphtheria. During an epidemic of diphtheria, Hahn and Sommer vaccinated part of the inhabitants of several villages: of 633 patients considered fully immunized only two developed mild diphtheria, but 10 of the group developed it during the first ten days. The disease continued to spread to some extent among those not vaccinated. Bauer finds that the persistence of the bacilli in carriers is not shortened by active immunization. He believes that not only all patients with antitoxin, but also those without natural antitoxin can be immunized, if sufficient doses and amounts of vaccines are injected. The interval between the injections of vaccine and development of antitoxin varies in different cases. According to Hahn it is usually not less than three weeks. Kleinschmidt and Viereck found it shorter—even eight days. Patients with natural antitoxin usually show early and considerable antitoxin production. They also generally

show a somewhat greater local susceptibility to vaccines. This, according to von Behring, is due to sensitization from previous infections with the Klebs-Loeffler bacillus. According to von Behring, the higher temperature of fever will destroy antitoxin at an increased rate so that an amount of antitoxin, which generally protects, fails to do so in measles and scarlet fever. Schick and Karasawa find, however, that no change in antitoxin content is caused by measles. Von Behring considers that 0.01 unit per cubic centimeter is sufficient to protect healthy persons. Much less than this probably suffices except under unusual conditions, as in scarlet fever. During the past twelve months the attempt has been made to immunize actively against diphtheria the patients in the scarlet fever wards of the Willard-Parker Hospital. For this purpose mixtures of diphtheria antitoxin and toxin were prepared, either slightly antitoxic, neutral or slightly toxic to the guinea-pig. The injections were made subcutaneously or intramuscularly in doses of from 0.25 to 1 c.c. of undiluted vaccine; a few of the non-immune persons received as high as from 3 to 5 c.c. at each injection. The dose was repeated two or three times at intervals of from three to seven days. The injections were made posteriorly in the intrascapular region, in some over the insertion of the deltoid. The local reactions consisted as a rule of varying degrees of redness, induration, pain and tenderness; in part they seemed to depend on the size of the dose and in part on the individual susceptibility. Persons with natural antitoxin gave somewhat more frequently the stronger local reactions. The constitutional symptoms were as a rule rather mild, occasional temperature reactions of from 1 to 3 degrees were noted after larger doses of the strong vaccines. The authors found that active immunization produced a very decided increase of antitoxin in a relatively short time in all persons who had natural antitoxin. These, however, were immune to diphtheria before the injections were made. In a series of 700 scarlet fever patients tested by them for natural immunity by the Schick reaction, 400 gave a negative reaction. 57 per cent. were, therefore, naturally protected and needed neither active nor passive immunization. Less than one-quarter of the remaining 43 per cent. which were probably susceptible to diphtheria, reacted to active immunization with mixtures of diphtheria toxin and antitoxin to a degree sufficient to immunize them. A larger percentage developed a trace of antitoxin which was possibly enough to give a slight protection. In their conclusions they say that those who are definitely exposed to infection should be passively immunized even if the toxin-antitoxin injections have been given. The use of the Schick test will eliminate the necessity of immunizing about two-thirds of those exposed, as those not reacting are probably immune. This natural immunity probably continues for a considerable period of time, possibly indefinitely. Active immunization is indicated when there is no immediate danger of infection and when it is desirable to lessen the number of susceptible persons. It is too early to decide whether active immunization should be attempted on a large scale. The lack of a sufficient response of at least 50 per cent. of those susceptible to diphtheria and the fact that the immunity lasts for but one or two years are drawbacks that will probably limit its usefulness.

The Present Status of Organic Iodin Preparations—McLean (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1382) says that the larger number of commercial preparations of organic iodin resolve themselves naturally into two classes: (1) iodin products of the higher fats or fatty acids and (2) iodized albumins. The chief iodized fats and fatty acids on the market at the present time are iodifin, sajodin, and iodinal. The preparations contain varying amounts of iodin but are sufficiently similar in their characteristics to allow of their being considered together. The advantage over the alkaline iodides claimed by the manufacturers are chiefly as follows: (1) absence of gastro-intestinal irritation, (2) slower absorption, (3) longer retention in the body and a more uniform rate of excretion, and (4) less tendency to produce iodism. The first claim is in general well substantiated, as all of these substances are bland and unirritating, the iodin being so firmly bound as to be inactive locally. These substances are absorbed without much change in their composition, the absorption being similar to that of fatty acids. While 75 per cent. of the iodin given in the form of potassium iodid is excreted in the urine within twelve hours, and the highest amount in the urine is in the second hour, the absorption and elimination of the iodized fats is much slower. When sajodin is given, iodin does not appear in the urine until after from one to three hours, and while the highest point in the excretion is reached within twelve hours the amount excreted remains high for thirty hours, giving a much more uniform rate of excretion. The iodin is excreted in inorganic form and probably is effective in the body only after it is separated from its organic molecule. The fact that relatively more iodin is found in the nervous tissues probably has little bearing on the efficiency of these substances in cerebral syphilis as their lipoid solubility would not favor their entrance into syphilitic tissue. The lessened tendency to iodism claimed by many observers may be explained by the slower and more uniform release from the lipoid combination in the form of available iodin. Where continuous small amounts of iodin are desired, as in arteriosclerosis, bronchial asthma, lead poisoning, etc., this iodin may be supplied in a form non-irritant to the stomach as an iodized fat or fatty acid, and the probability of iodism would not be great. When large amounts of iodin are desirable, as in cerebral syphilis, etc., the therapeutic effect seems to depend on the same property that causes the toxic effect, that is, the high concentration of iodin, and any effort to decrease the concentration would result in a loss of therapeutic efficiency. The iodized albumins on the market are chiefly iodalbin and iodo-casein. They are relatively unstable and iodalbin contains some free iodin and much more easily available iodin. The absorption of iodin is somewhat retarded and these preparations are less irritant to the stomach than the soluble inorganic salts. Iothion and iothion oil are recommended for local applications and for percutaneous administrations. They are apparently efficient in case percutaneous use is desirable. Another class of preparations, the iodized tannins, are not strictly organic preparations. They are prepared in the form of wines or syrups, and contain tannin with a small amount of loosely combined iodin. They decompose rapidly in the stomach and their action is the same as that of a corresponding amount of potassium iodide.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M D.,

OF PHILADELPHIA.

The Epifascial Neosalvarsan Injection of Wechselmann in Children.—HANS KERN (*Berlin klin. Woch.*, 1914, li, 1742) describes the method as used in an orphanage in Berlin. The combined treatment has been employed for some time, and besides the exhibition of mercury in some acceptible form, from four to six injections of neosalvarsan are employed. The use of neosalvarsan alone was discontinued because the results were not permanent enough. On account of the difficulty of giving neosalvarsan intravenously in children, especially between the second and seventh years, the epifascial method of Wechselmann was adopted and has proven very satisfactory. This method consists of depositing the solution exactly upon the fascia. The guide to this location is a sensation of roughness felt on drawing the tip of the needle over the fascia. This sign, however, frequently fails in children owing to lack of development in the fascia. The concentration of the solution of neosalvarsan was gradually increased during the application of this form of treatment from month to month until 100 per cent. solutions were being used. Infiltration of tissue followed the procedure at first but with increasing skill in technique gradually disappeared until in a series of 88 injections but 3 cases showed slight infiltration. The conclusion was that it was the technique and not the concentrated solution that caused infiltration. The method is naturally more difficult with small children than with adults, and the impression frequently was that the epifascial injection had become really an intramuscular one. However the expected infiltration did not appear. No clinical difference was noted in the action of the intravenous and epifascial method; the latter, however, has a slower, steadier action and avoids the sudden stormy flooding of the intravenous method. The author recommends the epifascial method in children. It takes the place of intravenous injection and infiltration disappears or diminishes with improvement in technique, which, if not simple, can easily be learned.

Vaccination against Varicella.—KLING (*Berlin klin. Woch.*, 1915, lii, 13) gives his technique and results in vaccinating against varicella. During an epidemic of varicella KLING began to vaccinate healthy children against the disease and found the reaction very slight, the efflorescence almost invariably limited to the point of vaccination and the fever and constitutional signs absent. From a practical standpoint it was significant that all children successfully vaccinated remained immune to the contagion of the disease. In all there were 135 cases vaccinated, only 45 of which failed to give a good positive reaction. In 10 cases a few vesicles appeared on the body, besides the local reaction, and in 3 cases the vesiculation was more general, in all the others

the reaction was localized. All of the 135 cases with positive reactions remained free from the contagion during months of observation, while in 108 children who were unprotected or in whom the vaccination had failed to "take," 73 per cent. contracted the disease. It therefore appears that this process of vaccination is of utility in protecting against the severe forms of varicella. The technique of vaccination against varicella follows the main principles in all vaccination, in that the child from whom the vaccine material is taken should be free from syphilis and tuberculosis and be normally healthy. The operation in all respects should be aseptically performed. The vesicle from which the serum is derived should be from a fresh crop, contain clear serum, and should not be surrounded by a marked inflammatory areola. The vaccination-lance is preferred to the Pirquet needle. The skin on the arm is prepared in the usual manner, the lance is inserted into the vesicle, so that the serum covers the point and a light stab is made on the prepared skin surface, deep enough to slightly draw blood. About three stabs are made, then the lance tip is again covered with serum from this vesicle and three more stabs are made. It has been shown that where one or two stabs only are made, only a small percentage of reactions occur. Usually the reaction will occur in only one or two of the stabs, the rest remaining negative. A sterile dressing is applied for two days when it is removed as the punctures will have healed. As soon as the reaction sets in the sterile dressing must be again applied to prevent secondary infection.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Diathermy in the Treatment of Pelvic Inflammation.—The noted Spanish gynecologist, RECASENS, in an article recently contributed to one of the German journals (*Monat. f. Geb. u. Gyn.*, 1915, xli, 130) says that the "operative madness" which prevailed during the last twenty years of the past century and the first few years of this, with regard to the treatment of inflammatory conditions of the adnexa is gradually giving place to more conservative and rational methods. It has been conclusively demonstrated that many cases which were formerly considered only fit subjects for radical surgery may, if properly treated, attain at least a complete symptomatic cure without operative interference. The best of the conservative methods, in his opinion, is the application of heat, for the purpose of inducing hyperemia, which latter is as effectual in causing resolution of chronic inflammatory processes in the genital organs as it is in the Bier treatment of joints, etc. In the past, however, great difficulty has been experienced in actually applying an efficient quantity of heat to the internal genital

organs; the various methods by which this was attempted, such as hot applications, douches, and even abdominal and vaginal electrically heated coils, were all more or less unsatisfactory, in that they were not able to drive the heat into the deeper tissues, where it was wanted. These difficulties are entirely overcome, however, in Recasens' estimation, by diathermy, in which process an electrical current, which can be passed accurately between two electrodes placed in any desired positions, and whose strength can be absolutely regulated, is transformed in the tissues through which it passes from electrical to heat energy, thus applying the latter along its whole course. For most purposes, Recasens employs a large electrode in the lumbosacral region, and another on the lower abdomen, passing the current from the latter to the former, and thus exciting a condition of hyperemia in all the pelvic organs. In other cases, the dorsal electrode is replaced by one in the vagina; it must be large enough practically to fill up the entire vagina, and in this case the current is sent from the vaginal to the abdominal electrode. When working in this way, the strength of current must be considerably less than when both electrodes are on the external surface. The current must be so regulated that the heat development takes place slowly but progressively, and that it is maintained at its height for thirty to forty minutes. Recasens says his best results with this method of treatment have been obtained in cases of chronic salpingo-oöphoritis with adhesions; in a few sittings he has seen the formerly fixed uterus become movable, the pains disappear, and exudate, where present, absorbed. In chronic inflammatory processes associated with pus formation, however, he has seen practically no benefit, either subjectively or objectively. While unable to offer any positive explanation for the results secured, the author ventures the opinion that possibly the heat has some effect in inhibiting the growth of pathogenic organisms in the infected tissues.

Nerve Distribution in the Ovaries.—In a very elaborate series of investigations, Wallart (*Ztschr. f. Geb. u. Gyn.*, 1914, lxxvi, 321) has studied by means of special staining technique the distribution of nerve fibers in human and various types of mammalian ovaries. He finds that the nerves enter the ovary at the hilus in the form of large, very tortuous bundles, the great tortuosity being evidently a provision to allow for changes in the size of the ovary incident to ovulation. Gradually giving off branches to the stroma, the nerve bundles eventually reach the cortex, where they break up into such an enormously rich network of fibers that in suitably stained specimens this region of the ovary appears to consist in large part of nerve tissue. There is also an exceedingly rich nerve supply to the walls of bloodvessels throughout all portions of the organ. An interesting relation was noted between the nerves and the Graafian follicles; while these are completely surrounded by a rich network of fibers, no penetration of nerves could ever be demonstrated within the epithelial portion of the follicle, *i. e.*, within the membrana granulosa, which tissue, together with the developing ovum, appears to be without direct nerve connection. A few fibers were found in mature corpora lutea, but only in the connective-tissue septa containing the bloodvessels—never running between the lutein cells. After degeneration and retrogression of the

corpus luteum sets in, however, nerve fibrils can often be seen in close relation to the individual cells. This late appearance of nerves in the corpus luteum may be due, WALLERT thinks, to faulty technique the large amount of fat in the fresh corpus luteum seriously interfering with the staining reactions, and thus preventing satisfactory demonstration of nerve fibers, or it may stand in some relation to the gradual evolution of what he considers a true "interstitial gland" from the remains of the corpus luteum. At any rate, WALLART always found an exceedingly rich network of fibers associated with the terminal stages of this structure, even including the apparently inert mass of connective tissue known as the corpus fibrosum, which represents the terminal form of the extinct corpus luteum. He thinks, therefore, that even this structure has a distinct secretary function, by which the ovary is to some extent brought into relation with other ductless glands. Although not able to demonstrate positively the presence of ganglion cells in the ovary, WALLART discovered numerous bodies so strongly suggestive of them as to warrant the belief that in all probability ganglionic elements are in reality present.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL,

AND

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

Cholesterin in Blood.—MILKOWITSCH (*Russki Wratsch*, 1911, xxii) determined in a number of experiments the influence of cholesterin, lecithin, adrenalin, and other substances upon the process of phagocytosis. He used the Wright method. He employed the Staphylococcus aureus and tubercle bacillus in conjunction with normal human serum and leukocytes. He comes to the conclusion that both cholesterin and lecithin increases the phagocytosis of Staphylococcus aureus and tubercle bacillus. ROEHMANN (*Berlin klin. Woch.*, 1912, No. 42) found in the red blood cells, but not in the blood plasma, an enzyme which acting like a lipase splits the cholesterin-ester. He calls it a cholesterase. It is important to determine whether other tissues contain this cholesterase and whether an increase of cholesterin ester in amyloid kidney and in arteriosclerosis has a relationship to this ferment. It is suggested that the accumulation of cholesterin in the liver is associated with the cholesterase of the red blood cells which are destroyed by this organ. The deviation of the complement in the

Wassermann reaction is enhanced by the presence of cholesterin. It would appear that the sera giving a positive Wassermann contained more cholesterin than others. It may be that this increase is directly related to an excess amount of cholesterase in the serum. Citronberg (*Biochem. Zeitsch.*, 1912, xiv, 281) has shown that the blood of horses is capable of decomposing cholesterin-esters without the addition of liver extract. This decomposition does not take place in serum alone, but it appears that the cholesterase is contained within the red blood cells. It is indicated, in fact, that the red cells not only contain the cholesterase but also the cholesterin-ester. Pringsheim (*Münch. med. Woch.*, 1912, 1757) reports the case of a man, aged thirty-four years, who after a severe cold developed hemoglobinuria without marked change in the blood picture. The Wassermann was positive. Mercurial treatment was of no value. The patient then received five injections of 0.05 grms. of cholesterin in a 10 per cent. emulsion intramuscularly in a period of eleven days. The hemoglobinuria disappeared. After eight days he had another attack as severe as original. The resistance of the red blood cells was normal to saponin solutions. Buerger and Beumer (*Berlin. klin. Woch.*, 1913, No. 3) studied the lipoid content of the blood. The greatest cholesterin and lecithin values of the serum was observed in diabetic lipemia and cholemia. In a case of eclampsia they also found an increase. Less than the normal quantity was found in pernicious anemia, chlorosis, malignant cachexia, and in inanition. It is true that others have stated to have found an increase under conditions similar to these. A constant relationship, therefore, is not necessarily found in given diseases since the content in lipoids is influenced by the diet and the nutrition of the patient. In every serum some free cholesterin was found, equaling about 30 per cent. of the fats present. Kanders (*Biochem. Zeitsch.*, 1913, lv, 96) used the method of Windaus and determined the cholesterin content of the serum of the horse, dog, cow, rabbit, guinea-pig, and sheep. He found the cholesterin content to increase in the following order: cow, horse, dog, sheep, guinea-pig, and rabbit. In the order of cholesterin or cholesterin-ester content of the red blood cells, are dog, guinea-pig, rabbit, cow, and sheep. He found that human sera with positive Wassermann reactions had a lower cholesterin ester content than the negative. Obakevitsch (*Russki Wratsch*, 1913 No. 30) determined the cholesterin content of blood by the colorimetric method of Grigaut. The cholesterin content in a litter of blood serum normally varies from 1.4 to 1.8 grams. A fatty diet readily increases the cholesterin content. Hypercholesterinemia was found in pregnancy, nephritis, cholelithiasis, arteriosclerosis, lues, and during convalescence from acute infections. On the other hand, hypocholesterinemia was found in acute and subacute infections, anemias, and hemolytic jaundice. Gaucher and Desmoulier (*Bull. de l'Acad. de Med.*, Paris, 1912, No. 26) found a striking parallelism between the cholesterin content of the serum and the Wassermann reaction. Cantieri (*Wien. klin. Woch.*, 1913, No. 48) reported the treatment of splenic anemia in a young child by injecting cholesterin-esters of olein and palmatin. He reported marked improvement in the blood picture and a diminution in the size of the spleen. Stuber (*Biochem. Zeitsch.*, 1913, li, 211) found that cholesterin diminished the phagocytic activity. Lecithin had no particular effect upon

the phagocytosis but it inhibited the action of the cholesterin. Intravenous inoculation of 70 to 90 c.c. of a 0.5 per cent. to 1 per cent. emulsion of cholesterin reduces the phagocytic index in cats enormously. The reaction may persist for days. On the other hand lecithin slightly increases the index as well as neutralizing the depressing influence of cholesterin previously inoculated. Lecithin heated to 70 degrees reduces its activity. Wacker and Hueck (*Archiv. f. Exper. Path. u. Pharm.*, 1913, lxxiv, 416). Normally the cholesterin in the blood is distributed in the serum as well as the cells. The white cells contain five times as much cholesterin as the red blood cells. The serum contains both free cholesterin and cholesterin esters. The separation of fibrin carries no cholesterin with it. The normal cholesterin content is fairly uniform but is more or less disturbed by diet, muscular activity, and tissue destruction. The feeding of free cholesterin increases the cholesterin and cholesterin-ester content of the blood serum. The same may be observed in the inoculation of cholesterin or oleic acid cholesterin ester underneath the skin. The blood cells play but little part in this alteration of the cholesterin content of the blood. A cholesterin diet leads to the deposition of fat in various organs and cholesterin fat mixtures may be observed in the cortex of the adrenal, liver, kidney, spleen, bone marrow, gall-bladder and adipose tissue. They also found that prolonged muscular exercise led to a diminution of the cholesterin esters in the adrenal while that in the blood was slightly increased, while rapidly fatiguing exercise led to a diminution in the blood serum and a slight increase in the adrenals. Fischl (*Wien. klin. Woch.*, 1914, No. 27) found an increase of cholesterin in the serum of patients suffering from various dermatoses (urticaria, eczema, mycosis fungoides, xanthoma). He believed that this increase of the cholesterin is associated with a protective reaction of the serum.

Mixed Vaccines against Typhoid and Paratyphoid Fevers.—Kabeshima (*Centralb. f. Bakt.*, 1914, 74, H. 1) reports upon the use of mixed vaccines as used in the Japanese Marine. A vaccine containing B. typhi, B. paratyphi A and B were administered to many individuals. The local and systemic reaction which followed the inoculation of the mixed vaccine was not greater than that observed in simple ones. In experiment it was shown that the individuals possessed an immunity to infections of each organism and that the use of such vaccines had a definite practical value in the army.

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ORIGINAL ARTICLES

AN EXPERIMENTAL STUDY IN EXCLUSION (FUNCTIONAL) OF THE PYLORIC ANTRUM.

By Willard Bartlett, A.M., M.D.,
ST. LOUIS, MISSOURI.

(From the Surgical Laboratory of Washington University.)

My problem is not to determine the relative values of pyloric obstruction and exclusion of the pyloric antrum, but to study the latter, which involves a class of cases—ulcers of the stomach, away from the pylorus—in which the results of simple gastro-enterostomy are relatively unsatisfactory; cases in which resection would seem indicated were it not for the fact that chronic perforation into liver, pancreas, or other important neighbors make it a hazardous procedure. I have excluded the pyloric region twenty-seven times on the human subject, as reported at the 1914 meeting of the American Medical Association. The first fifteen patients were operated upon by transverse section of the stomach with blind closure, as first suggested by Doyen, with which no other method has been definitely proved experimentally to compare in efficiency. These experiences convinced me that the technical difficulties and dangers attendant on this procedure warranted experiments, which are reproduced herewith, looking toward a simpler and safer method which could guarantee the same result. Ten of my last twelve patients had the pyloric antrum excluded by original methods, which I shall here show to have been satisfactory on dogs.

A large number of methods have been proposed for obstructing the pylorus and excluding the pyloric region. They will be considered together, since it is difficult to separate the two historically, although they are by no means to be considered a clinical entity.

Berg[1] has practised gastro-enterostomy with pyloric exclusion since 1901 on bleeding ulcers in the pyloric region, for duodenal fistula or accidental wounds of the duodenum, and for simple or callous ulcers of the pyloric end of the stomach. His operation consists of a gastro-enterostomy in the usual manner, with the addition of an occluding ligature of heavy Pagenstecher thread passed behind the stomach just proximal to the antrum; then taking a few stitches through the peritoneum and muscularis to prevent slipping, he slowly ties the ligature, being careful not to interfere with the circulation. He says this method of exclusion does not increase the mortality or the length of the operation. Pool[2] reoperated a case upon which a gastro-enterostomy had been performed six months previously without relief of symptoms. A simple ligation of the pylorus with catgut suture was considered the safest procedure and gave a good result. He excluded a second case in a similar manner and a gastrojejunostomy was done with a satisfactory result, but he says the permanency of this closure is doubtful. Momburg[3] treated two cases by tying silk ligatures tightly around the pylorus and suturing omentum in the furrow thus created. Corner[4] says that when doing a gastro-enterostomy for pyloric ulcers he excludes the pylorus by placing a ligature on the pyloric end of the stomach as suggested by Berg. Renton[5], surgeon of the Western Infirmary of Glasgow, says the operation they have usually performed during the last three years is the posterior gastro-enterostomy of Robson, with exclusion of the pylorus, where necesssary, with a purse-string suture. Ward[6] gives a case after the Berg method, with a good result. Parlavecchia[7] merely throws a strong non-elastic ligature around the stomach at the point where the incision would be made by the usual technique, as proposed by Doyen, and proliferation of cicatricial tissue soon shuts off the part completely. On dogs it required only from two to four minutes longer than a simple gastro-enterostomy. As far as we can learn no exhaustive series of animal experiments have ever confirmed these results. The universal experience with ligatures on hollow viscera has been that they cut through into the lumen and are passed out with other intestinal contents, the peritoneum speedily becoming agglutinated outside of the constriction.

Leriche[8] tried ligating the pylorus of the human subject with

[1] Jour. Amer. Med. Assoc., March, 1913.
[2] Ann. Surg., November, 1913.
[3] Zentral. f. Chir., October, 1913, No. 42.
[4] Lancet, London, 1913.
[5] British Med. Jour., April, 1912.
[6] Lancet, London, July 7, 1906.
[7] Policlinico, Rome, April, 1910, xvii.
[8] Lyon Chirurg., 1913.

catgut, and though the immediate results were good the Rœntgen rays soon showed the operation to have been a complete failure. He then did the Doyen exclusion on the same patient, with complete success. In a second case he tied a silk string around the stomach in such a way that it was divided into a small cardiac cavity and a larger pyloric one, but Rœntgen rays soon demonstrated the re-establishment of the viscus. There was a time when Ochsner thought he had definitely excluded the pylorus by wrapping a silver wire about it. Brewer[9] uses a strip of aluminum, 1 cm. wide and 5 cm. long (thickness not stated), which is passed under the pylorus and rolled together with the fingers tightly enough to close its lumen without devitalizing the tissue. Nine dog experiments are recorded after gastro-enterostomy had been done. In all of these cases where the animal lived more than nine days the band was found hidden by new tissue and the vicinity was usually free from adhesions. There was never a necrosis, and the lumen was non-patent in every instance. No dog was allowed to live more than two months and ten days after the operation. Wilms[10] separates a strip of fascia from the anterior aspect of the rectus muscle or from the fascia lata and throws it around the pylorus, tying or suturing it so as to exclude the pylorus completely. It is easy, safe, and shortens the operation for exclusion, giving no reflex disturbance of the stomach. When we visited Professor Wilms at his clinic in 1912 he stated that Rœntgen-ray examinations of patients, some months following operation, show the pylorus to be closed. Kolb[11] practised exclusion of the pylorus by ligating with a strip of fascia or omentum in cases of bleeding ulcer of the stomach with duodenal stenosis. He treated in all 18 cases, 3 with the omentum and 15 with fascia, 9 cases were reëxamined, the pylorus found to be closed, and the chyme passing through the new opening in one hour. Technique: the strip of fascia lata is about 3 cm. wide, free of all fat and muscle. It must not be tied too tightly and the strip does not relax if sutured to the serosa with silk or catgut.

Bircher[12] has done Wilms' operation, but is convinced that the strip of fascia undergoes early absorption. He found that strings of linen or catgut wrapped around the viscus accomplish the same result, but are not permanently effective. In 15 cases Bircher took the hepatico-umbilical ligament, cut it loose from the abdominal wall, finding it to be from 5 to 6 cm. in length, wrapped it once or twice, as the length permitted, around the pylorus, and fastened it in position with a few stitches. Rœntgenoscopy from one-fourth to one year after operation shows that the obstruction is lasting.

[9] Surg., Gyn., and Obst., vol. xviii, p. 145.
[10] Deutsch. med. Woch., January 18, 1912.
[11] Deutsch. chir. Kong., 1913.
[12] Zentralbl. f. Chir., October, 1913, No. 40.

Hercher[13] had four cases in which he excluded and suspended the pylorus (after gastro-enterostomy) with the ligamentum teres hepatis. Hoffmann[14] uses the same method with the ligamentum teres hepatis. Polya[15] thinks that the closure of the lumen thus is the only safe means of exclusion. He thinks in the ligamentum teres hepatis he has found a material which, on account of its form and suppleness, is even better for the purpose than the strip of fascia used by Wilms. He had seven cases, of which five were successful. Gobell[16] excludes the pylorus after the Wilms method. Naselli[17] has proved in six animal experiments that it is impossible to exclude the pylorus by ligature method. His ligature consisted of an aponeurotic band from the fascia lata, from the anterior abdominal wall, or the tendon Achilles. In no case did he get the permanent physiological result desired. He did secure slightly more stenosis in instances where he first crushed a furrow with forceps and then tied his strand in this. In no case did the tissue ligature cut into the lumen. In the beginning the lumen is closed by longitudinal folds of mucous emmbrane but later there is an atrophy of the encircling tissue, the folds straighten out, and the canal is reëstablished. In consequence of this a gastro-enterostomy made at the same time as the ligation will eventually close up if the animal lives long enough. Surely the autoplastic method of obstructing the pylorus has a distinct advantage if as is claimed the fibrous band remains viable. It is said to become firmly adherent to the peritoneum and hence does not cut its way into the viscus. The permanency of these results must, however, remain an open question until experimenters have had time for most remote observations. Blad[18] discusses the methods in vogue for closing the pylorus in a gastro-enterostomy, and reports a case in which he folded in the pylorus and duodenum with silk sutures, forming a role about 6 cm. long and as thick as the little finger. Examination seven months later showed most of the chyme expelled through the new opening, but also part through the pylorus. Mertens[19] kinks the pylorus by sewing together the anterior surfaces of the stomach and duodenum, attempting in this way to obstruct the lumen. He had four cases, two of which were examined at the expiration of seven weeks and the pylorus found to be obstructed. He admits that an examination after a much longer time is necessary to determine the permanency of closure. Sequinot[20] shows the inefficiency of a gastro-enterostomy in all cases where a true stricture of the pylorus does not exist, and after showing the advantages of exclusion gives a procedure of infolding. He gave three cases,

[13] Zentralbl. f. Chir., August, 1913, No. 44.
[14] Ibid.
[15] Ibid.
[16] Ibid.
[17] La Clinica Chirurgica, May, 1913.
[18] Ugesk. f. Læger, 1912, xxv.
[19] Zentralbl. f. Chir., October, 1913, No. 40.
[20] Thèse de doct., Paris, January, 1913.

two of which were successful. Mariani[21] did an exclusion in this way: the stretched pylorus was kinked on itself and sutured to the duodenum and below to the rectus muscle and subcutaneous tissue. Functional results were good at once. He[22] later reports two cases, the first one dying of pneumonia and the second giving a good functional result. The Rœntgen rays showed food passing through the gastro-enterostomy, but he does not state how long after operation. It is pretty well established that no form of infolding or kinking has more than a temporary effect in producing occlusion.

In 1893 Doyen[23] was probably the first to suggest exclusion of the pylorus when he reported to the French Surgical Congress that he had in two cases done this for ulcer by cutting across the stomach just proximal to the pyloric antrum and making a blind closure of the resulting ends. Von Eiselsberg[24] independently proposed exclusion of the pylorus in 1895, reporting two cases of pyloric cancer in which adhesions made resection impossible. The intense pain which had been a leading symptom in both cases was completely relieved and, as a matter of course, the operation goes by his name in all German descriptions of it. Haberer[25] has done twenty-four exclusions, using the Doyen-von Eiselsberg technique. All the patients are well today but two, one of whom died of jejunal ulcer and a second who was reoperated for the same. He thinks this the operation of choice for duodenal ulcer, and it can take the place of difficult technique in benign cases. It is indicated in perigastritis of the pyloric region, and it should guard against cancerous degeneration of the ulcer. Threatened perforation may also be prevented. Jonnesco[26] in 1906-07 operated upon nine cases of pyloric and duodenal ulcers after this method of Doyen-von Eiselsberg. Jianu[27] discusses the advantages of exclusion and gives a report of two cases operated upon after the method last mentioned. Girard[28] says in cases of duodenal ulcer the operation is usually incomplete without an exclusion of the pylorus. If the employment of Doyen's method is impracticable he recommends a separation of the seromuscular layers and the introduction of a longitudinal suture. In greatly exhausted patients he uses a plicature of the anterior wall of the stomach or ligation as indicated by Körte. He gives two cases of partial exclusion by means of several plications of anterior wall. Leriche and Bressot[29] review fifty-nine exclusions of the pylorus and duodenum. By exclusion of the duodenum they mean cutting the pylorus across and closing each

[21] Policlinico, Rome, August 17, 1913.
[22] Zentralbl. f. Chir., November, 1913, No. 44.
[23] Franzosicher Chiro. Kongress, 1893.
[24] Arch. f. Klin. Chir., Band 50, 1895.
[25] Ibid., 1913, Band. 100, Heft 1.
[26] Revue de Chir., 1907.
[27] Wien. klin. Woch., 1910.
[28] Verhand. d. deutsch. Gesellsch. f. Chir., Berlin, 1911.
[29] Lyon Chir., Lyon, October, 1911, Band. vi.

stump, finishing with a gastro-enterostomy. The operation for exclusion of the pyloric antrum is more difficult being on the stomach tissue itself. All results were good with no deaths. Leriche[30] says all procedures intended to exclude the pylorus, excepting those which cut the stomach in two, may be regarded as parodies on surgery. He has done three exclusions of the duodenum by means of a modified Doyen operation at the pylorus, cutting across the sphincter, and he states that this is extremely easy, takes but a few sutures, and requires not over ten minutes for its performance. Jianu and Grossman[31] review the history of exclusion of the pylorus and also give results of experiments on dogs. They conclude that vacuolar degeneration of the excluded stomach mucosa rapidly procedes and favors healing of ulcer, also wards off hemorrhage, perforation, and cancerous degeneration later. Küttner[32] says in the surgical treatment of duodenal ulcers that the ideal method is that of gastro-enterostomy with the Doyen-von Eiselsberg method of unilateral exclusion of the pylorus, but the operative mortality is increased 10 per cent. He also uses Wilms' method, with a strip of fascia or Bier's method of crushing. Von Tappeiner[33] experimented on seventeen dogs in comparing results of the following five procedures to occlude: (1) infolding by suture; (2) narrowing the pylorus by what is called submucous plastic (this means manipulation of flaps formed of muscularis and serosa); (3) ligation of the pylorus with foreign material; (4) ligation of the pylorus with a pedunculated strand of serosa and muscle from the anterior abdominal wall; (5) ligation of the pylorus with strips of fascia after Wilms' method. He lost but one animal and examined all the others four, seven, or ten weeks later. As a result of these experiments he concludes that none of the five compare in efficiency with transverse section of the stomach as done by Doyen. Of these five methods, however, Wilms' ligation with a strip of fascia seem to be most efficacious. The great argument against Doyen's idea is the difficulty of execution.

The question of pyloric exclusion was discussed at a recent meeting of the Deutsche Gesellschaft in Berlin. Some were in favor of it, especially von Eiselsberg, others, including Kocher, think the methods without exclusion give the best results, but no conclusion was reached.

All my dog work was done under full ether anesthesia, every care being given to the animal's comfort later.

It may not be out of place before reciting the details of my experiments to state in a general way the method of studying the material secured. As soon as possible after death the stomach together with lower esophagus and upper jejunum were removed

[30] Lyon Chir., Lyon, October, 1913.
[31] Arch. f. Verdauungskr., April, 1910.
[32] Deutsch. chir. Kong., 1913.
[33] Beitr. z. klin. Chir., 1912.

en bloc. These viscera were distended with water until normal roundness was maintained, double ligated, and then hardened in 4 per cent. formalin solution. Some days later they were emptied, injected with barium, and rœntgenograms made. These together with illuminating diagrams are shown in Figs. 5 and 16. Transverse section was next made across the stomach on both sides of the septum and very close to it. After study of this interesting object in its entirety it was cut into thin transverse sections, of which one is shown herewith (Fig. 17).

Experiment I. December 19, 1912; large brown collie. We made a two-inch posterior no-loop gastro-enterostomy. There was a tear through the omentum, which was repaired.

February 7, 1912, the dog was killed because of distemper. The autopsy showed the gastro-enterostomy to be patent and there were no macroscopic lesions of the bowel or peritoneum. This was a control operation.

Experiment II. April 17, 1911; a small white and black fox terrier bitch. The pyloric region was excluded by mattress sutures including four thicknesses behind a transverse clamp, through which pressure was applied across the stomach for fifteen minutes. An anterior row of peritoneal sutures covered up the mattress row. An anterior gastro-enterostomy was done.

October 25. The dog was sacrificed and the gastro-enterostomy found to be patent. A white scar ran across the anterior and posterior surfaces of the stomach just distal to the gastro-enterostomy opening at the point where the clamp had been applied. There was no change in the stomach lumen. Distal to the cross-scar the outer surface of the stomach had a yellowish tinge and the mucous membrane was deeply bile-tinged over the corresponding area.

It had been thought possible to crush through the mucosa and cause an agglutination of the deeper mesoblastic structures, these being held in approximation by the mattress sutures. The futility of this plan was strikingly shown at autopsy some six months later; in fact the stomach showed but slight evidence of operative interference.

Experiment III. Januray 27, 1912; small black slut. At a distance of about two inches from the pylorus a slender rod was inserted under the stomach, lifting it up, and a clamp applied beneath. A transverse incision was made down to the muscularis of the posterior wall. The submucosa and the mucosa were cut as short as possible and allowed to retract. The anterior and posterior muscularis and serosa were drawn together by interrupted sutures, which were then hidden by a Lembert layer. The operation was finished by a posterior gastro-enterostomy.

February 2, the dog died. The belly was full of thin fluid blood and the intestines were matted around the pylorus. A furrow

transverse to the stomach and about 3 cm. from the pylorus indicated the site of the exclusion. A longitudinal section showed a complete septum formed by a double layer of the anterior wall attached to the posterior wall without intervention of the mucosa.

Experiment IV. February 17. This is a repetition of Experiment III. February 24, 1913, the dog died. The autopsy showed the belly full of bloody pus, the stomach was small, and the upper intestines engorged with bile. A deep groove on the anterior and posterior walls showed the site of the obstruction to be about 3.5 cm. from the pylorus; on section a complete septum was seen, two-thirds of which was formed by all the layers of the anterior wall. The gastro-enterostomy was found to have been made in the transverse colon.

The last two experiments prove only one thing, namely, that the simple method used is entirely too dangerous to be considered further. Both dogs died of peritonitis on the sixth and seventh days respectively. A complete septum was found in each case; however, the period of observation is too short to establish its permanency.

Experiment V. January 6, 1912; small white dog with bronze head. We incised the anterior wall of the stomach to the submucosa, both layers of which were divided transversely without wounding the posterior muscularis, the proximal and distal submucosa being closed blind. The anterior serous and muscular coats were sutured with two rows and the operation was completed with a gastro-enterostomy. Result: the dog was lost. The foregoing experiment represents a development of technique tending in the direction of greater safety. It is to be regretted that the result is not known.

Experiment VI. January 17; small black dog. At about three inches from the pylorus the wall was cut transversely to the submucosa, which was separated from the muscularis all the way around and the latter divided transversely. Both ends of the submucosa were then closed blindly and the muscularis and peritoneum sewed so that the anterior and posterior wall layers came together between the ends of the blind submucosa.

February 4 the dog died. The stomach and loop for the gastro-enterostomy were found to be greatly dilated. There was an obstruction and the stomach contents were found in the esophagus. The peritoneum was clean. At a point 3 cm. from the pylorus, furrows on both walls were external evidence of the site of the exclusion. A longitudinal section revealed a complete septum formed by a double layer of the anterior and posterior stomach walls, meeting end on without intervention of the mucosa.

Experiment VII. January 20, 1913; small white bitch. This is a repetition of Experiment VI, with the single exception that the incision in the anterior wall through the serosa and muscularis was made in the long axis of the stomach and quite near the pyloric region, on either side of which the submucosa was sewn blind.

Experiment VIII. February 24, 1912. This is an exact replica of Experiment VII. March 9. The dog was healthy, so was killed with chloroform. The exterior of the stomach showed little effect of the effort to obliterate the lumen. There was an incomplete septum seen on section.

In Experiments VI, VII, and VIII a technique based upon accepted surgical principals was devised, with the result that no dog died directly in consequence. One was killed on the fourteenth day while the other two died on the fifteenth and eighteenth days respectively. In the last two mentioned a complete septum was found, while in the fourteenth day animal it was only partially in evidence. While this form of exclusion is apparently leak-proof (in three instances at least) it is not satisfactory so far as simplicity and neatness are concerned. It is the identical operation which was described later by Porta[34] as having been adopted at the Biondi clinic. I had done this some months before his article appeared, but discarded it for the reasons given.

Experiment IX. February 10, 1912. A rod was passed transversely under the stomach and the lifted portion was caught in clamps. A shoemaker stitch was placed between the rod and clamp and everything cut through onto the rod. After cutting away the redundant mass the whole was inverted with Lembert sutures and a gastro-enterostomy done as usual.

February 17 the dog died. The stomach was dilated and an intussusception was present in the small intestine. A deep furrow on the anterior and posterior walls indicated the site of the infolding. A heavy complete septum was formed equally from both anterior and posterior walls; no mucosa intervened between the other tissues.

Experiment X. February 3, 1912; small white bitch. This experiment repeats Experiment IX, although the mattress stitches were introduced in a slightly different manner.

The animal died March 4. There was great dilatation of the stomach. A furrow on the exterior marked the site of the operation and a fine mucosa-lined canal persisted. Judging by the amount of dilatation there must have been a high degree of partial obstruction.

The same principle is involved in the two experiments just described, though the technique differed somewhat One animal died in seven days without any evidence of a leak, while the other lived thirty days. The septum was practically complete in the last-mentioned animal, while the other lived too short a time to be of value in this regard. Too much hemorrhage at the minor curvature characterized these operations.

After the foregoing ten experiments had been made a clinical experience suggested to the writer that partial transverse division of the stomach might be sufficient to create complete functional

[34] Deutsch. Zeit. f. Chir. Bd. 125, No. 5–6.

exclusion of the pyloric region. It came about in this way: A large callous ulcer was widely excised from the minor curvature, the stomach being cut about half way across, and in closing the defect the wound sutured transversely to the long axis of the viscus. Still complete obstruction ensued and was relieved only when a gastro-enterostomy was done some days later. At the second operation no mechanical explanation could be elicited, the stomach lumen being unimpaired (I am told by Dr. William J. Mayo that this phenomenon has appeared so often at Rochester that he does an immediate gastro-enterostomy whenever a large excision of the lesser curvature is made).

The ensuing twenty-eight studies are based upon the idea of a functional disturbance or at just distal to a partial transverse incision through both stomach walls (as opposed to the complete transverse incision of Doyen-von Eiselsberg). In addition I have created a partial septum in each instance while closing the defect.

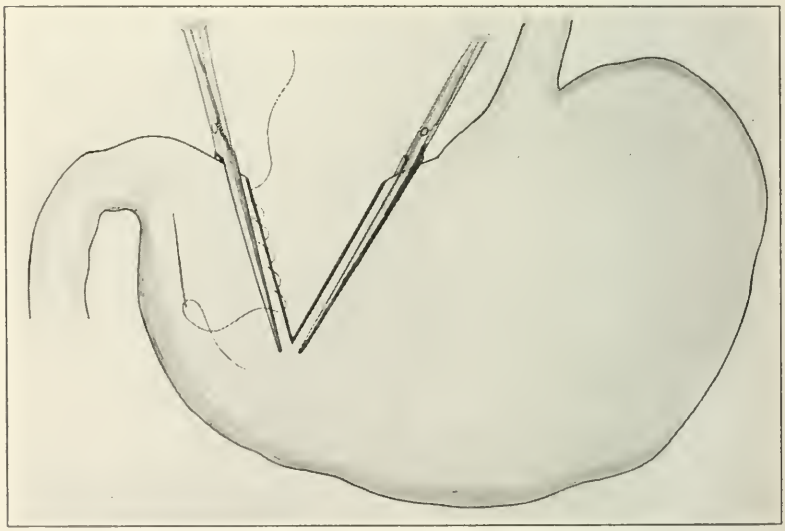

Fig. 1.—Clamps have been placed two-thirds of the way across the stomach at the minor curvature; both walls cut between them and a whip stitch partly introduced.

Experiment XI. December 24, 1912; a small dog. A transverse incision was made into the minor curvature half-way across the stomach between two clamps (Fig. 1) which had been placed about one-fourth of the way from pylorus to cardiac. A shoemaker's stitch was carried clear across behind the clamps closing the wound and then two rows of mattress sutures (Fig. 2) were applied in such a way that a septum was established as the first row was entirely hidden.

March 24, 1913, the dog died. In the minor curvature and extending almost across the anterior and posterior walls of the stomach was a deep furrow which practically cut off the pyloric portion from the rest of the viscus. This first named was shrunken to less than one-fourth of its original dimensions. Contraction of the deep scar in the minor curvature had led to the pylorus approaching the cardia to a considerable extent. Viewed from either side the septum appeared to be complete. Water could not be poured through it and its centre presented a uniformly smooth appearance no matter from which side it was viewed. It measured 3 cm. from the greater to the lesser curvature and a mucous-lined canal at the greater curvature was seen completely collapsed,

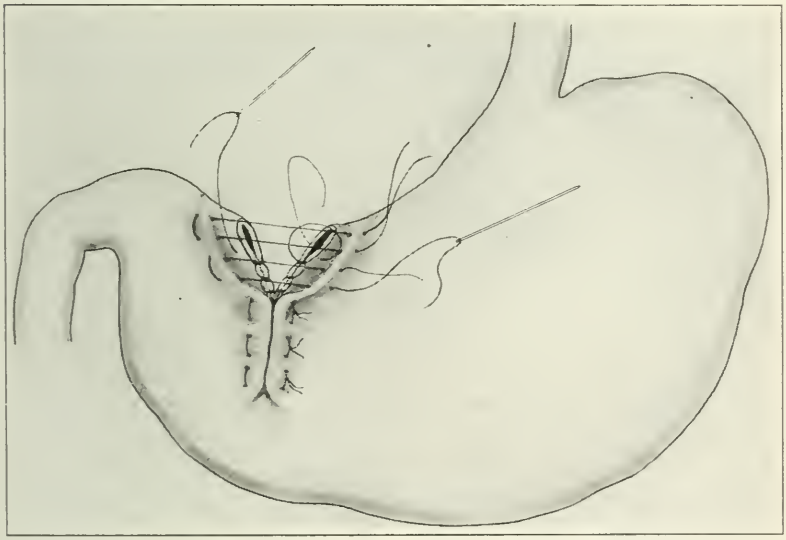

Fig. 2.—Mattress stitches cover the first row in front and behind.

probably due to the cicatricial band around it. Had dilatation been possible it would probably have admitted a rod almost 1 cm. in diameter.

No practical use can be made of this result, however successful it may have been, since the minor curvature furnishes a comparatively inaccessible and very vascular field. However, the lower border of the viscus is open to neither of these objections and will be used in future experiments of this kind.

Experiment XII. January 8, 1913; medium sized white half bulldog. A deep cut (Fig. 3) was made into the greater curvature just proximal to the pyloric antrum and a whip-stitch made outside of both clamps. The first row was then inverted by a Lembert

row (Fig. 4), leaving a defect, and a posterior gastro-enterostomy was done.

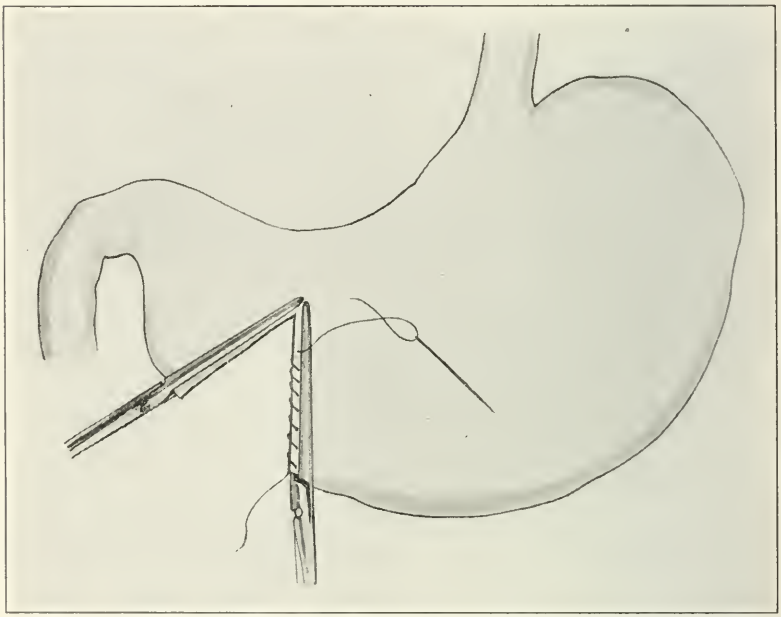

Fig. 3.—The stomach has been divided two-thirds of the way across at the greater curvature and the resulting defect partly closed blind.

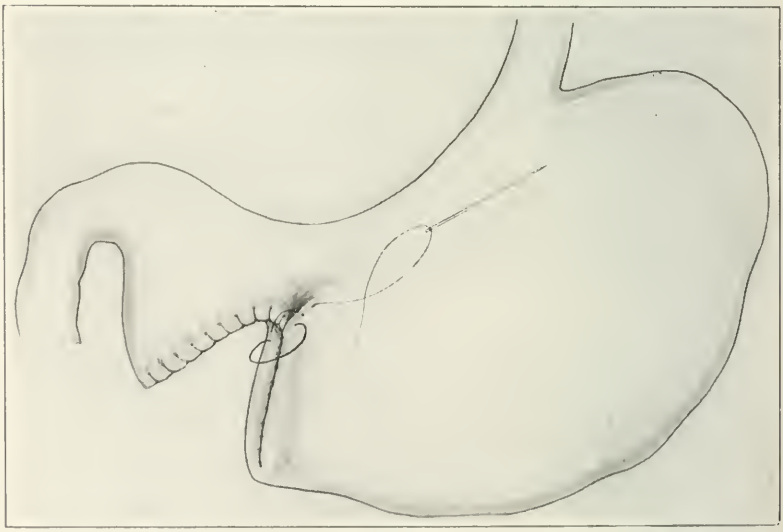

Fig. 4.—The first row is inverted by a continuous Lembert suture, leaving a triangular defect.

January 20 the dog died. There was no peritonitis but great emaciation, a moderate dilatation of the stomach, and also a dilatation of the jejunum below the gastro-enterostomy opening. The heart muscle was flabby. A deep furrow on the anterior and posterior surfaces showed the new septum. There was practically no distortion or change in either segment and the organ looked very much as it did when it was dropped back into the abdomen at the completion of the operation. Viewed from either side the septum measuring $3\frac{1}{3}$ cm. from the greater to lesser curvature, was entirely covered with mucous membrane excepting just under the minor curvature, where it was perforated by a mucous-lined canals maller than a goose-quill in size, which when split lengthwise and spread out was lined by folds of mucous membrane and appeared slightly larger than before it was cut.

Experiment XIII. January 20, 1913; a small white slut with a yellow head. This is an exact repetition of Experiment XII.

April 2 the dog died of distemper. The stomach was quite large and a deep furrow clear around it demonstrated the position of the new partition. The specimen gave the impression of intestine springing from the stomach wall as is the case where an end-to-side anastomosis has been made. Postmortem rœntgenoscopy showed bismuth making use of the new opening instead of the excluded pyloric portion. Viewed from the stomach side the septum, measuring $3\frac{3}{4}$ cm. from greater to lesser curvature, appeared to be absolutely complete and bulged well forward into the cavity of this viscus. There was a mucous-lined canal tightly folded together, through which a lead-pencil might be forced were the walls of the canal not so rigid.

Experiment XIV. February 12, 1913; a medium sized black animal. This repeats Experiment XII.

February 15 the dog died. The autopsy showed acute purulent peritonitis, the exclusion suture line leaking when water was forced into the specimen. There appeared to be a complete septum, although it was impossible to harden the specimen injected with the walls on tension on account of the leak. It is only fair to state in connection with the death of this animal that an experimental intestinal anastomosis was carried out with what seems to have been faulty technique after completion of the stomach work.

Experiment XV. April 10, 1913. This is exactly the same as Experiment XII.

August 30. A rœntgenogram, with bismuth in the stomach, demonstrated the absence of the pyloric portion and the mixture escaping only through the gastro-enterostomy opening.

September 4. The dog well nourished and playful, was killed with chloroform. A deep groove on the anterior and posterior surfaces represented the plane of the new septum, distal to which the stomach was shrunken in a most interesting manner. It was

not to be distinguished in appearance or size from the duodenum which was extremely pale and shrunken.

Postmorten Rœntgen ray findings: The accompanying roentgeno-

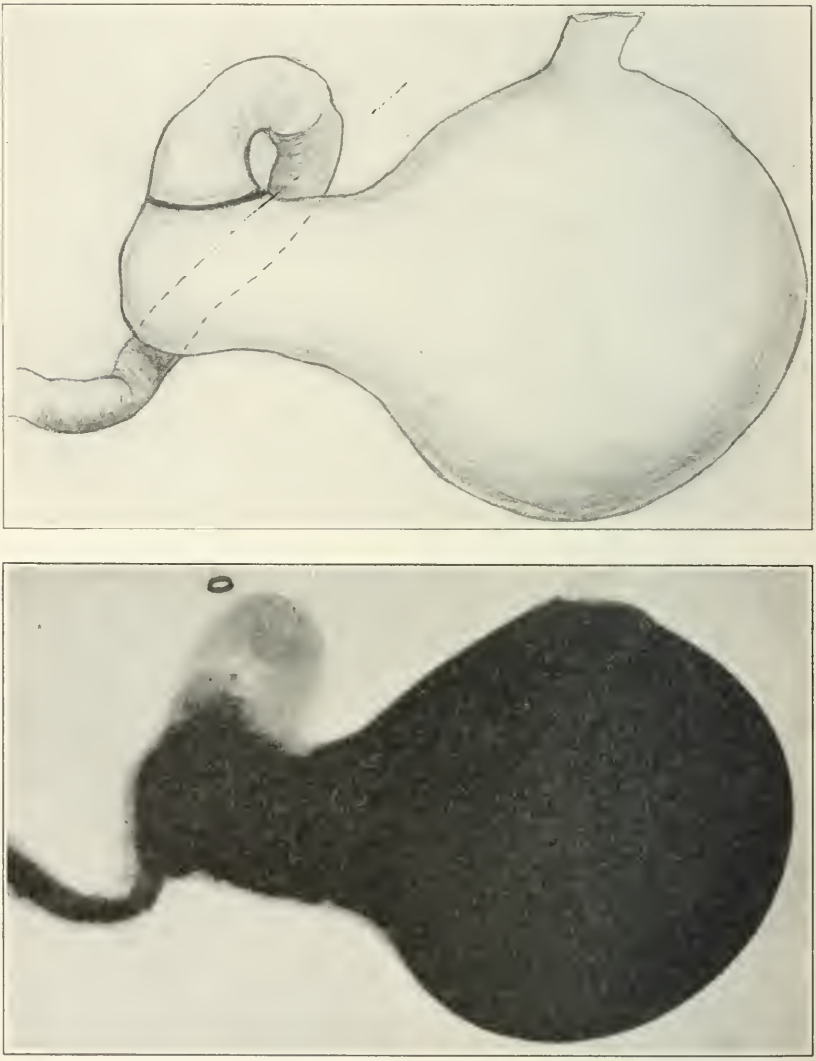

Fig. 5.—Illustrates the postmortem Rœntgen-ray appearance of the stomach in Experiment XV.

gram (Fig. 5) shows the septum to be complete and bismuth, leaving the stomach only through the gastro-enterostomy opening.

Viewed from the stomach side the septum from greater to lesser curvature measured 3.5 cm. and appeared to be absolutely complete.

A short double heavy suture hung from the centre and was surrounded by concentric folds of mucous membrane. There was a mucous-lined canal through which a goose-quill might have been introduced if only the surrounding ring of scar tissue could have been stretched.

Since only one of the last-mentioned four stomachs leaked it may be justly inferred that the operation rather than the method is to be blamed. No cause can be assigned for the death at twelve days, nor will any attempt be made to draw a conclusion so early. The specimens recovered after the animals had lived about three and five months respectively demonstrated anatomically the efficiency of the procedure as was done functionally by Rœntgen rays in the animal (Experiment XV) which lived longest.

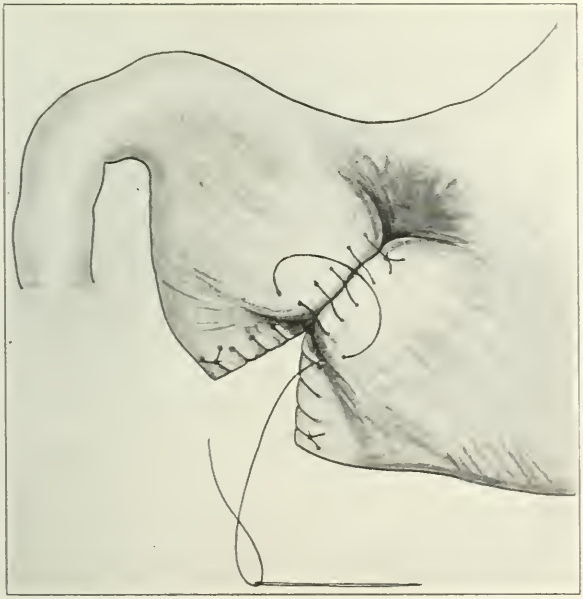

Fig. 6.—Here a defect, similar to the one made in Fig. 3, is closed blind by an inner through-and-through stitch, which is inverted by a continuous Lembert row down the front and up the back.

Experiment XVI. January 18, 1913; small slender white shut. An incision was made into the greater curvature, the clamps were separated, and a running stitch was taken clear across outside of both clamps. These suture lines were held together and a continuous Lembert suture (Fig. 6) was carried around them down posteriorly and up anteriorly. This inverted a septum and restored the external appearance of the stomach. Approximately the pyloric one-quarter of the stomach was excluded. The operation was finished with a posterior gastro-enterostomy.

March 10. No cause could be found for the death of the dog. It was emaciated but showed no peritonitis, adhesions, or obstruction. A faint furrow extending clear around showed the presence of the septum in this instance. The excluded portion was so shrunken so far as diameter was concerned, that it closely resembled the small bowel which served as its continuation. The septum, measuring 2 cm. from greater to lesser curvature, appeared to be absolutely complete when viewed from the stomach side, and was covered with deep folds of mucous membrane. A fine canal completely lined with mucosa penetrated the septum at the lesser curvature.

Experiment XVII. January 24, 1913; slender white, yellow spotted fox terrier. This is a complete repetition of Experiment XVI.

February 8 the dog died, but no cause was revealed by the autopsy. There were practically no adhesions about the visceral

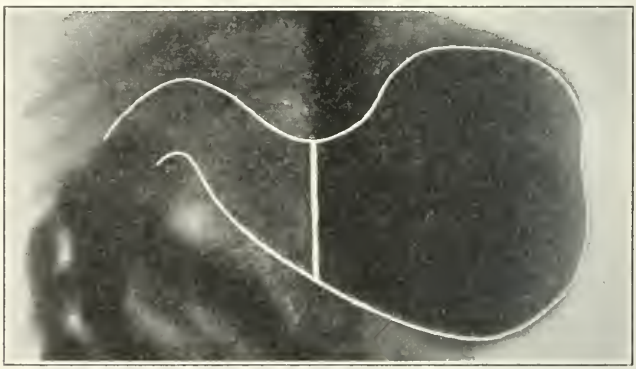

Fig. 7.—This rœntgenogram was taken in life seven months after the operation and shows the pyloric region to have been practically cut off.

wounds, no obstruction and no peritonitis. The location of the septum was clearly defined by a groove running entirely around the organ, the excluded portion being considerably shrunken, although retaining its normal outlines. Seen from the interior of the stomach the septum, which measured 3 cm. from the greater to the lesser curvature, appeared to be complete and bulged markedly into the stomach cavity. Water could not be poured through it and no opening could be discovered by dissection of the septum.

Experiment XVIII. February 3, 1913; small white fox terrier bitch. This is a duplicate of Experiment 16.

August 30. A Rœntgen ray test (Fig. 7) showed the pyloric region to be excluded, bismuth running out only through the new anatomatical opening.

September 4. The dog, well nourished and in good spirits, was killed with chloroform and the atnopsy revealed faint adhesions from the exclusion line to the under surface of the liver. The

peritoneum was otherwise apparently normal. A deep furrow in the anterior and posterior surfaces represented the exclusion line, the excluded portion being shrunken to a point where it represented not more than one-fifth of the stomach's total cubic capacity. Viewed from the interior of the stomach the septum, from greater to lesser curvature measuring 3 cm., appeared to be absolutely complete, with folds of mucous membrane radiating from the centre of the same and a thread four inches long hung free by one end in the stomach cavity. If an opening existed it could not be found by dissection of the septum.

Experiment XIX. February 21, 1913; small black slut. This experiment is an exact replica of Experiment XVI.

On March 8 the dog died. There was no sign of obstruction or peritonitis. The septum looked just as it did at the time of operation.

Experiment XX. March 1, 1913. The technique here was carried out identically as in Experiment XVI.

March 17 the dog died. Autopsy showed no peritonitis nor obstruction. A very deep furrow particularly on the posterior wall marked the site of the artificial partition. There was considerable rotary distortion of the stomach, although comparatively little deformity had taken place otherwise. Viewed from the stomach side the septum, measuring from greater to lesser curvature 4.5 cm. in length, was almost complete. At the minor curvature was a mucous lined canal barely large enough to admit a ray of light, but through which water could not be poured. A lead-pencil might have been forced through were it not for scar thickening of its wall.

In Experiments XVI to XX inclusive an anatomical result was intended and obtained similar to that characterizing the group which preceded them. The technique of producing the septum was slightly different in the two sets of experiments. None of these last five animals was lost as a result of peritonitis or obstruction; three died at the end of fifteen, fifteen, and sixteen days respectively. Although no cause could be determined at autopsy, death occurred too early to permit of conclusions being drawn. Two stomachs were recovered at the expiration of about two and seven months respectively, both showing what is now regarded as a characteristic shrinkage of the excluded portion. The Rœntgen rays proved before death that the seven months' stomach possessed no functionating pyloric portion.

Experiment XXI. January 4, 1913; Medium-sized black, short-haired slut. We made a cut into the greater curvature at the usual distance from the pylorus, then made a whip-stitch outside of the clamps, and everted all four layers by mattress sutures (Fig. 8). The peritoneum was then whipped over all and a no-loop posterior gastro-enterostomy done. The stomach, as viewed from the exterior, was entirely reëstablished, leaving a septum.

March 1 the animal was sacrificed because of the mange. No peritoneal involvement was found. The gastro-enterostomy was patent. Very deep infolding on the anterior and posterior walls of the stomach showed where the partition was made. The excluded portion was considerably shrunken and was distinctly paler in color than the rest of the viscus. The septum, which measured from the greater to the lesser curvature 5 cm., presented an opening at the minor curvature about the size of a lead-pencil. It was a mucous-lined canal through which water could easily be poured.

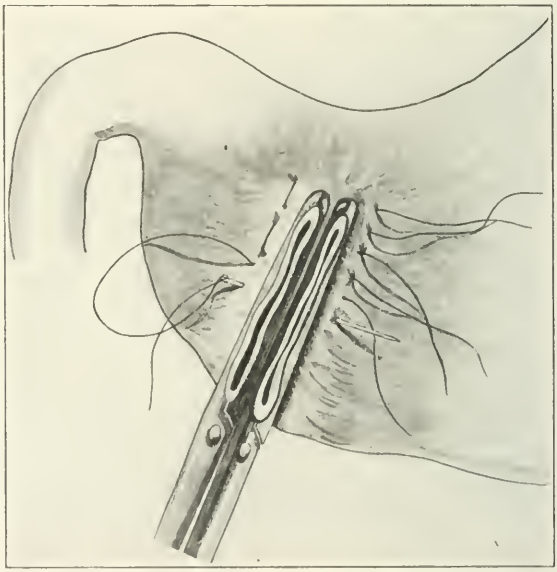

Fig. 8.—A defect similar to that in Fig. 3 is being closed with through-and-through mattress sutures; these will be inverted by a continuous Lembert row.

A septum similar to the nine which preceded it was produced in a slightly different manner in Experiment XXI. The result seems to have been anatomically all that one could desire if permanent conclusions can be drawn at the expiration of two months.

Experiments XI to XXI inclusive were all made by cutting into the greater curvature except the first, which involved the minor curvature. Ten septa have been excised and examined as to complete closure. Of these, seven were found to extend practically across the lumen of the stomach, which is all the more surprising when one considers that no complete operation was attempted. Each of the other three presented appreciable mucous-lined canals just where one had been left at the operation. In one instance this was large as a pencil, in the second as large as a goose-quill and in the third merely large enough to admit a ray of light. Specimens

were examined at the expiration of three, fifteen, fifty-two, seventy-two, ninety, one hundred and fifty, and two hundred ten days respectively.

Rœntgen-ray determinations in Experiments XI to XXI inclusive prove that partial transverse section of the stomach results in complete functional exclusion of the pyloric region in addition to extreme shrinkage of the same. In accomplishing this we have up to date cut through either the minor or major curvature with consequent danger of hemorrhage from the large vessels which are necessarily encountered. As a natural step in the evolution of the

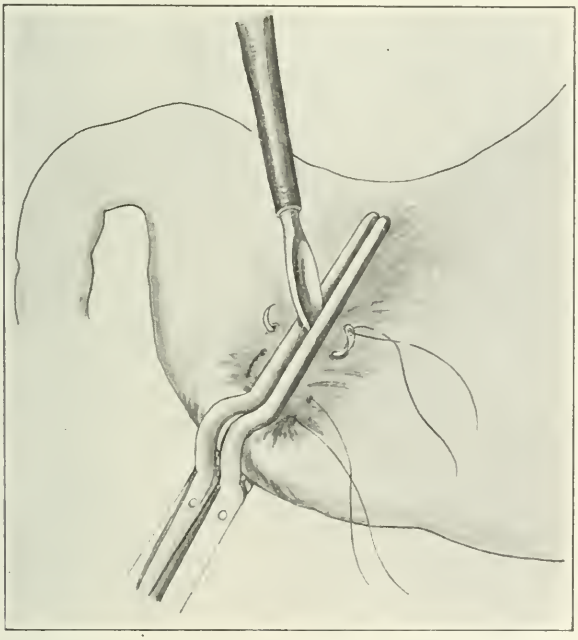

Fig. 9.—The clamps leave both curvatures free; through-and-through mattress sutures are introduced behind them, and both walls of the stomach are divided only as far as crushed.

method we commenced with No. 22 to use an incision similar in length, location, and general direction to that employed in the preceding eleven animals, but so placed across the axis of the stomach that it interrupted the lumen without involving the region of either curvature. This procedure was employed in Experiments XXII to XXXVI inclusive.

Experiment XXII. March 4, 1913. We did a gastro-enterostomy and then placed two clamps across the stomach (Fig. 9) about one-quarter of its length away from the pylorus. The blades were so bent as to leave the greater curvature free and of a length which prevented them reaching to within 1 cm. of the lesser curva-

ture. The viscus was then cut half-way across leaving one-fourth of it intact at either curvature. Mattress sutures taken behind the clamps, everted the cut edges; they then were hidden by a continuous Lembert suture.

August 30. No pyloric region showed in a rœntgenogram, while bismuth escaped through the gastro-enterostomy opening only.

September 4. The dog, well nourished and playful, was killed with chloroform. The excluded portion was represented by a contracted mass which represented not more than one one-hundredth of the cubic capacity of the stomach, having its boundary well defined by a deep groove on the anterior wall. Postmortem rœntgenoscopy showed the bismuth to have been directed entirely from the normal channel by the new partition. Viewed from the stomach side the septum seemed complete with one mattress stitch hanging into the lumen. The centre of this diaphgram was indicated by a deep round depression surrounded by circular furrows of mucosa. Cross-section through the middle of the excluded portion of the stomach showed its wall to be enormously thickened, contracted, and the mucosa reduced to a very small amount.

Experiment XXIII. March 8, 1913. A cut was made nearly across the stomach at its middle, using an original exclusion clamp (Fig. 10) which left both curvatures free. After five mattress sutures had been introduced behind the clamp the crushed stomach was divided through the slit in the upper blade of the instrument. The mattress stitches were tied and the row inverted with a continuous Lembert suture. An anterior gastro-enterostomy was made well to the left of the midline.

April 3 the dog died of distemper. A deep annular constriction divided the stomach into two portions, the pyloric being greatly reduced in caliber although not much effected in length. There was not even a peritoneal adhesion in the vicinity of either of the visceral wounds. A postmortem rœntgenogram is shown. An inspection of this septum showed a faint ray of light penetrating it at the greater curvature. Water did not leak through the opening and rows of deeply folded mucosa radiated from it. Two loops of thread hung free into the stomach cavity.

Experiment XXIV. March 12, 1913. This was an exact replica of Experiment XXIII except that a posterior gastro-enterostomy was done.

On April 7 the dog died of distemper. There was no peritonitis or adhesions except of the omentum to the suture lines. Deep grooves on both surfaces demonstrated very plainly where the exclusion was made. The pyloric portion was so changed in consequence that it resembled the intestine in every way, with the single exception that it was double the caliber of the viscus last named.

Postmortem Rœntgen ray findings: bismuth left the stomach

only through the gastro-enterostomy opening and could not be made to pass through or around the new septum.

Viewed from the stomach or intestinal side the septum appeared to be complete, when, however, it was held to the light a small defect could be noted at the minor curvature, although water could not be poured through the same. A deep linear groove from which folds of mucosa run transversely was apparent on both sides of it.

Experiment XXV. April 12, 1913. This also was a repetition of Experiment XXIII with a posterior gastro-enterostomy.

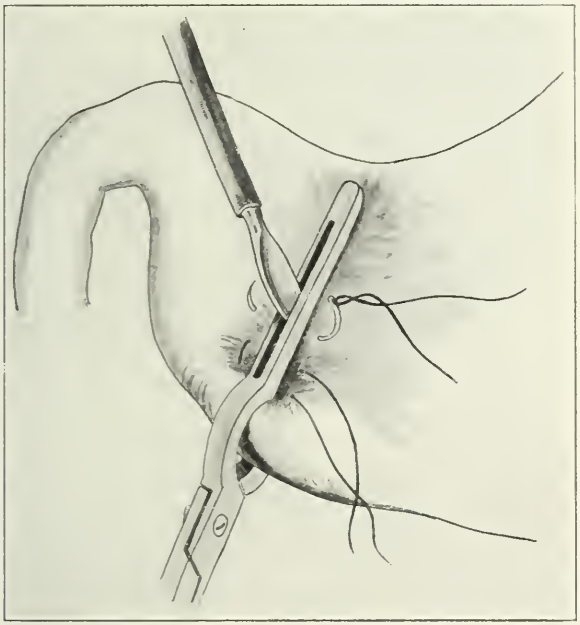

Fig. 10.—Demonstrates the use of an original clamp, which shows both curvatures free and has a slit in the upper blade through which both stomach walls are partly divided after through-and-through mattress sutures have been introduced behind it.

April 24 the dog died. It was thin and the autopsy showed no pathological condition on the peritoneum, bowel, or lumen. This stomach was very small and showed a considerable portion of it to have been excluded. The part so treated bore every resemblance to a segment of intestine, being merely slightly greater in diameter than the latter. Postmortem Rœntgen ray findings were to the effect that no bismuth passed through the pyloric portion of the stomach, but all of it followed the course of least resistance through the gastro-enterostomy opening. The septum in this instance viewed from both sides looked as though it were complete. The site of the suture line was indicated by a linear depression from which folds of mucosa radiated.

Experiment XXVI. April 19, 1913. A metal spatula was introduced through a slit in the gastrocolic ligament to protect the structures behind the stomach, then a metal "skewer" (Fig. 11)

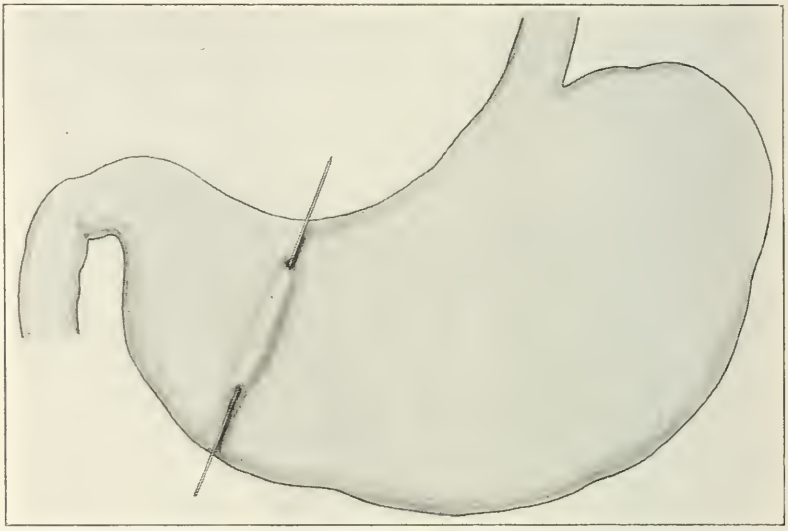

Fig. 11.—A skewer has been thrust through both stomach walls and out again; it holds them up for about half the distance across the axis of the organ.

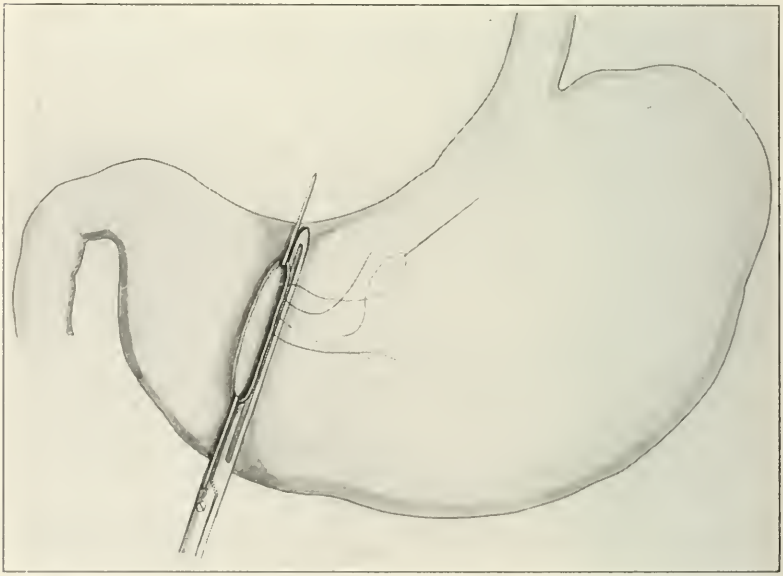

Fig. 12.—A clamp with slit blades has been placed behind the skewer, through-and-through mattress sutures having been introduced in the slit or between clamp and skewer if preferred.

was thrust directly through both walls of the stomach into the lesser peritoneal cavity and out again so as to encompass about one-half the distance between the two curvatures. A clamp (Fig.

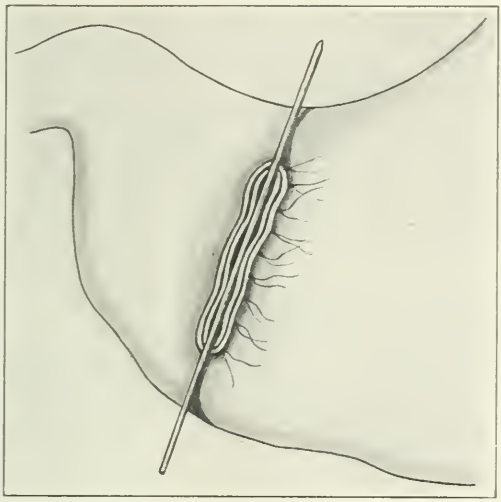

Fig. 13.—The mattress sutures have been tied and the skewer cut out.

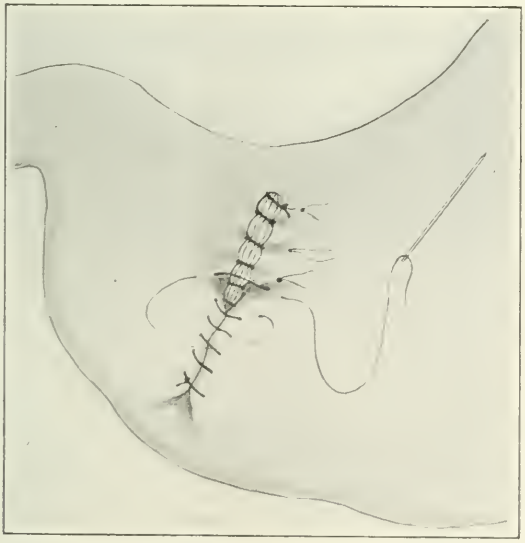

Fig. 14.—A whipover suture acts as a hemostatic and is buried by a Lembert row.

12) was placed behind the "skewer" and several mattress sutures introduced between the "skewer" and clamp; as a matter of course these embraced the whole thickness of both walls of the stomach. The "skewer" was cut out (Fig. 13) with a sharp knife and the

mattress sutures tied before the clamp was removed. A hemostatic running stitch of silk or linen united the four exposed cut edges (it may be inverted before removal of clamp). The ridge of tissue formed by the mattress sutures was inverted (Fig. 14) with a continuous Lembert row.

May 6 the dog died. The peritoneum was full of thin fluid blood and a few clots. There were many adhesions between the anterior wall of the abdomen, pylorus, and liver. A well-defined groove showed the presence of the artificial partition, and the excluded portion was deformed to the extent that its proximal end looked as though it had been implanted laterally into the stomach wall. The septum appeared to be absolutely complete when the gastric aspect of it was considered. Its centre was represented by a deep depression from the sides of which hung two silk sutures. It was on the intestinal side that the most marked change was noticed. The lumen of this excluded area was not greater than that of the bowel. Its muscular wall was enormously thickened and the mucosa contained within this tube was reduced to a few thin folds.

Experiment XXVII. April 22, 1913. This is exactly the same as Experiment XXVI.

May 6 the dog died, with no evidence of disease anywhere. The characteristic grooves particularly deep on the posterior aspect in this instance demonstrated the position of the new partition. The distal portion of the stomach was shrunken to the point that it bore a striking resemblance to the adjacent intestine. Postmortem Rœntgen ray examination showed bismuth leaving the stomach through the gastro-enterostomy only, but none of it making use of the normal channel. Viewed from the stomach side the excised septum appeared to be absolutely complete. Two black mattress sutures projected into the lumen of the stomach.

Experiment XXVIII. April 25, 1913. This repeats Experiment XXVI in every essential.

August 30. A rœntgenogram made this day showed the stomach to have no functionating pyloric portion. Bismuth escaped through the gastro-enterostomy only.

September 4. The dog, well nourished and playful, was killed with chloroform. The lesser peritoneal cavity, posterior to the exclusion line, was partially obliterated. The pancreas was hard and nodular throughout. The aspect of this specimen was altered on account of an anterior gastro-enterostomy having been made. However, a deep furrow extending around the stomach illustrated plainly the location of the new septum. The excluded portion was shrunken though not to the extent apparent in earlier specimens. Postmortem Rœntgen-ray findings indicated that bismuth could not be forced into the pyloric portion of the stomach, but that it passed out only through the newly made opening. Viewed from the stomach side this septum showed an opening

on the minor curvature which was 1 cm. in diameter. The persisting obstruction measured from the edge of this opening to the greater curvature was 2 cm. in length. On the greater curvature side no opening could be found for the finest probe. A piece of silk hanging from the last-named area proved that it was the artificial new structure.

It is interesting to note in this connection that the greatly shortened and thickened excluded portion of the stomach failed to propel bismuth through the pylorus, although admitting a small amount into its own cavity, the septum being incomplete. This is shown by a radiogram taken four months after the operation as well as by another taken after the stomach had been removed from the body and injected with bismuth under pressure.

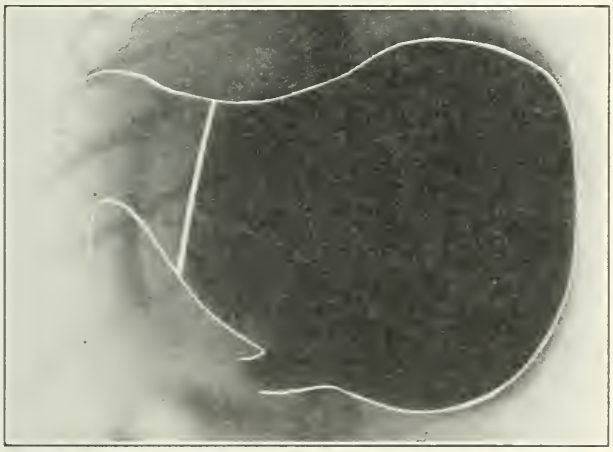

FIG. 15.—This is a roentgenogram taken during life four months after the operation. It shows bismuth leaving the gastro-enterostomy opening but none entering the pyloric region.

EXPERIMENT XXIX. May 1. This experiment essentially repeated Experiment XXVI.

August 30. The functional absence of its pyloric portion was apparent in a rœntgenogram (Fig. 15) of this stomach. Bismuth escaped only through the gastro-enterostomy opening. A deep groove, particularly well marked on the anterior surface of the stomach, showed the pyloric portion so shrunken as to be almost unrecognizable, the pyloric ring having been drawn to within 2 cm. of the exclusion line. Postmortem Rœntgen rays (Fig. 16) showed no bismuth passing through the excluded portion, but it left the stomach freely *via* the gastro-enterostomy opening. Viewed from the stomach side this septum presented an irregular opening about 8 mm. by 3 mm. in size. This was toward the greater curvature. The rest of the septum was intact and presented two long silk threads hanging free in the stomach cavity.

Experiment XXX. May 3. This was an exclusion similar to Experiment XXVI.

The dog, which died June 9, was very thin. The autopsy showed

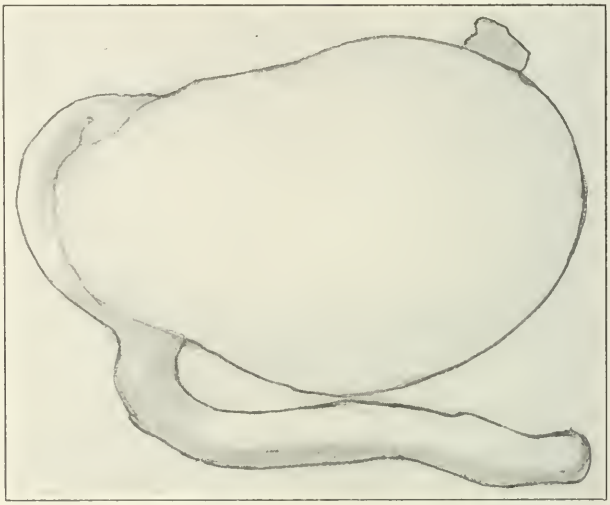

Fig. 16.—This illustrates postmortem appearance in Experiment XXIX.

no peritoneal involvement, the gastro-enterostomy having been made by mistake into the tranvserse colon. The stomach was small and distorted in a peculiar manner. A deep circular furrow showed

the point where the exclusion was made. The portion of the stomach excluded preserved, to a certain extent, its outline, but was considerably smaller than at the time of operation, as shown by a postmortem rœntgenogram of the experiment. Viewed from inside the septum appeared to be complete. It was scarcely to be distinguished from the rest of the stomach wall on one side or from the intestine ending blind on the other.

Experiment XXXI. June 6, 1913. This experiment was carried out similar to Experiment XXVI.

June 30 the dog died. Little can be stated definitely about this stomach, since it was removed by one of the other men in the surgical department and not hardened while distended.

Experiment XXXII. June 10. This is a repetition of Experiment XXVI.

June 23 the dog died but was destroyed by mistake.

Experiment XXXIII. November 10. One-fifth of this animal's stomach was excluded by the method used in Experiment XXIII, the partial division of the viscus being made by actual cautery.

January 27, 1914, the dog died. It was emaciated, although nothing discovered at autopsy explained this condition. The peritoneum was practically normal and the exclusion line as well as the gastro-enterostomy opening was practically free from adhesions. The excluded portion was pale and contracted to a fraction of what it had been. A furrow which ran clear around the viscus showed where the exclusion was made. The septum, measured from minor to major curvature extended about 3.5 cm. across and presented an almost round opening approximately 0.75 cm. in diameter. A heavy suture hung into the cavity of the stomach. The edges of this opening were lined with a continuous mucous membrane which united the cavity of the stomach with this shrunken partially excluded pouch.

Experiment XXXIV. April 14, 1914. Here Experiment XXVI was somewhat improved upon. After a skewer was thrust through both stomach walls a long clamp with slit blades (Fig. 12) was applied immediately behind the same; mattress sutures were then introduced, tied, and cut in the "slit" and the skewer burned out with the cautery. After all surfaces were whipped over the slit clamp was removed, the field buried, and the operation completed with a posterior gastro-enterostomy. The animal is still alive.

This is the technique now recommended to other experimenters.

Of the preceding Experiments XXII to XXXIV inclusive the last two mentioned will not be considered, since the time elapsed has not been sufficient to warrant any conclusion. Of the remaining eleven, one dog died on the twelfth and another on the thirteenth day without known cause of death. Another died on the fourteenth

day with autopsy wholly negative and another on the seventeenth. Another died on the twenty-fourth day. Two died on the twenty-sixth day with no cause of death ascertainable at autopsy. While I will not endeavor to draw conclusions from results obtained upon a dog which died at thirty-seven days or less, I will merely state that the appearance of the specimens was highly gratifying. In every instance the excluded portion of the stomach was shrunken to a degree which made a striking contrast with its size before the operation. A deep furrow marking the site of operation would make one think that a complete instead of a very incomplete division and suture of the viscus had been made. In none of this last series, Experiments XXII to XXXIV was there a leak nor did autopsy reveal a cause of death which might be traced to the operation as such. The remaining three animals of this group were sacrificed at four, four one-half and six months respectively after Rœntgen-ray examination had shown during life that the pyloric region had been functionally obliterated and that the gastro-enterostomy alone drained the stomach. Nine septa in this group, Experiments XXII to XXXVI, were excised and examined, five of them seeming complete at twelve, fifteen, eighteen, thirty-seven and one hundred eighty-four days respectively. Two twenty-six day specimens were complete with the exception of a cleft so tiny that a faint ray of light penetrated them. The remaining two, examined at one hundred twenty-one and one hundred thirty-two days respectively, showed an opening in each, the largest of these being 1 cm. in diameter. For practical purposes it would seem as though a high degree of obstruction must have resulted when an opening of this size is compared with the original lumen of the stomach at a point some 6 cm. from the pylorus, where the exclusion line was placed. The procedure is remarkably simple where a "skewer" is used, is entirely free from bleeding or soiling, can be quickly accomplished, and apparently gives permanent results.

Experiment XXXV. February 10, 1914. The stomach was partially divided, by the skewer method, into two equal cavities as nearly as this could be ascertained. A low anterior gastro-enterostomy was done and then the stomach was cut transversally in two, very close to the pylorus. The duodenal stump was covered with two rows of sutures and dropped. The open end of the stomach was sutured between the lips of the abdominal wound at its upper angle, the rest of the wound being closed in layers.

February 16 the dog died. The divided pyloric portion of the stomach remained where it had been sutured in the angle of the wound, but the rest of the laparotomy wound was wide open, the animal emaciated and covered with filth.

Experiment XXXVI. February 16, 1914. We did identically the same experiment as that reported in Experiment XXXIV, the

animal living but two days, obviously too short a time for any physiological determinations to be made.

February 20, 1914, the dog died of peritonitis.

Experiment XXXVII. February 24, 1914. The stomach was divided transversally at about its middle, and the two resulting ends were closed blind, after which a high gastro-enterostomy was done. An ordinary bone button had been placed in the excluded cavity, and this, with the stomach wall stretched over it, was anchored between the lips of the skin wound by a suture which closed one angle of the rectus sheath incision behind it after anchoring the stomach peritoneum to the skin. The rest of the laparotomy wound was closed in layers.

February 27 the dog died of pneumonia.

So far as gross comparison at the operating table in this experiment goes, transverse section of the stomach does not seem to make any immediate difference in the motility of the excluded half. Peristaltic waves were as strong and as frequent after complete division of the organ as they had been before it.

Experiment XXXVIII. March 10, 1914. The same operation was done as in Experiment XV, the stomach being almost completely divided into two pouches, the greater lying to the left and the lesser representing about one-third of the total capacity. After the lesser pouch had been closed up its lower extremity was sutured to the peritoneum and skin of the upper angle of the wound to be opened later. The remainder of the laparotomy incision was closed in layers and the whole smeared with collodion.

The animal died the day following operation. The excluded portion of the stomach was distended with thin foul-smelling contents, and it was supposed that the animal died of absorption caused by stomach obstruction due to drawing a part of the organ up into the incidion.

It was hoped that Experiments XXXV to XXXVIII inclusive would throw some light on the chemistry of the partially excluded stomach; however, none of the animals survived.

Experiment XXXIX. March 18, 1914. A band of fibrous tissue one-quarter inch wide was stripped from the exact midline embracing all between skin and peritoneum. It was tied transversely around the stomach at about its middle, a silk stitch united the two portions of the band where they crossed, while each free end was fastened to the fibrous ring with one silk stitch. An anterior gastro-enterostomy was done. Sacrificed October 1, 1914. There were no adhesions and the obstruction were complete. The fascial band could not be identified.

Experiment XL. March 24, 1914. An aluminum strip was rolled about the stomach so as to exclude the pyloric one-fourth. The metal was $\frac{5}{16}$ inch wide and 0.04 inch in thickness. The ends overlapped about $\frac{5}{8}$ inch, and were held so only by the

stiffness of the material. A posterior suture gastro-enterostomy was done.

Experiment XLI. March 31, 1914. The same operation was done as in Experiment XXXIX. The metal band being $\frac{1}{4}$ inch wide and 0.011 inch thick. The ends were rolled over each other so as to catch firmly.

Dogs XL and XLI were sacrificed October 1, 1914, and in each instance the ring was buried in scar tissue and surrounded with unusually strong adhesions. Both stomachs were entirely obstructed the bands *not* having cut through.

A metal band as used by Brewer is surely easy to apply around the stomach, and my two dogs have experienced no ill effects from it, yet I can hardly bring myself to leave a metal foreign body in the peritoneal cavity in view of the fact that similar results are claimed for an autoplasty. It must be added that no published observation of ultimate results dates back longer than two months and ten days.

It has not been proved experimentally that any of the constriction methods are able to permanently exclude a considerable portion of the stomach. My own three experiments are too recent to be of value, and mere pyloric obstruction by this means can have no part in this discussion of exclusion of the pylorie antrum.

The constriction methods all possess the theoretical objection that they leave a folded-up intact mucous membrane, *and therein go contrary to the process of nature in which a destructive process of the inner coats is the first step in the formation of a more or less annular scar which results in the hour-glass stomach.*

As a result of these experiments I have to offer two methods which seem to have been about equally efficient. The one was employed, in principle at least, in Experiments XXII to XXXVI inclusive (see Figs. 9 to 16 inclusive). It is the easier of the two, violates a recognized surgical principal in *leaving mucous membrane between layers which are supposed to heal together*, and while I have been unable to demonstrate that it is dangerous, still I have not the temerity to recommend or advise its further use on the human subject before more similar experiments have been done by others.

The second method referred to was used in Experiments XII to XXI inclusively (see Figs. 3, 4, and 5). It is more difficult, takes a little longer, and encounters more bloodvessels than does the other. Still it employs only time-tried and proven principles hence must be recommended in the absence of further experimental proof to the contrary.

All authors who have had experience with pyloroplasty will bear testimony to the fact that shrinkage and closure are to be feared after an incision into the interior of the stomach. This principle makes the reason for my own experiments apparent and their favorable outcome logical.

During one operation (Experiment XXXVIII)) at least, peristaltic waves were seen to travel uninterrupted the entire length of a stomach which had just been completely divided transversely. This is in line with the thought that gastric motility is governed by automatic centres within the organ, and will furnish food for thought to those who write of "placing the ulcer-bearing area at rest" by various simple methods.

Conclusions. 1. My first ten experiments demonstrate that almost any form of operation which removes a cuff of mucosa plus submucosa, with approximation of denuded muscular coats, results in the formation of a diaphragm. Blind suture closure of the layers from which a section has been removed seems a necessary safeguard. However, none of these methods is considered simple or safe enough to warrant use on the human subject.

Fig. 17.—Illustrates cross-section of the septa obtained as a result of fourteen experiments done by the two methods proposed in this paper.

2. My results detailed in the body of this article, as well as those obtained on ten human subjects (reported at 1914 meeting of the American Medical Association) seem to indicate that both of my incomplete exclusion methods, Experiments XI to XXXIV inclusive, accomplish practically what the more difficult Doyen-von Eiselsberg procedure does: cognizance being taken of the fact that I have no animal observation more remote than two hundred and ten days (Fig. 17 illustrates cross-section of the septa obtained). One advantage which cannot be denied these forms of exclusion is that no prolapse of the major portion of the stomach is possible with subsequent functional disturbance, since the organ is not completely divided nor the two halves detached from each other.

3. The pyloric antrum was found to undergo a surprising diminution in its size after partial exclusion no matter what technique was used. This would seem to be due to tonic muscle contraction,

since comparison with control specimens from the pyloric antrum of a normal stomach shows the excluded muscularis to be greatly thickened. Histological study of many sections from the areas effected in eighteen experiments demonstrates no other abnormality.

6. I will go no farther than to suggest that the obstruction may have been of *functional* nature in stomachs which were cut only half way across, found at autopsy to possess an incomplete septum, and showed tonic contraction of the excluded area.

My thanks are due to Dr. Ellis Fischel for kindly coöperation in part of these experiments.

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GASTRIC HEADACHES.

By William Fitch Cheney, M.D.,
CLINICAL PROFESSOR OF MEDICINE, STANFORD UNIVERSITY MEDICAL SCHOOL, SAN FRANCISCO, CALIFORNIA.

Headaches of any kind are a great affliction; but they are so common and so rarely serious in their consequences, they often recur throughout so many years of life without inducing fatal results, that they do not receive the same consideration by the profession as do other and more threatening ailments. After excluding cerebral neoplasm and meningitis, chronic nephritis and arteriosclerosis it is too often the physician's custom to assure the patient that his headaches are of no consequence and need cause him no alarm; while if any treatment at all is given, it is frequently empirical, without any definite conclusion as to the cause of the paroxysms or rational effort to prevent their recurrence.

It is the object of this paper to call attention to headaches due to disturbance of the stomach; to the fact that they are not an infrequent occurrence; that they present characteristics which fairly well identify them; that it is possible by stomach investigation in these cases to prove the existence of gastric disorder, as well as by other examinations to exclude disease elsewhere; and that the headaches can be made to disppear by therapy directed to the underlying gastric disturbance. If these facts are not universally accepted, it is probably because the matter cannot be satisfactorily explained. It is difficult to understand how disorder

of the stomach can cause violent pain in the head, and no adequate scientific explanation for it can really be given; but it is equally difficult to explain in another case how constipation causes headache, and why the pain disappears promptly after the lower bowel is emptied.

The headaches due to gastric disease are usually periodic. They repeat themselves throughout months or years. They may occur but once in a month, or once or several times in a week. Over certain periods they may become practically constant, during which periods headache is never entirely absent, though worse or better at certain times in the day. But the most common story is of sudden, unexpected attacks of pain in the head, coming after days or weeks of good health. Such headaches are of variable duration, but rarely last over twenty-four hours. The patient wakens with the pain in the morning, and it grows more intense as the day goes on; or it may come on in the evening, persist during the night, and pass off after the patient rises. These headaches may be so severe and prostrating as to incapacitate the sufferer for any kind of work while they last; but more often they are not so violent as to prevent the patient from going about his usual occupation, even though he feels miserable and unfit. Sometimes nausea and vomiting accompany the pain, giving rise to the popular term "sick-headaches;" but in other cases there may be no disturbance whatever of the stomach to make the digestive organs even suspected. Following the attack no disturbance of health is left, unless it be a sense of soreness over the scalp at the site of previous pain and a feeling of mental unclearness and confusion; but these sensations are transient and the paroxysm is usually followed by complete restoration to normal. Repetition of these attacks may go on indefinitely before the real cause is discovered. The longer the interval of freedom the less the patient is inclined to seek advice; but as the attacks become gradually more and more frequent, not only their increasing interference with daily duties but also the alarm aroused as to their significance, at last impels the patient to ask medical aid.

The site of the pain alone is by no means sufficient to determine a gastric origin. Perhaps the most common type is hemicrania, one-sided pain, though not always on the same side. The pain is described as boring in character, through one eye or temple; or it may be the entire half of the head, even back to the base and the nape of the neck, that aches and throbs; while the opposite side is entirely free from discomfort and as clear as ever. But this one-sided headache is caused frequently by the autointoxication of chronic intestinal stasis; it is the characteristic type of the paroxysm known as migraine; and it sometimes occurs as a manifestation of uremia. On the other hand the headache of gastric origin often involves the whole forehead and vertex with a throbbing distention

and fulness, not limited to any one area; so that it becomes absolutely impossible to construct any diagnostic chart of headaches, as has been attempted, in which certain locations of pain serve to determine infallibly the diseased organ giving rise to the pain.

Turning now to the manifestations of gastric disease in patients with a headache history, there may be none at all, and the headaches may constitute the only symptom of the underlying stomach disorder. On the other hand, minor evidences of the latter are frequently found to exist when inquiry is made for them; though the patient has not thought them of enough importance to mention; such as belching, or water-brash, or a sense of distention constantly after meals, or an abnormal appetite or a persistent sour taste in the mouth. In a third group of cases there is definite complaint of habitual indigestion, of the hyperchlorhydria type, or atony type, or chronic gastritis type; with headaches recurring intercurrently from time to time, when the gastric manifestations are all intensified.

It follows that no diagnosis can be made without careful examination of the stomach's functions. Whether there is complaint of indigestion or not, a test meal and gastric analysis will be needed to reveal the cause of the headaches. The most frequent disturbance found in such cases is one of motility; what is designated as myasthenia or atony, due to a weakness of the muscular wall. With this the secretion may or may not be normal, but the significant feature is the delay of food in the stomach. If patients with this gastric abnormality indulge in a meal unusually heavy or coarse, putting still further strain upon a weakened organ; or if they eat their usual meal when tired or exhausted by mental or physical exertion, thus creating demands for power in excess of the existing supply, then a headache is likely to result. Conversely, if care is taken, the food is selected for its freedom from bulk or undue coarseness, and is eaten only under favorable conditions, headaches gradually become less frequent and ultimately disappear altogether.

In another case, analysis reveals a hyperchlorhydria, and headaches are found to follow the taking of food that is too acid or too spicy; while if care is observed to avoid all irritating substances, no headaches occur, especially if at the same time treatment is directed to decreasing the hyperacidity. In the third place, there are undoubtedly cases of low-grade chronic gastritis, of the subacidity type, with abundant mucus found in the stomach contents, that may have few symptoms of indigestion, but the most depressing and incapacitating headaches, recurring more or less constantly until the gastric condition is discovered and improved.

In the diagnosis of gastric headaches, therefore, the history makes us only suspect, the gastric analysis makes us reasonably certain; but only after elimination of all other possible causes can this one be accepted as the basis for therapy. Examination of heart, urine, blood, eyes, sinuses, and reflexes must be made and disease elsewhere

disproved before chronic recurring headaches can be properly attributed to disturbance of gastric function. There is no doubt a danger on the one hand that the stomach may be assumed as a cause of headache without sufficient search being made for more serious possibilities; but there is also the frequent error, after serious disease is proved not to exist, of losing interest and of failing to give relief by treating the organ really at fault.

The following case histories illustrate not only the methods employed to reach a diagnosis of gastric headches, but also the measures adopted to cure them:

Case I.—A man, aged forty years, sought advice for the relief of chronic headaches, that had recurred throughout seven or eight years. Formerly they came only about once a week, but recently as often as every second or third day. The pain was either across the forehead, or at times through one eye and temple. Nausea usually accompanied the headache, but he rarely vomited. The attacks had gradually grown more severe as well as more frequent, and seemed to come with less provocation than formerly. He complained also of a poor appetite and much belching of gas after eating, but no pain. The patient was a large, well-nourished man, and physical examination showed no abnormality in any organ. After the Ewald test meal, however, the total amount of contents obtained was unusually large, 176 c.c.; and even after its removal a loud succussion splash could be elicited over the stomach. The analysis of this material showed a total acidity of 72, with free HCl 36, and combined HCl 20. On inflation the greater curvature was found 4 cm. below the navel, but there was no peristaltic wave. The diagnosis made in this case was of atony with hyperchlorhydria. The treatment advised was a soft, non-irritating diet, with restriction of acid and highly seasoned foods, and tincture of nux vomica before each meal. The nervous condition of these patients is usually a most important factor, to which the gastric atony and hyperchlorhydria are really secondary. This patient, for instance, was an insurance broker, with long hours of close confinement in an office and intense mental application. He was urged, therefore, to give his body more exercise every day, to live more out-of-doors, and to devote less strenuous application to his work. Under the influence of these various methods of treatment his headaches practically disappeared, recurring only at long intervals and then only after some immoderate conduct, either in diet or in work.

Case II.—A man, aged thirty-seven years, complained particularly of headaches, recurring for years, but gradually growing more frequent and severe until at the time preceding consultation they averaged once a week. They came usually after luncheon, gradually growing worse during the afternoon, and persisting until he went to bed and to sleep. No nausea accompanied the attack.

The pain was usually one-sided, through one eye and temple; but sometimes all over the top of the head. His appetite and digestion were good, he said, except for occasional belching. This patient used tobacco to excess, smoking many cigars each day. He also took habitually a cock-tail before lunch and dinner and wine with these meals. The man was large, plethoric, rather obese; and no abnormality was found in any organ except that the liver was slightly increased in area and its lower border palpable. The Ewald test meal showed considerable mucus, poor trituration of gastric contents, a total acidity of 70, free HCl 36, and combined HCl 20. On inflation no displacement or dilatation of stomach was found. The diagnosis made was hyperacid gastritis. The man was given a soft, non-irritating diet, suited to his hyperchlorhydria; and a powder of soda, rhubarb, and magnesia after meals. He was also instructed to abstain absolutely from alcohol in any form; to limit his cigars to three per day; and to take more physical exercise. His headaches at once disappeared and had not recurred six months after his consultation, when he last reported.

Case III.—A girl, aged nineteen years, complained that she has been suffering for four years with headaches, though she had never had any other illness of any kind. At first these came irregularly, never more often than once a week; but gradually they had grown more frequent, and for three months past had been present nearly every day. As a rule she awoke each morning with headache, and this persisted until toward evening, then went away. She always slept well and had no recurrence until next morning. The pain was felt above the eyes and over the top of the forehead and head. Sometimes it was severe pain, sometimes only a dull ache. She wore glasses, having been told her trouble was due to her eyes; but the glasses had never made any difference in the headaches. This patient was a rosy, well-nourished girl, apparently in good health; and no abnormality could be found about any of her organs on physical examination. After the Ewald meal the contents obtained were very poorly triturated, with an abundance of thick, ropy mucus; the total acidity was only 10, and ordinary tests gave no reaction for free HCl. On inflation the greater curvature was found 4 cm. below the navel. In this case the diagnosis seemed clearly one of chronic gastritis of the subacidity type, and the case was treated accordingly. Particularly was it necessary here to reform the diet, which had been in every way improper, both in quality and quantity. This regulation of diet with tincture of nux vomica before meals and a cascara prescription at bedtime quickly put a stop to the headaches, which ceased altogether within a week, and have never recurred since.

There is one point that impresses anyone who sees such cases often, and that is the frequent coincidence of constipation with the headaches and the gastric findings. The question that arises is

whether intestinal stasis is not the primary trouble to which the gastric disorder is secondary. In this interpretation the headaches would be explained as autotoxic and the stomach condition as reflex. The objection to this theory is that laxatives alone do not remove the symptoms, but that a proper diet seems the essential feature in treatment, the determination of what is proper depending on investigation of the gastric functions. This arrangement of dietary with other measures to overcome gastric atony and faulty secretion are often sufficient to regulate the bowels without the addition of laxatives to the therapy.

The cases outlined have been selected simply because typical of the different kinds of gastric disorder that may be responsible for chronic headaches. Such cases are numerous in the practice of every physician, but unfortunately they are not always recognized, and therefore are not appropriately treated. Other ailments of more serious character usually interest the physician more, but the writer's experience has been that no class of sufferer, from any sort of disease, is more grateful than the victim of chronic headaches recurring throughout months or years, who finds himself at last freed from this annoying and incapacitating disturbance of health.

THE USE OF DAHLIA IN INFECTIONS.[1]

By John Ruhräh, M.D.,
BALTIMORE.

For a long time anilin dyes have been known to exert certain antiseptic actions, and this has been the subject of a considerable amount of study, and certain practical applications have been made as the result. As early as 1886 Pfeffer showed the effects of certain anilin dyes upon the cells of the higher plants, and in the following year Rozsahegyi pointed out the harmful action upon certain bacteria. He also observed the selective action of the dyes. For example, the bacillus of rabbit septicemia grows readily in the presence of carmin and vesuvin, while it will not grow in the presence of gentian violet. The bacillus of chicken cholera does not grow in the presence of vesuvin but will grow in the presence of gentian violet. These observations did not attract much attention, but a few years later, in 1890, a number of communications were made dealing with this subject. Stilling showed that the dye not only exerts an antiseptic action but also actually kills certain bacteria, and at his request the firm of Merck & Company put out a mixture

[1] Read at the 26th Annual Meeting of the American Pediatric Society, Stockbridge, Mass., May 28, 1914.

of methyl violet 6B, dahlia, and benzoyl violet. This was called blue pyoctanin. Stilling mentions the fact that Kramenski suggested the use of pure anilin and of anilin dyes as inhalations in the treatment of tuberculosis of the lungs, and it seems that the curative action of anilin upon wounds has been known to workers in the dye factories, where it is the custom to treat skin wounds by dusting them with various dyes. The selective action of these dyes led to their use in culture media, and Drigalski and Conradi used crystal violet in a dilution of 1 to 100,000 in a culture medium designed for the isolation of the typhoid bacillus. They believed that it hindered the growth of various cocci without interfering with the growth of the typhoid bacillus. Churchman[2] recently published the details of a study of the effect of gentian violet upon various bacteria and found that the various forms of organisms could be separated into violet positive or those in which the growth is inhibited and violet negative in which the growth is not inhibited. For almost all bacteria this relation of the growth to gentian violet is quite constant. Simon and Wood[3] have made a study and have established the fact that an acid dye irrespective of its color in the standard concentration of from 1 to 100,000 is devoid of bactericidal properties while a basic dye likewise irrespective of its color possesses inhibitory power. Among the basic dyes may be mentioned basic fuchsin, methyl violet, crystal violet, Hoffman's violet, and dahlia. Among the acid dyes the acid fuchsin, roth violet, and acid violet. Simon states that this inhibitory effect upon the growth of bacteria is not referable to the color but to their chemical structure (Triamino triphenyl methanes). A second contribution by Simon and Wood[4] contains an account of numerous experiments with various dyes in which they show that the inhibitory action upon the growth of certain bacteria which has been demonstrated to be common to all the triaminotriphenyl methanes is not an exclusive property of this group of anilin dyes but is manifested also to a greater or less extent by other strongly basic dyes. A theory is given concerning this which need not be discussed at this time. They have also demonstrated that certain bacteria belonging to groups ordinarily susceptible to dyes may grow in their presence and many organisms may overcome the susceptibility by adaptation. This has also been announced from Ehrlich's laboratory. Similar studies have been made by May[5] and by May and Heidingfeld.[6] They found that in studying the fuchsins, essentially the same thing that is the most basic, rosalin acetate, is also most toxic for bacteria while the acid fuchsins are not toxic at all. They found that a 1 to 1000 solution of basic fuchsin would kill in five minutes typhoid,

[2] Jour. Exper. Med., xvi, 221 and 822; ibid., 1913, xvii, 373.
[3] Amer. Jour. Med. Sci., February, 1914, 247.
[4] Ibid., April, 1914, 524.
[5] Jour. Amer. Med. Assoc., April 20, 1912, 1174.
[6] Ibid., May 31, 1913, 1680.

paratyphoid, tubercle bacillus, staphylococci, and the oidium albicans. They also found that the 1 per cent. solution did not produce any irritation of the mucous membranes and could even be injected into the bladder. They also found that 1 per cent. ointments which could be used in the treatment of ulcers and abrasions were non-irritating. Stronger ointments would occasionally produce some irritation. They suggest that the base of the ointment be made of five parts of petroleum and five parts lanolin.

About two years ago in searching for an efficient local application for streptococcic infections of the throat, Dr. Charles Simon suggested the use of dahlia. I started this as a local application, beginning at first with weak solutions, and I soon found that the saturated, that is about 4 per cent., solution could be applied to the mucous membranes of the throat or in fact other parts of the body without producing either pain or subsequent irritation. The drug seems to penetrate only to short distances and for the deeper seated affections has no value, but for superficial involvement of the mucous membranes whether the infection is due to streptococcus or to other organisms the effect is quite striking. In some cases but little effect is noted, it is true, but in others there is marked lessening of the intensity of the inflammation and coincidently a marked lessening of the constitutional symptoms. It has the advantage over other applications in that it is not painful, does not produce irritation, and is markedly antiseptic. The only disadvantage is the color, which, of course, will stain fabrics with which it comes in contact, although most of these stains can be removed if the garment is immediately washed out in cold water. For ulcerations about the mouth it may be used either by applying a saturated solution or a mouth wash varying in strength from 1 to 1000 or 1 to 10,000 may be used. The stronger solutions need not be used very frequently. The dahlia not only kills the offending organism but it has a marked stimulating effect upon the healing. Externally upon skin surfaces the drug may be used with marked benefit particularly upon ulcerations. I have used it with remarkable benefit upon vaccinations which were slow in healing, and upon other abraded surfaces, especially those which are infected. I have not had an opportunity of using it in erysipelas, but Dr. Louis P. Hamburger, of Baltimore, and Dr. T. B. Johnson, of Frederick, have used it in a number of cases, with the most satisfactory results. Dr. Johnson informs me that he has used it with remarkable success in both acute and chronic eczema, in herpes, tinea tonsurans, and furunculosis. In one resistant case of tinea sycosis in which the whole surface of the beard was tremendously involved, the patient was cured after five or six daily applications. It may be used with reasonable hope of success in skin lesions caused by or accompanied with pus organisms.

TUBERCULOSIS IN THE AGED.

By John B. Hawes, 2d, M.D.,

ASSISTANT VISITING PHYSICIAN, DIRECTOR TUBERCULOSIS CLINIC, MASSACHUSETTS GENERAL HOSPITAL; SECRETARY OF MASSACHUSETTS TUBERCULOSIS COMMISSION.

Pulmonary tuberculosis is ordinarily looked upon as a disease of early adult life. Of late years, and particularly at present, the subject of tuberculosis in infancy and childhood, its peculiar manifestations, and the modifications demanded in its treatment occupy the attention of the medical world. There remains one phase of the tuberculosis problem which also has its special characteristics, and which demand more study than it has hitherto received. I refer to pulmonary tuberculosis in the aged. This paper is based on a study of seventy-four patients, sixty years old or more, who are or have been under treatment in the Massachusetts State Sanatoria.

I have been able to find scarcely any mention of this subject in the modern text-books on tuberculosis or general medicine. Thomson, in 1912, speaking of prognosis in tuberculosis, writes that "beyond forty the outlook becomes less hopeful with increase in years." Bandelier and Roepke devote one or two lines to the same subject, and are in accord with Thomson. Laënnec, in 1826, comments on the frequency of tuberculosis in the aged; his pupil, Louis, out of 205 cases, found 11 over sixty years, and made a detailed study of this condition. The chief, if not the only, writers on senile tuberculosis for the ensuring years consisted of a group of French investigators: Moureton in 1863, Broussé in 1886, Marfan in 1893, Potain and Parisot in 1894, Barré in 1895, Froment in 1903, and Etienne in 1905. Squire, of Philadelphia, discussed this subject in 1906, and Stoll, of Hartford, in 1912. In 1914 Nascher, of New York, published a volume on *Geriatrics*, diseases of old age, in which he devotes a few pages to tuberculosis in elderly persons.

Frequency. Barré, of Paris, in 1895, found a proportion of 2.29 per cent. of cases sixty years old or more out of 92,141 deaths from phthisis during the years 1884–1893 in ten large hospitals in that city. My own percentage is less than this. Out of 6832 consumptives in the four Massachusetts State Sanatoria during the past four years I found 74 who were sixty years old or more, or 1.08 per cent. The difference in the basis for calculation in the two cases is of course obvious and accounts for the disparity between the two sets of figures.

Etiology. Barré believes that this condition in elderly persons is apt to be a sequel of some other process, such as bronchiectasis, or chronic bronchitis, etc. Less often it is the awakening of a

hitherto quiescent lesion. Hart confirms this view. Nasher likewise believes it to be only rarely a primary infection, but usually the result of some previous inflammatory lung condition. In the cases I have studied the process was far more often a continuing or awakening of an old tuberculous focus rather than an infection with tuberculosis superimposed on some other condition.

Symptomatology and Course. Fever, according to Barré, is comparatively rare except when the patient is suffering from an acute exacerbation. Shortness of breath is apt to be marked. The course is very slow and chronic, but progressive. Crespin comments on the comparatively slight constitutional disturbance arising from a marked lesion in old age, compared with that in younger persons. Hart emphasizes the extreme chronicity of this condition, its tendency toward healing by the formation of fibrous tissue, and slight tendency toward dissemination. He calls attention to the apparent reduced virulence of the organism in these cases. Squire, commenting on the lack of constitutional disturbance, writes as follows: "Tuberculosis when it attacks lungs already damaged by the degeneration of old age may add but little to the discomfort of the individual who is already short of breath and 'wheezy.' But the sputum may be loaded with tubercle bacilli and a great source of danger to others." He takes the opposite view from Hart, and states, as his opinion, that the tendency is to advance and not to cure, and that the progress though slow is continuous and progressive. Potain comments on the lack of fever, and emphasizes the frequent combination of emphysema with tuberculosis. He, likewise, is pessimistic as to cure, stating "le tuberculeux sénile ne guérit jamais." The patient is always in danger of some grave disaster; the least complication may bring about his death. My own opinion is hardly so pessimistic as those given above. While the chances of a real cure may be regarded as *nil*, and while the disease will undoubtedly cause the patient's death, my experience has been that this condition, under proper treatment, is compatible with years of useful and comfortable, though semi-invalid, life.

Diagnosis. This is often a very difficult matter. It is well-nigh impossible to tell when the patient who for years has suffered with chronic bronchitis, emphysema, or asthma, may develop tuberculosis in addition to his other troubles. Fever is often absent; other symptoms, such as cough, sputum, and shortness of breath, may be already present and well accounted for by the existing condition. Loss of weight, weakness, etc., are common in old age as well as in tuberculosis. In the lungs themselves asthma and emphysema often mask areas of consolidation, rales, etc. Stoll calls attention to the value of d'Espine's sign, intense whispered voice heard on auscultation over the spines of the vertebræ below the third or fourth dorsal in this class of cases. He believes a positive d'Espine's sign to be

almost pathognomonic of tuberculosis when found in elderly persons. The experience of the superintendents of our Massachusetts sanatoria, and my own observations, would not lead us to expect an enlargement of the bronchial glands in a process such as this, nor to confirm this statement in regard to the value of d'Espine's sign. It is well known that d'Espine's sign, when present in children, is of distinct value in the diagnosis of enlarged bronchial but not necessarily tuberculous glands. In adults its presence or absence is of little significance. The various tuberculin reactions and serum tests are of little or no value in diagnosis. The Roentgen-rays, however, may be of great help.

Finally, then, as our chief help in diagnosis there remains the sputum examination. This should be done at regular and frequent intervals in every case of chronic bronchitis or similar conditions in elderly persons. In no other way can it be definitely determined when a person suffering from an innocuous disease, such as chronic bronchitis with asthma and emphysema, may become a person most dangerous to others on account of his wholesale distribution of tubercle bacilli.

Treatment. There is no class of patients more in need of adequate treatment and supervision both for their own sakes and for others as these senile consumptives. There is also no class more neglected in this respect. The menace to the immediate family and to the public which this group of consumptives offers has been frequently commented on by various writers, but cannot be given overemphasis. As Crespin said sixteen years ago, the process and the tubercle bacilli which cause it may be benign for the patient but quite the reverse for others. It has been the experience of many physicians to find case after case of phthisis occurring in one family and to be quite unable to discover the original source of infection until often by accident a grandparent or some other older person apparently in fairly good health, except for a slight cough, is found to be expectorating sputum loaded with tubercle bacilli. The sound advice to examine the children in any family in which there is a case of pulmonary tuberculosis might well be enlarged so as to include all elderly persons with any cough whatsoever.

As far as the treatment of the patient himself is concerned it is well to remember that the strict sanatorium régime is rarely wise or necessary. Squire advises a warm, dry climate and small doses of iodide of potassium. Nascher is of the opinion that sanatorium and health resort treatment is rarely required, that high altitudes are dangerous, and moist atmospheres are bad. Dr. H. D. Chadwick, superintendent of the Westfield State Sanatorium in Massachusetts, writes as follows on the treatment of this class of consumptives: "From my experience with these patients I am strongly of the opinion that sanatorium treatment as it is given in large institutions during the winter is not the best thing for aged people. They

cannot be made comfortable during the cold weather in open wards. They should have private rooms whenever possible." Dr. Carl C. MacCorison, of the North Reading State Sanatorium in Massachusetts, comments on the difficulty in keeping these patients warm. As a class they make excellent patients, but are quite unsuited for the open construction of a sanatorium for incipient and early cases. In other words, one will accomplish more in these cases by keeping the patient warm and comfortable day and night in air which is fresh and pure, but not necessarily cold, than by demanding rigid adherence to a strict outdoor régime.

The 74 cases I have studied were divided as follows as regards age: 60 to 64 years, 48 cases; 65 to 69, 20 cases; 70 to 74, 4 cases; and 2 over 75 years, one 82 and one 88. There were 54 males and 20 females. On admission the stage of disease was as follows: incipient, 2; moderately advanced, 24; advanced, 40; not tuberculous, 8. Of 62 patients discharged the classification was as follows: apparently arrested, 8; improved, 20; progressive, 6; died, 16; not considered, 12. The sputum was positive in 43 cases, negative in 24, and not obtained or examined in 7. Of these 74 patients, 28 gave a definite family history of tuberculosis involving 53 immediate members of the family; 38 gave a negative history; and in 8 instances no information could be obtained. Out of the 74, 30 gave a definite history of influenza and only 2 a history of chronic bronchitis or winter cough. Of the 8 patients who after careful study were considered non-tuberculous, 3 were cases of asthma and 5 arteriosclerosis. In only a few of those patients who had tuberculosis was asthma a complication, while in no case was empysema mentioned in the records. I fear that this is owing to the fact that these cases were not recognized until the tuberculous process was well advanced and more in evidence than the asthma or emphysema. There are at present in our midst a far greater number of consumptives among elderly persons in whom the evidences of the tuberculous process is masked by asthma, emphysema, and chronic bronchitis than my figures, 74 out of 6832 cases or 1.08 per cent. would indicate.

Summary. 1. *Incidence.* Out of 6832 consumptives of all ages in Massachusetts State Sanatorium during the past four years, 74 or 1.08 per cent. were sixty years old or older. These figures probably do not nearly represent the actual number of elderly consumptives in Massachusetts today. Barré's figures, 2.29 per cent., are far nearer the truth. Taking 2 per cent. as a conservative estimate and 10,000 as an extremely low figure to represent the number of active open cases of consumption in Massachusetts, would give 200 consumptives of this class at present in this State. This number, though small in itself, constitutes one of the most dangerous groups of consumptives that we have, and one that is a constant menace to the lives of those around them.

2. *Course.* The course of tuberculosis in the aged is a chronic one, with intervals of comparatively good health. There is marked tendency to fibrous tissue formation. While a definite cure or permanent arrest never occurs, this condition is compatible in many cases with years of fairly comfortable life.

3. *Diagnosis.* The diagnosis of senile tuberculosis is often very difficult. Asthma, emphysema, and chronic bronchitis may so mask the tuberculous process in the lungs as to render its detection very hard. Constitutional symptoms may be lacking. Tuberculin tests are of no value. Roentgen-ray examination is often of great service. Repeated and frequent sputum examinations are essential in these cases. Such examinations should be made at frequent intervals in every case of chronic lung trouble in elderly persons.

4. *Treatment.* This is largely palliative and preventive. Treatment in a sanatorium where a strict outdoor régime is carried on is rarely necessary or advisable for these patients. A warm, dry climate is best. Small doses of iodide of potassium are sometimes beneficial. The utmost care of the sputum must be exercised.

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GENERALIZED TELANGIECTASIA IN ASSOCIATION WITH SYPHILIS, WITH THE PATHOLOGICAL PICTURE OF PERIPHERAL VASCULAR SCLEROSIS.

By John H. Stokes, A.B., M.D.,
INSTRUCTOR IN DERMATOLOGY AND SYPHILOLOGY, UNIVERSITY OF MICHIGAN.

(From the Department of Dermatology and Syphilology, University of Michigan, Ann Arbor, Michigan.)

The case of generalized telangiectasia which forms the basis of the present study, occurred in the practice of Dr. John Tanner Holmes, formerly instructor in dermatology and syphilology in this department. It is through his courtesy in transferring the patient to the care of the University Hospital at the close of his connection with this clinic that the author is enabled to present the following report:

Generalized telangiectasia of the cutaneous bloodvessels is well recognized as one of the rarest of dermatological conditions. Joseph,[1] in *Mracek's Handbuch* (1904), mentions 9 reported cases. Subsequent studies, among which should be mentioned those of Mosny and Malloizel,[16] Ehrman,[17 18] Lanceplaine,[15] Colcott Fox,[20] Trawinski,[21] Fearnsides,[22] Frick,[23] and others have, however, more than trebled this number. The case of angioma serpiginosum described by Wise[24] bears certain resemblances to the author's case, and will be discussed later. The recognition of the condition as a morbid entity is not as yet complete, and while many of the reports accord in essential particulars the etiology is as yet obscure. In the absence of satisfactory conceptions on this point, classifications of a descriptive or morphological type cannot escape an element of vagueness and uncertainty. In the hope of placing the case under discussion in as definite a relation as possible to those presented by other investigators, critical analysis of the literature is deferred until the findings in the present case are detailed.

The patient is a widow, aged thrity-four years, clerk by occupation, who came under observation complaining of spreading redness on the arms, legs, and body of five years' duration.

History. *Family History.* In direct and collateral lines of descent this is negative. Special inquiry into evidences of hereditary syphilis, hemophilia, familial tendency to epistaxis, vicarious menstruation, evidences of cardiovascular degeneration, such as apoplexy, cardiac weakness, etc., and nevus formation failed to reveal anything of interest.

Personal History. Patient was of normal birth. Good health as a child, with good recoveries from ordinary children's diseases. At nine years of age she began to suffer from nose-bleeding. The attacks averaged one a week and showed a certain periodicity. The

hemorrhage was severe, the blood "gushing from the nose and spattering those about who tried to help." The patient states that it could only be controlled by putting her feet in hot water and tying cords tightly about her arms and legs. This recurrent epistaxis ceased abruptly with the patient's first menstruation at the age of twelve years, and she cannot recall a single attack since. Menstruation is normal in amount; flow three days; regular; no pain. A small telangiectatic nevus below the right eye has been present and undergone no change since she can remember.

Patient married at twenty-one years; has two living healthy children, both normal births; no miscarriages; no deaths. So far as she knows her husband was healthy up to final illness (aged thirty-two years at death).

Husband was examined as an out-patient in the neurological clinic of the University Hospital some time before his death, with the following history and findings (appended from the records through the courtesy of Professor Camp): *Complaint,* stomach trouble with pain and attacks of vomiting, frontal headache, memory defect, irritability, and fatigue. *Examination* showed unequal pupils, slow reaction to light, pupils dilate again; no choked disk; no sensory changes; deep reflexes normal. The husband was later operated upon, according to the patient's statement, at another hospital, a gastro-enterostomy being done, with fatal termination. No pathological change was said to have been discovered in the abdomen. No Wassermann reaction on either blood or spinal fluid was obtained in the University Hospital, but the presumptive diagnosis with the above findings is tabetic gastric crises.

The patient denies extramarital exposure, and has never, so far as she knows, presented evidences of active syphilis, although she was much troubled by "canker sores" five or six years ago. She has never been nervous and always of a matter-of-fact, placid, almost phlegmatic temperament. There is nothing in the history to suggest either hyper- or hypothyroidism, although special inquiry was made. No rheumatism, no urinary disturbances, no hemorrhoids or rectal bleeding. Three years ago (two years after onset of present trouble) she had an attack of mumps, which was said to have affected the ovaries, but made a good recovery. Never uses alcoholic liquors, has no dietary idiosyncrasies and no digestive disturbances. Nothing notable about occupation or habits except that she has been much on her feet. She is very constipated. Patient has never shown any special vasomotor instability, such as a tendency to blush.

Present Trouble. Began five years ago, three years before her husband's death. Dorsum of both feet first involved, two or three small pink spots becoming confluent, and a diffuse redness spreading up the leg. Wrists involved at about the same time, the condition spreading upward on both arms and legs, and involving the

trunk last. At no time have there been any signs of the trouble upon the face or the palms of the hands. While the telangiectases were spreading the patient gained fifteen pounds in weight, and from a rather well-nourished woman has become somewhat obese. For the last four years the patient has suffered much from headaches and a sense of fulness, and from a "drawn feeling" in the head and eyes. Dizzy at times for the last four years, but for the last two has been much worse, and patient has noticed it while walking. Has had to use aspirin for the relief of the headache during the past year. Skin itches slightly, and there is some scaling. Troubled with chilly feelings, less marked at the present time. Vascular condition seems about stationary for the past few months. Patient complains that she cannot perspire. Hands and feet never swell, are always warm, and she is not short of breath on ordinary exertion. She has noticed that the redness is more marked when the parts are dependent, and that when she rises in the morning the affected skin is almost white.

General Physical Examination of Patient. A decidedly fleshy woman, well developed, in early middle life. Pupils somewhat sluggish to light, accommodation normal. No eye signs of exophthalmic goitre. Visual fields normal. Flush over the face. *Thorax* hyperresonant; breath sounds markedly accentuated in left upper portion. *Heart* markedly enlarged; impulse heaving; apex in fifth intercostal space, anterior axillary line. Tic-tac rhythm; no murmurs. *Abdomen* negative. *Pelvis:* some suffusion of mucosa of portio and vagina, otherwise negative. *Pulse* normal; radial artery negative.

Dermatological Examination. Face slightly suffused over the flush area; slight capillary dilatation. A pin-head papular nevus forms the centre of a small spider angioma below the outer canthus of the right eye. *Scalp,* marked seborrheic dermatitis; no telangictases; no atrophy; hair fairly abundant. Port-wine nevus at the nape of the neck not conspicuous. *Skin,* except for a few pigmented nevi and the telangiectatic lesions to be described, presents no notable abnormality.

Special Lesions. The telangiectasia of which the patient complains is generalized over the larger part of the body, but with marked variations in the intensity of the involvement. The scalp, neck and shoulders and the palms of the hands and thicker portions of the soles seem to be the only entirely free areas. The backs of hands and the face and the flexor surfaces of the arms are relatively free. In the main the process is diffuse, but macular involvement of some of the comparatively normal skin is present, and deeper red patches are in places superposed upon areas of moderate telangiectasia, as, for example, over the buttocks. In general the configuration of the dilated venules is arborescent, stellate, or lace-like. The degree of dilatation varies greatly. On the legs below the knees,

delicately beautiful telangiectatic figures of the arborescent type are visible with the naked eye. Elsewhere, naked-eye examination gives only impressions varying from that of an exaggerated *cutis marmorata* to the appearance of a reddish or livid mottling or an extensive blotching suggestive of hypostasis or suggillation, in which the telangiectasia is only visible with the aid of a lens. Four types of lesions are distinguished on close examination. The first is the diffuse or mottled, dark-red to purplish flush over extensive areas, such as the entire extensor surfaces of both arms from the shoulders to the wrists. All the larger sites presenting this type of involvement, including the buttocks and lower abdomen and the thighs above the knees, exhibit the arborescent configuration imperfectly, which leads to various degrees of mottling. Below the knees the telangiectasia takes the second form, approaching the type of the nevus araneus, with confluence of the individual capillary and stellate groups to form a continuous tracery. The third type of lesion is the macule, which is usually seen on comparatively free areas, but which is occasionally superimposed upon the diffuse lesion. The macules are oval or irregular in outline, do not exceed a centimeter in diameter, and show only a diffuse redness to the naked eye, without any suggestion of special structure. They are not elevated or depressed, have no sharp border, no involuting or atrophic centre. The fourth type of lesion is found only over the shoulders from the deltoid region to the middle of the upper arm, and consists of pin-point purplish or reddish angiomatous puncta which, under the lens, look like glomerular tufts or minute senile angiomata. They are scattered about irregularly over the surface mentioned and exhibit no definite configuration.

In addition to the foregoing types of vascular lesions there is a single, oval, annular patch of brownish hyperpigmentation, about 12 mm. in diameter, to the right of the median line and about 2 inches below the umbilicus. This shows neither induration nor atrophy. No other lesion of this type could be found on the remainder of the body. All the involved parts of the skin, but especially the extremities, showed a slight furfuraceous scale. In a single small patch below the outer condyle of the right humerus the scale was thicker and more adherent, and there was a suggestion of atrophy. This patch later disappeared and the skin resumed the appearance of the telangiectatic surroundings.

There were no suggestions of annular or gyrate configuration, of white spots, of central involution, of induration or nodule formation of edema, purpuric hemorrhage, atrophy, or follicular changes associated with the telangiectasia.

Inspection of the lesions, region by region, reveals the following additional points of interest. Even in apparently normal regions, close inspection discloses an involvement of the deeper vessels, and occasional tortuous venules and loops can be made out. The sym-

metry of the diffuse type of involvement is in marked contrast to the asymmetry of the macular type. Of the latter lesion, five patches occur below the left scapula and an equal number low on the right buttock. There are four typical macules on the left side of the abdomen and one over the inner condyle of the left humerus which are without fellows on the right side. The region of the mammary glands is almost the sole site of thoracic involvement anteriorly. The arborescence is radiating, with the nipple as a centre, and there is marked accentuation in and immediately around the areola. Another striking feature is the marked accentuation of the process in scars. The vaccination scar is the site of a vivid telangiectasia, and the striæ albicantes are made conspicuous in the same way. Two symmetrical patches of lichenification and hyperpigmentation on the adjoining surfaces of the thighs, due to chafing, are free from involvement, the ectasia being sharply limited at their borders. Along the anterior and outer surfaces of the thighs are typical deep, spider-web varicosities of the larger superficial veins forming a radiating, dusky purple network beneath the red mottling and tracery of the minute capillaries. This is presumably simply a phase of a general accentuation of the process in the more dependent portions of the body, which is easily apparent. The deep veins of the legs, however, show no external signs of involvement.

Mucous Membranes. Negative to ordinary inspection.

Glandular System. Left epitrochlear palpable; one large gland in left inguinal group. Otherwise negative.

Osseous System. No nodes on long bones, no tenderness, no bone changes suggestive of lues hereditaria.

Special Reactions on the Part of the Skin Lesions. Pressure. In practically all parts of the body, sufficiently heavy pressure caused a momentary disappearance of the erythema. The length of time that the area pressed upon remained blanched was greatest where the ectasia was moderate. Under glass pressure the red area first became yellow and then pale. In the most intensely affected parts all the pressure that could be brought to bear, scarcely sufficed to blanch the skin completely. Rapid stroking in even markedly involved regions, such as the arms, was fully as effective. *Posture* had a very marked effect. The backs of the hands, ordinarily little affected, showed marked arborescent reddening when the arm hung at the side for some time, and the hand and forearm well above the wrist could be blanched by elevation above the head. The legs paled distinctly on elevation. *Interference with venous return* accentuated the dilatation. *Cold* in the form of the ice-bag caused slight blanching, persisting after the removal of the bag itself for quite an appreciable interval, after which erythema seemed to develop, so to speak, between the original arborescences, forming a distinctly brighter flush. *Heat* was followed almost at once by an excessive reaction in the form of blotchy erythema, as compared with a

normal arm used as control. *Temperature to touch:* As a rule the skin was warm but not excessively so. The extremities were seldom cold even in a cold room, and not distinctly cyanotic. There was none of the blueness of vasomotor astbenia. *Hemorrhage:* As ascertained in the biopsies, it was no more profuse than from a normal skin, even without the use of adrenalin in the anesthetic. *Emotion* was entirely without effect.

Clinical Laboratory Findings. *Urine.* Three examinations, including a morning and evening specimen and one after diuresis (copious water), were negative for albumin, glucose, acetone, indican, bile, casts, blood, pus, crystalline sediment, and specific gravity.

Blood. Two counts, taken a week apart, gave the following results: (1) Reds, 5,580,000; whites, 7500; hemoglobin (Miescher), 88 per cent; (2) reds, 5,440,000; whites, 7250; hemoglobin (Meischer), 87 per cent.

Differential count: polymorphonuclears, 61 per cent.; small lymphocytes, 27 per cent.; large lymphocytes, 8 per cent; transitionals, 2 per cent.; eosinophiles, 2 per cent.; mast cells, none seen in 200 cells.

Coagulation Time. Two careful observations were made, two weeks apart, the first result being four minutes forty-five seconds, and the second four minutes; both results thus well within normal limits.

Blood-pressure. Four observations were taken, one week apart, using the Mercer and Faught mercury column instruments. Systolic pressure varied between the limits of 113 mm. and 128 mm.; diastolic between 90 mm. and 118 mm.

Wassermann Reaction. This could only be taken on the blood, the patient refusing a lumbar puncture. The reaction was positive once and negative once.

Urea Content of the Blood. This was determined through the courtesy of the medical service, and was found to be 0.32 gm. per liter. From the standpoint of nitrogen elimination, then, the renal function is apparently normal.

Stool examination was entirely negative.

Special Investigations. Believing that the value of this case as an etiological study of an obscure dermatosis would be greatly enhanced by expert judgment on certain special phases, the generous coöperation of the chiefs of the ophthalmological, otological, medical, neurological, and roentgenological departments of the University Hospital was enlisted in the preparation of the special reports which follow.

The examinations were planned to throw light on the following features of the case: (1) The condition of the cardiovascular system as a whole. (2) The condition of the nervous system with reference to any known organic or functional lesion that might

bear on a possible vasomotor origin for the dermatosis. (3) The question of the existence of syphilis in this patient and its role, if any, in the picture of cutaneous vascular pathology which she presents. Incidentally the otolaryngological examination cleared up the question as to telangiectases on the mucous membranes of the upper respiratory tract, a point of special interest in view of the history of epistaxis in childhood and the known association of this condition with Osler's syndrome.

Otolaryngological Examination. This examination was performed by Professor R. Bishop Canfield, whose report is appended:

"The examination of the mucous membrane of the nose and throat reveals nothing abnormal, although when my attention was called to her condition by Dr. Stokes, I was inclined to think that I could detect a general suffusion of the mucous membrane of the nose. This was not marked enough, however, to consider abnormal. The ears show a marked decrease in bone conduction, although the high limits are normal. The fact that she retains good hearing in both ears makes this decrease in bone conduction typically luetic."

The examination of the fundus of the eye was performed by Professor Walter R. Parker, who in addition to finding the fields normal reports the following:

"*Ophthalmoscopic Examination.* O. D.; media clear. The head of the nerve is markedly congested, edges obscured; small central physiological cup; the lamina cribrosa are not seen. The head of the disk is elevated one to two diopters, but is not edematous. The veins are slightly engorged and tortuous; some arteriovenous compression; marked tortuosity of the smaller arteries. The retina is slightly edematous with marked striations, most marked in the vicinity of the disk; details of retina blurred. The foveal reflex is present. No marked choroidal changes.

"O. S.: the media are clear. The head of the nerve is markedly congested, edges obscured except down and out, all of which area is blurred. The head of the nerve is elevated from one to two diopters. Marked arteriovenous compression; distal dilatation. The veins are engorged and tortuous. The foveal reflex is present.

"Diagnosis. O. U.: active neuroretinitis with advanced arteriosclerotic changes."

The Neurological Examination. This proved still further the results of the two preceding examinations relative to the existence of syphilitic involvement of the central nervous system. Professor Carl D. Camp's report is as follows:

"Examined October 25, 1914. Sluggish pupillary reaction to light; absent knee-jerks and sensory changes strongly suggest the diagnosis of incomplete tabes dorsalis. The telangiectatic areas do not appear to have a metameric distribution, nor have they any definite relation to the distribution of peripheral nerves."

More specifically enumerated, the sensory changes included

loss of Achilles tenderness and marked increase in the distances at which the patient could distinguish compass points. Graves' sign and conjunctival anesthesia were present. There was no loss of sensibility to touch, pin-point or pin-head, and she differentiated heat and cold promptly over the entire body.

In order to investigate the dilatation of the heart, which had been foreshadowed by physical examination, and the condition of the aorta, and to determine whether any mediastinal tumor existed, whose pressure upon the sympathetic ganglionic chain might be a factor in the production of a vasomotor palsy, Professor J. G. Van Zuwaluwenburg fluoroscoped the thorax and prepared an orthodiagraph. His report follows:

"*Fluoroscopic.* The heart is evidently enlarged, particularly the left ventricle, reaching to the left thoracic wall.

" *Dimensions:* Mr, 25; ml, 97; long, more than 142; transverse 91; area. undetermined.

"The shadow of the arch of the aorta is exceedingly dense, more so than should be expected. This is particularly notable along the right margin, about two inches above the right auricle. It is probably due to calcification of the aorta."

The findings of the physical and fluoroscopic examinations were confirmed as regards the heart by an electrocardiographic tracing taken by Dr. F. N. Wilson through the courtesy of Professor Hewlett. No other special finding was noted.

With a view to ascertaining whether a record of the flow of blood through the arm, as determined by the plethysmograph, would contribute anything of interest to an understanding of the dynamics of the patient's circulation, Professor A. W. Hewlett undertook such a study. His conclusions are quoted as follows:

"The records from the arm show a rate of blood-flow in the arm of between 2 c.c. and 2.5 c.c. per 100 c.c. arm volume; the primary pulse wave puts in about 0.5 c.c. of blood. Both of these are about the lower limits of normal. Tracings are characterized also by a rather unusual degree of reflection of the primary pulse wave.

"It is hardly possible with our present knowledge to interpret these findings satisfactorily, but they might be due to a rather marked constriction of the arterioles in the arm, without a corresponding change in the larger arteries."

Professor Hewlett's opinion, based on functional investigation, is a remarkable confirmation of the clinical findings as above enumerated and of the direct pathological study of the lesion itself as detailed below.

Examination of the Patient's Children. The patient's children, both girls, aged ten and twelve years, were examined for stigmata of inherited syphilis and for signs of vascular ectasia. Neither showed essential stigmata of the former disease. The older girl presented very definite saber tibiæ with other suggestions of

abnormal ossification, such as ulnar deviation of the middle fingers, some saddling of the bridge of the nose, and a high, narrow palatine arch. There were no telangiectases. The younger girl had a prominent forehead with a suggestion of bosses, marked ulnar deviation of the middle fingers, very striking scaphoid scapulæ, and some epiphyseal enlargement, especially of the distal ends of the femora. Both had a negative Wassermann. The findings could not be rated as more than suggestive; certainly not diagnostic. The bone conduction test for specific auditory nerve involvement, conducted by Professor Canfield, showed a marked decrease in bone conduction, with practically normal hearing in both children.

It is of interest to note that the younger girl presented a telangiectatic lesion of the nevus araneus type, about 1 cm. square, over the left scapula, about which no history could be obtained.

Histopathological Study. With the consent of the patient a biopsy was performed, two pieces of affected skin being excised. The first consisted of a typical macular lesion below the left scapula. The second was taken from a region of typical diffuse arborescent telangiectasia about three inches below the right knee on the internal surface. The macular lesion was fixed in absolute alcohol and later transferred to 5 per cent. formalin. The piece from the diffuse area was fixed in 5 per cent. formalin alone. The material was embedded in paraffin and the sections cut at 10 microns. The stains employed were Unna's polychrome methylene-blue, polychrome-eosin, polychrome-acid orcein, polychrome-neutral orcein, Van Gieson, carbol-methyl-green pyronin (Unna-Pappenheim), and hematoxylineosin. The only essential difference observable between the two pieces of material was a more marked dilatation of certain of the vessels in the specimen from below the knee. The pathological changes were as follows:

Epidermis. On the whole the changes are not marked. Slight atrophic thinning was apparent with moderate hyperkeratosis. Occasional intracellular edema was noted, affecting especially the basal layer and the deeper portions of the rete Malpighii. Occasional polymorphonuclear and round cells had invaded the epidermis, the latter being the more numerous.

Corium. The vascular supply of the corium and hypoderm was the seat of the significant pathological changes. The capillary loops in the papillæ were markedly dilated, much as is seen in a psoriasis. The subpapillary vessels presented a variety of changes representing phases of the essential process of obliterative endarteritis and periarteritis of certain vessels with compensatory dilatation of others. In conjunction with these changes, varying degress of of perivascular round-cell infiltration have occurred. Topically enumerated, examples of the following changes were easily found in all the sections examined:

Simple endothelial swelling in normal or dilated capillaries;

endothelial proliferation, all degrees to total obliterative endarteritis; perivascular thickening, affecting media and adventitia of the larger arterioles, with normal endothelium; periarteritis with obliterative endarteritis; simple ectasia (compensatory?) in otherwise normal vessels; ectasia with endothelial swelling and various degrees of proliferation; ectasia with normal endothelium and perivascular thickening.

New formation of capillaries was well marked, and there were numerous examples of the formation of capillary tufts from the lengthening and doubling of single vessels upon themselves. These tufts lay with their long axes in the lines of least resistance in the connective tissue. The cellular infiltrate appeared with the earliest signs of endothelial swelling, and was associated in varying degree with all stages of the endarteritis and periarteritis. The infiltrating cells were uniformly mononuclear lymphocytes, often arranged in arcs and concentric rings around the affected vessels. In no case was the infiltrate massive in character. There were no hemorrhages, no pigment deposits, no perivascular edema, or other evidence of acute injury to the vessel walls. Typical fibroblastic proliferation was evident around some of the small vessels, but nothing in the least suggestive of a neoplastic change could be discovered. There was a marked general increase in mast cells throughout the corium, especially conspicuous in the deeper layers and about the larger capillaries. The collagen and elastin were not noticeably involved.

Hypoderm. A marked sclerosis of the larger arterioles was apparent, affecting the media and adventitia rather than the intima. Many of the vessels had walls at least as thick as their lumina. In them the endothelial involvement was evidently less intense, concentric rings of large pale-staining nuclei in the outer coats showing the process to be essentially periarteritic.

The series of figures presented with this study are drawn from actual fields, and depict stages in the endarteritis and periarteritis associated with various degrees of round-cell infiltration. In Fig. 1, endothelial swelling, the earliest stage of the process is practically the only change. Fig. 2 shows a perivascular round-cell infiltration well established, endothelial swelling in the dilated capillary which is cut in cross-section, and swelling of some of the endothelial cells in one of the capillaries cut in longitudinal section, with lack of involvement in the main stem. One of the branches of the main trunk forms a capillary tuft just beyond the limits of the field. Fig. 3 illustrates the beginning encroachment of the proliferating endothelium upon the lumen and the decided increase in connective tissue about even very small vessels. In Fig. 4 the endarteritis is well advanced, the perivascular infiltrate less conspicuous. Fig. 5 is typical of the stage of practically complete obliteration. Longitudinal and cross-sections of vessels were found, which would not have been out of place in a syphilitic primary lesion. Fig. 6 is

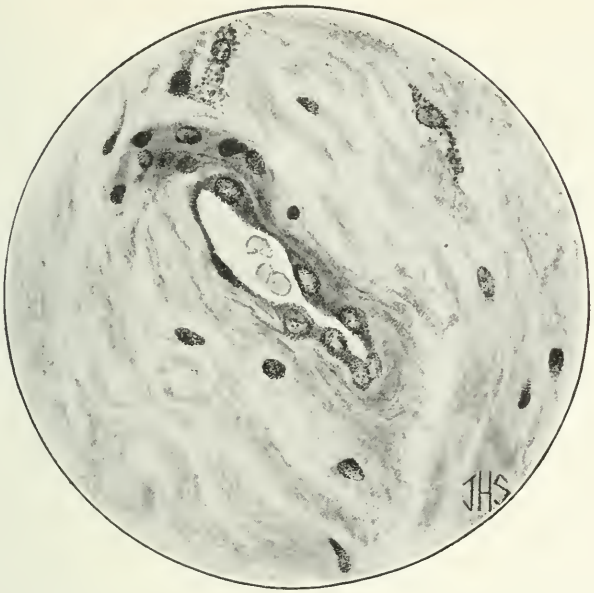

Fig. 1.—Capillary of the sub-papillary rete, showing endothelial swelling and a few perivascular round cells. Mast cells at the margin of the field. Polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

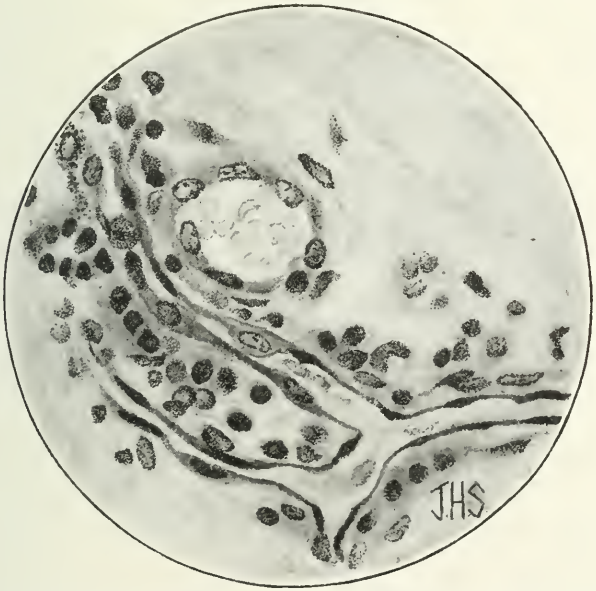

Fig. 2.—Capillaries, showing endothelial swelling and well-marked round-cell infiltration. Polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

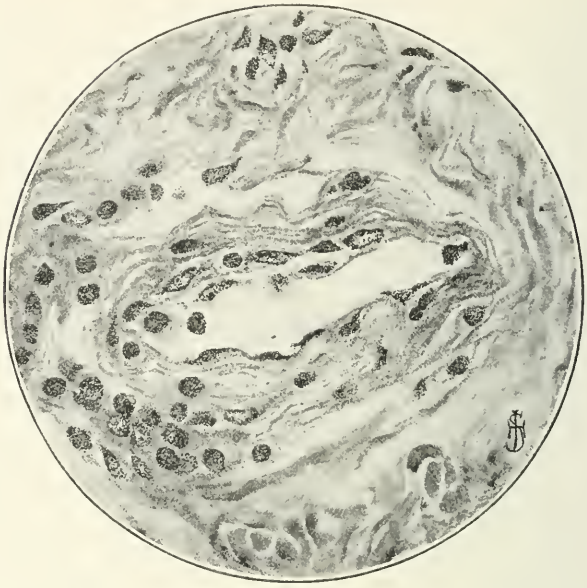

FIG. 3.—Perivascular fibrosis, endothelial proliferation, in a small vessel of the sub-papillary rete. Round cell collection to the left. Orcein-polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

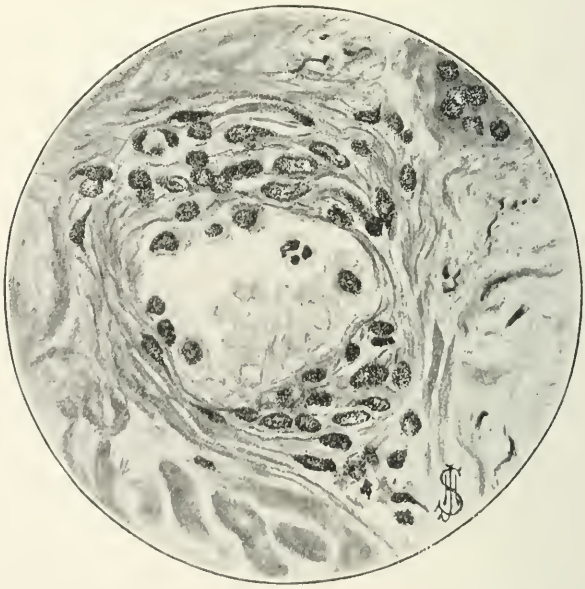

FIG. 4.—Endarteritis, partial obliteration. Infiltrate less marked. Orcein-polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

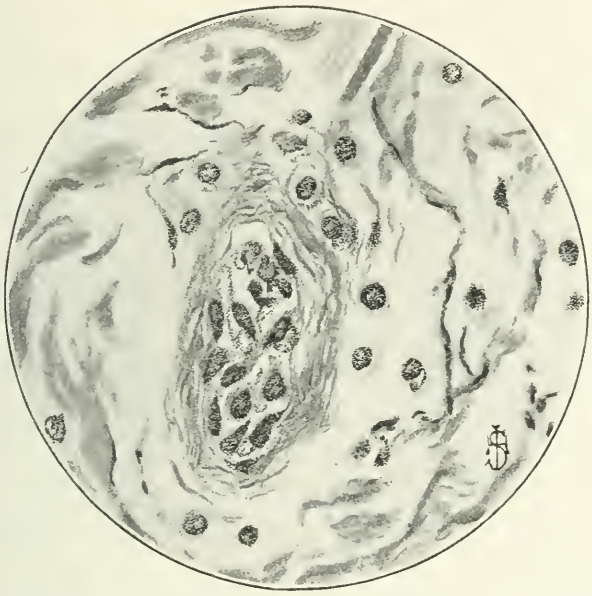

FIG. 5.—Endarteritis; practically total obliteration. Capillary fibrosis. A few scattered round cells. Orcein-polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

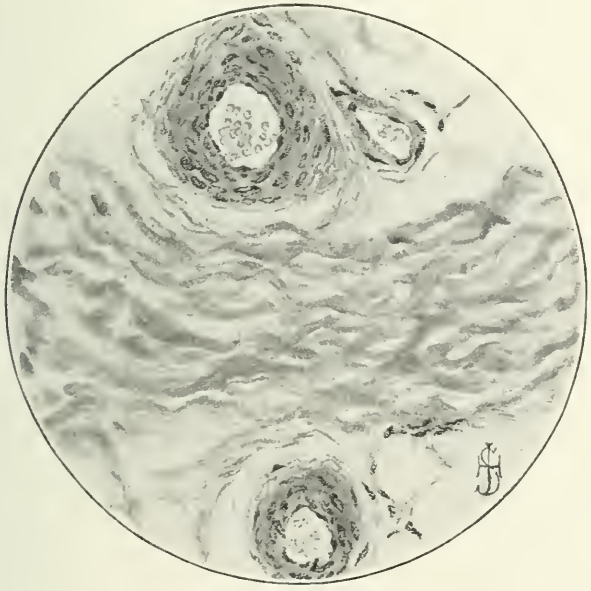

FIG. 6.—Sclerotic changes in the vessels of the hypoderm, confined to the media and adventitia, endothelium practically normal.

drawn from the subcutaneous fat of the specimen from the leg. The same condition was present in the excised macule.

Summary of the Case. The salient points in the foregoing presentation of my case of generalized telangiectasia may be summarized as follows:

1. A history devoid of hereditary or congenital elements bearing on present trouble.

2. Prior to marriage nothing of interest except epistaxis in childhood, ending with the establishment of menstruation.

3. Syphilis of the nervous system in the patient's husband (gastric crises).

4. The appearance in the wife eight years after marriage of seemingly idiopathic telangiectatic lesions in the skin, generalizing slowly through a period of five years. Lesions macular, punctate, and diffuse, the two latter symmetrical, the former asymmetrical in distribution. No other distinctive configuration, no symptoms, no notable secondary changes in the skin, such as hemorrhage, pigmentation, or atrophy. No involvement of mucous membranes.

5. The absence on examination of any demonstrable abnormality in the blood.

6. The absence on examination of any abnormality in the renal excretory mechanism.

7. The absence of any directly toxic influence known to have a degenerative effect on the cardiovascular system, such as alcohol, jaundice, lead.

8. The absence of evidence of vasomotor asthenia, of involvement of the nervous system other than that associated with tabes dorsalis or of involvement of the sympathetic system. Nothing to connect the distribution of the vascular phenomena with that of peripheral nerves.

9. The absence of any demonstrable abnormality of internal secretion—hyper- or hypothyroidism, pituitarism, ovarian or adrenal changes.

10. The presence of active syphilis in the patient in the form of involvement of central nervous system: active neuroretinitis; eighth nerve involvement; incomplete tabes dorsalis; positive, later negative Wassermann reaction on the blood.

11. Pathological changes in the cardiovascular system in the form of (*a*) hypertrophy of the heart and possibly a patch of calcification at the base of the aorta (electrocardiographic and fluoroscopic examinations), and (*b*) in the retina, demonstrable peripheral arteriosclerosis far in advance of the patient's years.

12. Experimental data (plethysmograph) tending to show a constriction of the peripheral arterioles in one of the most affected portions of the body (arm) without involvement of the deeper vessels.

13. Further evidence for a lack of extensive involvement of the deeper vascular trunks in the form of a normal blood-pressure.

14. Final microscopic demonstration in macular and diffuse types of skin lesions, of extensive endarteritis obliterans, and of periarteritis in the vascular supply of the skin, of the type often associated with syphilis. Accompanying this is a low-grade perivascular round-cell infiltration, new formation of vessels in the affected skin, and some ectasia (compensatory?) of vessels as yet uninvolved.

It is proper to remark that in thus seeming to summarize the case in favor of syphilis as the etiological factor, the writer is none the less aware of the virtues of conservatism, and of the possibility that something has slipped through the meshes of the net. In preference, however, to the blank confession of ignorance involved in the terms "idiopathic" and "essential," it would seem allowable to advance the most tenable hypothesis. In making syphilis the prime etiological factor in this case, due allowance should be had for a possible predisposition on the part of this patient's cardiovascular system to the injurious effects of a syphilitic infection. Of such vascular weakness or abnormality the epistaxis in childhood may have been an evidence. So far as this investigation shows, the telangiectatic lesions are scarcely to be interpreted as cutaneous syphilides in the strict sense. Rather the changes detailed above so strongly suggest those usually associated with syphilitic involvement of the cardiovascular system that the writer is inclined to look upon the case under discussion as one of peripheral vascular sclerosis in which syphilis has been the cardinal etiological factor.

Discussion of the Literature. The subject of generalized cutaneous telangiectasia is, as previously intimated, far from satisfactory elucidation. From the confused mass of reported observation and description, attempts have been made to select and distinguish certain groups, primarily upon the basis of certain clinical resemblances and associations. It would seem advisable for the present to rate these as syndromes rather than as clinical or pathological entities.

Among the notable contributions to the effort to group these clinical phenomena, Osler's[26] syndrome of hereditary recurrent epistaxis associated with cutaneous and mucous membrane telangiectases is one of the best known.* With this are included for the purposes of this paper the cases of multiple papular telangiectases on the skin and mucous membranes which have engaged the

* A case of acquired telangiectases reported by Osler[27] was accidentally overlooked by the writer until after the preparation of the statistical study. Patient was a male, very neurotic, exhibiting factitial urticaria, and having several attacks of possibly renal colic with hematuria while under observation. Telangiectases of wide distribution. Hands suggest Raynaud's disease. Spleen enlarged. Cardiovascular system not entirely normal apparently, but no definite diagnosis on this point or explanation of the cutaneous condition is offered. Vidal's and Levi's cases are cited.

attention of British writers, notably F. P. Weber,[28] Kelly,[29] and others. Purpura annularis telangiectodes Majocchi constitutes another clinically well-defined group. Angioma serpiginosum of Hutchinson seems also to present a well-recognized clinical identity. Dubreuilh[30] and others have directed attention to the so-called senile angiomata. In spite of these attempts at classification there remains a residual group of cases which Lanceplaine[15] acting under Brocq's direction, undertook to systemmatize under the caption of essential or primary telangiectases, recognizing in the designation the existing ignorance of their etiology. A better illustration of the overlapping of the types enumerated could scarcely be desired than that afforded by Lanceplaine's inclusion of Majocchi's original cases in his discussion. Again, from the clinical description at least, Lanceplaine's thirteenth case might pass for one of angioma serpiginosum. Similar disagreements among authors can be noted in almost every paper on the dermatoses in question.

With Ehrmann's[17 18] publication in 1907 of a report on four cases an effort to introduce an etiologically unified group of generalized telangiectasias with syphilis as a basis, was made. Trawinski,[21] in 1910, followed Ehrmann's lead in reporting another case of generalized telangiectasia associated with syphilis. In 1908 Colcott Fox,[20] in reporting a peculiar case of obscure etiology, attempted a general survey of the entire field, without, however, mentioning Ehrmann's work. Fox's division of the subject included (1) nevi, under which he grouped angioma serpiginosum, and (2) Majocchi's disease. He then adopted Lanceplaine's three groups: (1) telangiectases complicating various dermatoses, (2) telangiectases symptomatic of disturbances of the general circulation, and (3) essential or primary telangiectases. Lanceplaine's subclassification of the essential forms is based solely upon morphology, a weakness to which Fox calls attention. Fox himself included the senile angiomata of Dubreuilh among the essential forms. His fourth group is limited practically to Osler's syndrome. The etiological study of telangiectasia received a renewed impulse with the publication of a series of 6 cases by Fearnsides,[22] in 1912. In this series, chronic diarrhea with marasmus and edema form the background for the cutaneous manifestations. The most recent consideration of any of the above-mentioned groups is that of Wise,[24] which is based upon a clinical case of angioma serpiginosum, and contains a comprehensive review of the literature connected with that dermatosis.

In the effort to place my case in proper relation to those discussed by the authors mentioned above, I was impressed by the tentative character of most of the generalizations, and their application rather to the specific case than to any group as a whole. The absolute necessity for narrowing the field, led me to eliminate for the time being, for purposes of discussion, the well-defined groups, such as Osler's syndrome, Majocchi's disease, and angioma serpig-

inosum. An effort was made to collect, for comparison, the cases dealt with in the literature as belonging to the primary or essential group of acquired generalized telangiectasia. To this group, on the whole, rather than to any of the others mentioned above, except that of Ehrmann, my case seemed to bear the most resemblance. In place of the conventional abstract of the literature it was thought worth while to make a critical analysis of a combination of these nondescript or isolated cases and of the less well-known groups, such as those of Ehrmann and Fearnsides, in order to see whether a composite picture might not be forthcoming. In this composite picture it was hoped that etiological generalizations might stand out with enough distinctness to justify at least a partial discarding of the terms "essential" or "idiopathic." The usual difficulties which beset such a study from case reports were encountered in full measure, and were in themselves no small explanation of the reason why the etiology is still shrouded under the mystic term "essential." Several of the standard references in the literature, cited by one author after another, were hardly more than clinical notes or skeleton presentations. In spite of this difficulty, however, 33 cases, including the present one, were submitted to a parallel column analysis. The cases reported by the following writers constitute the material for this portion of the study: Tanturri[2] (1879) (Jullien's abstract); Vidal[3] (1880); Mandelbaum[4] (1882); Gastou[5] (1894); Morrow[6] (1894); Terrell[7] (1896); Levi et Le Noble[8] (1896); Chauffard[9] (1896); Kopp[10] (1897); Letienne et Arnal[11] (1897); Brocq[12] (1897); Levi et Delherm[13] (1901); Gaucher et Crouzon[14] (1902); Lanceplaine[15] (1904), three original cases (II, III, XIII); Mosny et Malloizel[16] (1905); Ehrmann[17] (1907), four cases; Hyde[19] (1908), case IV; T. C. Fox[20] (1908); Trawinski[21] (1910), Fearnsides[22] (1912), six cases; Frick[23] (1912), author's case (1914). Gastou, it should be recalled, reported two cases in the same discussion, a father and daughter. Details about the latter case were, however, very meager.

The findings are presented in groups, representing parts of a detailed topical outline into which each case was fitted. The outline proved to be too complete for a number of the less carefully worked-up cases, and accordingly only a few of the items carry figures covering the whole series of 33 cases. The totals represent the number of cases in which data are given.

Family History of Patients. This was limited to the direct line of descent, and for practical purposes included only the parents.

Item.	Positive.	Negative.	Doubtful.	Total.
History of hereditary transmission	1	21	0	22
Neuropathic heredity	1	12	0	13
Cardiovascular disease in parents	5	10	0	15
Syphilis in the parents	1	12	0	13
Other constitutional diseases in the parents (diabetes, 1; tuberculosis, 1, rheumatism, 1)	3	13	0	16

The single case of hereditary transmission and that of syphilis in the parents are one and the same, the combination occurring in Gastou's[5] two cases. The father developed telangiectases in association with cardiovascular and late central nervous manifestations. The daughter, whose mother sustained a typical series of syphilitic pregnancies, developed a localized telangiectasia in early life, which generalized rapidly after a pregnancy. The figures as a whole, however, negate the idea that there is any hereditary influence directly concerned in the transmission of telangiectases of the essential type from parent to child. On the other hand the indirect influence of a weakened cardiovascular resistance may be inferred to some extent from the fact that of 15 cases, one-third had a parentage in which one or both members developed serious involvement of the circulatory system in the course of their lives. The influence of other constitutional diseases can hardly be judged from these figures:

Age Incidence of Telangiectases.

Under 10 years	2 plus 4 (Fearnsides' syndrome).
10 to 20 years	3 " 2 " "
20 to 30 years	8
30 to 40 years	2
40 to 50	4
50 to 60 years	1
60 to 70 years	1

It would appear that the highest age incidence is in early adult life between the ages of twenty and thirty years. Fearnsides' syndrome was mentioned separately in these figures, because as a picture associated thus far mainly with a disease of children it seemed a little out of keeping in this detail with the problem presented by acquired telangiectasia in later life.

Sex Incidence. Many writers have noted the preponderance of females over males in connection with the development of generalized telangiectasia. The results in this series show 22 females affected as against 11 males.

Systemic Disease in the Patient. This is taken to mean chronic systemic disease of a serious character. The acute exanthemata are, of course, excluded.

Syphilis	11
Chronic lead poisoning	1
Hyperthyroidism	2
Nephritis	3
Hemophilia	1
Arthritis	1
Diarrhea with edema (Fearnsides)	6
	25
Counted twice	3
Total	22

Of the 11 syphilitic cases, Gastou II[5] is not spoken of as syphilitic by the author, but the description of the case justifies the diagnosis of hereditary syphilis. Ehrmann IV[17] is not specifically diagnosed as syphilitic, but endarteritis and general arteriosclerosis, especially cerebral, were demonstrated at autopsy, and the case is included with three of undoubted specific infection. Lanceplaine III[15] presented Argyl-Robertson pupils, primary optic atrophy, and other symptoms of tabes, although not definitely denominated such in the report. Lanceplaine XIII is not rated in this table, although the patient had a history of Bartholinitis and an undiagnosed ulcer in the mouth.

Two points stand out conspicuously from this table. The first is the prominence of systemic diseases which have a well-known tendency to attack the cardiovascular system, in association with so-called "essential" telangiectases. Syphilis, plumbism, hyperthyroidism, or nephritis are present in 22 and possibly 23 out of 33 cases. Chauffard's[9] case of hemophilia was associated with purpura and other evidences of actual injury to the vascular system. While the exact mechanism by which a prolonged diarrhea with loss of fluid, in Fearnsides syndrome, affects the vessel walls, may be a matter for discussion, the definite association of stasis manifestations and exudation of fluid (edema) with the picture in his cases, seems to support the view that we have to deal with a direct insult to the vessels which manifests itself in part in the development of telangiectases. Without yielding too much to the attractions of the argument *post hoc propter hoc*, it would seem a legitimate conclusion that diseases of a known cardiovascular degenerative type may be in definite etiological relation to a cutaneous vascular disturbance heretofore regarded as idiopathic and "essential." The second point is subsidiary to this, and calls attention to the leading role played by syphilis as a cardiovascular degenerative influence and possible etiological factor in the production of many generalized telangiectasias.

Actual Cardiovascular Changes Demonstrable by Examination or Autopsy. This is in effect an objective confirmation and amplification of the general data embodied in the previous table, and dealing with the cardiovascular system at large. Cardiovascular changes demonstrable: positive, 13; negative, 8; doubtful, 7; total, 28.

The cases grouped under the heading "doubtful" include four of Fearnsides' in which the patient presented no demonstrable lesion other than edema and stasis manifestations and did not come to autopsy. Vidal's[3] case presented merely "palpitation," Fox's[20] case had a bradycardia with vasomotor asthenia, and Tanturri's[2] case is reported to have had a weak pulse and stasis signs. As the table stands, nearly 50 per cent. had involvement of the cardiovascular system concomitant with the local lesion in the skin.

Renal Involvement. This was positive in only 3 cases, negative in 21, and doubtful in 1. This relatively rare association of renal insufficiency with cutaneous telangiectases would seem to relegate it to a subsidiary rank among etiological factors. It is impossible to determine definitely from the descriptions whether the renal disturbance was primary or was secondary to cardiovascular changes.

Visceral Changes.

Pulmonary (emphysema, pleural adhesion)	5 cases in 13
Hepatic	3 cases in 16
Gastro-intestinal	9 cases in 16
Spleen	1 case.

The gastric manifestations were largely symptomatic, such as hyperacidity in nervous patients and gastritis in alcoholics. *Apropos*, pulmonary symptoms, in Brocq's[12] case the telangiectases extended rapidly after a severe pneumonia, possibly as a result of cardiac strain incident to this particular infection.

Disorders of the Central Nervous System. In view of the prominent part which supposed neurological factors have played in the opinions of various writers who have discussed etiological possibilities in generalized telangiectasia, the findings under this heading were of more than ordinary interest. A rough classification into functional and organic conditions was made. Where a definite neurological entity existed it was classed as positive. Where the patient was described as merely "nervous," the case was rated as doubtful.

Functional Disorders.

	Positive.	Doubtful.
Hysteria	3	3
Miscellaneous	3	3
Total	6	3

Organic Disorders.

Syphilis of the nervous system	3
Alcoholic polyneuritis	1
Chronic lead poisoning	1
Convulsions and imbecility	1
No definite syndrome	1
Total	7

Of the functional cases, one occurred in a syphilitic. Of the organic cases it will be noted that 5 out of 7 were due to agents whose influence was also apparent in the form of cardiovascular changes. In other words, in these 5 cases the telangiectasia could scarcely be the result of central nervous disturbance. Rather the central nervous disturbance and the cardiovascular phenomena were effects springing from a common cause—syphilis, alcohol, lead.

Disorders of Internal Secretion.

Hyperthyroidism	2 cases.
Climacteric	1 case.
Puberty	1 case (doubtful).
Ovariotomy	1 case.

The objection to the *post hoc* type of reasoning applies with full force to the last three cases given above. Terrell's[7] report is fragmentary and incomplete and the process had begun well before the menopause. Kopp[10] frankly lays the blame on puberty as the only etiological factor. Gaucher and Crouzon[14] made a rather incomplete analysis of their case, a woman, aged twenty-eight years, upon whom an ovariotomy was performed after six years of pelvic inflammatory disease. The question of syphilis was apparently not considered. The relation of the ovariotomy to the telangiectases suggests the chronological rather than etiological. The cardiovascular changes of Basedow's disease were present in the 2 cases of hyperthyroidism (Létienne et Arnal[11] and Hyde[19]).

Site of Onset of the Telangiectases. Investigation of the site of onset was made in the hope of determining whether there was a possible *locus minoris resistentiæ* for this disease and what deductions might be drawn from it. It was found that 6 cases had begun upon the face, 8 below the elbows, and 10 below the knees. Only 7 appeared upon the remaining parts of the body. The localization to the most dependent portions of the body of 18 out of 33 cases at onset is decidedly of interest as indicating that the lesion tends to occur in the weakest part of the peripheral circulatory system. The involvement of the face in hyperthyroid cases was explained by Hyde[19] on the ground that it was a highly vascularized site, close to the heart, and subject to "special exposure to the bombardment of the left ventricle." This rather plausible explanation seems applicable to the entire range of cases under consideration. It justifies the inclusion of the face with the parts of least resistance in the peripheral vascular system.

Associated Dermatological Conditions. While a considerable variety of dermatoses appeared in individuals affected with general telangiectasia, the following were the only conditions whose constancy suggested a relation to the vascular abnormalities.

Urticaria	3 cases.
Dermatographia	4 "
Vasomotor asthenia, pronounced	3 "
Tertiary syphilides	4 "
Nevi (numerous)	2 "
Edema (Fearnsides' syndrome)	5 "

Allowing for one case counted twice, 9 cases in a total of 28 presented cutaneous conditions commonly associated with peripheral vascular changes. If edema be included the total rises to 14 out of 28 cases.

Lesions Present. With a view to ascertaining whether the clinical descriptions could be combined to form an approach to an average type, the separate lesions described were catalogued as follows. Practically every case presented several types at once and accordingly appears under a corresponding number of entries:

Macules	19 cases.
Papules	3 "
Puncta (angiomatous)	7 "
Diffuse undifferentiated erythema	9 "
Bands	3 "
Aborescences and visible telangiectatic network	18 "
Mottled areas (livedo or *cutis marmorata*)	4 "
Annular and gyrate figures	2 "
Induration in the lesions (excluding papules)	9 "
Secondary changes (in 26 cases):	
Atrophy	3 "
Pigmentation	5 "
Depigmentation	2 "
Scaling	11 "
Purpura	5 "

From this *resume* certain objective features seem to stand forth with some definiteness. The efflorescence is a combination of macules and arborescences, with a certain amount of diffuse erythema. About 25 per cent. of the cases show some slight induration on palpation. Annular and gyrate figures are an insignificant part of the picture, which differentiates it rather sharply, morphologically from the angioma serpiginosum group, as does also the relative unimportance of the "cayenne pepper grain." Atrophy and depigmentation, similarly, are uncommon secondary changes, while slight scaling ranks as the commonest. Even this is easily overemphasized, so that typically the telangiectasia exists without apparent secondary change in the affected skin. On objective grounds alone then, there seems to be good reason for differentiating the syndrome under discussion from that of angioma serpiginosum and Majocchi's disease.

Symptoms. Itching was present in moderate degree in 7 cases, absence of symptoms specially noted in 6 cases, no mention made of the subject in 19 cases.

Blood Examination. Examined in 7 cases, normal in 4 cases. One case had a red count of 6,500,000 (Trawinski)[21] and 3 per cent. of mast cells. Two cases showed moderate secondary anemia, the first of them with leukopenia. The second was Chauffard's[9] case of hemophilia, with lowered coagulation time and leukocytosis.

Mucous Membrane Lesions. In 8 cases in which the mucous membranes were specially examined, 3 were involved and 5 were not.

Prognosis. While under observation, 8 cases remained stationary and 6 progressed. Death occurred from the following causes in 4 cases: cerebral and general arteriosclerosis, hemiplegia, terminal

pneumonia (Ehrman);[17] chronic ulcerative iliocolitis following typhoid, with marasmus, edema and acute endocarditis (Fearnsides);[22] generalized visceral tuberculosis with chronic diarrhea, marasmus, and edema (Fearnsides); suicide (Frick).[23] Autopsy on this case showed carcinoma of the liver, of much more recent origin than the telangiectasis.

Improvement was noted in 4 cases, 3 of which were suffering from diarrhea and edema (Fearnsides). Two cures are recorded, one by Fearnsides, which occurred when the child's diarrhea was gotten under control, and one by Ehrmann. The latter case was one of syphilis of two years' standing, in which a patch of telangiectasis the size of a palm appeared on the hip. It cleared up in the course of two years of mercurial treatment. Mercury, on the other hand, is stated to have had no effect in three other old syphilitics (Mandelbaum,[4] Lanceplaine III[15] and Trawinski[21]).

Summary of the Literature. The impressions gathered from the foregoing comparative review of the literature may be summarized as follows:

1. It would appear that from a number of reported examples of so-called primary, idiopathic, or essential cases of generalized telangiectasia it is possible to segregate a new group on the basis of certain clinical considerations. In this group, well-known factors in cardiovascular pathology, such as syphilis, chronic plumbism, hyperthyroidism, and nephritis, may be suspected of forming the etiological background for the cutaneous manifestations.

2. Clinical examination and autopsy by revealing extensive cardiovascular disease, further support the suspicions aroused by this association and lend color to the belief that the cutaneous manifestations are simply unusual phases of the general involvement.

3. In the list of cardiovascular degenerative agents here enumerated, first rank must be assigned to syphilis.

4. The absence of annular and serpiginous lesions in the majority of the cases, the insignificant part played by atrophy, hemorrhage, depigmentation, follicular involvement, etc., would seem to differentiate it clinically from Majocchi's disease and angioma serpiginosum. The picture is a relatively simple one from the stand-point of clinical description—macular lesions and arborescent telangiectases with a certain amount of diffuse erythema; occasionally angiomatous puncta; slight induration on palpation in perhaps one-fourth of the cases. The most notable secondary change is a moderate scaling.

5. To this clinical picture my case in the main conforms, both from the stand-point of presumptive etiology and objective characteristics.

Discussion of the Pathology. Thus far the discussion of the possibility of regarding certain of the so-called "essential" forms

of the generalized telangiectases of the skin as simply rare aspects of the vascular pathology of syphilis, lead-poisoning, etc., has been confined to clinical considerations. It is unfortunate that a parallel comparative study of the local pathology cannot be carried out, owing to the fact that of the 33 cases here considered only 7 were subjected to histopathological investigation. Of the 7 available reports, several are fragmentary. The available material may be briefly reviewed as follows:

Mandelbaum's[4] Case: Histopathological examination by Stroganoff. Patient was an old syphilitic with macular, arborescent, and even nodular telangiectatic and angiomatous lesions, generalized over most of the body. The pathological changes consisted of moderate atrophy of the papillary body, with marked hyperpigmentation. New formation of bloodvessels was apparent in the subpapillary rete. The ectasia was not accompanied by any thickening of the perithelial connective tissue or changes in the endothelium.

Gastou's[5] Case I: Histopathological examination by Darier. Old syphilitic with advanced central nervous manifestations. Daughter developed general telangiectases also. The father presented a generalized telangiectasia of a plexiform type with large patches and mottled areas suggestive of ecchymoses. Fragmentary report. Moderate perivascular infiltrate the only positive finding. No pronounced ectasia apparent.

Ehrmann's[17] Case IV: Picture of generalized arteriosclerosis and endarteritis. Lethal exit following hemiplegia at forty-five years. Telangiectases and livid mottled patches over trunk and extremities. Blueness and mottling of hands and feet. Suggestion of purpura about the feet. Histopathological examination of the skin showed endarteritis of the finer capillaries of the affected skin, comparable to that described for Raynaud's disease. From this finding Ehrmann argues that localized sclerosis of the skin vessels may give the clinical picture of telangiectasia. The mechanism operates in his opinion, through the accumulation of blood in the arteriovenous network as a result of the diminished elastic recoil of the arterioles. While not making the vascular changes synonymous with syphilis, he lays great stress upon its etiological importance, and in addition to the 4 cases reported, mentions that he has seen 3 other cases of peripheral cutaneous vascular disturbance associated with late lues. A second paper (1908),[18] to which the writer has unfortunately not been able to secure access, presumably further analyzes this point of view and extends its application.

T. C. Fox's[20] Case: Grouped papular telangiectases on the trunk, appearing in association with an obscure syndrome of vasomotor asthenia, rectal hemorrhages, and epistaxis in childhood. The histopathological study disclosed nothing more than vascular dilatation.

Trawinski's[21] Case: Macular, arborescent, and striate telangiectases in direct association with gummatous infiltrates in the skin. A careful histopathological study disclosed atrophy of the papillary body and vascular changes enumerated as follows: (1) dilatation; (2) marked perithelial proliferation with thickening of vessel walls; (3) some perivascular round-cell infiltrate; (4) involvement of the media in certain vessels, but apparent absence of pathological change in the endothelium; (5) no signs of hemorrhage. There was no follicular involvement. Numerous plasma cells were demonstrated with polychrome methylene-blue and occasional discrete collections of round cells. So striking was the pathological change in the vessels that Trawinski proposes the designation *perivasculitis syphilitica telangiectatica* for the picture as a whole.

Fearnsides'[22] Case I: Generalized tuberculosis with diarrhea and edéma; lethal outcome. A rather indefinite report mentions dilatation and extravasation of blood around some of the smaller vessels and the absence of infiltration. The findings at least substantiate the view that the telangiectases and edema were due to actual injury to the vessel wall.

Frick's[23] Case: Generalized telangiectasia, indefinite syndrome. Autopsy showed carcinoma of the liver with metastases, more recent than the skin lesions. Rather indefinite biopsy findings seem to establish nothing except vascular dilatation.

It is apparent that no trustworthy general conclusions can be drawn from these findings. My case (see page 677) would seem to align itself with those of Ehrmann and Trawinski, both of which showed very definitely the minute changes of peripheral vascular sclerosis, and both, as in my case, in association with syphilis.

While in general angioma serpiginosum has been excluded from the foregoing consideration of generalized telangiectasia, the pathological study of Wise's[24] case, conducted by Pollitzer, is an exceptionally complete one, and the findings present several striking points of resemblance to those in the present case. For that reason they are here briefly reviewed. The epidermal changes in Wise's case consisted of marked intracellular edema with some round-cell infiltration of the deeper parts of the rete Malpighii and the basal layer. In certain of the indurated lesions this process was a striking feature of the picture. It will be recalled as present to only a slight degree in my case just described. Apart from some edema and degeneration of the collagen in Wise's case the principal changes in the corium were vascular, and include new formation of capillaries, many of them abnormally sinuous, endarteritis, and moderate perivascular lymphocytic infiltration (early stages). These cells often form single rows or collars about the adventitia of the smaller vessels. The condition did not apparently progress to the point of complete obliteration of the vessel lumina. Summarizing, Pollitzer repudiates the idea that the picture thus presented is that of an

angioma, and characterizes it as "a low-grade inflammation, affecting primarily the capillary areas of the papillary and subpapillary rete, with secondary effects in the epidermis."

Reference to my description and figures will call attention to the really remarkable resemblances between Pollitzer's account of Wise's case and the author's own. That Pollitzer was fully alive to the questions raised by the dissimilarity between Wise's case and the conventional histopathological architecture of angioma serpiginosum is evidenced by the following statement: "It seems equally certain that there has been included in this group (angioma serpiginosum) another class of cases with similar clinical appearances which is of an entirely different nature anatomically and etiologically. One is a progressive superficial capillary hemangioma, the other a subacute inflammatory process, limited to the papillary and subpapillary layers, most probably of toxic origin."

In the light of the foregoing considerations it must be conceded that exclusively clinical studies have failed to properly differentiate the widespread acquired vascular dilatations affecting the skin. Resort must be had to complete and thorough investigation of the etiological possibilities in the individual case and to systematic biopsy and histopathological study.

I regret that inability to secure Majocchi's original paper[25] on purpura annularis telangiectodes and a lack of pathological material illustrative of this rare dermatosis make it inadvisable to institute searching comparisons between my case and the group just mentioned. According to a summary by Trawinski,[21] obliterative endarteritis with its sequelæ in atrophy and sclerosis of the cutis forms the basis of the pathological picture. Majocchi is quoted as advancing an angioneurotic hypothesis and a theory of direct action by some toxin upon the vessels themselves. According to the latter view, cardiac disease, lues, infectious diseases, etc., any toxin or toxin-producing agent which can excite endothelial reaction and proliferation may serve as the basis for Majocchi's syndrome. The acceptance of such a view would seem to include purpura annularis telangiectodes in an etiology shared by cases of the essential type. The occurrence of hemorrhage, so often emphasized as a differential point in Majocchi's disease as against the other telangiectatic syndromata, would seem to lose much of its force when it is recalled that weakening of a vessel wall in a sclerotic process not infrequently results in rupture. Such an occurrence is familiar enough in the brain in the various forms of cerebral hemorrhage due to arteriosclerosis. Furthermore, obliterative endarteritis in Majocchi's disease may bear the same relation to cutaneous atrophy and fibrosis that anemic infarct due to obliterative endarteritis of the terminal vessels of the coronary system bears to fibrosis and sclerosis in the heart muscle.

Conclusions. 1. Cardiovascular degenerative conditions, among which syphilis is most conspicuous, appear to stand in etiological relation to a considerable percentage of the obscure dermatoses heretofore grouped under the meaningless terms "essential," "idiopathic," and "primary" telangiectasia.

2. The conception of a low-grade inflammation due to definite etiological factors, such as syphilis, lead, alcohol, hyperthyroidism, etc., forms a more substantial starting-point for further study than relatively intangible angioneurotic theories of the etiology of generalized telangiectases.

3. Much of the existing confusion in the classification of telangiectatic cutaneous lesions can be ascribed to overreliance on purely clinical data, whose value as exclusive criteria in these cases is open to grave doubt.

4. While not all acquired cutaneous telangiectases will be aligned under the schema just mentioned, there is reason to believe that more searching analysis of etiology and pathology will readjust classification in this field. Such study may even lead to the inclusion of clinical cases of angioma serpiginosum or Majocchi's disease under a new group of peripheral vascular scleroses with telangiectasia of known etiology.

I feel it a privilege to acknowledge the cordial coöperation of my chief, Professor Wile, in the form of invaluable criticism and suggestions bearing on the work and in the generous use of departmental facilities. I also acknowledge with thanks the courtesy and interest of the members of the clinical faculty whose examinations have contributed so materially to the thoroughness of the investigation where it concerned the fields of their special departments.

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ON THE USE OF STRYCHNIN IN BROKEN CARDIAC COMPENSATION.[1]

By L. H. Newburgh, M.D.,
BOSTON.

(From the East Medical Service of the Massachusetts General Hospital.)

Many English and American clinicians are in the habit of prescribing strychnin for persons suffering from acute and chronic heart failure. Strychnin is used for this purpose because it is believed that it increases the work of the heart and that it slows and steadies the pulse. Yet an unbiased examination of the evidence will show that there is no sound basis for this belief. Pharmacologists have not been able to demonstrate that strychnin increases the output from the heart. Clinicians have not shown that broken cardiac compensation can be relieved by strychnin. But since physicians continue to employ strychnin in the treatment of heart disease despite these facts, it is important to furnish data about which there can be no reasonable doubt. Such data, to be absolutely convincing, must be quantitative. One may measure the effect of a drug on broken cardiac compensation by recording the rate of the pulse, the rate of the respiration, the weight, the fluid intake, and the urinary output, before, during, and after its administration.

Earlier Studies. *Pharmacological Observations.* Igersheimer,[2] in 1905, reviewed the work of earlier observers and added important new data. It is to be noted that the pharmacologists always used amounts of strychnin which were many times the therapeutic dose—amounts which invariably caused convulsions. For example,

[1] Aided by a grant from the Council on Pharmacy and Chemistry of the American Medical Association.

[2] Ueber die Wirkung des Strychnins auf das Kalt und Warmblüherherz, Arch. f. exp. Path. u. Pharm., 1905, liv, 73.

in two instances, Igersheimer gave rabbits 0.055 gram and 0.375 gram. For men of average weight this would mean 3 grams and 12 grams. It is not safe or reasonable to assume that effects obtained with such large quantities would also follow therapeutic doses. But even if we do assume that such effects would be produced by amounts which may safely be given to patients, there is nothing in the pharmacological data which would lead us to believe that strychnin is indicated in the treatment of heart disease.

An examination of the literature shows that the earlier observations made on the hearts of warm-blooded animals are conflicting. Sometimes a slight acceleration, at other times a slight slowing, was noted. Igersheimer carefully studied the action of strychnin on the isolated and intact rabbits' heart. He could produce no change in rate until he had injected several times the amount which would cause convulsions in non-curarized animals. As the dose was gradually increased the heart beats became less frequent and weaker and the blood-pressure fell.

In 1911 Cameron[3] published his observations on the effect of strychnin on the heart. His technique was so elaborate that it is difficult if not impossible to analyze his results. He, however, sums up his work thus: "Strychnin in large or small doses tends to increase cardiac tonicity, except when the slowing is too great or when the slowing is associated with increased blood-pressure or when the increase in blood-pressure alone is sufficient to counteract the tendency to increased tonicity." A drug which can increase tonus only under such ideal conditions can have but little value in the treatment of heart disease even if the increased tonus is desirable. But is the type of increased tone said to be caused by strychnin ever advantageous if, as Cameron himself points out, it is accompanied by a decrease in systolic output?

It is apparent that the laboratory studies of the action of strychnin show that doses permissible in man can be of no direct use in the treatment of heart disease.

Let us now turn to the evidence gathered by clinical observers.

Clinical Observations. James Mackenzie,[4] speaking of "cardiac tonics," has written the following about strychnin, "the most popular remedy of this class is strychnin. I have carefully sought for its special effect on the heart and found none. When I inquired into the evidence for its supposed good effect I found that it was practically all clinical, and clinical evidence endows the drug with the most diverse properties. It is recommended as a cardiac stimulant in slow acting hearts, and even in heart-block it is said to quicken the beat. It is also recommended in the too excitable heart, as when there are extrasystoles, and in the rapid heart

[3] Johns Hopkins Hosp. Rep., 1911, xvi, 549.
[4] Diseases of the Heart, London, 1908, p.267.

of acute myocardial affections. It is said to be beneficial in cases of low blood-pressure and equally beneficial in the cases of high tension and even in angina pectoris. The evidence that can show a drug to possess the property of exciting the sluggish and of soothing the excited, of raising the low pressure and of relieving the high, speaks more for unreasoning faith in the drug than for the beneficial properties of the drug itself."

In the studies of Parkinson and Rowlands[5] the observations were made in such a manner that any immediate effect of strychnin when given subcutaneously in severe heart failure would be recorded quantitatively. The data were collected from fifty cases after they had been in the wards three to eight hours. The rate and character of the pulse and the rate of respiration were recorded with the Mackenzie polygraph, and the systolic blood-pressure with a Leonard Hill sphygmomanometer. Readings were made ten minutes, five minutes, and just before the injection of one-fifteenth grain of strychnin, and every five minutes for one hour after the injection. The work was controlled by giving the last ten patients an injection of water instead of strychnin. The following results were obtained:

On no occasion was any increase in blood-pressure produced. The average slowing of the pulse after the injection of strychnin was 3.3 beats per minute. The slowing which followed the injection of water was somewhat greater. There was no effect on the irregularity of the pulse. Neither the rate nor the amplitude of respiration were changed. There was no objective improvement in any case. These data fully warrant the conclusion which Parkinson and Rowlands reach, namely, that "strychnin has no effect which justifies its employment as a rapid cardiac stimulant in cases of heart failure."

The evidence which shows that a single dose of strychnin does not benefit persons suffering from heart failure does not prove that the prolonged use of the drug may not be a material aid in the relief of broken cardiac compensation. We have accordingly investigated the possible effect of the administration of large doses of strychnin over a period of several days in persons suffering from chronic heart failure.

Prolonged Use of Strychnin. *Method.* The cases were studied in accordance with the following plan: The patients upon entrance to the ward were placed on a diet of liquids and soft solids and the liquids were limited to 1000 c.c. in the twenty-four hours. If there was sufficient dyspnea or cough to prevent sleep, morphin or codein was ordered. The bowels were moved with various cathartics. The weight was noted. The temperature, pulse, and respirations were recorded twice daily. The twenty-

[5] Strychnin in Heart Failure, Quart. Jour. Med., 1913, vii, 42.

four-hour fluid intake and urinary output were noted. The patients were kept in bed throughout the period of observation. For the first few days after entrance the clinical course of the affection was watched. Many patients will entirely recover their compensation as a result of this *regime* without the aid of digitalis. It is important to exclude all such cases from a series in which the effect of any given drug upon the heart is to be studied. Only those patients who showed no persistent slowing of the cardiac or respiratory rates, no increased output of urine and no loss of weight after three or four days, were considered unimproved. Failure to observe this precaution may cause an error of as much as 50 per cent. The patients who did not recover their compensation were then given strychnin, and the effect upon the pulse, respiration, urinary output, systolic and diastolic pressures, weight, and subjective symptoms noted. Finally, digitalis bodies and diuretics were given in order that the effect of strychnin might be compared in the same patient under otherwise uniform conditions, with the effect of remedies whose efficiency is established beyond doubt.

Strychnin was studied in this way in eight cases of broken cardiac compensation. Table I shows the total dose of strychnin, the size of the individual doses, and the period of time over which the drug was given to each patient. Further details will be found in the accompanying case histories and charts.

TABLE I.

Case No.	Total amount of strychnin administered.	Duration of strychnin period in days.	Mode of administration of strychnin.	Remarks.
1	0.3 grain	3	0.03 grain three times a day.	
2	0.4 grain	4	0.03 grain three times a day.	
3	1.4 grain	3	0.1 grain every three hours on the first day; every two hours on the second day; every hour on the third day.	Finally omitted because of toxic symptoms.
4	2.0 grain	3	0.1 grain every two hours when awake.	Finally omitted because of toxic symptoms.
5	0.2 grain	1	0.1 grain at 9 A.M. and 5 P.M.	Discontinued because patient was growing steadily worse.
6	0.3 grain	1	0.1 grain every three hours.	Discontinued because patient was growing steadily worse.
7	1.6 grain	5	0.1 grain every six hours.	
8	0.3 grain	3	0.03 grain three times a day.	

EXPLANATION OF CHARTS.

Chart I.

Case II. A. P. Q., aged sixty years. Arteriosclerosis; weak heart ; broken cardiac compensation; dyspnea; right hydrothorax; ascites; edema of legs; continuous irregularity of the pulse, many beats not reaching the wrist. After being in the hospital four days without improvement, he was started on strychnin sulphate, gr. $\frac{1}{30}$, s.c., three times a day. The blood-pressure, taken at short intervals following the first dose, showed no change. After four days of strychnin there was no slowing of the pulse or decrease in its irregularity. The temperature remained subnormal. There was no change in either systolic or diastolic blood-pressure; no diuresis; no subjective improvement. There was an increase in weight. Strychnin was discontinued, and digipuratum given. Gratifying improvement in all the signs noted as unimproved during the strychnin period, followed. The decrease in the irregularity of the pulse was striking.

Chart II.

Case III. A. C., aged thirty years. Mitral stenosis; broken cardiac compensation; dyspnea; continuous extreme irregularity of the pulse; ascites; edema of the ankles. The patient had been in this condition for some time and she made no improvement for the first three days in the hospital. She was started on strychnin on the fourth day. It was omitted at the end of three days, because the patient showed physiologieal effects at that time. During this period she had been given a total of one and two-fifths grains of strychnin. She, however, made no improvement. There was no slowing of the pulse, no loss of weight, no diuresis, no subjective betterment. On the seventh day she was started on digipuratum. Thereafter she made a steady and satisfactory improvement. The increase in the loudness of the pulmonic second sound was striking. Blood-pressures were not charted on account of the extreme irregularity of the pulse.

Chart III.

Case IV. M. K., aged fifty-five years. Arteriosclerosis; chronic nephritis; broken cardiac compensation; dyspnea; attacks of cardiac asthma; enlarged liver; edema of the legs. After being in the hospital four days without showing any improvement he was started on strychnin sulphate, gr. $\frac{1}{10}$, s.c. On the first day after having been given 0.7 grain of strychnin, he was "jumpy" and felt excited. The strychnin was omitted. The next day 0.7 grain was given. On the third day the patient had 0.6 grain; and the drug was finally omitted that evening because the patient twitched every time he was touched. During the first "strychnin day" he had an attack of acute dyspnea, during which the systolic pressure went up to 300 mm. Hg. As will be seen by the chart, there was no change during the strychnin period. Digipuratum was then started and resulted in rapid marked objective and subjective improvement.

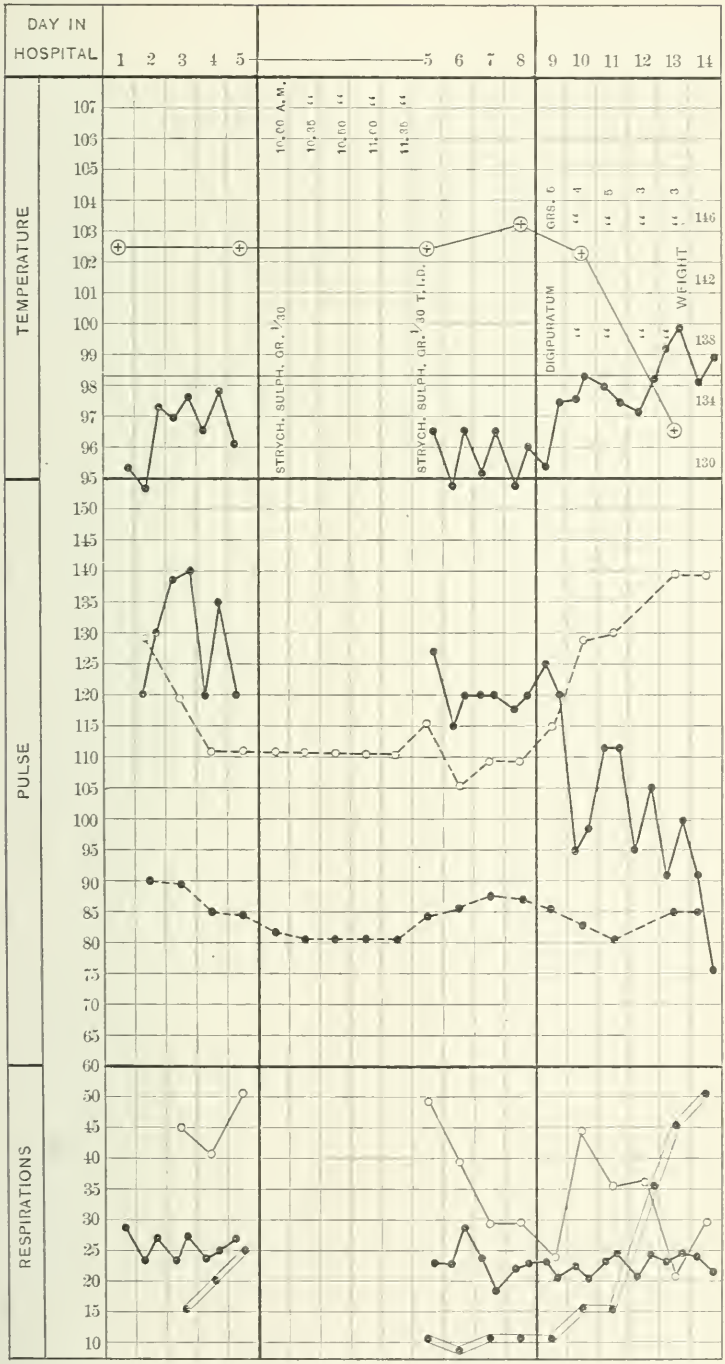
DAY IN HOSPITAL
1 2 3 4 5 5 6 7 8 9 10 11 12 13 14
TEMPERATURE
PULSE
RESPIRATIONS
STRYCH. SULPH. GR. 1/30
STRYCH. SULPH. GR. 1/30 T.I.D.
DIGIPURATUM
WEIGHT

Chart I.

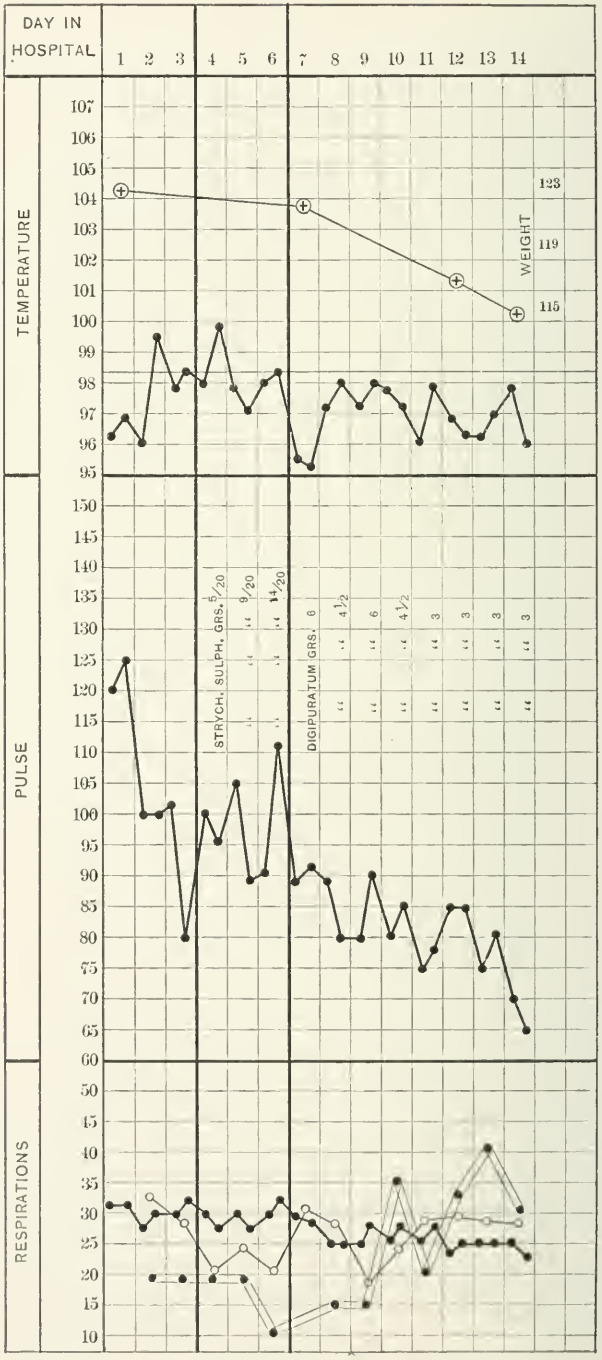
DAY IN HOSPITAL
1 2 3 4 5 6 7 8 9 10 11 12 13 14
TEMPERATURE
PULSE
RESPIRATIONS
WEIGHT
123
119
115
STRYCH. SULPH. GRS. 5/20
" 9/20
" 14/20
DIGIPURATUM GRS. 6
" 4½
" 6
" 4½
" 3
" 3
" 3
" 3

Chart II.

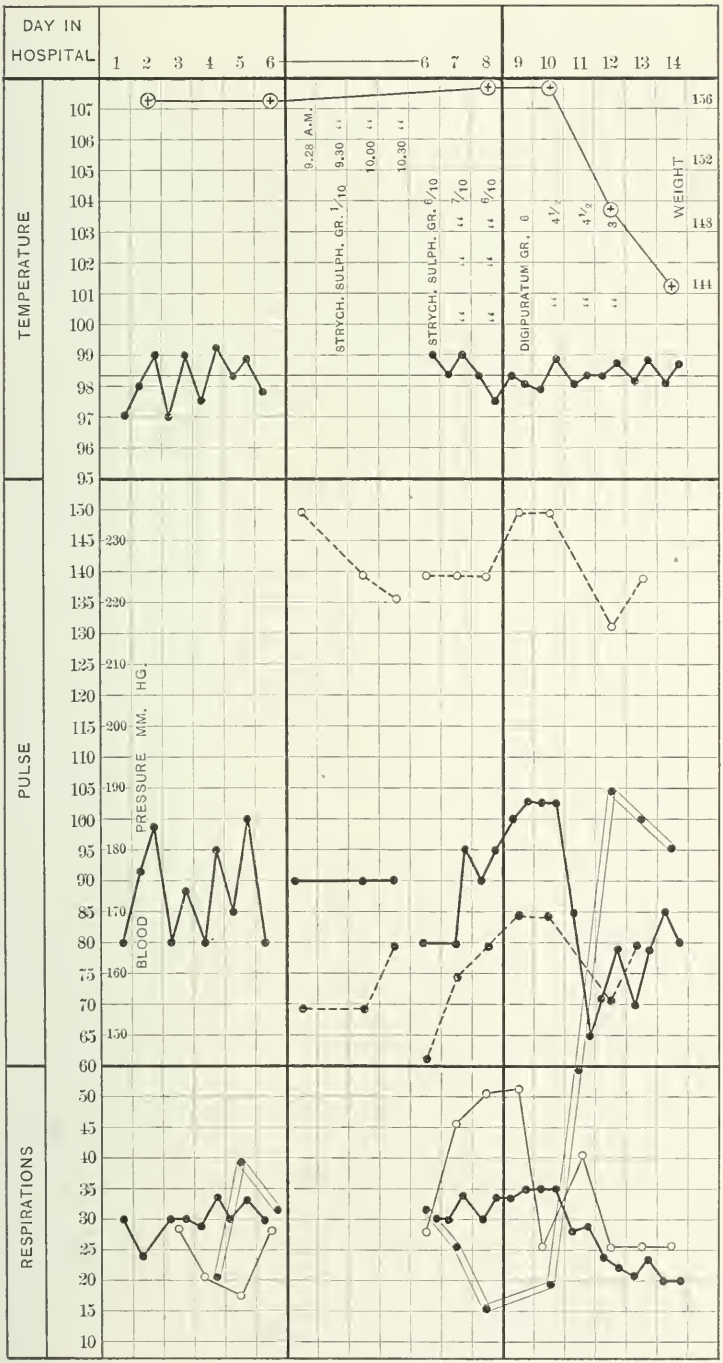
DAY IN HOSPITAL
1 2 3 4 5 6
6 7 8
9 10 11 12 13 14
TEMPERATURE
PULSE
RESPIRATIONS
BLOOD PRESSURE MM. HG.
9.28 A.M.
9.30 " STRYCH. SULPH. GR. 1/10
10.00 "
10.30 "
STRYCH. SULPH. GR. 6/10 7/10 6/10
DIGIPURATUM GR. 6 4½ 4½ 3
WEIGHT
156
152
148
144

Chart III.

Case Histories. Case I.—M. V., aged twenty-seven years. Aortic regurgitation; mitral regurgitation; broken compensation; dyspnea; right hydrothorax; ascites; edema of legs. After being in the hospital four days without improvement he was started on strychnin sulphate, gr. $\frac{1}{30}$, s.c., three times a day. After three days there was no slowing of the pulse, no change in the blood-pressure, no diuresis, and no subjective improvement. There was, however, an increase in weight. Strychnin was discontinued and diuretin and digipuratum given. The patient made no improvement, and died twenty days after entering the hospital.

Case II.—See history accompanying Chart No. I.[6]

Case III.—See history accompanying Chart No. II.

Case IV.—See history accompanying Chart No. III.

Case V.—M. A., aged fifty years. Obesity (weight, 232 pounds); broken cardiac compensation; hydrothorax; ascites; general edema; rapid, feeble pulse. After being in the wards three days he had lost no weight; his dyspnea had increased and his heart sounds had become weaker. The urinary output had fallen. During the previous twenty-four hours he had shown marked Cheyne-Stokes breathing. For the past few hours the periods of apnea were becoming longer. The systolic blood-pressure was about 110 mm. The diastolic pressure could not be determined by the auscultatory method. On the fourth day the patient was given strychnin, gr. $\frac{1}{10}$ s.c., at 9 A.M., and 5 P.M. During the day his breathing became so much worse and his general condition so much poorer that vigorous treatment was indicated. The strychnin was accordingly omitted and camphor, grs. 3, s.c., each two hours, given. The next morning there was gratifying improvement. The patient was then started on digipuratum and diuretin. His compensation was quickly and completely restored.

Case VI.—M. L., aged thirty-six years. Mitral disease; very severe break in compensation; general anasarca; right hydrothorax and ascites. On the fourth day after entrance the following note was made: "Since entrance the pulse has become progressively more rapid—at first hard to feel it is now almost imperceptible. The systolic blood-pressure is estimated with much difficulty at about 130 mm. The diastolic pressure cannot be obtained by the auscultatory method. In view of the fact that the patient is certainly worse than at entrance, she is started on strychnin sulphate, gr. $\frac{1}{10}$, s.c., each three hours. At 4 P.M., after three doses of strychnin, the patient seemed worse and her condition was such

[6] The temperature, pulse, and respiration, are represented in the usual way.
The weight is represented thus ⊕——⊕
The fluid intake thus ○——○
The twenty-four-hour urinary output thus ●═══●
The systolic blood-pressure thus ○----○
The diastolic blood-pressure thus ●----●
The dosage and the time of administration of the drug is printed on the chart.

that it was deemed unfair to withhold digitalis any longer. Strychnin was omitted and she was given strophanthin, gm. 0.001, intravenously, and camphor, gr. $1\frac{1}{5}$ s.c., each two hours." The next day she was started on digipuratum, and caffein was substituted for camphor. None of these procedures caused any significant change in the patient's condition. She continued to fail and died several days later.

Case VII.—L. M. A., aged fifty-three years. General arteriosclerosis: auricular fibrillation; myocardial degeneration; broken cardiac compensation; general edema; hydrothorax; ascites. The blood-pressure was not recorded because the irregularity of the pulse prevented its accurate measurement. Repeated estimations, however, showed that it was neither abnormally high nor low. The patient improved very slightly if at all under the routine treatment, which lasted for the first twenty days in the hospital. This was followed by a strychnin period of six days, during which time she was also having digitalis to the point of toxicity. It will be noted that the addition of the strychnin did not make the digitalis any more efficient than it had been during a previous period, when it had also been given to toxicity. The administration of the strychnin resulted in neither a subjective nor an objective improvement. $1\frac{6}{10}$ grains of strychnin were given in four days.

Case VIII.—E. P. T., aged sixteen years. Chronic endocarditis; mitral and aortic disease; adherent pericardium; hydrothorax; ascites; enlarged liver; general anasarca; gradual failure to death. After having been in the wards for several months, during which time he continued to fail in spite of a variety of therapeutic procedures, he was put on strychnin sulphate, gr. $\frac{1}{30}$, s.c., three times a day. During this period all digitalis preparations were omitted. At the end of three days there was no change in any of the objective signs, and certainly no subjective improvement. Strychnin was accordingly discontinued and routine treatment reinstated. The patient continued to fail, and died several weeks later.

Results. None of the patients were benefited by strychnin. The compensation was not improved in the slightest by the drug. Four patients subsequently recovered their compensation as the result of digitalis administration. Two patients died in the hospital. The other two were discharged unimproved. The failure of strychnin to have its reputed effect cannot be explained by assuming that the patients under observation were beyond all therapeutic aid, because, as was pointed out above, half of them did regain cardiac compensation when given digitalis. These four patients did not recover during the strychnin period solely because strychnin does not improve the work of the heart.

Conclusions. Neither pharmacological nor clinical evidence justifies the use of strychnin in the treatment of acute or chronic heart failure.

MULTIPLE NEURITIS AS A COMPLICATION OR SEQUEL OF TYPHOID FEVER.[1]

By Thomas A. Claytor, M.D.,

CLINICAL PROFESSOR OF MEDICINE, GEORGE WASHINGTON UNIVERSITY; PHYSICIAN TO THE GARFIELD MEMORIAL, THE PROVIDENCE, AND THE TUBERCULOSIS HOSPITALS, WASHINGTON, D.C.

My interest in this rather unusual complication was aroused by the following case: S. B., male, aged forty-two years, lawyer, was taken ill September 20, 1913, with what proved to be a long and severe attack of enteric fever. The fever continued for seventy-six days, the highest point reached being 104.4° F. At one time or another during the attack the following complications were noted: agonizing backache (lower lumbar region), diarrhea, irritable bladder, bronchitis, hemorrhage, nephritis, and neuritis.

The diet throughout the attack was as liberal as the patient could be induced to take, consisting of milk, eggs, custard, cocoa, cream, blanc mange, jelly, milk toast, crackers, scraped beef, minced chicken, rice, cereals, bread and butter, soft cheese, and well-cooked fruit. He was, therefore, in spite of the unusually long attack, in good physical condition when the temperature became normal, except for the neuritis.

The backache, in a most severe form, began to give trouble on the tenth day and continued until the sixteenth day. The suffering was so great as to require the administration of morphin hypodermically. This intense pain in the back coming on so late in the attack, gave me some anxiety later when the paralysis manifested itself, as it suggested the possibility of a spinal origin. On the fiftieth day he complained that his feet and legs felt stiff and that there was tingling. For two days there was the pins and needles sensation from the knees downward.

On the sixty-first day, as the fever seemed very tenacious, a dose of 500,000,000 dead typhoid bacteria was given, which was followed at intervals of two days each by two more doses of 1,000,000,000 each. The fever then gradually subsided and became normal on the seventy-sixth day.

There was some complaint of tender toes, but pain due to the peripheral neuritis was conspicuously absent, which would account for the fact that the condition was not suspected until attempts at movement demonstrated partial paralysis. Notes on the examination of the nervous system, made early in January, 1914, are as follows: The feet are slightly swollen and the skin is glossy; sensation to wool, good everywhere; slight hyperesthesia over the distribution of tenth and eleventh dorsal segments, posteriorly

[1] Read before the District of Columbia Medical Society, October 14, 1914.

and anteriorly, and also over the anterior surface of both thighs; spacing sense diminished in the hands, heat and cold sense unchanged; pin-prick felt everywhere; tenderness on deep pressure of the muscles of the thighs and less so of those of the calves (this sign had been much more marked two weeks earlier); some asteriognosis, which became very marked later; can tell position of the hands, but there is some loss of coördination in the upper extremities; loss of deep muscular sense at ankles and knees; marked incoördination on attempting to walk; wrist-jerks normal but elbow reflexes weak; knee-jerks exaggerated; ankle reflexes normal; no Babinski sign; plantar reflexes present; cremasteric reflex diminished on the right; abdominal reflex active; sense of vibration absent over legs and much diminished from the lumbar region downward over the trunk; marked steppage gait; great difficulty in placing the feet, liable to step much farther than intended; complains of a sensation about his waist, as though the pajamas were tied too tightly; no sphincter involvement.

By January 23, there had been great improvement in locomotion; the patient was then able to take a few steps without even the aid of a stick. The sense of position of the knees was perfect and that of the ankles much improved. There was still asteriognosis and lack of coördination of the hands. The most annoying symptom and the slowest to disappear was the paresthesia, which, by the way, was made much worse by the galvanic current. He felt so strongly on this point that he was unwilling to persist in the usual method of treatment. The treatment after the patient refused to continue the electricity consisted in gentle massage with persistent exercise or reëducation of the various groups of muscles.

After six months he was able to play nine holes of golf with but little fatigue. Now, eleven months after the onset of the neuritis, the paresthesia is just as pronounced as at first, and he still tires rather easily; the muscular power is good, but he gets a pain in his back in the original spot when he exercises too much.

The comparative rarity of this complication in typhoid fever may be gathered from McCrae's[2] statement that in a series of 1500 cases, of which he made a study, there were but 11, or 0.7 per cent., which developed neuritis (he does not say how many of this number were of the multiple variety).

As no one observer sees many instances of this condition, I have thought it worth while to collect from literature the following reports of cases, and from them to attempt to draw some conclusions:

Case I.—Man, aged twenty-four years; typhoid fever; highest temperature, 105° F.; relapse. During convalescence complained of pain in the legs, slightest contact with bedclothes causing the

[2] Osler, Modern Medicine.

greatest suffering. Examination: Loss of patellar reflexes; some atrophy; double foot-drop; reaction of degeneration; no marked disturbance of sensation. Able to walk with crutches six months from the beginning of the fever. Walked without difficulty at the end of another month. Slow but complete recovery.[3]

Case II.—Woman, age not given; severe typhoid fever; delirious for four weeks. Four days after subsidence of fever the patient complained of severe pain in the right arm and leg with loss of power in these parts. In ten days the pain subsided, but returned later with great violence and spread over the whole body; greatest intensity in the left leg which showed some edema and hyperesthesia. There was loss of knee-jerks; muscular atrophy; double foot-drop; reaction of degeneration; little loss of sensation. Result not given.

Case III.—W. R., aged twenty-eight, tuberculous. Typhoid fever four weeks, bed-sores, septic fever. Then developed hyperesthesia, most marked in the lower extremities; extensive paralysis of legs and arms followed by marked atrophy. Gradual return to power but not complete recovery. Death due to nephritis.[4]

Case IV.—Man, aged twenty-eight years. During the third week of typhoid fever great difficulty was noted in delivery of sputa; then dyspnea with regurgitation of fluids through the nose; one week later weakness in the legs; some paresthesia of feet and ankles; knee-jerks present; muscles of face and arms became weak; pupils dilated and unequal, also weakness of other ocular muscles; deafness; lessened sensation all over body, including the conjunctivæ; loss of knee-jerks; leukocytes, 14,800; pulse, 160; respirations, 40; temperature, 100°. Death.

Autopsy. Median, anterior crural, spinal accessory, hypoglossal, glossopharyngeal, oculo-motor and trifacial nerves removed. Wallerian degeneration and slight inflammation demonstrated. No disturbance of brain nor medulla.[5]

Case V.—Male, aged thirty years. On the fifteenth day of an attack of typhoid fever, pain appeared in the right arm; at the same time there was difficulty in mastication with escape of fluids from the right side of the mouth, and inability to close the right eye was also noted; face was drawn to the left, some weakness of right frontalis; tongue protruded to right; no pain in face; weakness of all muscles of the right arm, with tenderness on deep pressure of the muscles, and diminished reflexes. Result not given.[6]

Case VI.—Male. Six days after having been discharged as cured of an ordinary attack of typhoid fever complained of difficult vision especially of diplopia, also of difficulty in swallowing, regurgi-

[3] Preston, George J., Maryland Med. Jour., November 7, 1896, 55.
[4] Ibid.
[5] Lazell, E. W., Colorado Medicine, 1909, vi. 207.
[6] Gordon, Alfred, Amer. Med., December 31, 1901, 1130.

tation of fluids through the nose; then paralysis of arms and legs with loss of reflexes and ataxia and paresthesia over the affected limbs. Gradual improvement until at the end of two months recovery was almost complete except for some paresis and ataxia which still remained.[7]

Case VII.—Male. Well-marked attack of typhoid fever, no severe symptoms. Three days after discharge there were shooting pains in the legs; next day marked paresis of both legs with slight anesthesia, ataxia; temperature, 100° F.; knee-jerks normal. Temperature normal on eighth day; knee jerks absent, paresis increased but not complete paralysis. Great improvement by the eighteenth day. Late complete recovery.[8]

Case VIII.—M. K., white, male, laborer, aged thirty-eight years. Convalescent after about seven weeks. Then there was noted considerable swelling of both lower limbs which were very painful, some numbness and tingling in the distribution of the left ulnar and left politeal nerves,left foot-drop; anesthesia corresponding to distribution of the left external popliteal; hyperesthesia of plantar surfaces of foot and toes; left hand grasp weakened. Result not stated.[9]

Case IX.—Male, aged twenty years; ill for fourteen weeks with typhoid fever. In second week there was swelling of right arm and leg, very painful, preventing motion; knee bent at 45°. After slow convalescence patient began to get about and the leg gradually straightened, so that in a few weeks he had practically free motion of joints. The arm was slower to improve so that there was slight motion of elbow and wrist; the hand assumed the bird-claw appearance; in hand some loss of pain, tactile and temperature sense; tendon reflexes lessened in right arm; patellar reflex very faint on right, normal on left. This observation was made one year after the febrile attack.[10]

Case X.—J, L., female, in bed about two months with typhoid fever. Four days after getting up developed a temperature of 102°, with great sensitiveness and severe pain in the legs; legs and thighs flexed; any attempt to straighten them causing great pain; incontinence of urine for one day only; bedsores formed; temperature soon normal. When admitted to hospital two weeks later: Emaciated and anemic; some edema of left foot; great wasting of leg and thigh muscles; both knees rigidly bent; marked paresis in all attempted movements of feet, legs and thighs, tenderness of muscles of legs; no anesthesia; plantar and abdominal reflexes present; small amount of albumin; pulse rapid and feeble. The legs were straightened by weights; sensory disturbances dis-

[7] Kebler, Cincinnati Lancet-Clinic, 1889, xxiii, 35.
[8] Gordon, Alfred, loc. cit.
[9] Aldrich, Charles J., Med. News, August 16, 1902. 295.
[10] Moyer, H. N., Chicago Clinic, 1899, xii, 229.

appeared; motor power gradually returned, so that in five months from the onset the patient was able to walk about the ward.[11]

Case XI.—E. H., aged fifteen years. Had typhoid fever for about four weeks; shortly after defervescence began to have difficulty in talking and the voice had a nasal twang; soon there was numbness in ends of fingers and weakness in all the limbs, more marked on left than on right; no pain; swallowing difficult, regurgitation of fluids through the nose; knee-jerks absent on both sides; tactile sense good; reaction good to faradic but slow to galvanic current. Gradual improvement.[12]

Case XII.—J. W., girl, aged eighteen years, was seen eight months after an attack of typhoid fever of average duration. During the fever one day she found that she could not straighten out elbows, wrists, or knees; rigidity persisted. When seen there was marked wasting of the muscles; knee-jerks were variable; plantar reflexes absent; no clonus; elbows semiflexed and rigid; movements of hands and fingers feebly performed; some movements impossible; almost complete anesthesia over right thumb and index finger. Ultimate complete recovery.[13]

Case XIII.—Man, aged forty-two years. Shortly after recovery from typhoid fever it was noticed that there was partial loss to cutaneous sensibility, chiefly to pain, in feet and lower part of the legs; feet felt sore and there was pain in legs after walking; foot movements feeble; all muscles below the knees moderately atrophied; knee-jerks exaggerated.[14]

Case XIV.—Girl had severe attack of typhoid fever; in four weeks abdominal reflexes found to be exaggerated; legs painful and flexed; two months later was able to sit up in bed but could not lift either leg, and was unable to walk; no reaction to faradic current; in a short time, the right leg regained power, but the abdominal muscles on the right side bulged when child cried or moved. Recovery almost complete five months subsequent to attack.[15]

Case XV.—Boy, aged thirteen years. Had severe typhoid fever; passed from delirium into a state of mental dulness; fed by tube; loss of rectal control; gave much trouble by biting and eating the sheets; mental equilibrium recovered in about three months from onset of fever, when mind was a complete blank as to everything which had passed. At this time he complained that his left foot felt heavy; had noticed numbness and feeling of pins and needles for some days, he said. Decided foot-drop; increased knee-jerk; ankle clonus; reaction of degeneration in the tibialis anticus group; some atrophy; no loss of sensation. Recovery in about four months.[16]

[11] Ross, George. Amer. Jour. Med. Sci., 1889, xcvii, 25.
[12] Ross, George, loc. cit. [13] Bury, Judson S., Med. Chron., 1892, xvi, 145.
[14] Bury, Judson S., loc. cit.
[15] Humphreys, F. R., Hunter Society, London, 1889–90, 41.
[16] Abercrombie, John, Medico-Chir. Trans., 1897, lviii, 159.

Case XVI.—Girl, aged sixteen years. During a severe attack of typhoid fever complicated by hemorrhages, suddenly became totally blind. Both pupils widely dilated, especially the right; had been quite deaf but could hear quite well at this time. In about eight or nine weeks recovered vision completely.[17]

Case XVII.—Man, aged thirty years. Always feeble-minded; severe typhoid fever for two months; relapses; hemorrhages; convulsions; bed-sores; gangrene. As early as the sixth week he complained of pains in the legs; during convalescence paralysis noted; painful contractions of knee-joints; right knee swollen and right leg edematous; wasting of peroneal and quadriceps muscles; some wasting of thenar and hypothenar eminences; sensation good everywhere; reaction of degeneration present. Result not given.[18]

Case XVIII.—Man, aged twenty-six years. Moderately severe typhoid fever in 1887. After recovery went abroad apparently perfectly well, but in 1888 developed aching pain in right knee, which soon became very painful and symptoms of synovitis developed; ligaments all completely relaxed; paralysis of the extensors of the leg with wasting; no loss of sensation; gradual improvement so that in about four months he was able to leave the hospital. After eight months was able to use the leg well in walking but unable to jump and kick as before.[19]

Case XIX.—Woman, aged twenty-seven years. Had severe typhoid fever; hemorrhages; suppurative parotitis; optic neuritis. About a month from the onset of disease complained of dimness of vision. A few days later, examination showed an intense papillitis with some hemorrhage among the swollen nerve fibers; each disk strikingly dappled with rounded white spots; no changes in the retina beyond the disks; pupils widely dilated; vision reduced to perception of the hand movements; later numerous hemorrhages in the retina adjacent to papilla and no perception of light with motionless pupils. In less than three months there was considerable improvement; vision restored to 6/36; patient able to see to do her housework and go about the streets by day, though not at night.[20]

Case XX.—Man, aged fifty years. After six weeks of moderately severe typhoid fever, he complained of pain on the inner side of each elbow radiating down the ulnar side of each forearm to the little and ulnar side of each ring finger; both legs slightly swollen with muscular tenderness of calves; no paralysis. These symptoms disappeared in about two weeks. About two and a half months later the fingers of the right hand were all stiff and complete extension was impossible; marked wasting of the interossei; anesthesia, analgesia, and thermic anesthesia along the ulnar

[17] Davis, Clark W., Cincinnati Lancet-Clinic, 1889, xxii, 43.
[18] Lloyd, James H., Uni. Med. Mag., 1894–95, vii, 379.
[19] Stoney, W., Med. Press and Circ., 1889, xlvii, 562.
[20] Cattle, C. H., The Medical Magazine, 1907, xvi, 262.

side of the hand and over the ulnar distribution of the fingers; no response to faradic current. Left hand similarly affected, but to a much less extent. After three months there was no further improvement in the right hand, but the left was restored to normal.[21]

Case XXI.—Man, age unknown, recovering from typhoid fever of average severity at end of fourth week, complained of slight pain in left hand extending up the arm, pain becoming worse with numbness, flashes of heat and cold, formications, etc.; no change in electrical reaction; no change in reflexes; pain on motion; gradually were added cutaneous and muscular hyperesthesia; the left lower limb began to be involved from the thigh down. The above lasted about three weeks. Within the next ten days the hand movements became less painful, less efficacious, especially extension. Later almost complete paralysis of the extensor muscles of the hand, while flexion was very limited, the arm was swollen and edematous from the shoulder to the wrist. The lower limb showed diminution of movement of the foot on the leg. All reflexes normal. Almost complete recovery in about three months from onset of symptoms of neuritis.[22]

Case XXII.—Man, aged twenty-eight years. Five days after the temperature had become normal began to feel ill, temperature rose to 38° C. and remained high for about a week. He had severe pain in both shoulders and in the lumbar region; both lower and upper limbs were practically without motion; parasthesia and hyperesthesia very pronounced. Duration and result not given.[23]

Case XXIII.—Man, aged twenty-seven years. During an attack of typhoid fever developed pain in both knees, right became red and swollen; fluid evacuated and showed presence of typhoid bacilli. After the knee was well the muscles of both legs showed diminished function, the right more than the left; atrophy of muscles with reaction of degeneration. Recovery in about six months.[24]

Case XXIV.—Woman, aged twenty-three years. After having been ill with typhoid fever about a month she complained of pain in the right foot and then in the arm. Nothing, however, was found on examination. In ten days dorsal and plantar reflexes in right foot abolished; faradic current showed slight response on part of peroneal nerve and none in tibialis anticus on the right side. Galvanic current; response of peroneal nerve at the cathode, weaker than at the anode. The left leg was not normal either, especially as regards the faradic current. Sensory subjective phenomina became very marked, especially on the right side. Not quite well after about four and one-half months.[25]

[21] Whit, H. J., Philadelphia Med. Jour., January 19, 1901, 125.
[22] Bassi, Ugo, Revista Veneta di Scienza Mediche, 1887, vi, 585.
[23] Lozano Monzon, R., Rev. de Med. y. Cir. Pract., 1897, xli, 281.
[24] Unlig, R., Thesis, Göttingen, 1904.
[25] Schmidt, Friedrich, Thesis, Nurnberg, 1891.

Case XXV.—Man, aged twenty-five years. One week after the temperature had become normal from an attack of typhoid fever the temperature again rose to a moderate degree and the patient complained of severe pains in the legs; within a few days the pain gradually disappeared, but there developed a weakness in both limbs which within a month became a general paralysis. Examination showed some consonants not clearly pronounced; face expressionless, stary; chin dropping; eyes narrow and cannot be closed; mouth drooping, unable to whistle. Conjunctival and corneal reflexes abolished on both sides. Other cranial nerves normal. The fingers flattened; interspaces more pronounced than normally; movements normal except abduction and adduction. The feet in position of varus, general muscular atrophy; knee- and ankle-jerks lost. There was paresthesia in all the extremities; Lasegue's symptom present on both sides; deep sensibility normal; no trophic changes. Marked reaction of degeneration on both sides of the face and in lower extremities along the sciatic nerves while along the femoral nerves it was only partial. No D. R. in upper extremities. Patient in the hospital about fourteen months but ultimately made a complete recovery.[26]

Summary. I have collected from the literature 25 cases which are sufficiently fully described to be of value, which, with my own, make a series of 26. Unfortunately the duration and final result are not given in quite a number, nor are all the reports very full in other respects. There were 19 males and 6 females; in one instance the sex was not mentioned. The first symptom noted was, in 14 instances, pain; in 3, failing vision; in 2, paresthesia; in 1 each, hyperesthesia, paresthesia, swelling of the limbs, difficult speech, rigidity of joints, anesthesia, increased reflexes.

Symptoms of the condition were recognized during the course of the fever in 14 instances; after the fever had subsided in 12. The earliest was the second week of fever. It is impossible from the data to say what was the longest period after apparent complete recovery at which the symptoms of neuritis first appeared, but usually it was a few days to a week after the temperature had become normal. Pain was present 17 times, absent 9 times. There was altered sensation in 19, no change in 4, and no mention of this condition was made in 3 instances. Paralysis was noted 25 times; in one case it was not mentioned. The reflexes were lost in 9, exaggerated in 4, diminished in 2, normal in 1, and not noted in 1. Of course, it should be understood that the reflexes were variable, depending somewhat upon the stage of the attack at which the examination was made. There were no contractures in 20, while in 6 they were noted. The cranial nerves were involved in 7, not affected in 19; the spinal in 24, not so in 2, while both were

[26] Mancini, Wien. med. Wochen., 1910, lx, 1035.

Case.	Sex.	Age.	First symptom.	When noted.	Pain.	Altered sensation.	Paresis or paralysis.	Reflexes.	Contractures.	Cranial nerves.	Spinal nerves.	Atrophy.	Duration.	Result.
1	M.	24	Pain.	Convalescence.	+	+	+	Lost.	−	−	+	+	7 months.	Recovery.
2	F.	..	Pain.	Four days after normal temperature	+	+	+	Lost.	−	−	+	+	?	Not given.
3	M.	28	Hyperesthesia.	Fourth day of normal temperature.	−	+	+	?	−	−	+	+	?	Death (nephritis).
4	M.	28	Paralysis.	Fifth week of fever.	−	+	+	Lost.	−	+	+	?	?	Death.
5	M.	30	Pain.	Fifteenth day of fever.	+	?	+	Diminished.	−	+	+	?	?	Not given.
6	M.	..	Failing sight.	Six days after discharge.	−	+	+	Lost.	−	+	+	?	2 months.	Recovery.
7	M.	..	Pain.	Three days after discharge.	+	+	+	Lost.	−	−	+	?	Improved in 18 days.	Recovery.
8	M.	38	Pain.	Convalescence.	+	+	+	?	−	−	+	?	?	Not given.
9	M.	20	Swelling of limbs.	Second week of fever.	+	+	+	Diminished.	+	−	+	+	1 year.	Improved.
10	F.	..	Pain.	Four days after recovery.	+	+	+	?	+	−	+	+	5 months.	Able to walk.
11	..	15	Difficult speech.	Convalescence.	−	+	+	Lost.	−	+	+	?	?	Improvement gradual.
12	F.	18	Rigid joints.	During fever.	−	+	+	Lost.	+	−	+	+	?	Recovery.
13	M.	42	Anesthesia.	After recovery.	+	+	+	Exaggerated.	−	−	+	+	?	Not given.
14	M.	..	Increase of reflexes.	Fourth week of fever.	+	−	+	Exaggerated.	+	−	+	?	?	Recovery almost complete in five months.
15	M.	13	Paresthesia.	End third month of fever.	−	+	+	Exaggerated.	−	−	+	?	4 months.	Recovery.
16	F.	16	Blindness.	During fever.	−	−	+	?	−	+	−	−	9 weeks.	Recovery.
17	F.	30	Pain.	Sixth week of fever.	+	?	+	?	+	−	+	+	?	Not given.
18	M.	26	Pain.	After complete recovery.	+	−	+	?	−	−	+	+	8 months.	Recovery.
19	F.	27	Failing sight.	Four weeks from onset.	−	−	+	?	−	+	−	−	3 months.	Partial recovery.
20	M.	50	Pain.	Seventh week of fever.	+	+	+	?	+	+	+	+	3 months.	Partial recovery.
21	M.	..	Pain.	End of fourth week of fever.	+	+	+	Normal.	−	−	+	+	3 months.	Recovery.
22	M.	28	Pain.	Fifth day of normal temperature.	+	+	+	?	−	−	+	?	?	Not given.
23	M.	27	Pain.	During fever.	+	?	+	?	−	−	+	+	6 months.	Recovery.
24	M.	23	Pain.	Fourth week of fever.	+	+	?	Lost.	−	−	+	?	4½ months.	Recovery.
25	M.	25	Pain.	After week of normal temperature.	+	+	+	Lost.	−	+	+	+	14 months.	Recovery.
26	M.	42	Paresthesia.	Fiftieth day of fever.	−	+	+	Exaggerated.[27]	−	−	+	+	11 months.	Recovery not yet complete.

[27] Only the knee-jerks were exaggerated.

affected in 5 cases. Fourteen cases showed atrophy, 2 none; in 10 there was no mention made of the condition. The duration varied from three months to fourteen in which complete recovery occurred. Unqualified recovery took place in 11, improvement in 7, death in 2, and the result was not given in 6 cases. It must be remembered, however, that many of these reports were probably made before the final result was known, and it seems likely that quite a fair proportion of those recorded as improved ultimately recovered.

POST-OPERATIVE NERVOUS AND MENTAL DISTURBANCES.[1]

By Joseph M. Aikin, M.D.,

PROFESSOR OF NERVOUS AND MENTAL DISEASES, COLLEGE OF MEDICINE, UNIVERSITY OF NEBRASKA, AT OMAHA, NEBRASKA.

About three years ago Dr. W. B. Kern suggested that he and I secure opinions of medical men whose observation and judgment would be valuable in estimating the potency of pelvic surgery—especially oöphorectomy—in causing nervous and mental disorders. We purposed accepting the data thus obtained as the basis of a report to our State Medical Association. Out of fifteen replies received, several denied its etiologic power, a few cited cases and denied its causative power, a few cited cases and were positive of its primary etiological importance, while the majority were sure of its power to establish nervous and mental disorders, but failed in giving evidence proving their assumption. Our intended paper was not written. When your program committee wrote the theme "post-operative," without regional location on the body and notified me to try the case on its merits, I proceded to secure testimony that would incriminate the surgeon. It seemed to me the evidence was adequate to convict surgery as the direct cause for many nervous wrecks and fit subjects for our insane hospitals. I heard Dr. Alfred Gordon read a paper on "Nervous and Mental Manifestations following Castration in Women," in the Section on Nervous and Mental Diseases in the last American Medical Association meeting. The gist of Dr. Gordon's paper, corroborated by its critics, commended surgery when the pathology demanded it and the recupera-

[1] I am indebted to the following list of physicians, also Audrey Goss, of John Crerar Library, Chicago, for personal opinions and abstracts which form the data for my conclusions: H. G. Brainerd, Los Angeles, Cal.; B. F. Bailey, Lincoln, Nebr.; Charles W. Burr, Philadelphia, Pa.; Edwin N. Brush, Towson, Maryland; Alfred Gordon, Philadelphia, Pa.; J. T. Hay, Lincoln, Nebr.; A. F. Jonas, Omaha, Nebr.; W. B. Kern, Hastings, Nebr.; William W. Richardson, Norristown, Pa.; M. G. Schlapp, New York; George Tilden, Omaha, Nebr.; W. A. Searl, Guyahoga Falls, Ohio; J. H. McBride, Pasadena, Cal.; G. H. Harding, Jr., Columbus, Ohio.

tive power of the patient justified establishing the conditions necessary by that therapeutic measure. The essayist and his audience were a unit in condemning surgery as a cure for existing psychic or neuritic conditions, and censured the surgeon who neglected or ignored the alienist, neurologist, oculist, and internist when deciding for surgery on any person of an unstable nervous system. I secured a series of abstracts from papers that were published in medicial journals, both domestic and foreign, on the subject of post-operative neuroses and psychoses. Among the domestic papers the *American Journal of Obstetrics* contained an exhaustive article on alleged post-operative insanity cases. An analysis of the clinical histories there recorded failed to prove that surgery caused the mental or nervous symptoms in question. In this article was a clinical report of six cases by Dr. T. Gaillard Thomas in 1890, which attracted much attention to the subject of post-operative insanity in this country. Commenting on this report Dr. Landon Carter Gray ventured the opinion that Dr. Thomas had described a "new genus of insanity." As a matter of fact, Thomas had not described a single case with sufficient accuracy to prove that the psychic state admitted was not a logical sequence from causes other than surgery. For additional evidence to incriminate surgery as a primary cause for post-operative psychic and neuritic manifestations I obtained full abstracts from fifteen papers by German, French, Swiss, Italian, and English writers on the subject. A careful reading of all these abstracts revealed a uniformity of vagueness in their clinical reports. From a wearisome amount of testimony investigated the evidence did not prove more than a negligible percentage of post-operative mental or nervous disorders primarily traceable to surgery. One noticeable fact established by the evidence is the gradual disappearance of post-operative insanity since the advent of aseptic surgery. Cleanliness during a surgical operation is more easily obtained than we are sure will be maintained during all the after-treatment. Post-operative nervous and mental disorders are rapidly becoming an avoidable accident. Either sepsis, the administration of some drug, or poor judgment by the surgeon who operated on a patient ripe for a mental or nervous collapse caused them. Of these three possible factors the latter is probably the most frequent ultimate cause for post-operative psychoses or neuroses. If the pathology of the case warrants surgical treatment only the imminence of a mental or nervous disorder more serious than the affliction which surgery may relieve should weight against that procedure. An artificial leg may be preferable to a tuberculous joint; surgery effecting complete drainage of sepsis from a cavity, or enucleating a cancer that spells much suffering and certain death, may be more objectionable to the patient than a neurosis or psychosis from which recovery is possible. Any disorder of the nervous

system developing soon after a surgical operation is a complex affair evolving symptoms varying in degree and differing in type. It is questionable if the term post-operative insanity has any just claim as a clinical entity in medical literature. The fact that it appears in a few days or weeks subsequent to some surgical operation is alone responsible for its coinage. The same observation applies to traumatic neurasthenia, also the antepartum and lactational insanities. To that list may be added the post-typhoid neuroses and psychoses, for they are no less frequent than the post-surgical cases. The content of the nervous or mental syndrome incidental to a surgical operation, an accidental trauma or the parturient period, is not essentially different from nervous and mental symptoms evolved when no one of these conditions prevail. Removal of the germinal glands prior to the reproductive period of the animal prevents its complete masculine or feminine development, but facts are wanting to prove that it initiates nervous and mental disorders. If during the reproductive period the possibility of parentage is eliminated by gonococci or spirochetes the evidence of experience incriminates them as primary factors producing nervous and mental disorders. The cases are numerous where surgery alone relieves the already barren women of destructive and painful conditions initiated by venereal infections. It is sometimes a mark of social distinction to have undergone a surgical operation. The surgeon's knife may easily become the "scapegoat" bearing silent testimony to ease the remorse and suffering directly due to moral turpitude. If from any cause the power to conceive—or power to impregnate—is destroyed prior to its normal termination the mental impress of lost parental power certainly tends to initiate nervous and mental disturbances. I think it possible and quite probable that in the majority of post-operative nervous and mental disturbances the forces making surgery necessary were more potent than the operation in evolving such conditions. Were we to balance the evidence in which surgery established relief from nervous and mental disorders against that proving it the direct cause of them, I think the advantages from the wise exercise of surgery would far exceed the disadvantages it may precipitate.

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11. Truelle. Psychoses dites post-operatoires, Thèse de Paris, 1899.

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A STUDY OF THE URINARY NITROGEN AND SULPHUR PARTITION IN A CASE OF RHEUMATOID ARTHRITIS TREATED WITH INTRAVENOUS INJECTIONS OF RADIUM SALTS.

By Jacob Rosenbloom, M.D., Ph.D.,

PITTSBURGH, PENNSYLVANIA.

(From the Biochemical Laboratory of the Western Pennsylvania Hospital, Pittsburgh, Pennsylvania.)

I. Introduction. It is of great interest to establish the effects of radium on metabolism. This paper contains a study of the effects of radium given intravenously on the urinary nitrogen and sulphur metabolism. But little work has been done from the metabolic standpoint. Gudzent[1] claimed to have found a disappearance of uric acid from the blood after inhalations of air containing 2 to 4 Mache units of radium per hour. He also claimed the emanation of radium caused an increase in the solubility of sodium urate. Kerb and Lazarus[2] found that radium emanation had no effect on the solubility of sodium urate. Kehrer[3] claimed that radium emanation caused a mobilization of uric acid in the body. Knafll-Lenz and Wiechowski[4] found no increase in the

[1] Berl. klin. Woch., 1911, xlviii, 2098; Zeit. f. klin. Med., 1913, lxxviii, 266.
[2] Biochem. Zeit., 1912, xlii, 82.
[3] Arch. f. Verdauungs.-Krank., 1913, xix, 98.
[4] Zeit. f. physiol. Chem., 1912, lxxvii, 325.

solubility or decomposition of sodium urate by radium emanation. Fine and Chace[5] found that radium administered as the bromide and inhalation of emanation in strengths as high as 100 Mache units per liter for long periods of time failed to show any influence upon the uric-acid concentration of the blood and produced no definitely increased output of uric acid in the urine. Skorzowski[6] claimed to have found that radium therapy in the gouty leads to an increased output of nitrogen, uric acid, and neutral and oxidized sulphur.

These papers are all that I have been able to find in the literature as regards the metabolic effects of radium in man, and it may readily be noted how much work yet remains to be carried out in this field.[7]

II. Experimental. The patient on whom this study was carried out was the subject of a severe case of rheumatoid arthritis of many years' standing. Throughout the experiments he was placed on a constant diet, and the methods for the estimation of the various urinary constituents were the same as those mentioned in previous communications.[8]

Table I demonstrates that following the intravenous injections of 100 micrograms of radium element the urinary nitrogen shows a marked increase on both occasions. This increase persisted for about three days. The proportions of urinary nitrogen as urea-nitrogen, uric acid-nitrogen, ammonia-nitrogen, amino-acid nitrogen, creatinin-nitrogen, and undetermined-nitrogen remained about the same following the injections. The uric acid in grams and uric acid-nitrogen, both of which are of special interest, also show the non-effect of the radium on their excretion in the urine.

Table II shows that following the intravenous injection of 100 micrograms of radium element there was produced a marked increase on both occasions in the total sulphur of the urine, and this increase persisted for three days. On the urinary sulphur partition it may be noted that a marked increase in the neutral sulphur of the urine was produced by the radium. This effect continued for about three days following the injection. This finding of effects ceasing after three days following the injection may be considered as an indication for giving the radium about every fourth day, as by this method one would be renewing the effect that it has on the metabolism.

[5] Jour. Pharm. and Expt. Ther., 1914, vi, 219.

[6] Zeit. Expt. Path. u. Ther., 1914, xiv, 116.

[7] For biological effects of radium see London, Das Radium in der Biologie und Medizin, Leipzig, 1911; Lazarus, Handbuch der Radium Biologie und Therapie, Wiesbaden, 1913; Salomon in von Noorden, Metabolism and Practical Medicine, 1907, iii, 1220.

[8] Amer. Jour. Med. Sci., 1911, cxlii, 7; 1913, cxlvi, 731; 1914, cxlviii, 65; Arch. Int. Med., 1913, xii, 276; 1914, xiv, 263.

TABLE I.—THE URINARY NITROGEN PARTITION.

Day.	Urine. Volume c.c.	Total nitrogen gm.	Urea nitrogen. gm.	Urea nitrogen. Per cent. of total nitrogen.	Uric acid. gm.	Uric acid. Nitrogen gm.	Uric acid. Per cent. of total nitrogen.	Ammonia nitrogen. gm.	Ammonia nitrogen. Per cent. of total nitrogen.	Amino-acid nitrogen. gm.	Amino-acid nitrogen. Per cent. of total nitrogen.	Creatinin. gm.	Creatinin. Nitrogen.	Creatinin. Per cent. of total nitrogen.	Undetermined nitrogen. gm.	Undetermined nitrogen. Per cent. of total nitrogen	Remarks.
1	700	6.40	5.2	81.2	0.23	0.08	1.3	0.265	4.1	0.275	4.3	0.57	0.21	3.2	0.37	5.8	
2	700	5.10	4.2	82.3	0.27	0.09	1.8	0.204	4.0	0.206	4.04	0.71	0.26	5.1	0.14	2.7	
3	1000	7.84	6.4	81.6	0.25	0.08	1.02	0.29	3.9	0.172	2.2	0.81	0.29	3.7	0.59	7.5	100 micrograms of radium element intravenously.
4	1590	7.74	6.5	83.8	0.30	0.10	1.3	0 25	3.2	0.25	3.3	0.93	0.34	4.4	0.30	3.8	
5	1540	7.33	6.2	84.6	0.27	0.09	1.2	0.29	4.0	0.31	4.2	0.93	0.34	4.6	0.10	1.4	
6	1010	7.24	6.0	82.9	0.28	0.09	1.2	0 23	3.1	0.25	3.5	0.80	0.29	4.0	0.38	5.2	
7	1400	6.34	5.2	82.0	0.22	0.07	1.1	0.27	4.2	0.26	4.1	0.56	0.20	3.1	0.34	5.3	100 micrograms of radium element intravenously.
8	1380	7.54	6.3	83.6	0.28	0.09	1.2	0.29	3.8	0.28	3.7	0.91	0.33	4.3	0.25	3.3	
9	1240	7.82	6.7	85.7	0.34	0.11	1.4	0.26	3.3	0.23	2.9	0.93	0.34	4.3	0.18	2.3	
10	1280	7.12	6.0	84.2	0.28	0.09	1.2	0.25	3.5	0.21	2.9	0.78	0.28	3.9	0.29	4.1	

TABLE II.—THE URINARY SULPHUR PARTITION.

Day.	Urine.									
	Total sulphur.	Total sulphate sulphur.		Inorganic sulphate sulphur.		Ethereal sulphate sulphur.		Neutral sulphur.		Remarks.
	gm.	gm.	Per cent. of total sulphur.	gm.	Per cent. of total sulphur.	gm.	Per cent. of total sulphur.	gm.	Per cent. of total sulphur.	
1	0.57	0.50	87.7	0.48	84.2	0.02	3.5	0.07	12.3	
2	0.48	0.41	85.4	0.35	72.9	0.06	12.5	0.07	14.6	
3	0.80	0.56	70.0	0.51	62.5	0.05	7.5	0.24	30.0	100 micrograms of radium element intravenously.
4	0.96	0.61	63.5	0.54	56.2	0.07	7.3	0.35	36.4	
5	0.84	0.59	70.2	0.55	65.4	0.04	4.8	0.25	29.7	
6	0.76	0.69	90.8	0.57	75.0	0.12	15.6	0.07	9.2	
7	0.86	0.60	69.7	0.54	62.8	0.06	6.9	0.26	30.2	100 micrograms of radium element intravenously.
8	0.96	0.64	65.3	0.54	56.2	0.10	9.1	0.32	33.3	
9	0.94	0.62	65.9	0.52	55.3	0.10	10.6	0.32	34.1	
10	0.62	0.558	90.0	0.49	79.0	0.068	11.0	0.062	10.0	

It will be recalled that the urinary sulphur is made up of sulphates, both inorganic and ethereal, and certain less highly oxidized compounds which are called, following Salkowski's[9] suggestion, "neutral sulphur." The neutral sulphur compounds are many and include the following: Uroferric acid,[10] uroproteic acid,[11] oxyproteic acid,[12] urochrome,[13] thiocyanic acid and its salts,[14] cystin and similar substances,[15] taurin and taurincarbamic acid,[9] methyl mercaptan,[16] ethyl sulphid,[17] thiosulphuric acid,[18] and sulphurous acid.[19]

This effect of intravenous injection of radium producing such a marked increase in the excretion of the urinary neutral sulphur is of great interest. It will be recalled that Folin claims that the truest index to the endogenous or cellular metabolism is represented by the urinary uric acid, creatinin, and neutral sulphur. As we have found that the intravenous injection of radium in dosage of 100 micrograms has no effect on the amount of creatinin and uric acid excreted, it must be that the radium influences some part of the endogenous metabolism related to the neutral sulphur but not implicating the other two constituents. It may be that the radium affects the intracellular oxidation, thereby increasing the amount of neutral or unoxidized sulphur.

III. Summary. 1. The intravenous injection of 100 micrograms of radium element produced an increase in the amount of nitrogen excreted in the urine. No constant effect was noted in the percentage excretion of urea-nitrogen, ammonia-nitrogen, uric acid, ammonia-acid nitrogen, creatinin-nitrogen and undetermined nitrogen.

2. The injection also caused a marked increase in the amount of total urinary sulphur and in the amount of neutral sulphur excreted.

3. The effect of intravenous injection of 100 micrograms of radium on the nitrogen and sulphur metabolism lasted for about three days following the injection.

The writer wishes to thank Dr. W. H. Cameron and Dr. J. R. McCurdy for their coöperation.

[9] Virchows Arch. f. path. Anat., 1873, lviii, 472.

[10] Ztschr. f. physiol. Chem., 1903, xxxvii, 251.

[11] Arch. f. exper. Path. u. Pharm., 1897, xl, 29.

[12] Centralbl. f. d. med. Wissensch., 1897, p. 577; Berl. d. Deutsch. chem. Gesellsch., 1902, xxxv, 2959; Ztschr. f. physiol. Chem., 1905, xlv, 83; Pflüger's Arch. f. d. ges. Physiol., 1899, lxxv, 87.

[13] Ztschr. f. physiol. Chem., 1907, liv, 204.

[14] Proc. Roy. Soc., London, 1870, xvi, 18; Virchows Arch. f. path. Anat., lxix, 351.

[15] Ztschr. f. physiol. Chem., 1885, ix, 125; 1888, xii, 254.

[16] Arch. f. exper. Path. u. Pharm., 1891, xxviii, 206.

[17] Ztschr. f. physiol. Chem., 1894, xx, 253.

[18] Ergebn. d. Physiol., 1902, i, 458.

[19] Strümpell, Arch. d. Heilk., 1876 (quoted from Mann, Physiology and Pathology of the Urine, 1908, p. 18).

ENDOCARDITIS OF THE PULMONIC VALVE CAUSED BY MICROCOCCUS ENDOCARDITIDIS RUGATUS.[1]

By G. R. Callender, M.D.,
FIRST LIEUTENANT, MEDICAL CORPS, FORT BAYARD, U. S. ARMY.

Case.—Patient, H. K. B., aged thirty-eight years. Family and past personal history unimportant.

Personal History. On March 1, 1914, the patient had an attack of tonsillitis, lasting only a few days, which was accompanied by constipation and stiffness and soreness of muscles.

March 10. Entered the hospital with a temperature of 102°, headache, muscular soreness, and pain in the right knee and left shoulder. The pains disappeared in a few days, leaving fever, sweating, and constipation. Following this a cough developed, accompanied by a small amount of expectoration. Urine was reported negative. The blood was negative for malaria; blood cultures on March 12 and 24 were negative. Wassermann was negative.

March 17. A blood examination showed 4000 leukocytes (of which 65 per cent. were polymorphonuclears), 15 per cent. small lymphocytes, 8 per cent. large lymphocytes, 11 per cent. mast cells, and 1 per cent. eosinophiles.

March 28. Leukocytes numbered 8000, of which 88 per cent. were polymorphonuclears, 5 per cent. lymphocytes, 1 per cent. mast cells, 2 per cent. transitionals, and 4 per cent. large mononuclears. Hemoglobin, 80 to 85 per cent.

April 19. Patient was admitted to Fort Bayard. On admission the patient complained of weakness. His mind seemed to be dull. There was considerable cough. Expectoration was negative for tubercle bacilli. Temperature, 101° to 103°. Physical examination showed dulness over the anterior part of the right upper lobe and both bases. There were abundant moist rales over the posterior surfaces of both lungs.

Urine contained considerable albumin and numerous granular casts and renal cells.

May 4. Urine examination was as follows: Amount in twenty-four hours, 210 c.c.; specific gravity, 1.022; large amount of albumin; numerous renal cells and erythrocytes. Late on this date the patient died. Death was preceded by a dyspnea of rapid onset.

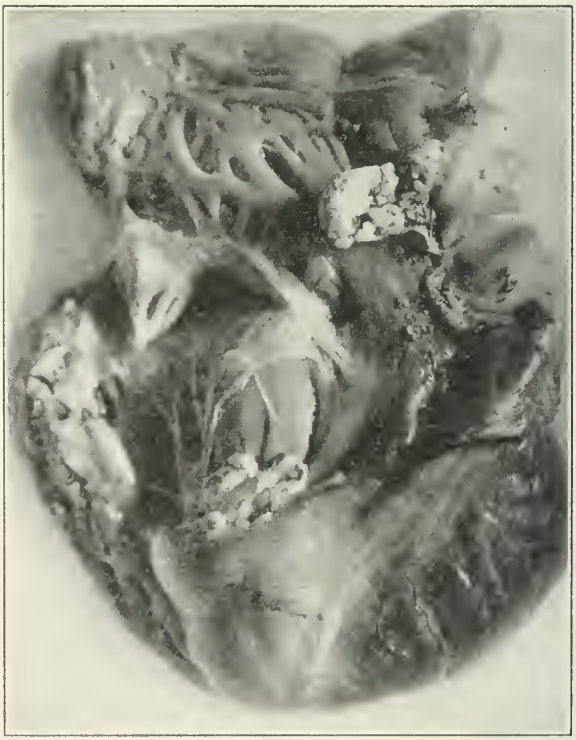
May 5. Autopsy.

Heart. Free in pericardium, which contains 125 c.c. clear amber fluid. The heart muscle is rather pale and soft and the

[1] Published with the permission of the Surgeon-General, U. S. Army.

right ventricle is dilated. The valves of the left heart and the tricuspid valve are normal in appearance, except for the large size of the tricuspid orifice.

The central cusp of the pulmonic valve presents a fibrinous vegetation adherent to the inner surface, 3 cm. in length and 1.5 cm. in diameter, of a dirty yellow color, very friable. There are smaller vegetations of a pinkish color on both of the other cusps, and the leaflets are thickened and contracted. There are numerous



Heart, showing large vegetation on central cusp of pulmonic valve and smaller vegetation on the other cusps.

small granulation-like masses on other portions of the valve on the endocardium adjacent to the valve and on the intima of the pulmonary artery. There is a clot, rather firm and friable, adherent to the larger vegetation, blocking still further the valve orifice. These vegetations are composed largely of fibrin with bacteria and leukocytes. The bases of the larger vegetations are firmly adherent by the ingrowth of connective tissue. Weight of heart, 360 grams.

Other conditions found at autopsy were healed tuberculosis of

the apex of right lung and bronchial glands; pulmonary edema; chronic and acute passive hyperemia of the liver and spleen; acute exudative and degenerative nephritis.

This case is of interest because of the unusual location of the lesion and because of the organism causing it. The diagnosis of lesions of the right heart are always difficult, but are dwelt on sufficiently in the various text-books, and will not be made the subject of remark here. Cultures from the vegetations were made on blood-agar, and the organism found to be the Micrococcus endocarditidis rugatus. This organism was described by Weichselbaum in 1889. Inoculation experiments made on dogs cause an endocarditis, while in rabbits and guinea-pigs local lesions only occur.

The writer had the opportunity of working with this organism while assistant to Professor Leary, of Tufts College Medical School. The organism was obtained from a fatal case of acute endocarditis, and various cultural tests and animal inoculations were made, though little was added to the knowledge of the organism as supplied by Weichselbaum. It was found to undergo autolysis rather easily, and resembled in this respect the Gram-negative group of cocci of which the meningoeoccus and gonococcus are members. The organism grows slowly on blood-agar, adhering to the medium in spreading, raised, tenacious colonies, of a dirty yellowish-white color with darker centres.

Smears stained by Gram's method, from the lesions, showed most of the cocci to be Gram-positive. In smears from culture the young cocci retain the stain while many of the older organisms do not, and there are numerous large involution forms produced. Old cultures kept below 37.5° C. are especially rich in large Gram-positive involution forms.

HERPES ZOSTER OF THE CEPHALIC EXTREMITY, WITH A SPECIAL REFERENCE TO THE GENICULATE, AUDITORY, GLOSSOPHARYNGEAL, AND VAGAL SYNDROMES.

By Norman Sharpe, M.D.,
NEW YORK.

Introduction. That herpetic inflammations attack the sensory ganglia of the cephalic extremity other than the ganglion of Gasser, and constitute distinct clinical entities, has been known for the past several years; yet, judging from the reports that have appeared in recent literature of herpes zoster of the face, ears, or neck, with or without motor-nerve involvement, this fact has not been generally recognized.

Herpes zoster, as an independent disease, has long been known. It was the zona of the Greeks and the cingula of the Romans. The etiology is still in doubt, but the consensus of opinion is that it is due to a specific agent. In 1863 von Bärensprung[1] first showed the lesion to be in the sensory ganglia on the posterior spinal roots; but more recently Head and Campbell developed the pathology of herpes zoster and placed it on a firm basis. Their observations were, however, confined to the glanglia of the spinal roots and the Gasserian ganglion. Still more recently Ramsay Hunt, entering a hitherto unexplored field, in a series of convincing articles, has shown that the sensory ganglion of the facial nerve (the geniculate ganglion), the peripheral ganglia of the acoustic, of the glossopharyngeal, and the vagus nerves, may also be the seat of herpetic inflammation, and has outlined a definite syndrome and zoster zones for each ganglionic distribution. These ganglia have been shown to be of the same anatomical construction and embryological derivation as the spinal ganglia and the ganglion of Gasser.

Beyond a few remarks on the etiology and pathology of herpes zoster in general, this paper will be confined to a consideration of the herpetic inflammation of the sensory ganglia of the cephalic extremity, omitting, however, the Gasserian ganglion, which has already been well and abundantly studied.

As stated above, nothing is positively known concerning the etiology of zona, but as Head and Campbell pointed out, and as others have emphasized since, the inflammatory lesion in the sensory ganglia is similar to that attacking the anterior horn cells in acute anterior poliomyelitis. It is most likely an acute infectious condition caused by a specific agent, as only those nerve structures are attacked which contain unipolar cells, of which the spinal ganglia and the Gasserian ganglion are types. Hunt's[2] work in demonstrating that the peripheral ganglia of the seventh, eight, ninth and tenth nerves, which contain unipolar cells and, like the spinal glanglia, are developed from the neural ridge and subject to the inflammation of herpes zoster, has strengthened the belief that zona is an acute infectious condition caused by a specific agent.

On account of the similarity of this condition to that of anterior poliomyelitis, Head and Campbell gave to herpes zoster the name of posterior poliomyelitis, a rather misleading term, and one which should be restricted to designating inflammatory conditions of the posterior horn.

Pathology. The pathology consists of an acute inflammation of the sensory ganglion on the posterior root, in whose skin zones

[1] Beiträge zur Kentnisse des Herpes Zoster, Charite Annalen, 1863.

[2] Herpetic Inflammation of the Geniculate Ganglion; a New Syndrome and its Complications, Jour. Nerv. and Ment. Dis., 1907, xxxiv, 73.

the vesicles are found, as Head and Campbell[3] have shown in their twenty-one autopsies, the herpetic eruption having appeared from three days to seven hundred and ninety days previous to death. In those cases in which the eruption appeared but a few day before death the affected ganglion was found swollen and edematous, the vessels intensely engorged, and small foci of hemorrhage scattered throughout the ganglion. This was accompanied by degeneration and destruction of some of the nerve cells. They also found degeneration of fibers in the posterior root central to the ganglion, and in some cases degeneration of afferent fibers in the peripheral nerve leading to the affected ganglion. In those cases in which weeks or months had elapsed between the herpetic inflammation and death there was found replacement of the degenerated cells in the ganglion by scar tissue.

Though these observers stated that the inflammatory changes were confined to the ganglion (including afferent and efferent nerve fibers) in whose skin zone the eruption was found, yet their own data show, and as Hunt has demonstrated in a case of his own, the adjacent ganglia, both above and below, show evidences of inflammation similar to that of the affected ganglion, though in a lesser degree. Therefore, although the specific inflammation attacks chiefly one sensory ganglion, with eruption in its skin zone, the adjacent ganglia do not escape involvement, though the inflammation is rarely severe enough to cause herpes in their respective skin zones. This is important to remember, especially when dealing with herpes zoster of the cephalic extremity, where the different ganglia are closely associated, as it explains those cases in which the eruption is in the zone of one ganglion, and there are complications which can be attributed only to the involvement of other ganglia.

Zona usually attacks the ganglia of one side only, and the eruption and neuralgic pain are strictly confined to the skin zone governed by the affected ganglion.

Owing to the specific nature of the affection a second attack of herpes zoster is rare, and in fact is less common than a second attack of measles. Head and Campbell found but four such cases in over four hundred. In some cases reported recently this fact seems to have been overlooked, as the reports spoke of previous attacks, and in other respects did not correspond to true herpes zoster. As Dabney[4] says, symptomatic herpes, accompanying or following caries, arsenical or other chemical poisoning, and seen in certain brain diseases, must be differentiated from true herpes zoster.

[3] The pathology of Herpes Zoster and its Bearing on Sensory Localization, Brain, 1900, xxiii, 353.

[4] Herpes Zoster Oticus, New York Med. Jour., February 7, 1914.

Formerly herpetic eruptions in the auricle were ascribed to inflammation of the Gasserian ganglion or of the ganglia of the second and third cervical ganglia; but Cushing's[5] studies of the anesthesia following extirpation of the Gasserian ganglion show that the fibers of the fifth nerve do not innervate the area in which the eruption of herpes zoster oticus is found. The sensory innervation of the ear by the fifth nerve includes the tragus, the anterior wall of the canal, and the anterior half of the tympanum. The sensory representation of the second and third cervical nerves upon the auricle is the area posterior to a line drawn from the middle of the pinna down along the edge of the helix, under the antitragus, and forward, including the larger part of the lobe. Thus there is a part of the ear, composed of the posterior half of the tympanum, the posterior wall of the canal, the concha, the antitragus, and the fossa of the antihelix which is innervated by neither the fifth nerve nor the second and third cervical. This area is innervated by fibers from the seventh, the ninth, and tenth nerves, and it is in this area that the eruption in herpes zoster oticus is found.

Hunt,[6] in his work on the pathology of herpes zoster oticus, with or without facial palsy and acoustic symptoms, and in his later work on localizing the lesions of the peripheral ganglia of the eight, ninth, and tenth nerves, and mapping out their skin zones in the external ear and in the buccal cavity, has rendered comprehensible the various symptoms presented by herpes zoster in these localities.

Symptomatology. Following Hunt's[7] classification we group herpes zoster of the cephalic extremity as follows:

1. Herpetic inflammation of the geniculate ganglion (herpes zoster oticus).
2. Herpetic inflammation of the geniculate ganglion with facial palsy and acoustic symptoms.
3. Herpetic inflammation of the auditory ganglia with acoustic symptoms.
4. Herpetic inflammation of the glossopharyngeal and vagal ganglia.
5. Herpes zoster facialis or occipitocollaris with facial palsy and auditory symptoms, alone or in combination.

1. *Herpetic Inflammation of the Geniculate Ganglion.* It has long been known that the facial nerve is a mixed nerve, having a ganglion, the geniculate, a sensory root, the pars intermedia of Wrisberg, and afferent sensory fibers in the superficial petrosal

[5] The Sensory Distributions of the Fifth Cranial Nerve, Bull. Johns Hopkins Hosp., 1904, xv, 213.

[6] A Further Contribution to the Herpetic Inflammations of the Geniculate Ganglion, Amer. Jour. Med. Sci., August, 1908.

[7] The Symptom Complex of the Acute Posterior Poliomyelitis of the Geniculate, Auditory Glossopharyngeal and Pneumogastric Ganglia, Archiv Int. Med., 1910, v, 631. (Full bibliography to date.)

nerves and the chorda tympani. The geniculate ganglion is situated on the seventh nerve just at the opening of the Fallopian aqueduct (Fig. 1). Anatomically it corresponds to the sensory ganglia of the spinal roots, like them being developed from the neural ridge and being composed of unipolar cells. In this situation in the aqueduct the ganglion, the facial, and the auditory nerves are closely associated, being contained in a common sheath. When the specific inflammation attacks the geniculate there is preherpetic pain, otalgia, more or less severe, and following this, usually two to

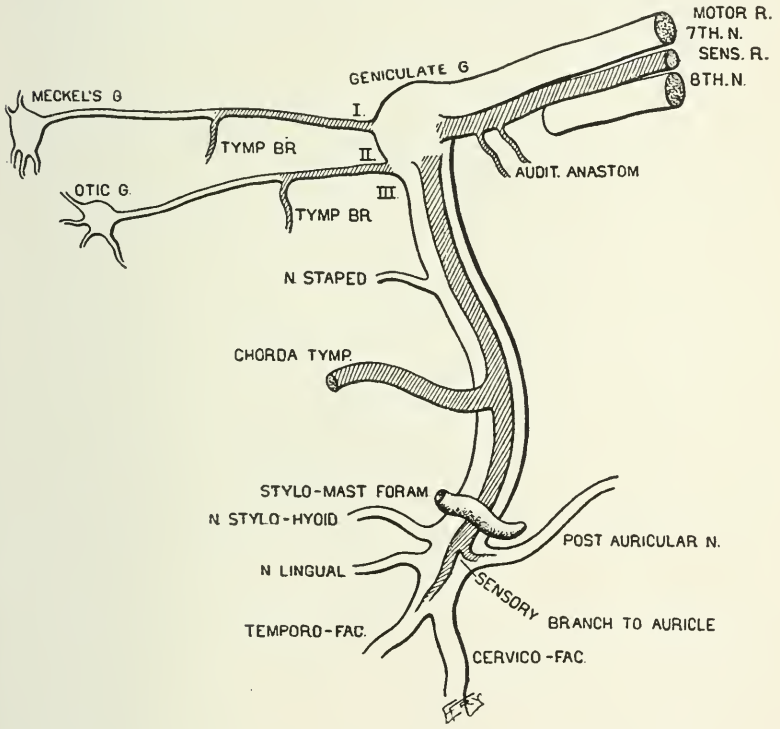


Fig. 1.

eight days, the characteristic vesicular eruption in the zoster zone of the ganglion. This zone, which is somewhat cone-shaped includes the posterior half of the tympanic membrane, exterior auditory canal, the concha, the antihelix and its fossa, the antitragus, and a portion of the lobule. If the inflammation in the geniculate extends to the facial and auditory nerves, as it is prone to do because of their close association in the internal canal, there will appear facial palsy and auditory symptoms. Dejerine,[8] who

[8] Report of a Case of Herpetic Inflammation of the Geniculate with Facial Palsy, Revue Neurol., Année 20, 1912, xxiii, 467.

has accepted Hunt's geniculate syndrome, reports a case of herpes zoster oticus accompanied by facial impairment. In his case the eruption, which was more widespread than that shown in Fig. 2, occupied a large part of the geniculate zone, being placed on the concha, the fossa of the antihelix, and the lobe of the ear.

2. *Herpetic Inflammation of the Geniculate with Facial Palsy and Acoustic Symptoms.* In the course of zona of the geniculate ganglion, if the seventh nerve is involved, facial palsy supervenes. The paralysis, which is always complete, involving all three branches of the facial nerve, may come on at the time the eruption appears or not until from five to twelve days later, showing that the disease

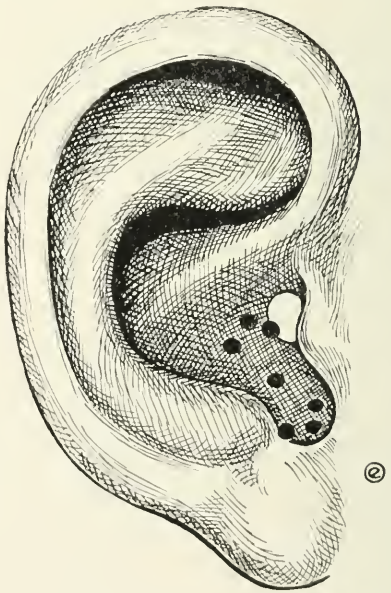


Fig. 2.—Eruption in Case I.

had not reached its height with the appearance of the eruption. Hennebert[9] has reported a case in which the eruption on the concha and on the mastoid was followed in five days by facial palsy. The auditory symptoms, which are due either to an extension of the inflammation from the geniculate to the eighth nerve in the auditory canal, or to a simultaneous inflammation of the auditory ganglia, vary from hypacusis with tinnitus to severe expressions of Ménière's syndrome (nystagmus, vertigo, nausea, and vomiting).

Muck[10] reports a case of herpes zoster of the geniculate (herpes

[9] Zona Otique, Archiv internat. de laryngol d'otol. et de rhinol., 1913, xxxv, 365.

[10] Neuritis des Trigeminus, des Fazialis und des Akustikus als symptomenkomplex eines Herpes Zoster Oticus, Ztschr. f. Ohrenh., Weisb., 1912, lxiv, 217.

zoster oticus) in which, following the eruption on the auricle, there was involvement of the fifth, seventh, and eighth nerves, as shown by the presence of hypesthesia, facial impairment, and disturbances of hearing.

Dombrowski,[11] who discusses at length the various symptom-complexes of herpetic inflammations of the cephalic extremity, also states that a similar combination may occur.

In a recent article[12] Leonard Kidd, although he does not reject *in toto* the Hunt Syndrome, denies that the seventh nerve has a sensory cutaneous zone, and says that herpes zoster oticus is not due to an inflammation of the geniculate ganglion.

He states: "Now, if we recall the fact that the geniculate ganglion of man is a swelling on the course of the facial nerve, we must conclude at once that there could be no such thing as a true isolated geniculate herpes, without, at any rate, marked paresis of the facial nerve. It is certain, then, that all those cases of herpes auris, which are unaccompanied by facial palsy or paresis are of non-geniculate origin."

If this statement were to be accepted, we could not have a limited involvement of the Gasserian ganglion—as in those cases, not uncommon, in which the zoster eruption is strictly limited to the first, second or third dividion of the fifth nerve; also, according to this hypothesis, in cases of herpes frontalis, which is a very common and strictly limited Gasserian lesion, we should expect evidences of sensory involvement in the other distributions of this ganglion. This is, of course, by no means the case, and while it may occur, it by no means necessarily follows. Also, according to this theory of Dr. Kidd's, the motor roots of the spinal nerves, and the motor branch of the fifth nerve, should show, to say the least, frequent involvement; but on the contrary, the clinical facts indicate this to be extremely rare. Therefore the clinical evidence is all in favor of the possible occurrence of a limited selective inflammation with a resulting geniculate ganglionic herpes, without facial palsy.

In reveiwing the evidence furnished by comparative anatomy, Kidd recognizes the existence of a cutaneous facial component *in cyclostomes*, but says that this has yet to be demonstrated in the higher mammals. This may be true, yet the fact that it has existed in types as high as the cyclostomes, is strong presumptive evidence of its vestigial persistence in man. And a vestigial cutaneous representation is all that Hunt has claimed for this ganglionic distribution. Kidd admits that the facial nerve may carry fibers

[11] Contribution à Él'tude de la Paralysie Faciale Zosterienne. Syndrome de l'Inflammation Herpétique des Ganglion Geniculé, Thèse de Paris, Jouve and Cie., Paris, 1912.

[12] The Alleged Sensory Cutaneous Zone of the Facial Nerve of Man, Rev. of Neur. and Psych., Edinburgh, September, 1914, 393.

from the tympanic membrane and the mastoid cells. Why, however, he should admit this much of the geniculate distribution, and deny its cutaneous vestigial remnant, is rather difficult to understand. Kidd also states "If there were any facial cutaneous fibers in man, we should find in every case of Bell's palsy as complete a cutaneous anesthesia of its alleged auricular zone as any clinician ever found on the trigeminous cutaneous area, after a complete Gasserectomy." In this statement, Kidd shows his complete unfamiliarity with the geniculate zoster zone, its outline, size and relations with its neighboring zones. He ignores the fact that the ninth and tenth nerve have representation in part of this area. He also overlooks the fact that section or inflammation of *one* posterior spinal root, will not cause anesthesia in its cutaneous zone. This applies with a special force to this part of the auricle, where the sensory supply of the seventh, ninth and tenth nerves is vestigial in character, and the different zones are small, and to a certain extent, overlap. Kidd does not appear to be familiar with, as he does not quote from it, Hunt's comprehensive study of the zoster zones of the seventh, ninth, and tenth nerves.[13]

So that this rather spirited paper of Kidd's, who has approached his subject entirely from the critical and controversial side, contains no personal contribution except a discussion of the evidence. And even then does not present all the evidence, but omits entirely a citation of the most important contribution to the subject which he is discussing.

3. *Herpetic Inflammation of the Auditory Ganglia.* Herpes zoster attacking the eighth nerve ganglia (ganglion of Corti on the cochlear branch, and the ganglion of Scarpa on the vestibular branch) causes symptoms varying in severity from hypacusis with tinnitus to Ménière's syndrome (vertigo, nausea and vomiting, and prostration). That these symptoms are due to an inflammation of the auditory ganglia and not to an extension of inflammation from the geniculate to the auditory nerve can not be doubted. As proof of this, there are the cases in which the above symptoms occur, without an involvement of the seventh nerve, which, if involved, would be evidenced by facial impairment or paralysis. Considering the anatomical arrangement in the internal auditory canal, where the facial and auditory nerves are closely associated, being contained in a common sheath, and the geniculate ganglion seated upon the facial nerve, it is not conceivable that the facial would escape were the above symptoms due to zona of the geniculate ganglion.

4. *Herpetic Inflammation of the Glossopharyngeal and Vagal Ganglia.* The zoster zones of the peripheral ganglia of the glossopharyngeal nerve (ganglion petrosum and ganglion of Ehrenritter) and of the peripheral ganglia of the vagus nerve (ganglion jugulare and ganglion plexiforme) are represented upon the auricle and also

[13] The Sensory System of the Seventh Cranial Nerve and its Symptomatology, Jour. Nerv. and Ment. Dis., 1909, xxxvi, 323.

intra-orally. On the ear their zones are placed upon the posterior half of the tympanum, posterior wall of canal, and posteromesial surface of the auricle and adjacent mastoid region. Thus the ninth and tenth nerves occupy part of the geniculate zone. As the auricular branches of the ninth and tenth nerves unite it is impossible to separate their zoster zones. Of course, where several nerves have representation in such a small area, some allowance must be made for variation and overlapping. Intra-orally it is possible to separate the zones of the ninth and tenth nerves. The zoster zone of the glossopharyngeal is placed on the posterior surface of the tongue, pillars of the fauces, and the tonsil. Zona in this region (herpes zoster pharyngis) is difficult to diagnose, for usually there are but few vesicles, and they disappear rapidly. The eruption is strictly unilateral, may be accompanied by paralysis of the soft palate, and at times facial palsy due to simultaneous involvement of the geniculate. Zona in this locality must be distinguished from pseudo-herpes, which are bilateral, are found on the soft palate, uvula, and pharynx, and are due to blocking of gland follicles. The intra-oral zone of the vagal ganglia is placed more posteriorly, at the root of the tongue, at the entrance of the larynx, and the adjacent pharyngeal region. Herpes zoster of these ganglia, with eruption in this region, may be accompanied by brachycardia, singultus, nausea and vomiting due to involvement of fibers of the vagus by the inflamed ganglia.

5. *Herpes Zoster Facialis or Occipitocollaris with Facial Palsy and Acoustic Symptoms (Alone or in Combination).* In herpes facialis or occipitocollaris, facial palsy and auditory disturbances are sometimes seen. This is due to the fact that in cephalic zona the tendency is for invasion of more than one ganglion. In this type of zoster, although the chief focus of inflammation is in the Gasserian ganglion, with eruption in its skin zone (herpes zoster facialis), or in the ganglia of the second and third cervical nerves, with eruption on the neck or occiput (herpes zoster occipitocollaris), yet the geniculate or auditory ganglia are also involved, though in a less degree, facial palsy, or auditory symptoms, occurring without an eruption in the geniculate zone. Happel[14] reports a case of herpes occipitocollaris with facial palsy, though the true connection between the inflammation in the cervical ganglia and the facial palsy was evidently not recognized. In his patient the eruption appeared twenty-four hours after the preherpetic pain, and twelve days later paralysis of the facial nerve occurred. A month later the palsy still persisted, though the eruption had long since disappeared.

Motor nerve paralysis in herpes zoster occurs in other parts of the body but is rather uncommon. This is because the spinal ganglia and the ganglion of Gasser possess fibrous capsules which separate

[14] Report of a Case of Herpes Zoster Complicated by Bell's Palsy, Episcopal Hospital Reports, Philadelphia, 1913, i, 215.

them from the motor roots. But the ganglia of the seventh, eighth, ninth, and tenth nerves have no fibrous capsules, and are in close relationship with the nerve fibers; hence, slight inflammations of the ganglia tend to involve the nerve fibers, though not always.

If the examiner be alert the diagnosis of herpes zoster of the cephalic extremity with its various symptom-complexes is usually not a matter of great difficulty. But if the true condition is not recognized much harm may be done. The pain may at times be very severe and ear drums have been incised in the belief that the condition was one of middle-ear infection, or mastoid operations have been contemplated, even in the presence of an herpetic eruption. Occasionally there are but few vesicles present, and these situated on the tympanic membrane, and they are not found unless careful search is made.

Herpes zoster is not dangerous to life, though there is a belief among the laity that if the eruption extends around the body the patient will die. It is conceivable that if a bilateral involvement of the vagal ganglia should occur it might end fatally. The darting pains that often follow an attack of herpes zoster may be quite acute and persistent and cause great annoyance (Hunt[15]).

Treatment. In the treatment of herpes zoster many remedies are advised. Zinc phosphide and quinin internally and applications of soothing ointments are most in favor at present. When the nature of the condition is considered it is difficult to see how they can do any good, and they probably have none but a mental effect. Fortunately herpes zoster is a self-limiting disease. Opening the vesicles is futile and may give rise to infection. Hot applications, and at times cold, seem to give as much relief as any other form of treatment. In severe pain anodynes may be necessary.

Report of Cases. The following case is of interest, belonging to the type most commonly seen, herpes zoster of the geniculate with facial palsy, and also demonstrating the error that is generally made, that of attributing the symptoms to middle-ear or mastoid disease.

Case I.—L. S., female, aged sixteen years. Had never had previous attack of herpes zoster. Onset November 18, 1913, with severe pain in depths of right ear and in the auricle. At the height of the pain, which was intermittent, her physician suggested mastoid or middle-ear disease, and contemplated operation. Pain markedly lessened at end of two days, at which time paralysis of the right facial nerve occurred, complete in all three branches; with onset of paralysis vesicles were found in the auricle, as noted in Fig. 2. There was no discharge from the ear, no sore throat, no nausea or vomiting.

[15] Otalgia Considered as an Affection of the Seventh Cranial Nerve, Archiv Otol., 1907, xxxvi, 371.

January 13, 1914. Came to the Vanderbilt Clinic because of the facial palsy. Examination of the right ear revealed several small pigmented scars. They were situated on the concha and also just within the canal, as noted in Fig. 2; none behind ear. She complained of sticking pains in the right ear and slight tinnitus in both ears; no hypacusis. Facial palsy was complete with R. D. Palate was normal. She said taste sense was lost on the right side of the tongue for one month following the onset of the trouble. At time of examination taste sense was normal. The corneal and conjunctival reflexes on right side were diminished. The pupils were equal and reacted to light and accommodations.

March 16. Complete paralysis of middle and lower branches of right facial. Upper branch had partially recovered. Had occasional faint pain in depths of right auditory canal.

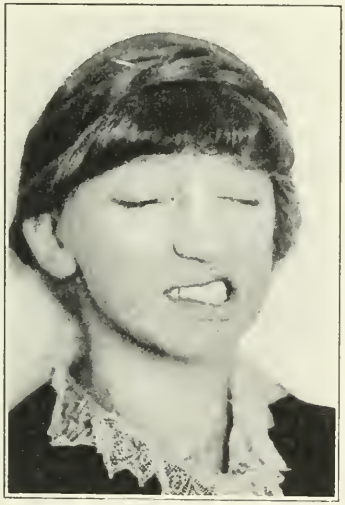


Fig. 3.—Facial palsy in Case I.

April 27. Upper branch of facial almost entirely recovered. Middle and lower branches partially recovered. Electric reactions K C C>A C C. The occasional sticking pains had disappeared. Scars on concha still visible.

Case II.—*Herpes Oticus with Facial Palsy.* Mrs. A. J., aged thirty-two years; widow. Personal and family history negative. Five weeks before present illness had a "cold," but had recovered. Felt well and was at work when present trouble began.

December 24, 1913, while at work, a paralysis of the right side of the face developed. Two days later had pain in canal of ear and behind ear, and a small ulcer appeared just behind antitragus. Had no tinnitus, no sore throat, no vomiting. Complains of a burning taste in the mouth which she refers to whole of tongue

and roof of mouth. No constitutional symptoms, and the only discomfort was pain at entrance of canal and tenderness of auricle, which lasted about three days.

Status. Pupils equal and react; hearing acute and equal on both sides; arm-jerks, knee- and ankle-jerks normal; pulse regular. Right seventh nerve paralysis, complete (can, however, close eye). Palate symmetrical; taste lost in right fifth nerve distribution. Auricle reddened and slightly swollen; in the concha, just behind the antitragus is a healing ulcer. Sense of smell normal. Other cranial nerves normal. Tactile and pain sense equal on both side of face.

January 12, 1914. No pain, and the auricle was not swollen. For several days has had considerable itching behind right ear in post-auricular (vagus) distribution. Facial innervation is almost normal in all branches. Tongue still feels rough and queer on right side.

Case III.—*Herpes Occipitocollaris with Facial Palsy.* R. M. L., male, aged sixty years. In the early part of February, 1914, he had pain in the neck and lower part of the face on left side. His neck felt as if there was a "kink" in it. Two days later an eruption of herpes appeared in the left side of the neck and over the angle of the jaw. The eruption was rather widespread, there being eighteen vesicles present. Three days after the appearance of the eruption, a left facial paralysis occurred. Hearing was slightly diminished on left side. No tinnitus. Had keen preherpetic pain, which lessened with appearance of facial palsy. Taste not impaired; no sore throat. Seen at Vanderbilt Clinic two weeks after onset of pain.

Status. General neurological examination negative. Complete left seventh nerve palsy; no nystagmus; corneal reflex present. No discharge from ear; no vesicles on or in the ear. Tactile and pain sense diminished over face and neck on left side.

Summary. The disease herpes zoster, in addition to its clinical, spinal, and Gasserian ganglia manifestations may involve other sensory ganglia of the cranial nerves. It may involve the ganglion of the facial nerve (the geniculate), the ganglia of the ninth nerve (ganglion petrosum and ganglion of Ehrenritter), and of the vagus nerve (ganglion jugulare and ganglion plexiforme). There are strong reasons for the supposition that the auditory ganglia (ganglion of Corti and ganglion of Scarpa) may be similarly involved. These ganglia may be involved singly or in combination.

The syndrome of the geniculate ganglion involvement is herpes zoster oticus, alone or with facial and auditory complications.

Herpetic inflammations of the ninth and tenth nerve ganglia occur, with herpes zoster oticus, herpes zoster pharyngis and laryngis, with pharyngeal and laryngeal palsies, occasionally with nausea and vomiting, brachycardia, hiccoughing, and other symptoms of vagal irritation.

Herpetic inflammations of the eighth nerve ganglia is indicated by symptoms referable to the vestibular and cochlear nerves; deafness, tinnitus aurium, nystagmus, nausea and vomiting, disturbances of equilibrium, the fully developed picture resembling a severe type of Ménière's disease.

The neural symptoms may be very slight, often clearing up in a few days or weeks, or they may be quite severe, leaving permanent disturbances of function.

In conclusion, emphasis is laid upon the fact that the clinical picture is by no means always limited to involvement of a single ganglion, and that multiple involvement of these ganglia is not infrequent, thus producing a great variety of clinical combinations which are readily interpreted if the fundamental pathological conceptions are borne in mind. It is by the careful study and recording of these cases that we shall achieve a definite knowledge of the sensory distribution (zoster zones) of these small and obscure sensory ganglia.

PILOUS CEREBRAL ADIPOSITY: A NEW SYNDROME.[1]

By Walter Max Kraus, A.M., M.D.,

SENIOR PHYSICIAN FOURTH MEDICAL DIVISION, BELLEVUE HOSPITAL, NEW YORK.

Many instances of genital dystrophy associated with obesity have been described since Froelich[2] first separated the syndrome from the general class of obesities, but we have not found any account of a class of cases complicated by an anomalous condition such as has been found in the following case. This condition is a marked increase of the body-hair, accompanied by a lack of the dry skin characteristic of the classical Froelich syndrome.

The case was in the service of Dr. Alexander Lambert in the medical wards of Bellevue Hospital, and it is through his kindness that I have been enabled to investigate it, and through his courtesy that I publish it.

Case.—A white man, aged thirty-one years; watchman; father living, and is alcoholic. Mother died of nephritis following childbirth. One brother died in infancy of unknown cause. One sister living and well. Other family history negative. The patient has been married since 1906. His wife is of an enteroptotic constitution, and has asthma. She has had one miscarriage and four normally born children. Three of these have died in infancy, one at twenty

[1] Presented at the meeting of the New York Neurological Society on November 10, 1914.

[2] Fall von Tumor der Hypophysis Cerebri ohne Akromegalie, Wiener klin Rundschau, 1901.

months, of meningitis; the cause of death of the others is not known. The living child is two years old and well.

Habits. The patient took from five to seven glasses of beer a day up to the present illness (1910). Smokes one to three cigars a day.

Infections. Of these the patient had measles, chicken-pox, diphtheria, and whooping cough. He has had some form of arthritis from the age of twenty-four years (1908) until one year ago (1913). The soles of the feet were sore. Later the tissues about the knees became red, swollen, hot, and painful. After several attacks there was some limitation of motion, but one year ago, after treatment at the Metropolitan Hospital, New York, the patient was cured. The joints are not at all affected now. Motion normal. Gonorrhea and syphilis denied.

Eyes. Internal strabismus of the right eye since the age of three.

Nose. Negative.

Ears. At seven an attack of otitis media followed by otorrhea, duration not recalled. After an operation (piercing the ear drum?) the trouble stopped. Hears equally well in both ears at present.

Throat. Negative.

Gastro-intestinal Tract. Negative.

Heart. Negative.

Lungs. Negative.

Lymphatic System. An attack of tonsillitis one year ago.

Kidneys. Nycturia. Once a night for seven years. One year ago the patient was at Bellevue Hospital with nephritis, edema of feet, but none of the eyelids. He says he was cured.

Genitalia. Negative.

Skeletal System. Negative.

Joints. Negative.

Skin. Negative.

Occupation. This will be noted under the account of the present illness.

Present Illness. Between the ages of three and four the patient fell from the fifth story of his residence to the ground. He says that the crown of his skull was fractured. He was unconscious for about fourteen hours. As a result of this accident he was sick for about six months. From that time until the age of thirteen the patient was entirely well. At thirteen he began to have attacks of Jacksonian epilepsy. These attacks began by a blurring of sight. Following this there were numbness and paralysis successively of the left leg, left side, and left arm, with finally a feeling of fulness in the tongue. The patient could not talk during the attacks, and after the attacks had a severe headache. Sometimes the left arm was seized by tonic spasm and was held out at right angles from the body. The patient in describing it says that "the devil himself couldn't bring it down."

These attacks came three to six times a year, and were not of

sufficient severity as to cause the patient to either tell his parents or seek the aid of a physician. At twenty-five, a little over twelve years after the first attack, the attacks ceased and have not since recurred.

In 1910, four years ago, at the age of twenty-seven years, the patient began to grow fatter. The following are his weights at this time and afterward up to the present:

Year.	Weight (pounds).
1910	150
1911	?
1912	204
1913	263
1914 (present time)	282

At about the same time as this increase in adipose tissue began, the following symptoms appeared: (1) The patient's hair began to increase over his trunk and extremities. (2) He felt sleepy and as time went on would fall asleep involuntarily in addition to sleeping a good deal voluntarily. This symptom became rather a serious matter, as the following incident shows. In 1910 while driving a large automobile beer-truck the patient fell asleep, allowing the truck to run into a saloon. This accident deprived him of his chauffeur's license. These narcoleptic attacks have continued since in addition to the hypersomnia. (3) The patient's appetite for food and drink increased. His desire for carbohydrates increased while that for fats decreased. He liked meat a good deal. He says that he always liked sweet things, but more so since he got sick. (4) He has had shortness of breath since he began to grow fatter. (5) He has sweated a good deal.

Three and a half years ago the patient noticed that his penis was smaller, and that shortly afterward (three years ago) his sexual desire grew less, until now he has none at all.

The patient says he smells, sees, tastes, and hears well. No headaches, vertigo, rhinorrhea, or fits.

Physical Examination (June 13, 1914). A white man, 5 foot $3\frac{1}{2}$ inches tall, very fat. He is up.

Eyes. React to light and accommodation, no von Graefe, Moebius or Rosenbach signs or exophthalmos or nystagmus. Right pupil larger than left; internal strabismus on the right. Tonsils are large, nearly meeting at midline. Crypts deep. Heart is normal. Pulse regular, 96 to the minute.

The skin is thick. Patient is sweating profusely. The sweat has an offensive odor. Hair in abundance covers the entire chest and abdomen (see Figs. 1, 2, 3, and 4). Legs and arms very hairy. Eczema about groins from sweating.

Penis very small. Testes small. Epididymes large.

Voice somewhat higher pitched than one would expect.

Nails. Lunulæ very small and short.

Hands. Typical "spade hands."

Fatty Tissues. Collar of fat about neck. Large jowls, supraclavicular pads and mammæ. Belly huge and pendant. Arms and legs huge with fat. (See Figs. 1, 2, 3, and 4.)

A depressed area is felt on the front of the crown of the head, about $4 \times 2\frac{1}{2}$ cm. in size.

The patient is intelligent, very jolly and good natured.

Ophthalmologic Status. Negative. Fields not reduced for form or color. Very slight blurring of nasal side of left disk.

Roentgen-ray shows a normal sella turcica.

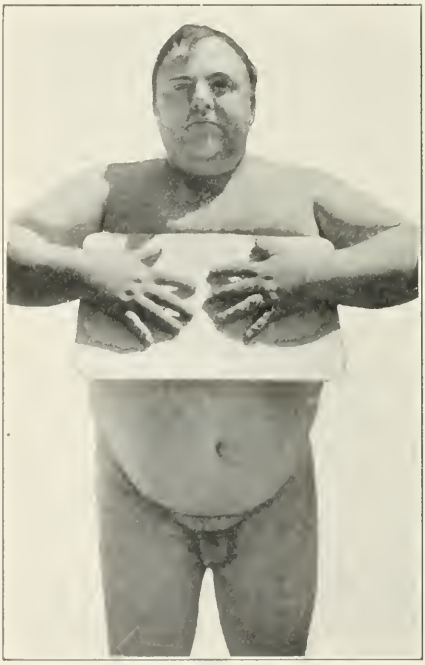


Fig. 1

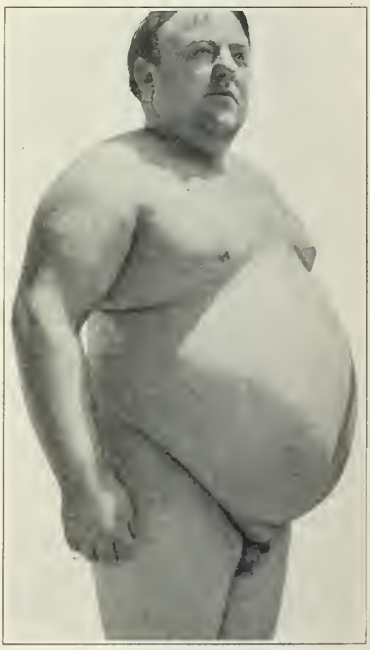


Fig. 2

Blood Examination. Red blood cells, 6,720,000; white blood cells, 10,800. Differential: polymorphonuclear neutrophiles, 56 per cent.; eosinophiles, 3 per cent.; transitionals, 1 per cent.; large lymphocytes, 19 per cent.; small lymphocytes, 11 per cent.; large mononuclears, 10 per cent.; hemoglobin, 110 per cent. (Sahli).

Blood flowed very freely and a bandage was needed after taking blood for a Wassermann.

Urine. Albumin ranged from one to six grams per day during two weeks' observation. Usually about three grams. No sugar. Many granular casts. Few white blood cells.

Carbohydrate Tolerance. 100, 150, 200, 300, 350, 400, and 500 grams of dextrose were all without effect in causing glycosuria. 700 grams, which the writer saw injected, showed a trace only of sugar in the urine.

Blood Pressure. Systolic, 170; diastolic, 120.

Wassermann. Negative.

Narcolepsy and hypersomnia were observed frequently, as the patient spent the days in the yard of the hospital.

In this case, increasing adiposity combined with genital retrogression and absent sexual desire led to the provisional diagnosis of Froelich's syndrome, adiposis genitalis.

FIG. 3

FIG. 4

Falta[3] in describing dystrophia adiposogenitalis says: "Adiposis genitalis may be considered a disease picture characterized by increase of fat in definite regions, as is found in eunuchs and eunuchoids; furthermore, by inhibition of development or by atrophy of the interstitial glands and the genital apparatus, accompanied by a corresponding inhibition of development or retrogression of the secondary sexual characteristics and the genitals; furthermore, when the disease occurs in youth, by inhibition of growth and

[3] Die Erkrankungen der Blutdrusen, Berlin, 1913.

ossification; finally, by lowering of the level of metabolism, to which may be added polyuria as a symptom of stimulation, and changes in the domain of the optic nerves, as a symptom of pressure. The etiology of this condition is a disturbance or absence of the normal functional activities of the glandular part of the hypophysis, caused by some disease-process in the hypophysis or its neighborhood."

Having defined the condition, we shall give a brief analysis of the symptoms found in this case. They may be separated into three groups: (1) hypophysial; (2) pressure; (3) unclassified.

Hypophysial: (*a*) adiposity, (*b*) high carbohydrate tolerance, (*c*) hypersomnia, (*d*) narcoleptic attacks, (*e*) genital atrophy.

Pressure: (*a*) joviality, (*b*) Jacksonian attacks, (*c*) tachycardia, (*d*) tachypnea.

Unclassified: (*a*) hypertrichosis, (*b*) bromidrosis, (*c*) blood changes.

It is difficult to form any clear conception of the basic cause of the trouble in this case. A fall on the head at four years of age, followed at thirteen by mild Jacksonian epileptic attacks, lasting thirteen years, leads one to believe that some neoplasm was present. Increasing accumulation of fat two years later points to an involvement of the glandular hypophysis, with the probability that in the interval the glandular part was gradually decreasing in power until its limit of safety was overstepped with ensuing appearance of the Froelich syndrome, complicated by atypical changes in the skin and blood. The absence of any evidence of involvement of the cranial nerves or of symptoms of a cranial neoplasm made it impossible to settle on any diagnosis other than hypopituitarism.

General Discussion. This case, though deserving of notice due to its relative infrequency, is of special interest in view of its variation from the usual type. This variation together with a few of the classical symptoms will be briefly discussed.

Hyperidrosis. The typical skin picture of cerebral adiposity due to hypopituitarism is dryness and hypoidrosis. In the above case there was *no* hypoidrosis but marked *hyperidrosis.*

Hypertrichosis. The usual condition of the hair in hypopituitarism is that of marked hypotrichosis. The female shows a diminution of hair; the male a female distribution of hair. This case therefore is quite anomalous.

Cushing[4] has reported a case (XLV) with hypertrichosis and dry skin. Therefore we have three of the four possible combinations: (1) the usual hypotrichosis and hypoidrosis; (2) Cushing's case with hypertrichosis and hypoidrosis, and (3) the case here reported with hypertrichosis and hyperidrosis. We have still to find the fourth group, having hypotrichosis and hyperidrosis.

The question of the growth and distribution of hair is but little

[4] The Pituitary Body and its Disorders, 1912.

understood. The few things which are known are in the main related to the glands of internal secretion.[5] Hypertrichosis is found in hypopinealism, hyperpituitarism (acromegaly and gigantism), hypergenitalism, and in hyperfunction of the adrenal cortex. The pre-adolescent hypotrichosis disappears as puberty begins. None of these furnish a good basis for the hypertrichosis in this case. The patient was an adult, which serves to make hypopinealism improbable. There were no ventricular symptoms, moreover, nor was the patient acromegalic. The genital functions were decreased rather than increased. There was no evidence of a lesion of the adrenal. This but serves to emphasize the difficulty in recognizing the significance of the hypertrichosis. We do not even know what causes the curious variations which we can see every day. We find men having a female type of hair on the chest and abdomen, scanty axillary hair, and yet hairy legs or arms, or both. We find men with hairy chests and abdomens and hairless legs or arms or both. We find men who look dirty after a daily shave and those who look clean before a bi-weekly shave. In women we find, frequently, an increase of hair on legs, arms, upper lips, or chins. The latter two are often, but not always, found after the menopause. There are also striking differences in the behavior of the growth and distribution of hair in men and women. The following facts suffice to emphasize this. Hypopituitarism causes the male to assume the female type of distribution of hair. The female never assumes the male type. Hyperpituitarism causes the male to become more masculine as to the distribution of hair. In hyperplastic tumors of the adrenal cortex, the male becomes more masculine in type of hair distribution, the female assumes the male type. Thus it would seem that the pituitary and the adrenal cortex, at least, have a stimulating action upon the secondary sexual characteristics which are the expression of masculinity.

Several conditions have been made responsible for the female distribution and scantiness of hair in both sexes. Among these are status thymicolymphaticus, infantilism, lymphatism, and eunuchoidism. But these are in all probability but primary conditions, causing changes in some gland or glands of internal secretion which are in turn responsible for the condition of the hair.

In fact we know practically nothing of the causes of changes in the hair either as to growth or distribution, and it seems unfortunate that a sign so easy of observation should be so little understood.

Adiposity. It seems that the fat men and women are too readily dismissed as merely such. I have seen two cases showing obesity with normal hair of late. One, a very fat man, about thirty years, who weighed about 280 pounds. Before he was eighteen he weighed about 150 pounds. His brother also weighs about 280 pounds and also was

[5] Biedl, A., Innere Sekretion, Vienna, 1913.

normal in weight before twenty-one years. I saw some three weeks before this another fat man like the above. It was striking to note how much, on casual examination, these two seemed like the case here reported. Here are two instances of *puberty obesity* due probably to a family tendency, and probably due to insufficiency of the pars intermedia of the hypophysis, the interstitial glands, the thyroid, or to some more general metabolic insufficiency. Related to this last is the obesity which turns eventually into diabetes, as von Noorden[6] has described it.

In order to recognize the cause of obesity associated with distressing symptoms, we must learn to recgonize not only the cause of fat in men and women, but must inquire carefully into their family history. It is interesting to note that Eppinger and Hess,[7] in their monograph on *Vagotonia* say that women who grow fat after pregnancy show some evidence of having had a previous condition, latent or active, of increased autonomic tonus. This is in the right direction, and though at the onset the hypotheses may be difficult of proof, some hypothesis is necessary as a basis of further investigation.

The *carbohydrate metabolism* is seriously impaired in many hypophysial dystrophies. Cushing has recorded among his cases with hypopituitarism one with a tolerance of 450 grams of levulose.

The tolerance for this sugar is about the same as that for dextrose.

The case reported was tested for tolerance to dextrose. Doses of 100, 150, 200, 300, 350, 400, 500, and 700 grams of dextrose were tried. The patient took the sugar without any appreciable discomfort, only vomiting once—with the 350 gram dose. The 700 gram dose was taken in the writer's presence. This gave a slight reduction only. This high tolerance is higher than any which the writer has noted in the literature and is in all probability the highest yet recorded.

The *blood* picture was also quite exceptional. Falta in his reported cases found the hemoglobin reduced as a rule, and no marked increase of the red blood cells. Our case showed hemoglobin of 110 per cent., red blood cells of 6,720,000. This finding lends increased interest to the case, since it is a mild, atypical instance of polycythemia.

The *narcolepsy* deserves a word of mention. Gelineau[8] described this condition in 1880. Among his cases were some of general obesity.

The *hypersomnia* is quite characteristic of hypopituitarism. Bailey and Jelliffe[9] in their article upon tumors of the pineal body,

[6] Die Fettsucht, Vienna, 1910.

[7] Die Vagotonie, Berlin, 1910, English translation by W. M. Kraus and S. E. Jelliffe, Jour. Nerv. and Ment. Dis., March, 1914, et seq.

[8] Gaz. des Hôp., 1880.

[9] Tumors of the Pineal Body, Arch. Int. Med., 1911, viii, 851–880.

state that "abnormal drowsiness or sleepiness has been characteristic in many, even in the early stages. It is probably a symptom of *increased intracranial pressure*, and furnishes, we believe, another proof that *local prsssure*, acting on the thalami, may be a cause of drowsiness, as well as increased pressure in the lateral ventricles acting on the cortex." Whether pressure accounts for the symptoms, in our case cannot be stated.

Cushing emphasizes hypopituitarism as a cause of hypersomnia, but adds that "in certain instances, however, there has been a sufficient increase of cerebral tension, due to the intracranial invasion of the growth to possibly account for the drowsiness; for the somnolence of tumor and of hypopituitarism are not unlike, and may indeed be attributable to the same cause. It is conceivable of course, that in *both conditions the somnolence may after all be due to a secondary hypophysial inactivity.*"

The presence of an abundance of hair combined with marked sweating stamps this case of cerebral adiposity as different from the classical type. And it is interesting that the skin differs in *two* of its most familiar functions.

Patients affected as above described deserve more attention, not only when they complain of distressing symptoms, but also when they are found in routine examinations. Fat, hairy men are not unusual, and although they may express no complaints, they are none the less abnormal. It is by studying not only the subjectively unwell but also the subjectively well that we have hope to complete our knowledge of both.

REVIEWS

Student's Manual of Gynecology. By John Osborn Polak, M.Sc., M.D., F.A.C.S., Professor of Obstetrics and Gynecology, Long Island College Hospital; Professor of Obstetrics in the Dartmouth Medical School; Gynecologist to the Jewish Hospital; Consulting Gynecologist to the Bushwick, Coney Island, Deaconess', and Williamsburgh Hospitals, Brooklyn, and the People's Hospital, New York; Fellow American Gynecological Society, etc. 100 engravings and 9 colored plates. Lea & Febiger: Philadelphia and New York, 1915.

The author states in his preface that this manual has been prepared primarily for the benefit of the medical student and general practitioner. With this object in view, he has purposely omitted all theoretical considerations, presenting only the essential and accepted facts in diagnosis and treatment.

The opening chapters deal with the physiology of the female genital organs and the various methods of examination applicable to gynecological work. While the more common diseases are clearly and fully described, those rarely seen are mentioned but dismissed in a few words. The two final chapters include the diseases of the urethra, bladder and ureter and the treatment of chronic constipation. Each disease is taken up from the stand-point of pathology, symptomatology, diagnosis and indications for treatment which include both medical and operative measures. The steps of the more important operations are presented in sufficient detail to enable the student to intelligently follow his course of clinical instruction. A series of excellent illustrations greatly enhance the descriptions of the text. It is by no means an easy task to boil down a subject to its fundamentals and present it in a readable style with sufficient comprehensiveness to meet the demands of the medical student and practitioner. Guided by his experience as a teacher and practical surgeon, the author has succeeded in meeting these requirements, and we can recommend the book as a valuable addition to the literature of Gynecology. F. E. K.

INFANT FEEDING: ITS PRINCIPLES AND PRACTICE. By F. L. WACHENHEIM, M.D., Attending Pediatrist, Sydenham Hospital and Mount Sinai Dispensary, New York City. Pp. 340. Philadelphia and New York: Lea & Febiger, 1915.

BEGINNING with an account of the modern teachings on metabolism, there follow chapters on breast-feeding, cow's milk and its modification, artificial feeding, disorders of digestion and metabolism, rickets, scurvy, and finally, the feeding of older infants.

This is an admirable presentation of the subject of infant feeding based upon modern conceptions. In fact, the chief basis for fair criticism would be that the author, perhaps too enthusiastically, stands for the modern view-point and is inclined to too great inflexibility in treatment. On the other hand, were a consensus of opinion available, it would probably be found that an easy majority agreed with him. The book sounds an insistent call to simplicity in milk formulæ, and to long interval feeding. The author accepts Finkelstein's teachings in great part, but, wisely, refuses unequivocal belief in the most vulnerable portion of the Finkelstein syndrome "the intoxications." He has preserved the very desirable virtue of conciseness without sacrificing the almost equally important quality of "readability." In fact, the book belongs to the class of medical works, none too large at best, whose perusal is a pleasure as well as a profit. The author is to be congratulated upon a most creditable and useful addition to pediatric literature. J. C. G.

AUGENVERLETZUNGEN IM KRIEGE UND IHRE BEHANDLUNG, MIT EINEM ABRISS ÜBER DIE DIAGNOSE UND BEHANDLUNG DES TRACHOMS. By PROFESSOR DR. C. ADAM, Priv. Doz. für Augenheilkunde in Berlin Während des II Balkankrieges; dirigierender Arzt der Augenabteilung des Militärhospitals in Belgrad. 46 Abbildungen. Berlin and Vienna: Urban and Schwarzenberg, 1914.

THE material of this brochure was obtained in the second Balkan war. It is written not for the specialist alone, but more particularly for the benefit of all physicians whose duties require them to render surgical assistance in the field and hospital. The work deals with all possible injuries direct and indirect of the eyeball and its adnexæ; it is presented in an attractive and interesting manner. Regarding the mechanism of ocular injuries, we find an excellent account of the explosive effect of bullets upon the orbit and eyeball; in consequence of the physical nature of fluid masses, the latter when enclosed by little yielding walls, are set in extremely rapid motion

and so acquire great *vis viva* when the cavity is penetrated by a shot. The movement takes place at right angles to the direction of the shot, and it is the impact of the fluid which is responsible for the injury to the hard and soft parts rather than the direct effect of the bullet itself. These effects have been established by numerous experiments upon the cadaver as well as in clinical observation. This principle serves to explain many otherwise inexplicable effects of shots to the contents and containing walls of closed cavities. The principle finds ample illustration in the pages of Prof. Adams' work; the author, indeed, was the first to apply the theory of explosive action to the special conditions of the eye.

T. B. S.

Röntgen–therapie (Oberflächen– und Tiefenbestrahlung). By Dr. H. E. Schmidt. Fourth edition. Pp. 253; 83 illustrations. Berlin: August Hirschwald, 1915.

This is a compact, comprehensive, and up-to-date little book dealing solely with the therapeutic aspect of roentgenology. It cannot be regarded as a text-book for one who is just taking up the study of this subject, but should prove itself of considerable value to the more advanced student who is about to begin work along this line. Very little space is devoted to apparatus, but all the modern methods and devices for exact dosage measurements are fully described in a concise manner. All pathological conditions in which roentgen therapy is applicable are considered briefly, the indications discussed, and the technique described. The author is to be commended for the omission of useless case reports so prevalent, as a rule, in books upon this subject. H. K. P.

General Surgery. By Prof. Dr. Ph. Bockenheimer; Professor of Surgery in the University of Berlin. Pp. 804; 1034 illustrations, including 64 colored plates. Leipzig: Dr. Werner Klinkhardt, 1914.

This is a text-book in the German language, on general surgery as distinguished from special surgery, and is based upon the material employed by Bockenheimer in his lectures in the University of Berlin. Its most striking feature is the profuseness of illustrations, which are well adapted to the purpose for which they are intended and explain the limitations of the text. It aims to introduce the student quickly to the general field of surgery, to permit the prac-

tising physician to become familiar with the approved newer ideas, and to give the specialist a clear synopsis of present-day general surgery. It is divided into three parts. Of special importance in the first part, devoted to the general surgery of operations, is a discussion of the most modern operating-room technique as well as of the newer methods of inducing anesthesia, the illustrations being employed to good effect. The second part, the largest of the three, is devoted chiefly to inflammatory and traumatic conditions, and the third part to tumors and cysts. The author does not confine himself to general surgery at all times, and this applies, particularly, to the first part, in which many valuable suggestions concerning special operations are offered. Such a book ought to be specially valuable to the undergaduate student of medicine.

T. T. T.

Outlines in Psychiatry. William A. White, M.D., Superintendent Government Hospital for the Insane, Washington, D. C. Fourth edition. Pp. 318; 6 illustrations. New York: Journal of Nervous and Mental Diseases Publishing Company.

This is the fourth edition of this well known work, which has been previously reviewed in this journal. The book has been somewhat enlarged, the new matter being an elaboration of the descriptions of the psychoses, there being, however, a new chapter added on the Binet-Simon Scale for Measuring Intelligence. One excellent addition is the inclusion of case histories which further elaborate the text. As has been previously said, for the beginner this is the best outline in psychiatry published in the English langua ge.

T. H. W.

Gastroscopy and Esophagogastroscopy. By William Hill, B.Sc., M.D. (Lond.), Surgeon for Diseases of the Throat, Nose, and Ear, St. Mary's Hospital, London. Pp. 45; 53 illustrations. London: John Bale, Sons & Danielsson, Ltd.

The author presents an historical review of the development of gastroscopy, pointing out the merits of both the oral and laparo methods, and discusses the advantages and disadvantages of the direct and indirect vision types. The blind introduction of instruments through the esophagus is rightfully condemned. The author directs attention to the improvements in gastroscopy embodied in the instrument devised by himself. On the whole the work is to be commended and the author congratulated on adding another stone to the foundation of gastroscopy.

B. A. T.

THE ANATOMIST'S NOTE-BOOK. A GUIDE TO THE DISSECTION OF THE HUMAN BODY. By A. MELVILLE PATERSON, M.D., (Edin.), F.R.C.S. (Eng.), Professor of Anatomy in the University of Liverpool; Examiner in Anatomy: University of London, Conjoint Board (Royal Colleges of Surgeons and Physicians), Indian Medical Service, etc.; Formerly Examiner in the Victoria University, and in the Universities of Cambridge, Oxford, and Durham. Pp. 351. London: Oxford University Press, 1914.

As stated in the preface, the object of this guide "is to give help to the student in the study of practical anatomy. It is intended essentially for use in the dissecting room, and is to be suplemented by means of a knowledge of osteology, and by means of a systematic text-book." Of the 351 pages, 26 contain blank outline diagrams, 149 are occupied by the text, and the remaining 176 are blank, to be filled in by sketches and notes.

Taking up the directions for dissection, we regret to see in this elementary book the omission of an outline of how to dissect. The selection of first-class instruments, the importance of keeping the scalpel sharp and the technique of honing, the proper way to hold the instruments, the correct method of reflecting the various layers, of cleaning the muscles, and of isolating vessels and nerves, could well be set forth both with profit to the student and with assistance to the demonstrator, who is very much rushed the first few days with a new class.

As to the terminology, no attempt has been made to follow the BNA. For the present we commend this, at least until medical students receive better instruction in Latin; it is better to select the more desirable term, whether it be in the new or the old nomenclature.

The book is singularly free from errors, clearly printed, and on paper suitable for sketching. The outline diagrams show by small circles where the superficial nerves pierce the deep fascia.

The book is carefully written by an antomist of experience, and if used as intended by the enthusiastic student must prove of unquestioned value in adding more permanent impressions to his cerebral photograph gallery. P. G. S., JR.

PLAIN RULES FOR THE USE OF TUBERCULIN. By R. ALLEN BENNETT, M.B. (Lond.), Physician-in-Charge, Devon County Council Tuberculosis Dispensary, Torquay. Pp. 48. New York: William Wood & Co., 1914.

WHILE taking the middle ground between the rabid enthusiasts on the subject of tuberculin as a curative agent and those who

regard it as, at best, only on trial, Mr. Bennett is a firm believer in its use in early cases. He gives simple directions and indicates his preference for the different preparations. He intimates that the presence of tubercle bacilli in the sputum is the only absolutely positive diagnostic test. This may be true, but if one were to wait for this, much valuable time would be lost, particularly in the class of patients in whom cough and expectoration is a late symptom. The rules here laid down show that there is no difficulty in giving tuberculin to ambulant patients and the simplicity of the technique should encourage those who have hesitated to use it on account of its supposed complexity. S. J. R.

Kirke's Hand-book of Physiology. Revised and Rewritten. By Charles Wilson Greene, A.M., Ph.D. Eighth American revision, with 509 illustrations, many in colors. New York: William Wood & Co., 1914.

When one pages through a physiological text-book of twenty years ago and compares it with a recent volume on the same subject the most striking difference is in the amount of histology contained. In the older works, structure is given first consideration, and only when the author feels that this is well understood does he advance to the study of function. The body is studied first of all as a mechanic would a locomotive, every component part is investigated in detail before considering its importance to the operations of the body or the machine, as the case may be. The physiologist of today assumes that the student has mastered the structure of the body, both macroscopic and microscopic, before the study of physiology is started. Curiously, however, he holds to the old method when considering the functions of the nervous system. Elsewhere he considers the subject in the manner in which an engineer would the locomotive, namely, to know at once how it works. The revision of Kirke's *Physiology* still retains evidences of the older method of teaching. But certainly the presence of this material does no harm, and undoubtedly is valuable to some students. It is true that many changes have occurred in our physiological teaching since the appearance of the first edition of this valuable text-book; nevertheless, much of the material therein found has not in any way been even modified. Here the splendid and clear presentations have not been surpassed even to the present time, justifying the frequent revisions of the book which have been made. This revision is a particularly good one, and one in which the American investigator has been well treated, for much material is taken from the products of the laboratories on this side of the Atlantic. E. L.

THE SCIENCE AND PRACTICE OF DENTAL SURGERY. Edited by NORMAN G. BENNETT, M.A., M.B., B.C. (Cantab.), L.D.S. (Eng.). Dental Surgeon to St. George's Hospital and the Royal Dental Hospital, London; Member of the Board of Examiners in Dental Surgery, Royal College of Surgeons of England. Pp. 797; 993 illustrations. New York: William Wood & Co., 1914.

IN the space allotted, a detailed review of this large volume is impossible, and is unnecessary for the readers of a medical journal. The contributors to the work may all be regarded as leaders of the dental profession in England, and the majority of them have both medical and dental qualifications. It is observed that not a few of them possess American dental degrees, and the influence of their American training is seen in the chapters written by them, and, indeed, almost all parts of the book attest the leadership of this country in dental art.

While intended primarily, of course, for the dental student and practitioner, the book nevertheless contains much matter for profitable reading by the physician. Of particular interest to the medical man and the surgeon will be found the chapters on affections of the third mandibular molar, bacteria of the mouth, diagnosis of the cause of facial pain, fractures of the jaws, oral spesis, reflex affections due to diseased teeth, and odontomes and other oral tumors. The last-named chapter is especially to be commended for its excellent classification and description of a somewhat confusing group of new growths.

While the technical side of dentistry receives its full share of attention, this happily has not been accomplished at the expense of the scientific aspect which a number of American dental books tend to treat with secondary consideration.

The book possesses in moderation the faults common to all works of multiple authorship, namely, more or less lack of harmony of style, overlapping of subjects, and in many places illogical sequence in the chapters. On the other hand, it has the advantage of expressing the views of a large number of authorities. The matter presented forms a bulky and unwieldy mass, which could with advantage have been divided into two volumes of moderate size.

In the preface the editor explains the use of certain peculiar anatomical terms found in various places in the book as being in conformity with accepted alterations in anatomical nomenclature. As a matter of fact, such terms as "inferior alveolar canal," "inferior alveolar nerve," "mandibular foramen" (for mental foramen) are not generally accepted alterations in nomenclature, and are certainly no improvement over the old terms.

The quality of the illustrations varies. Among the best are the numerous photomicrographs of Hopewell-Smith, upon whose recent acquisition as a teacher of dental histology and pathology

this country is to be congratulated. A full bibliography is given at the end of each chapter.

The book can be heartily recommended to the physician in search of reliable information on all matters pertaining to the teeth and associated parts. R. H. I.

DISEASES OF CHILDREN. By JOHN MCCAW, M.D., R.V.I., L.R.C.P., etc., Senior Physician, Belfast Hospital for Sick Children; Lecturer, Queen's University, Belfast. Pp.524; 9 plates; 14 illustrations. New York: William Wood & Co., 1914.

THE author has designed the book to fill the need for a work of "moderate dimensions and modest price." It comprises a condensed but reasonably complete description of the diseases common to infancy and childhood and is a distinct improvement upon the usual type of "compend." Apart from the personal touch given to treatment, the book appears to be chiefly a careful compilation. The author is well informed, and in the main presents the most recent accredited information upon the various subjects. Diseases of the special sense organs and the skin are not included.

J. C. G.

LECTURES ON CLINICAL PSYCHIATRY. By DR. EMIL KRAEPELIN, Professor of Psychiatry in the University of Munich. Authorized Translation from the second German Edition. Revised and Edited by Thomas Johnstone, M.D. (Edin.), M.R.C.P. (Lond.), etc. Third English Edition. Pp. 368. New York: William Wood & Co.

THIS third English edition of Dr. Kraepelin's excellent book on *Clinical Psychiatry* shows no change in the series of thirty-two lectures on the various types of nervous disease as described in the second English edition.

In order to bring the matter up to date, Dr. Johnstone has added a few short articles at the end of the volume on the serum diagnosis of general paralysis, maniacal-depressive insanity, and dementia præcox. The article on serum diagnosis of general paralysis is unsatisfactory, as the author has failed to incorporate the illuminating work of Nonne and his assistants. Dr. Johnstone succeeds better in his discussion of dementia præcox. Here he gives abstracts of the views of Meyer, Hoch, Jung, and Bolton.

The book is too well known to require further comment.

S. L.

Manual of Medical Jurisprudence, Toxicology and Public Health. By W. G. Aitchison Robertson, M.D., D.Sc., F.R.C.P.E., F.R.S.E., Lecturer on Medical Jurisprudence and Public Health, School of Medicine Royal College of Surgeons, Edinburgh. Second Edition. Pp. 560; 39 illustrations. New York: The Macmillan Company.

A very short time has elapsed since the appearance of the first edition of this typically constructed English volume. Comparatively few changes were rendered necessary. The passage of several new laws and the rapid advances made in the mechanical filtration of water called for a revision of chapters dealing with these topics.

The book should be an excellent one for the student while preparing himself for examination on these three main subjects; inasmuch as the essential features are collected in a convenient tangible order. The author is to be congratulated on assembling an immense amount of information between the covers of this volume.

A. A. H.

Tuberculin in Diagnosis and Treatment. By Dr. Bandelier, Medical Director of Sanatorium "Schwarzwaldheim" at Schoemberg, and Dr. Roepke, Medical Director of the Railway Sanatorium "Stadtwald" at Melsungen. Second English edition, translated from the seventh revised and enlarged German edition. Pp. 307; 25 temperature charts; 2 colored lithographic plates; 5 illustrations in the text. New York: William Wood & Company.

The authors have produced a most comprehensive treatise on the subject of tuberculin, considered from all stand-points. They have divided the work into three parts: (1) theoretical section; (2) section dealing with the specific diagnosis of tuberculosis; (3) section dealing with the specific treatment. The first part is extremely technical and discusses in detail the various theories accounting for the tuberculin reaction. The only one that is rejected is the non-specific theory. As far as the others are concerned the conclusion is that any one of them might be right. The theories concerning the curative action of tuberculin are dealt with in like manner. The authors disagree with Wright as to the value of the opsonic index in administering tuberculin.

In Part II they take up the various methods of tuberculin diagnostic methods and discuss them fully. They conclude that the subcutaneous test carried to the point of obtaining a focal reaction is the most satisfactory in adults. They affirm that the possibility of harm from the focal reaction is a negligible factor even in children.

Part III embraces a comprehensive survey of the various forms of curative tuberculin so complete as to make for confusion. Of these there are essentially only two forms: old tuberculin preparations, of which they find the albumose-free tuberculin (A F) most successful, and the bacillary preparations. Of the latter the sensitized bacillary emulsion (S B E) is the best. They conclude by urging its use in the treatment of all cases in some form or other and say that the general practitioner should not hesitate to use it in the ordinary ambulant type. S. J. R.

Embolism and Thrombosis of the Mesenteric Vessels. By Leslie B. C. Trotter, M.A., B.C. (Cantab.). Pp. 143; 6 illustrations. Cambridge University Press.

The work is a thesis written for the degree of M.D., Cambridge. The theme was suggested to the author by the occurrence of two cases at the University College Hospital during his tenure of office as house surgeon in 1910. He reports not only these two cases, but five others unreported before. He also includes statistics compiled from the analyzed records at Cambridge as well as statistics quoted by other writers.

The monograph is unusually complete, well arranged, and while a bit drawn out is probably no more so than is required for clearness. The lesions discussed are more or less obscure and often overlooked because of their apparent rarity in medical practice as well as because of their difficulty of diagnosis.

A perusal of this work will convince the reader that they are not so rare as previously thought, and will give him points which should help him in their diagnosis and in an intelligent understanding of their etiology and pathology. F. H. K.

A Manual of Bacteriology, Clinical and Applied. By R. Tanner Hewett, M.D., F.R.P.C., D.P.H. (Lond.), Professor of Bacteriology, University of London. Fifth edition. Pp. 668; 26 plates and 69 figures in the text. St. Louis: C. V. Mosby Company, 1914.

This book is intended as a laboratory guide for the student of bacteriology, and it serves the purpose very well in many particulars. It is well illustrated, printed in clear type, and has a serviceable index.

General bacteriological technique is outlined in the first four chapters. The fifth chapter is devoted to infection and immunity;

three chapters to saccharomycetes, hypomycetes, and the protozoa; two chapters to diseases known to be infectious in which the organisms are as yet not definitely known or classified; one chapter to bacteriological analysis of water, air, soil, sewage, and foods; and the final chapter to disinfection.

In discussing the various infectious diseases, special paragraphs are generally devoted to the consideration of pathogenesis, to toxin production, and to antiserum production. In the discussions on pathogenesis it is especially interesting to note that the author at once proceeds to inform the student with regard to the pathological conditions produced in man without confusing him with lengthy discussions of the experimental study of the disease processes induced in experimental animals, as is often the case in other text-books.

At the end of each chapter is given a section on clinical examination, in which are outlined the various steps which will aid the student in making bacteriological diagnosis. These sections are very valuable.

Several criticisms may be offered, namely, that the term "inoculation" is used when reference is made to the injection of toxins. The other criticism has reference to the citation of the earlier work on the separation of bacterial toxins from cultures. These are substances resulting from the decomposition of proteid matter. The student is left under the impression that the substances found (ptomains) have a relation to the disease-producing properties of the bacteria. This is not the case, as the substances referred to, in all probability, do not occur during the natural course of infection.

D. H. B.

The Student's Hand-book of Gynecology. By George Ernest Herman, M.D., F.R.C.F. (Lond.), F.R.C.S. (Eng.), Consulting Obstetric Physician to the London Hospital, etc. Second Edition, Revised by the Author with Additions by R. Drummond Maxwell, M. D. (Lond.), F.R.C.S. (Eng.), Assistant Obstetric Physician to the London Hospital, etc. Pp. 587; 6 colored plates and 194 illustrations in the text. New York: William Wood & Company, 1914.

The second edition of this book is issued in coauthorship with R. Drummond Maxwell, who has made some additions during the revision. Avoiding the form of a quiz-compend, the subjects have been handled briefly and concisely. Considerable space is given to symptomatology, to diagnosis, and to local treatment and palliative procedures. The underlying principles of operations are stated rather than any detail of technique. As is necessary in a book of this scope all speculative points are omitted and the book seems admirably suited for its intended purpose, the use of students.

F. P. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLIFTON SPRINGS SANATORIUM AND HOSPITAL, CLIFTON SPRINGS, NEW YORK.

An Experimental Study of the Effect of "Roentgenized" Serum on the Blood.—J. Glaubermann (*Münch. med. Wchnschr.*, 1914, lxi, 1867) has repeated some of the experiments of S. Wermel on the effect of blood serum exposed to Roentgen-rays (*x*-serum) when injected into the body. His experiments have been carried out on rabbits. He finds that the subcutaneous injection of *x*-serum produces characteristic changes in the blood. After a prompt leukocytosis of short duration, there is a temporary leukopenia, which reaches its maximum in one and one-half to two hours, and then gradually disappears in the course of the following twenty-four hours. There is also observed a rather marked lymphopenia, which gradually increases and is maximal at twenty-four hours. Comparison of the findings after injection of *x*-serum with those obtained by other observers after direct exposure of the organism to the rays shows a striking similarity. In each instance leukopenia and lymphopenia are found; the only difference seems to be that the reaction is more prompt after injection of *x*-serum and its duration shorter. With *x*-serum one has to deal with two antagonists, *i. e.*, the serum which causes a leukocytosis, and the Roentgen energy which works in the opposite manner.

The Influence of Menstruation on the Concentration of Glucose in the Blood.—H. Kahler (*Wiener klin. Wchnschr.*, 1914, xxvii, 417) has found a change in the concentration of glucose in the blood of patients during the menstrual period which, if substantiated by the work of others, must be borne in mind in studies of the blood sugar in females. In his determinations the author employed Bang's micro-method. He

found in the majority of the twenty-two patients examined (no normal individuals) that there was a well-defined rise in blood sugar which occured just before or during the menstrual period, usually followed by a drop, with the cessation of the bleeding, to the normal or to values which, for the given individual, may be looked upon as subnormal. In more than half the cases the variation between the highest and lowest readings amounted to 0.03 per cent. The author believes, therefore, that hyperglycemia is probably a physiological feature of menstruation in most women. Menstruation is so complex physiologically that the cause of the hyperglycemia is not at all clear. That it may be related to change in hepatic function the author thinks is probable, the more so since Chvostek has found evidence of hyperemia of the liver during the menstrual period.

Studies with the Abderhalden Test in Helminthiasis.—E. Manoiloff (*Wiener klin. Wchnschr.*, 1914, xxvii, 269) has tried the Abderhalden test in patients infected with intestinal parasites to determine whether enzymes specific for the parasites are present in the blood sera of the hosts. Substrata were prepared from Tenia solium and from Ascaris lumbricoides. The technique as described by Abderhalden was rigidly adhered to. In all, eighteen patients infected with tenia solium and four with Ascaris lumbricoides were examined. The reaction was marked and was specific in each case.

Studies with the Phenolsulphonephthalein Test.—O. Hess (*Münch. med. Wchnschr.*, 1914, lxi, 1835; 1874) gives the results of a study of the phthalein test in 300 cases of renal disease. The test he has found eminently satisfactory. It exceeds all previously described tests in simplicity and accuracy. The fact that it may be employed without previous preparation is a great advantage to the practitioner. He has found the test especially helpful in diagnosing chronic interstitial nephritis in cases where the clinical picture of the disease was not fully developed. He also finds that the severity of the disease it usually closely parallel to the phthalein elimination, and that the test is, therefore, of great value in prognosis. In acute nephritis, the author says, one must be cautious in drawing conclusions from the results of the text; however, he has found in the prognostically unfavorable cases that there is usually a marked decrease in the output of the dye. In unilateral renal disease the author's experience again coincides with that of the great majority of workers in establishing the value of the test. The author gives a comprehensive review of the literature. Many, if not all of the discordant results he attributes to errors in technique, mistakes in the collection of the specimens for examination, or to the use of unreliable preparations of the dye.

Studies on the Granular Form of the Tuberculous Virus.—S. Weiner (*Münch. med. Wchnschr.*, 1914, lxi, 1838) has made parallel examinations of 1050 specimens of tuberculous sputa for the acid-fast (Ziehl) organisms and for the granular bacilli first described by Much. The study extended over a period of a year and involved seventy-five patients who were under constant observation. In a large percentage of the tuberculous patients the granular virus was alone discovered. Acid-fast bacilli were not demonstrable, even with antiformin. Animal inocula-

tions from sputa showing only the granular bacilli gave positive results in fifteen of eighteen experiments. The tubercles in the infected guinea-pigs showed the granular bacilli only. In cases of tuberculosis which were improving the author was able to observe the change from acid-fast organisms which were originally present to the granular form of bacillus. Such observations were recorded not only in early cases but also in some advanced cases which yielded to treatment by means of artificial pneumothorax. In one of the latter, though the patient had been clinically cured for several years, Much's granular bacilli were still present in the sputum. These granular forms the author looks upon as a more resistent but less highly infectious form of the tubercle bacillus, the acid-fast organisms being the more active, vegetative form. In recurrences or in patients who are failing, granular bacilli may give way to the acid-fast organisms. The granular virus appears to be less toxic to the organism and more favorable from the standpoint of prognosis than the acid-fast form. For diagnosis and prophylaxis it is especially important to recognize the granular form, which is readily demonstrable, the author says, by Knoll's modified double staining method.

Studies of the Blood in Pertussis.—W. Schneider (*Münch. med. Wchnschr.*, 1914, lxi, 303) has studied the blood in a series of patients with pertussis, most of whom were under six years of age. Like others, he has found characteristic changes which make their appearance with the catarrhal symptoms. There is a leukocytosis which continues to the third week, averaging 27,100; it gradually falls with improvement of the patient. The highest leukocytosis in an uncomplicated case was 39,400, in a complicated case 85,800. The lymphocytes were relatively increased during the first week, in all 58 to 63 per cent. on the average. The highest percentage was 86. The large mononuclears and transitionals showed a slight increase, usually 6.2 per cent., never more than 10 per cent. This blood picture the author finds very valuable for diagnosis but of no assistance in prognosis.

Adrenalin Glycosuria in Man.—A. Landau (*Ztschr. f. klin. Med.*, 1914, xcvii, 201), has made observations on carbohydrate metabolism in nine individuals under the influence of adrenalin injected subcutaneously. He finds that the administration of 150 gm. glucose causes a distinct increase in the sugar content of the blood; this, however, is usually not sufficient to produce glycosuria. Glycosuria ensues, together with marked hyperglycemia, if a considerable quantity of glucose or of carbohyhydrate containing glucose is given and is followed by an injection of adrenalin. On the other hand if levulose is substituted for glucose the administration of adrenalin now causes no glycosuria. Landau finds that the diuretic property of adrenalin is quite distinct from its effect on sugar metabolism. Small doses of cocaine increase the effect of adrenalin on glucose, leading to more marked hyperglycemia and glycosuria. Pantopon injected with the adrenalin prevents the diuretic effect. This inhibition is produced in two ways: on the one hand pantopon retards the mobilization of the liver glycogen, and on the other it lessens the glycosuria by diminishing the secretory activity of the kidneys.

The Excretion of Uric Acid in Non-gouty Polyarthritides.—M. Ljungdahl (*Ztschr. f. klin. Med.*, 1914, xcvii, 177), has made an investigation of the uric-acid excretion in chronic non-gouty arthritides. He finds that the peculiarities of uric-acid excretion which were supposed to be characteristic of gout are not specific in the sense that differential diagnosis can be made on this basis alone in doubtful cases. Low values for endogenous uric acid may be observed quite constantly in chronic polyarthritides, regardless of their origin. The quantities of exogenous uric acid vary so markedly and so irregularly that they are quite valueless for diagnostic purposes. The time of excretion of exogenous uric acid seems to be less in the non-gouty than in patients afflicted with true gout. Nevertheless, this difference is neither sufficiently regular nor striking to be of diagnostic significance. Therefore, it is not possible, Ljungdahl concludes, to determine whether a polyarthritis is gouty or not by studying the excretion of endogenous and exogenous uric acid alone.

The Diagnostic Value of Pepsin Determinations in Organic Diseases of the Stomach.—C. Singer (*Deutsch. Arch. f. klin. Med.*, cxi, 188) has used a modification of Fuld and Levison's edestin method in studying the peptic activity of the gastric juice in more than 300 cases of organic disease of the stomach. The present conclusions are based on observations made only on cases where a histological diagnosis was possible. Singer finds that the peptic index and the chloride secretion usually vary in the same direction; exceptions to this rule result from a relatively greater reduction of the peptic index. In the early stages of duodenal ulcer the peptic index is usually high (over 60) and the chloride secretion is also high (above 6.0). According to the author's experience this relation observed in duodenal and gastric ulcers is practically pathognomonic. In the later stages of duodenal ulcer, or with complications, the peptic index may fall; in very chronic cases there may also be a decline in the chloride secretion. Cases of pyloric ulcer usually follow the same rule as duodenal ulcer but in the former the peptic index is usually lower. Cancer of the pylorus as a rule causes only a slight lowering of the peptic index and of the chloride secretion. In early cases the chloride secretion may even be increased. Gastric cancers which extend from the pylorus to the lesser curvature always cause a marked lowering of the peptic index (10) and nearly always a decrease in the chloride secretion (3).

The Diagnostic Value of the Determination of the Colloidal Nitrogen in the Urine.—G. Lehmann (*Deutsch. Arch. f. klin. Med.*, cxii, 376) has investigated on a fairly extensive scale the colloidal nitrogen of the urine. Salkowski has called attention to the importance of a relative increase of the colloidal nitrogen in the diagnosis of cancer. The author finds that this is not characteristic of cancer alone and arrives at the following conclusions: The Salkowski-Kojo quotient, *i. e.*, the relation of colloidal nitrogen to total nitrogen, is often high in cancer and in tuberculosis. This quotient may be definitely affected through the diet. In cancerous patients it is possible to change a high quotient to a low one by a purin-free diet, while in normal individuals the administration of purin bodies, such as sodium nucleinate

so alters the quotient that it may be confused with that which has been considered typical of cancer. Lehmann concludes, therefore, that without regulation of the diet, the Salkowski-Kojo quotient is entirely worthless in the diagnosis of carcinoma. Whether it may be possible, through the use of a fixed diet, to obtain values which will be serviceable in diagnosis remains to be determined.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The Diagnosis of Cancer by Means of the Abderhalden Dialysis Method.—Cytronberg (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1914, xxviii, 243) says that his investigations show that the Abderhalden carcinoma reaction is in the highest degree specific. He was not without failures in his results for the occurrence of which, unfortunately, no sure explanation has yet been given. We know that the practical value of the method is now only limited even in the hands of the skilful. On the other hand a whole series of experiments often showed no failures in diagnosis which cannot be attributed to accident. A positive carcinoma reaction in small skin cancer shows that an early diagnosis in cancer is possible by means of the dialysis method. These results were always proven by controls and by the clinical course. Although the practical value of Abderhalden's carcinoma reaction is still limited owing to the occurrence of certain errors, yet the correctness of the principle of the reaction is confirmed by Cytronberg's experiments.

Lymphatic Leukemia with Special Reference to the Large Cell Forms.—Nakamura (*Deutsch. Ztschr. f. Chir.*, 1914, cxxxii, 275) made a careful clinical and microscopical study of a case which came to autopsy, in which a tumor developed on the forehead after an injury. An acute large cell lymphatic leukemia developed. The primary, apple-sized, lymphoid tumor formation in the frontal region developed in connection with a light trauma. There were found numerous mitoses in the frontal tumor as well as in the lymph nodes and infiltration foci in some of the abdominal organs as the liver, spleen and kidneys. There was an exceedingly marked increase of the large lymphocytes in the blood. The lymphoid collections were always demonstrable in the tissues surrounding the bloodvessels in the above-mentioned organs. The

lymphoid cells infiltrated first the adventitia or the adventitia and media and finally reached the intima which was often absent, permitting the lymphoid elements to reach the circulation. This gives rise to the typical lymphatic leukemia. As long as the vessel walls are not broken through we have pseudoleukemia or aleukemic lymphomatosis. The aleukemic lymphomatosis is therefore a species or the beginning of lymphatic leukemia, since between leukemia and aleukemic lymphomatosis there is only a quantitative and not a qualitative difference. The tumor growth in leukemia is the result of the specific leukemia toxin and does not belong to the category of malignant tumors. Between Sternberg's leukemic omatosis and Kundrat-Paltauf's lymphosarcomatosis, there is an intimate relationship with a more gradual difference. The lymphatic blood change is brought about by a dissemination of the lymphocytes in consequence of a pathological growth due to the influence of a specific leukemic toxin. The lymphocytes deposited finally make their way into the blood. Sternberg's leucosarcomatosis has an intimate relationship with myeloleukemia.

Diagnosis and Treatment of Osteomyelitis.—Clofton (*Surg., Gynec., and Obst.*, 1915, xx, 6) says that the earliest symptom of osteomyelitis is pain in the shaft of the long bone (usually near the end), accompanying septic symptoms. In a few cases of profound sepsis, pain sense is lost. Soon there is swelling of the shaft near the joint, frequently at the epiphyseal line. At this stage the joint is not involved. Septic arthritis usually is an intense infection with less pain and several joints involved. Tuberculosis is a chronic disease that involves the epiphysis, and syphilis may give a similar picture. The Roentgen rays are of great value, except at the onset of the infection. The treatment in the acute stage is to drain to the centre of the medulla by removing a narrow channel of bone along one side of the shaft. Gutta percha tissue is used to drain this channel. The medulla should never be "cleaned out," as it is needed for the endosteal regeneration. In the subacute or chronic stage of osteomyelitis of the femur or humerus, treatment is planned to allow the shaft to heal after efficient and sufficient drainage. If sequestra have formed, these are removed, and the cavity wiped out with gauze. It is best not to curette these cavities or to attempt to sterilize with antiseptics. The iodoform beeswax of Mosetig-Moorhof is introduced into the cavity to act as a drain which is partially absorbed and partially extruded. Gauze should never be used as a drain in either the acute or chronic stage. Where one bone of the forearm or leg is involved (and at times the humerus), the treatment suggested by Nichols is followed. The shaft is removed superiosteally about five or six weeks after draining the acute infection. The periosteum at this time should show a sufficient thickening to cast a shadow on the Roentgen-ray plate. After removing the shaft the periosteum is sutured into a ribbon joining the ends of the remaining bone, and from this periosteum new bone is formed to replace the diseased shaft. In the meantime the bone supports the limb in its proper position. In about four months the new bone can support weight. The forearm can be used in less time. In a small proportion of badly infected cases, bone does not regenerate completely after removal of the shaft, and bone transplantation has to

be resorted to after healing is obtained. Chronic localized osteomyelitis cavities in the cancellous bone may be treated by healing under blood clot, or draining with Mosetig-Moorhof wax, after the bone detritus has been removed with rongeur and gauze.

Dislocation of the Semilunar Bone, with a Report of Eight Cases.—Runyan (*Surg., Gynec., and Obst.*, 1915, xx, 60) says that careful examination of all carpal injuries, and multiple Roentgen-ray plates, are necessary for diagnosis. Closed reduction can be accomplished in about one-half of the recent cases by the method of hyperextension followed by flexion while counter-pressure is maintained over the dislocated semilunar. Prompt diagnosis and treatment are essential in obtaining good results. The more speedily the dislocation is recognized and reduced, the better the result. Closed reduction should always be tried, irrespective of the length of time the dislocation has existed. Closed reduction being impossible, an anterior incision should be made and the dislocation reduced. Failing in this, it is necessary to excise the semilunar, but excision should be done only as a last resort.

Observations on Cerebral Surgery.—Kenyon (*Annals Surgery*, 1915, lxi, 17) reports on his personal experience during the last fourteen years in 160 cerebral operations of various kinds on every region of the head. He emphasizes early diagnosis, accurate localization and early operation in all cases, traumatic and pathological, before irreparable damage is done to the brain from hemorrhage, edema, blood clot, sepsis or prolonged pressure. A tumor should be removed before it has increased to such a size as to render its removal impossible. A method of procedure should be selected which combined exploration, radical removal or decompression, as the lesion seems to indicate. The skull should be opened by a large osteoplastic flap so that the intracranial condition may be accurately inspected and radically dealt with if that seems advisable. It gives the largest possible exposure without increasing the duration or the dangers of the operation. It enables the surgeon to combine in one operation exploration, radical treatment of the lesion, and also all the benefits of a decompression, if that be indicated. It provides by its accurate fit a restoration of the protecting cranium. Quoting Tooth, he says "Severe shock at the first stage is not generally repeated at the second stage and is therefore probably due to bone removal," Accordingly, anything which lessens the danger of this first stage should be adopted. The cutters best adapted for the making of an osteoplastic flap are the burr drill and the Doyen circular saw protected with washers. The power to operate these cutters is best obtained by using a small electric motor, light enough to be held by the operator, so constructed that the casing and wire may be removed for sterilizing, either by boiling or in steam. Continuous suction applied through a tube of appropriate size and shape furnishes a good retractor for the soft friable tumor mass. Continuous suction applied through a suitable tip, preferably a small malleable, metal tube which can be easily bent, is a most valuable adjunct to sponging and aids in furnishing a clear operative field, free from blood and cerebrospinal fluid. This is particularly useful

in operations on the Gasserian ganglion and for lesions in the cerebellar pontine angle, where the small size of the tube in the wound does not interfere with the operator although the wound is narrow and deep. Good illumination is most important when the wound is narrow and deep. This is best obtained by using a cystoscopic lamp on a long flexible holder, all of which, including the wire, should be sterilized.

The Injection Treatment of Infected Joints.—Cone (*Amer. Jour. Orthop. Surg.*, 1915, xii, 502) first used carbolic acid in the treatment of gonorrheal arthritis in 1893, injecting four drops of pure carbolic followed by ten drops of alcohol. He reports a series of cases in which he later changed to a 5 per cent. carbolic solution in alcohol. His present technique is as follows: It is always best to aspirate some of the joint fluid if under considerable tension. Select a point of marked fluctuation for injection. Use a long ordinary hypodermic needle that screws on. Anesthetize and clean the surface at the same time with pure carbolic followed by alcohol. Inject the carbolic, unscrew the syringe and fill with alcohol, injecting this in the needle in its original position. He uses 5 per cent. carbolic followed by alcohol as a rule, but does not specify the quantity injected. When he desires adhesions pure carbolic is used. It has been noted in the cases, in which the joint was operated on after the injection treatment had been tried that the pure carbolic forms lumps of caseous pus in the joint and does not seem to spread throughout the joint as does the weaker solution. From the results of treatment by this method it would seem that the method is most reliable in all cases where there has been no disorganization of the joint and the case is treated before extensive pus formation. Gonorrheal joints respond most readily. In tuberculosis there is no conclusion to be drawn, as we cannot tell how little has occurred, but since the bad cases did so well when operative interference was resorted to at least it would be well to use this treatment as part of the conservative fixation method. The same may be said of badly infected joints; the carbolic can do no harm and aids the favorable outcome of subsequent operative measures. One most striking point in this method is emphasized; no untoward results have occurred in its use—nothing but good resulting.

Experimental Contribution on Cholelithiasis.—Aoyama (*Deutsch. Ztschr. f. Chir.*, 1914, cxxxii, 234) says that if the cystic duct is ligated in healthy animals (rabbits and guinea-pigs), characteristicly formed elements develop in the gall-bladder. Whether this has anything to do with genuine stones is questionable. In one out of fourteen such experiments in rabbits a concrement similar to pure cholesterin was formed. To explain it an anomalous metabolism, a form of cholesterin diathesis, must be assumed. When rabbits or guinea-pigs are injected subcutaneously with cholesterin or the oleic acid of cholesterin and the cystic duct is ligated or narrowed, granules of a substance very much like cholesterin are deposited in the gall-bladder. This process is completed without the association of bacteria. The administration of cholesterin or the oleic acid of cholesterin by mouth leads by the same process to the same result. This fact teaches us that we should avoid food rich in cholesterin, especially that which disposes to chole-

lithiasis. Stagnation must be regarded as a causative factor in the formation of cholesterin stones. The gall-bladder plays a certain active role in the formation of stone. The results of these experiments explain to a certain extent the varying frequency of gall-stones in different countries. The formation of pure cholesterin stones needs no preceding metamorphosing process. It can develop as such from the beginning.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

Neosalvarsanized Serum in the Treatment of Syphilis of the Nervous System.—Yurari (*Wien. klin. Wchnschr.*, 1914, xxvii, 1207) has had excellent results with the intraspinal injection of neosalvarsanized serum according to the method of Swift and Ellis. He reports 10 cases in detail, in six of which number the cell count was markedly reduced. The Nonne reaction also subsided promptly, but the Lange and the Wassermann reactions were the last to be influenced. Clinically all of the cases showed improvement in the subjective symptoms; pains seemed to be especially favorably influenced. Naturally those symptoms dependent upon anatomical changes in the nervous system were not influenced.

The Specific Action of Salicylates in Acute Articular Rheumatism.—Miller (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1107), in the summary of his article, states that inasmuch as salicylic acid after absorption circulates and appears in the tissues as a salicylate, it cannot act as a germicide unless the increased carbonic acid tension in the joint, the result of inflammation, reconverts it into salicylic acid. Statistics show that patients receiving salicylate are free from pain much earlier than those not treated. Miller says that as the treated patients much more frequently relapse than the untreated, however, the total duration of pain in the treated and untreated patients may not be materially different. The period of stay in the hospital of patients receiving salicylate and of those receiving other forms of treatment is the same. Cardiac complications are not less frequent since the use of salicylates. Miller found that in rabbits the prophylactic use of salicylate is of no value in preventing arthritis after intravenous injections of hemolytic streptococci.

Results of One Hundred Injections of Salvarsanized Serum.—Riggs and Hammes (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 1277) report a series of 24 cases of syphilis of the central nervous system treated by intraspinous injections of salvarsanized serum. In 75 per cent. of the tabe-

tics the laboratory findings in the blood and spinal fluid have become normal in every way. Aside from this there has been decided clinical betterment, such as marked relief of the lightning pains, a practically normal return of the bladder functions, and an improvement in the general physical condition and in the gait. Two patients who clinically were typical tabetics, in whom the serobiologic findings were negative before the commencement of treatment, were greatly benefited by these injections. The results in paresis have not been so satisfactory as those in tabes, probably owing to the fact that most of the paretics were in the advanced stage when treatment began; but it can be said of paresis, as of cancer, that even a temporary amelioration of a disease so hopeless is a success for which to be grateful and not a failure to be despised. A greater number of injections are required before any favorable laboratory changes occur. Riggs and Hammes say that although cerebrospinal lues usually responds to antiluetic treatment, yet certain cases prove most refractory. It is in such cases that the intraspinal salvarsanized serum injections are especially indicated, favorable results being obtained after other methods have failed. In this series of cases there were four patients with cerebrospinal lues and one with tabes who improved both clinically and serobiologically under treatment, having received little or no benefit from intravenous injections alone.

The Treatment of Diabetes.—Allen (*Boston Med. and Surg. Jour.*, 1915, clxxii, 241) upon the theory that diabetes is caused by overtaxing a weakened pancreatic function, advocates fasting to control glycosuria and ketonuria. The form of treatment embodying this idea was first worked out on animals by Allen and his present article deals with the application of this treatment for diabetic patients. The first step is to fast until glycosuria ceases and then for twenty-four or forty-eight hours longer. At the same time, the ketonuria falls steeply. It quickly approximates what a normal individual would show under similar conditions and the aim is to keep it constantly down to this level. Plain fasting suffices for the purpose; but since alcohol is a food which does not produce glycosuria and is said to diminish ketonuria, it is generally given during fasting, especially if there is danger of coma. Alkalies may be useful for the first few days if coma seems imminent, but are then no longer needed. Continuing the sodium bicarbonate may cause the ferric chloride reaction to remain positive longer than it otherwise would, with no benefit to the patient. When the fasting patient has been free from glycosuria for twenty-four to forty-eight hours, the next step is to begin feeding very slowly and cautiously. It is desirable to individualize the diet to suit the needs of different patients. The one requirement is that the patient must remain free from both glycosuria and acidosis. Any trace of sugar is the signal for a fast day, with or without alcohol. The original fast, to clear up the urine in the first place, may be anything from two to ten days, but after that no fast need be longer than one day. Frequently the first thing given after the fast is carbohydrate. No distinction is necessary between different forms of starch, but there are advantages in using vegetables, following Joslins convenient classification on the basis of carbohydrate content. The first day after fasting, the only

food may be 200 grams of vegetables of the 5 and 6 per cent. classes. This is increased until a trace of glycosuria appears, which is checked by a fast-day. The purpose of such a program is to learn the carbohydrate tolerance and to clear up the last traces of acidosis. After this carbohydrate period, or sometimes in place of it, protein is given. On the first day, perhaps one or two eggs are given and nothing else. More protein, generally as eggs and meat, is added day by day, until the patient either shows glycosuria or reaches a safe protein ration. The purpose here is to learn the protein tolerance, and to cover protein loss as quickly as possible. Fat is somewhat less urgently needed, except in very weak and emaciated patients, and it can be added gradually, as conditions seem to indicate. An element of bulk is necessary to give the comfortable feeling of fulness, and to prevent constipation. This is the great advantage of green vegetables. When they are fed raw, or cooked in steam, or boiled and evaporated so that no water is thrown away, they contain a definite quantity of carbohydrate besides valuable salts; and this is the only form of carbohydrate that patients thus treated ordinarily receive. Some cases are so severe that even green vegetables cannot be tolerated. Under these conditions the vegetables may be boiled through three waters, throwing away all the water. Nearly all starch is thus removed, and the most severe cases generally take these thrice-cooked vegetables gladly and without glycosuria. One result of the initial program here described is the loss of weight. This is the thing which physicians have been accustomed to dread most but which, according to present indications, is beneficial in itself. In subsequent treatment, the patient is welcome to gain weight up to a certain point, provided he can do so without glycosuria or acidosis. The attempt to put on weight according to the time honored traditions of diabetic treatment is one of the surest way of bringing back all the symptoms and sending the patient down hill. It is probably one of the chief causes of past failures in treating severe diabetes. · In the severe cases it is found necessary to restrict all classes of food, and to test the tolerance of each patient for each particular class. Carbohydrate is given if possible, but is kept safely below the limit of tolerance. Protein must be kept fairly low, sometimes very low, with a dangerously low protein tolerance, the working rule has been to exclude all carbohydrate, then feed as much protein as possible without glycosuria. Fat has heretofore been considered as both safe and necessary in the diabetic diet. Allen believes that patients show a fat tolerance as truly as a carbohydrate or a protein tolerance. He has never seen glycosuria from fat alone; but there are patients whose urine is constantly negative on a given diet, who will show both glycosuria and ketonuria if butter and olive oil is added to that diet. The very severe diabetic may be both thin and weak, because he cannot metabolize enough food to be strong or well-nourished. But as long as his weakened function is not overtaxed, he seems able to retain such weight and strength as he has, at least for a considerable period. Any attempt to build him up with any kind or quantity of food beyond what he is able to metabolize perfectly, apparently hastens a fatal result. The number of diabetics admitted to the Rockefeller Hospital has been twenty-seven, including cases of all grades of severity and ranging in age from ten to sixty-nine. Every patient treated has been

made free from both glycosuria and acidosis. The number of deaths has been three. Of these two were untreated cases, one was admitted in coma and one died from cardiac complications. The fatal treated case was a twelve-year-old boy who did not follow the treatment. Allen says that no patient, up to the present time, died who has followed the treatment. However, he does not pretend that this method of treatment can save all patients. The author cites a few typical cases treated on this plan. He says that it clears up certain cases which heretofore have not been cleared up, and that the cases which could be cleared up heretofore are cleared up more quickly by this method. The cases have not been observed a sufficiently long time to give permanent results.

The Serum Treatment of Hyperthyroidism.—Beebe (*Jour. Amer. Med. Assoc.*, 1915, lxiv, 413) reports regarding the serum treatment of hyperthyroidism giving the results of 3000 cases treated by this method. He says that the precise result which will be obtained with any given patient cannot be precisely foretold. Beebe says that the results of the treatment may be classified as follows: Fifty per cent. of the patients have been cured in the sense that they are strong and able to meet all the demands made on them. They are of normal weight, have a normal heart, have no tremor, are not nervous, have no gastro-intestinal disturbance and perform all their accustomed tasks without undue fatigue. In some instances the goitre, although much reduced in size, is still enlarged, and in others exopthalmos persists to noticeable degree. The author furthermore states that a large portion of the 50 per cent. included in the list of cured show no evidence of the disease, and are normal persons. They pass rigid physical examinations and would never be suspected of having had the disease at any time. None of the cardinal or secondary symptoms can be discovered. Thirty per cent. of the patients treated show a very marked improvement, to such a degree that they meet all the usual demands of life without undue reaction. Under unusual physical or emotional strain they react more than normal persons do. The two symptoms which are the most evident with them are a gland larger than normal, and in many cases a mild exophthalmos. Some of this group ultimately improve to a point permitting them to be called well. The remaining 20 per cent. include those who have not been so markedly benefited, those who have been operated on, those who have not been benefited and those in whom the disease has proved fatal. The percentage of fatal cases in patients who have had serum treatment for a period of six months is very small.

Endamebic Pyorrhea and its Complications.—Evans and Middleton (*Jour. Amer. Med. Assoc.*, 1915, lxiv, 422) write especially concerning constitutional manifestations associated with endamebic pyorrhea. Fifty-two or 74 per cent. of the 70 pyorrhea cases showing endamebæ displayed constitutional symptoms or disturbances of more or less marked degree. The authors group these constitutional derangements under several heads: (*a*) Arthritic, mainly belonging to the type denoted as arthritis deformans, (*b*) neuritic, (*c*) digestive, (*d*) anemic, (*e*) miscellaneous. In all, 19 cases of arthritis were treated by local

injection of weak solutions of emetin hydrochlorid into the infected gums, usually combined with subcutaneous injection of the same remedy. Two of the patients were treated by the subcutaneous method alone. Decided improvement occurred in 12 cases, three had but slight relief from their arthritic pain and the remaining four showed no apparent improvement. Of 2 cases with digestive derangement as the prominent symptom complex, both were improved by local treatment, further improvement being noted in one following the administration of emetin hydrochlorid subcutaneously. The authors describe a large number of miscellaneous conditions associated with pyorrhea in a number of which they noted improvement following amebacidal treatment. In conclusion the authors state that constitutional disturbances are very frequent complications of endamebic pyorrhea, that arthritis, particularly of the type of arthritis deformans, is the most frequent complicating disorder, and that the results from the local and general administration of emetin hydrochlorid in the relief of the pyorrhea and the marked improvement of the arthritic condition are very encouraging in a large percentage of cases. In addition they believe that unexpected relations between pyorrhea and certain remote conditions are established through the response to the emetin treatment.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M.D., OF PHILADELPHIA.

Calcariuria (Phosphaturia) in Children.—H. KLEINSCHMIDT (*Berl. klin. Wchnschr.*, 1915, lii, 29) describes under the term calcariuria a cloudy or milky urine whose sediment is white and composed of calcium carbonate and calcium phosphate. It is characterized by an increased calcium output in the urine with no change in the phosphoric acid output. The total calcium output of the body is apparently not increased, as the more calcium is found in the urine the less is found in the feces. The urine in this condition is usually alkaline in reaction, but it has been shown that this sediment can occur in neutral or weakly acid urine. Many theories have been held as to the etiology of the condition, such as intestinal worms, inflammation of the large bowel, etc., but finally it has been considered a purely nutritional disturbance. Certain neurogenic conditions are almost invariably associated with calcariuria in children. Among them are insomnia, headache, anorexia, abdominal pain, pallor, sweating, itching, vomiting, diarrhea and hystero-epileptic attacks. Many observers differ on the question as to whether or not the definite chemical changes in the urine may be held responsible for the advent of the associated nervous phenomena. The author shows that in children with calcariuria, the nervous symptoms existed long before the urinary changes appeared, and that the children were neuropathic practically from birth. He cites in detail

the cases of two children with calcariuria and typically neurotic, who showed no change in their urine content on dietary changes at home, but in whom the abnormal condition disappeared suddenly on admission to hospital for treatment. Both the nervous signs and the calcariuria eventually returned after leaving the hospital, but the child who was there for a long period did not develop the condition for a long time after returning home. The author indicates his belief that the diet is not responsible for the urinary condition, and that the question is rather, how far the nervous condition is responsible for the urinary findings. He offers as the best treatment for the condition an absolute change of environment, such as removal to a hospital. The effect of this on the nervous phenomena is especially good and will cause a disappearance of the calcariuria if continued long enough.

Emulsions of Liquid Paraffin and Castor Oil in Chronic Dyspepsia in Childhood.—McNeil (*Edin. Med. Jour.*, 1915, xiv, 100) bases the following conclusions on 120 cases of chronic dyspepsia in children over one year old. Emulsions of liquid paraffin and castor-oil in non-purgative doses are of great value in this condition. McNeil gives the following types of dyspepsia: Malnutrition often with chronic diarrhea, rarely with constipation; enuresis with dyspeptic signs; recurrent vomiting; recurrent attacks of fainting and urticaria or eczema with dyspeptic symptoms. There may be diarrhea, rarely constipation, most frequently merely soft movements. A large number of these cases follow the common infections of childhood especially measles and whooping-cough. These cases are especially amenable to this form of treatment. Enuresis was cured in 8 cases out of 13 by this treatment. The action of the liquid paraffin and castor-oil is entirely local and confined to the mucous membrane of the intestinal tract and probably diminishes the congestion and catarrh of these surfaces and restores healthy activity in the digestive glands. The emulsion of liquid paraffin has the following formula: Paraff. liq., ʒiij; gum acac., ʒiij; gum tragacanth, gr. xij; ol. cass, ♏viij; aq. destill., ad. ʒvj. One drachm is given three times a day after meals. The emulsion of castor-oil contains: Ol. ricini, ʒiiss; gum acac., ʒvj; aq. aurant, ʒv; aq. cinnam., ad. ʒvj. The dosage is the same as that of the paraffin. As adjuvants McNeil occasionally uses powders, composed of hydrarg. subchlor., gr. j, with either sodii sal., gr. ij, and sod. bicarb., gr. v, or pulv. rhei., gr. j and magn. carb., gr. iij, one powder being given at night. In cases of enuresis it is a question which of the two emulsions does the most good, but probably it is the castor-oil emulsion. The separate disorders mentioned above, such as malnutrition, enuresis, recurrent vomiting, etc., seems to have certain clinical features in common, the general symptoms of chronic dyspepsia, which probably depend upon some unhealthy condition of the intestinal mucous membrane. The action of these two emulsions, therefore, seem to be logically explained.

A Ten-year Statistical Report on Scarlet Fever.—Barasch (*Deutsch. med. Wchnschr.*, 1915, xli, 4) offers a statistical report on scarlet fever, covering ten years and including 1438 cases, mainly in children, admitted to a hospital in Berlin. The total mortality was 15 per cent. This

compares with the general mortality of other observers as Heubner, Jurgensen, and others who report mortalities of from 13.4 per cent. to 16.6 per cent. The total mortality would be considerably decreased if we eliminate the 6.6 per cent. of cases admitted in a moribund condition or dying within three days of the onset. Nephritis was a complication in 16.1 per cent. of all cases; otitis in 13.8 per cent.; marked involvement of cervical glands 33.4 per cent.; sepsis in 9.1 per cent.; diphtheria as a complication in 16.4 per cent.; involvement of the joints or rheumatism in 5.9 per cent., and endocarditis in 1.3 per cent. The mortality according to age showed 50.7 per cent. under the fifth year, 31.4 per cent. between five and nine years, 9.9 per cent. between ten and fourteen years, and 2 per cent. between eleven and nineteen years. No treatment was found which could influence the course of the disease. A great number of different forms of treatment were tried from time to time but eventually all were discarded as not being as effective, or at least not more so than the regulation treatment there employed, which included principally bathing, diet, careful nursing and keeping the expenditure of energy or strength of the patient at a minimum. Among the methods tried out and discarded as being without much effect were the influence of the red light on the disease and the intra-tonsillar injection of carbolic. The regular treatment used comprised in particular ice caps or cold wet cloths around the throat, mild antiseptic gargles, or swabbing the throat, daily luke-warm baths, a diet practically salt-free and composed almost altogether of milk, or cocoa and gruel. This diet is continued to the nineteenth day in uncomplicated cases, before an increase is given. Tests made on blood-pressure seem to show an increase of 20 per cent. to 30 per cent. in pressure with the development of a nephritis. This complication is treated by diet and sweating especially by light baths. Uremia is treated by venesection, 10 grams of blood for every kg. of bodyweight. Nephritis usually developed between the fifteenth and twenty-fourth day, and the majority of cases developed in children between five and nine years old. Joint symptoms occurred more frequently in youths and adolescents than in children. The cases of endocarditis were all mild. The cases of sepsis were severe and the mortality was high.

The Treatment of Congenital Syphilis.—Findlay and Robertson (*Quart. Jour. Med.*, 1915, viii, 175) discuss the value of mercury and of salvarsan in the treatment of congenital syphilis. Mercury, while occasioning a negative Wassermann reaction, cures only in a few instances even with prolonged administration. Salvarsan is a more potent spirocheticide but works better when reinforced by mercury. Also it frequently clears up cases which mercury, given for long periods of time, has failed to affect. Congenital syphilis is a most obstinate form of the infection. The danger of a fatal toxemia in children following the use of salvarsan, has probably been over-estimated. Salvarsan possesses a very limited power when given rectally or through the medium of the mother's milk. The authors in giving neosalvarsan intramuscularly, found no untoward results except the pain, the induration and the occasional necrosis at the seat of injection. As these points were of importance in treating children they used the intravenous method. While the

veins in the arm can frequently be used, the veins of the scalp are preferable and usually are more prominent. The difficulties of this method is to keep the child's head absolutely quiet. This led to the use of concentrated solutions. In infants 3 to 4 c.c. of saline containing 0.05 to 0.3 gram of neosalvarsan are employed. Many hundreds of injections have been accomplished with concentrated solutions without any harm arising from them. A 5 c.c. record syringe is used and a No. 1 size needle. About 400 injections of neosalvarsan in concentrated solution have been used so far with a record of one fatal issue, occurring twelve hours after a second dose of 0.05 gram per kilo. The cases were out-patients, many living under the worst possible conditions. Most of the deaths were in no way associated with the method of treatment or the dose of the drug, but were due to the disease itself or to intercurrent disease such as pneumonia, measles, etc. The drug almost invariably caused an improvement even in those cases which subsequently died of intercurrent or syphilitic conditions. Of sixteen children that died within three weeks of an injection, nine were under three months of age at the beginning of treatment. With mercury and salvarsan the death rate under three months was 43 per cent., while in a series of 14 cases, also under three months, treated with mercury alone the death-rate was 71 per cent. Seven pregnant syphilitic women were treated by inunctions of mercury and neosalvarsan intravenously. Except for headache and sickness for a number of hours afterward this treatment had no effect on the kidneys or the pregnancy. Small doses should be injected frequently till the Wassermann reaction is negative. The inunctions should be kept up during the course of pregnancy. The children of these seven women were sound and healthy when born, with no evidence of syphilis, and at five or seven months had shown no sign of it. This form of treatment therefore appears encouraging.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

A New Method of Painless Childbirth.—Hellman (*Amer. Jour. Obst.*, February, 1915) calls attention to a preparation obtained by the action of chlorhydrate of morphin on living ferments, resembling beer at the leavening. This is a special method of fermenting opium, so that its toxicity becomes about one-fifteenth that of morphin, and the morphin is transformed into a substance that crystallizes in the regular way. This drug was described in July, 1914, by Dessaignes, in a paper read before the French Academy of Medicine. This drug makes the organism more susceptible to such drugs as strychnin and digitalin. It exaggerates vasomotor and general reflexes, and increases

salivary, intestinal, and renal secretion. Toxic doses are only reached when 2 or 3 eg. are injected for each kilogram of body weight, and the symptoms of poisoning are bloody and mucous diarrhea. The first toxic cerebral symptoms resemble those of drunkenness. When given to a patient in labor the drug acts on the brain and sympathetic centres without noticeable effect on the spinal cord. The action is prompt prickling or itching sensations which are experienced in two or three minutes. The patient becomes drowsy, and after ten to twenty minutes does not feel pain. In 84 cases there was complete analgesia, in 24 marked but not complete, and four patients denied relief. The analgesia lasts from thirty minutes to twelve hours, and but one injection was needed in 63 cases; 39 felt pain at the end of five hours; 9 received three injections, and 1 patient five injections. Uterine contractions were uninfluenced, and there was but one case of postoperative hemorrhage. On the average, in thirty-two minutes, the placenta was expelled. The patient was free from exhaustion, mental disturbance and after-pains, and involution and nursing were not affected. The usual vaginal operations, version, forceps and suture of the perineum, were performed without other anesthetic. In 112 labors 115 children were born, of whom 77 cried immediately after birth; 28 did not breathe at first, but soon revived. There was one fetal death from meningeal hemorrhage, and three premature children lived but a few days. Pinard stated that his results agreed with those of Dessaignes. The drug was given hypodermatically 1.5 c.c. for the first dose, 0.5 c.c. for succeeding doses. To test the remedy, Hellman used it in three cases at the Lebanon Hospital. His results were practically those already described. This preparation is known as toconalgine, and originated with French chemists in Paris.

The Action of Pituitrin upon the Uterus.—Lieb (*Amer. Jour. Obst.*, February, 1915) has studied the effects of various drugs upon the excised human uterus. Fluid extract of ergot had but little stimulating effect upon the isolated uterus and Fallopian tubes. Pituitary extract caused the uterine muscle to contract much more strongly and rapidly. The stimulation was persistent and not easily removed, even by repeated washings with fresh Ringer's solution. Upon the non-pregnant uterus or tube small doses have usually no effect, while large doses, which would stimulate the pregnant womb, may cause depression. The question arises, What is the cause of the differing effect upon the pregnant and non-pregnant uterus? It is probably the fact that during pregnancy the motor inervation of the uterus becomes predominate. There is possibly some substance which sensitizes the uterus to pituitary extract, and that substance is certainly not epinephrin.

Late Cesarean Section.—Zarate (*Arch. mens. l'obstetrique*, August, 1914) reports 4 cases in which Cesarean section was performed a considerable time after labor began. The first patient was in her second parturition and had been twenty-four hours in labor, with ruptured membranes. The second patient had contracted pelvis, gonorrhea, and had been sixty-two hours in labor, with ruptured membranes. The third patient had contracted pelvis with transverse presentation of the fetus, and had been eleven hours in labor. The fourth patient

had contracted pelvis. The interesting thing about this series of cases is that fact that all of the mothers did well. Fortunately, little or no effort had been made to deliver these patients before they were admitted to hospital. In dealing with cases of delayed labor where delivery must be accomplished by section, the reviewer ascertains as carefully as possible what has been done or attempted with the patient before admission to hospital. The surroundings of the patient in her lodging must also be taken into account. A further item of great importance is the known reputation of the physician who has sent her to hospital, for his skill and diligence in antiseptic precautions. From the stand-point of the patient, her age and general physical condition must not be forgotten. If the patient be young, the effort should be made to avoid hysterectomy, and thoroughly irrigating the uterus through the incision with hot sterile salt solution, and packing with 10 per cent. iodoform gauze should be practised. In a considerable number of cases this method has given excellent satisfaction. Where, however, the interior of the uterus is foul, greenish in color, and the patient's history states that repeated efforts at delivery were made, the removal of the greater portion of the womb, leaving the stump in the lower end of the abdominal incision, is the only safe procedure.

The Fetal Heart Sounds in Placenta Previa.— Baughman (*Amer. Jour. Obst.*, February, 1915) has studied the fetal heart sounds in placenta previa. He finds that comparison with heart sounds can only be made when we examine the fetal heart at the point of the abdomen of the woman nearest the middle of the back or the chest of the fetus. The exact location of the back or chest must be determined by external examination. In the interests of the child delivery should be accomplished as soon as possible after the diagnosis of placenta previa is made.

Pituitary Extract with Parturient Patients. — Esbensen (*Arch. mens. l'obstetrique*, September, 1914) has found in his clinical observations that pituitary extract in the majority of cases either produces or increases the vigor of the forces of labor. Uterine contractions become physiological in character, being rhythmical and increasing gradually. Pituitary extract will not cause miscarriage in a pregnant patient. When an abortion has actually begun and is in progress pituitary extract will increase somewhat the contractions of the uterus. In premature labor this substance acts essentially as it does at full term. In cases of labor at term pituitary extract has its best effect toward the end of parturition. The effect is less pronounced at the beginning. Good and efficient contractions of the uterus are not especially increased by pituitary extract, but they do not become tetanic in character because of this remedy. Where uterine contractions are very painful this substance will not lessen the pain, except in so far as it brings about more regular action of the uterine muscle. Considerable elevation of temperature during labor seems to arrest the effect of pituitary substance. In but one case was there observed atony of the uterus postpartum. Under proper precautions, and in skilled hands, pituitary extract given during labor is not dangerous for the child. Diseases of the heart are not a contra-indication to the use of this sub-

stance, nor are albuminuria and nephritis when they do not assume the extremely virulent and active type. A very small quantity of albumin is often found where this substance has been given during labor, and this must be kept in mind in using the remedy during eclampsia.

Salpingitis Opening into the Bladder through Suppuration. — Auvroy (*Arch. mens. l'obstetrique*, November, 1914) reports the interesting case of a patient who had salpingitis upon the right side, with enlargement of the womb, pain, and disability. The patient was kept for some time under observation in hospital, but without especial improvement, when operation was performed. The opening into the bladder through which the pus from the pyosalpinx had made its way could be distinctly seen by the cystoscope. The patient made a good recovery. In a second case section was performed because the patient had a history of infection and high fever. This was followed by rapid distention of the abdomen, with toxemia and death. In each of these cases the bladder had become involved by the adhesion of the affected tube, and an opening had developed into the bladder, into which pus had been discharged.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Physiology and Pharmacology of the Human Uterus.—A number of rather interesting experiments with human uterine muscle have been reported recently by Lieb (*Amer. Jour. Obst.*, 1915, lxxi, 209). The material was obtained in the operating room, strips of tissue being cut at once from freshly extirpated uteri and placed in jars containing 500 c.c. of oxygenated Ringer's solution. If the tests were to be made immediately, this was kept at a temperature of 38° C., but it was found that by keeping the solution at 5° C. the tissue could be preserved from one hundred hours or more, and would then show, upon being placed in warm solution, practically the same reactions as fresh tissue, although somewhat less in degree. The strips were taken from the outer, longitudinal layer of the uterine muscle, and were studied by being suspended in a cylinder containing warm, oxygenated Ringer's fluid, one end of the strip being attached to the lever of a kymograph. Under these conditions, the normal, non-pregnant human uterus shows slow but powerful contractions, which may be regular, or which may come at varying intervals. These contractions occur at the rate of 10 to 60 per hour; the Fallopian tubes—which were also tested in some instances—have a much faster rate of contraction, 120 to 200 times per hour. Their contractions are small, and fairly regular. From these experiments it is evident, says the author, that however much uterine contractions may be influenced by nerve impulses arising within the

central nervous system, these contractions cannot be wholly dependent upon such impulses, but must originate within the uterus itself. They may be due to an inherent function of the muscle cells, or may be the result of impulses formed in the nerve cells found within the walls of the uterus and tubes. Lieb inclines to the former view, as nothing corresponding to Auerbach's plexus in the intestinal wall is present in the genital organs, and it is improbable that ganglia scattered along the course of the nerve fibers are able to generate impulses which lead to coördinate contractions of the entire uterus. When sufficient epinephrin was added to the Ringer's fluid to make a 1 to 2,000,000 solution, a marked increase in the power of the contractions of both uterus and tubes was noticed, but this effect was fugaceous, and soon passed off. Ergotoxin added in sufficient quantity to make a solution of 2.5 to 100,000 caused powerful contractions, passing into very high tonus, with a suggestion of tetanus. The latter was soon broken through, however, by minute contractions, whose rate was approximately twice the normal. The effect was extremely lasting, but the doses required to produce this effect were far in excess of what are ever used clinically. Two other active principles of ergot caused practically similar reactions. Pituitary extract produced a marked effect upon segments of pregnant uteri, previous feeble and slow contractions becoming stronger and more rapid, with a great increase of tonus. This stimulation was very persistent, but in only one instance was a transitory tetanus produced, and then only when a very large quantity of pituitrin was used, sufficient to make a solution of 1 to 100. The effects on the non-pregnant uterus were rather surprising—small quantities generally produced no effect whatever; larger doses, such as produced marked stimulation of the pregnant uterus, caused either a very definite depression, or else did not influence the uterine movements at all. No such change in reaction between the pregnant and non-pregnant uterus was noticed in the case of epinephrin, so that this effect of pituitrin cannot be attributed to a reversal of the sympathetic innervation, *i. e.*, from inhibitory to motor, with onset of pregnancy. The most plausible explanation seems to be that some substance of unknown nature sensitizes the uterus during pregnancy to the action of pituitary extract.

Ectopic Pregnancy and the General Practitioner.—In a paper read before the recent meeting of the American Association of Obstetricians and Gynecologists, McClellan (*Amer. Jour. Obst.*, 1915, lxxi, 269) calls attention to the fact that extra-uterine pregnancy is far more common than is generally recognized, and that it is undoubtedly on the whole very badly managed in general practice, and yet it is on the general practitioner that the burden of recognizing the condition usually falls. "In a community well known to the writer," he says, "there are forty-eight able general practitioners, very few of whom have ever reported a case of extra-uterine pregnancy; however, two of their number each report from 2 to 5 cases every year. In this same community there have been a number of deaths, and many chronic invalids, reported to have had pelvic hematocele and pelvic abscesses following abortion, many of which were primarily no doubt overlooked extra-uterine pregnancies." McClellan lays great stress on the impor-

tance of going carefully into the history of the case, as this will generally point to some previous trouble with the generative organs, which will be at least a cause for suspecting the possibility of the existence of an ectopic gestation. He thinks that a much larger proportion of the cases should be diagnosed before rupture than is now done, but that since so large a number are not diagnosed until after this occurs, "it is most desirable that an established propaganda should be formulated which should serve as a guide to the treatment to be followed in this 'tragic stage.' . . . If the general practitioner takes the dictum 'to wait' seriously, he will delay the calling of a surgeon, on the assumption that a fairly large number of cases get well without operation, which of course can only result in a needless loss of life. On the other hand, there is sure to be an unnecessary risk taken if every case that has gone on to rupture is operated regardless of the state of collapse, and without waiting for the helpful effects of wisely selected treatment. . . . It seems equally clear that if called to a case where hemorrhage is persistent, quick operative intervention is advisable." In addition to the above excellent advice, the author very rightly emphasizes the value of the operating room as a teaching place where the general practitioner can be given the most impressive instruction in pathology as it occurs in the living body, since in no other way can the relation between the clinical picture and the pathological processes responsible for it be so forcibly impressed on his mind.

Simple Method of Establishing Vaginal Drainage.—Wood (*Surg. Gyn. and Obst.*, 1915, xx, 487) calls attention to the difficulties often encountered when it is desired to open the vagina for purposes of drainage at the end of an abdominal operation, since it is not always an easy matter to get into the vagina from above, and to go in from below involves a complete disarrangement of the aseptic sheets, and the presence of an extra sterile assistant to attend to the vaginal work. Wood obviates these difficulties by the following simple device. He has had a long curved Pean forceps sharpened at the points to form a trocar, and perforated by a hole drilled transversely near the tip large enough to take a catgut ligature. In cases where there is any probability that vaginal drainage may be required, before the abdomen is opened the vagina is sterilized, and with a curved needle a very light catgut suture is passed through the posterior fornix at a point where the cul-de-sac can be most easily penetrated. This ligature is now carried through the opening in the tip of the trocar-forceps and tied, the point of the instrument being thus held in close promixity to the point to be perforated by an easily broken ligature. The instrument is long enough for the handles to project six or eight inches from the vaginal orifice. It remains in place in the vagina throughout the abdominal operation, and if an opening in the cul-de-sac is desired, a nurse, who need not necessarily be sterile, simply passes her hand under the protective sheets from below, forces the instrument through, thereby breaking the ligature, and opens the handles so as to expand the blades sufficiently to dilate the opening and draw back a strip of gauze or drainage tube, as may be desired.

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
JOHN F. ANDERSON, M.D.,
DIRECTOR OF THE HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

The Chicken as a Possible Typhoid Carrier.—From the experiments of O. W. H. Mitchell and G. T. Bloomer (*Jour. Med. Research*, 1914, xxi, 247) it would seem that the chicken is highly resistant to the typhoid organism. It not only fails to take the disease, but also, as these experiments seem to indicate, it cannot be made a carrier either by feeding the organism or by intravenous inoculation. The limited time, however, in which the work was pursued and also the limited number of chickens used must be borne in mind in weighing the evidence adduced by these experiments, and a greater number of experiments covering a longer period should be done before it is said absolutely that the chicken cannot become a typhoid carrier.

Reaction of Cow's Milk Modified for Infant Feeding.—William Mansfield Clark, Ph.D. (*Jour. Med. Research*, 1915, xxxi) concludes that the hydrogen ion concentration of human and cow's milk have been compared with those of various formulæ of modified cow's milk. The addition of alkalis to modified milk for the purpose of neutralizing "the high acidity of cow's milk" is shown to be a practice based upon wrong principles. The addition of alkalis to modified milk for the purpose of preventing firm clots in the infant stomach is shown to be a procedure which not only may be unnecessary but one which involves a possible inhibition of both gastric proteolysis and lipolysis. Finally, the addition of alkalis to modified milk is criticised because of its probable influence in displacing from the intestine a normal bacteria fermentation and replacing it with those proteolytic or "putrefactive" processes which are responsible for many of the digestive disorders of infancy.

Experimental Polyneuritis.—W. Richard Ohler (*Jour. Med. Research*, 1914, xxi, 239) concludes from the results of his experiments, that fowls, when fed on an exclusive diet of white bread, whether with or without yeast, develop a definite polyneuritis. This condition has been demonstrated by histological studies of both nerve and muscle tissue. Furthermore, it can be stated with equal certainty that when fed on an exclusive diet of whole wheat bread fowls remain perfectly well. To say, then, that any exclusive diet may cause symptoms of polyneuritis is not true to fact. Apparently, there is some substance or substances present in whole wheat bread not present in white bread

which are essential to the health of the organism. In other words, it would seem that in the relation between whole wheat flour and highly milled white flour we are dealing with the same problem as in the relation between unpolished and polished rice. This problem arises, however, only where the diet is restricted and consists almost exclusively of white flour or polished rice, as the case may be. Whether or not polyneuritis gallinarum and beriberi are the same disease is still an open question. This much we know, that the results of dietary experiments in both fowls and mammals are generally uniform. In view of these uniform results it is perhaps not too much to assume that the experiments here reported (including the experiments with whole corn, wheat, grain, hominy, and rice, as well as those with different kinds of wheat bread) have added another link in the chain of evidence that beriberi is a "Deficiency Disease." Finally, these experiments go a long way toward proving that contention of Dr. Little that a restricted diet, consisting largely of white bread, is a large factor if not the single factor in the cause of beriberi in North Newfoundland and Labrador.

The Spread of Tuberculosis.—Dr. H. G. Lampson (*U. S. Public Health Reports*, January 8, 1915, xxx, No. 2) in his "Studies on the Spread of Tuberculosis in Five Counties of Minnesota" came to the conclusion that 79 per cent. of individuals fully exposed for a long period of time to open cases of tuberculosis, became infected. Only 28 per cent. of those partially exposed or exposed for a short period of time became infected. The percentage of infections from casual exposure such as everyone encounters, was small, 8 per cent. The more frequent infection of children is explained, at least in part, by their more intimate contact with the patient. At all ages, the intimacy and length of exposure are the determining factors in infection with tuberculosis.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL,

AND

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

The Bacteriology of Typhoid and Paratyphoid Fever at Autopsy.—One of the important findings by Grote (*Arb. a. d. path. Anat. Institut., Tübingen*, 1914, ix, 1) was the infrequency with which B. typhosus was isolated from the intestinal canal. Similar observations upon the living have been reported by many. It is suggested that the

organism multiplies but sparsely during its habitat in the bowel or that its growth is actually inhibited by the presence of other bacteria or through the bacterial effect of the intestinal juices. There is little evidence forthcoming to indicate the activities of the B. typhosi during its life in the bowel contents. The author believes that relatively few cases result from a primary invasion from the intestine but considers it a general infection with secondary localization in the lymphatic structures of the bowel. No relation can be indicated between the number or organisms which may be isolated and the intensity and distribution of the tissue change. The demonstration of B. typhosi at autopsy is best accomplished by cultures from the gall bladder. In every case studied, the author obtained pure cultures from this organ. He found no difficulty in isolating the organism from various parenchymatous organs, liver, kidney, spleen, and lung, as well as from blood and cerebrospinal fluid. Contrary to the former accepted belief he found considerable difficulty in isolating B. typhosus from the spleen. In three cases from which the paratyphoid organism was isolated the clinical symptoms had not suggested this infection. In one of these there were cholera-like manifestations, while in another, serious gastro-intestinal symptoms were prominent. An interesting case of a dual infection was reported by Benitker (*Cent. f. Bakt.*, 1914, lxxiv, 1). In this case an individual died of severe meat poisoning due to B. paratyphosus. There was evidence, however, of extensive typhoid ulceration of the ileum, whose character suggested some weeks' duration.

The Relative Virulence of Sensitized and Non-sensitized Typhoid Bacilli.—Besredka has shown that sensitized typhoid vaccines are less toxic and better tolerated in guinea-pigs than the non-sensitized. This has been verified by others who have shown that the sensitized vaccines produce a serum of higher protective quality than the untreated organisms. In view of this, the sensitized vaccine is recommended in practice in place of the usual vaccine of Wright. Cecil (*Jour. Infect. Diseases*, 1915, lvi, 26) has repeated the experiments using dead and living cultures and inoculating them intravenously. His findings are in agreement with previous work where the treatment has been subcutaneous or intraperitoneal. The sensitized vaccines are better tolerated and produce a greater immunity than the non-sensitized. Moreover the lethal dose of the typhoid cultures was much greater with the sensitized vaccine. He believes that the sensitized organisms undergo phagocytosis and bacteriolysis to a greater degree than the untreated one.

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ORIGINAL ARTICLES

SOME PROBLEMS IN THE PATHOLOGY OF SYPHILIS.[1]

By John A. Fordyce, M.D.,

PROFESSOR OF DERMATOLOGY AND SYPHILOLOGY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

It is proposed in the present paper to discuss some of the phases of syphilis which have resulted from the intensive investigations of the past ten years. These problems include the question of immunity, a few of the most striking anatomicopathological changes met with in the disease, as well as its effects on the cardiovascular and nervous systems, and the lessons to be deduced from the knowledge which has been gained.

Immunity. One of the most interesting and perhaps least understood problems in the pathology and biology of lues is the question of immunity. Formerly it was taught that like many of the other infections one attack of syphilis conferred a lifelong immunity, that a syphilitic mother might transmit an immunity to her child, while, conversely, the mother of a syphilitic child was rendered insusceptible to the disease, as postulated in the well-known laws of Profeta and Colles-Baumès. Since the work of Neisser, Finger and Landsteiner, Levaditi, Uhlenhuth and Mulzer, and others, however, our conception of immunity in syphilis has undergone considerable modification.

Investigations along these lines and in microbiology have shown that syphilis is closely allied with the protozoal affections, especially

[1] Read before the Harvey Society, February 13, 1915.

those caused by trypanosomes and piroplasomes. These diseases differ from those of bacterial origin in the manner in which they respond to the introduction of organisms into the system. While in the great majority of infectious processes acquired immunity is expressed by a protection more or less absolute against a new attack and the disappearance of the causal agent from the body, or its innocuousness to the host if it persists, diseases of protozoal origin behave in a different way. Levaditi has demonstrated, for instance, that animals suffering with a spirillary infection are immune to a new inoculation. Their serum has a high antibody content, but the blood still harbors parasites and is capable of producing a fresh infection in healthy animals. So with the serum of guinea-pigs inoculated with Nagana or Surra trypanosomes. This is trypanocidal for these organisms *in vitro*, but *in vivo* they have acquired an insensibility to the trypanolytic antibodies, for the blood and tissues of the animals still contain parasites. The same is true of human subjects suffering from sleeping sickness in whose serum trypanolytic, agglutinating and other protective bodies have been demonstrated. Carrying the analogy to syphilis we find that an individual may harbor spirochetes for forty or fifty years, while his skin and mucous membranes exhibit an insusceptibility to re-inoculation under natural exposure. However, as soon as he is freed from his infection he is again in as susceptible a state as he was prior to his first attack.

It is a well-known clinical observation that after the development of the initial lesion a syphilitic is immune to a fresh infection. Why have the integument and mucous membranes ceased to react to organisms introduced from without when they are susceptible to their action from within? The opinion has been generally held that for infection to take place one of the first laws of its requirements is fulfilled by a surface covered by squamous epithelium. The earlier experiments on animals seemingly corroborated this view, for inoculations were only successful where scarification of a squamous-celled area was performed. Improved laboratory technique has, however, overcome the difficulty, positive results now being obtained in animals by the introduction of the virus into the testicle, peritoneal cavity, under the skin or directly into the circulation, especially the heart.

In human syphilis, while it is more usual for the general infection to be preceded by the development of a primary lesion, somewhere on the cutaneous or mucous surface, it is not rare for the local reaction to be altogether absent. To illustrate: a male nurse in my hospital service pricked himself with a needle used for obtaining blood for the Wassermann test directly after he had withdrawn it from the vein of a patient with florid syphilis. He was carefully watched for the development of a chancre at the site of injury, but the first macroscopic manifestation was a late secondary papule

on his foot. Similar cases are reported in the literature. Another instance is exemplified in a personal communication by Dr. Dade, in which he related the infection of a young girl by blood transfusion. Her brother, whose blood was used for the treatment of her anemia, was at the time of the operation in the second incubation period of the disease. She in due course of time developed a secondary rash. Congenital lues is a further example of syphilis without the development of an initial lesion. Neisser came to the opinion, from his many experimental observations, that in certain cases infection might take place through the integument without visible or even microscopic changes, the organisms gaining access to the lymphatic or blood stream direct.

When spirochetes are successfully implanted, what takes place? As soon as they have become acclimated to changed nutritional conditions at the site of inoculation, as shown by Levaditi and Yamanouchi, they multiply, call forth microscopic changes in the cutaneous vessels, and enter the lymph and blood stream. This is known as the first incubation period and varies in length in different subjects. Just how far the organisms penetrate beyond the local sore and satellite lymph nodes in human subjects in this stage is not known, but it has been demonstrated by Neisser that the spleen and marrow of inoculated monkeys contain virus thus early in the infection. Now, as the chancre is forming a peculiar reaction on the part of the host is also developing. At first it is so feeble that the individual is for some time susceptible to re-inoculation. In animals it has been found that superinfection is possible if made eight days before the evolution of the primary lesion. Not rarely we see patients with multiple chancres. In some instances they develop simultaneously as the result of multiple inoculations; in others they appear successively either from auto-inoculation or contamination with a fresh virus. Human and animal experiments are at one in showing that superinfection lesions do not develop in the typical manner of those implanted on a virgin soil. Their incubation period is shorter and their clinical characteristics simulate those of the stage the patient is in at the time; that is, papular if close to the secondary period and ulcerative if in the tertiary stage. In other words, they are the expression of an altered tissue reaction. The hypothesis has been advanced by Krause and Volk that this immunity has a regional development, beginning at the site of the primary sore and progressively involving the mucous and cutaneous covering. Neisser has suggested that the susceptibility to re-infection returns in an inverse manner.

During the second incubation period the refractory state continues to develop until it attains its maximum with the outbreak of the secondary rash. Even now, however, it is only relative, for laboratory experiments have yielded positive results if special methods are employed, namely, larger amounts of active virus

introduced subepidermically. From a clinical stand-point, however, this refractory state, or anergy—the term usually applied—is complete as far as ordinary infection is concerned, disappearing only with the cure of the disease, when the patient is again in a receptive condition.

It has been demonstrated further that the anergy is a specific one, the attempts of Neisser, Baermann, and Halberstädter to induce it by inoculation with Spirocheta pertenuis, of Hidaka with Spirocheta duttoni, and of Uhlenhuth with Trypanosoma lewisii having proved futile. None of these infections protected against that of syphilis, while, on the other hand, luetic animals were all susceptible to frambesia, relapsing fever, and dourine. Little is known of the nature of this state of resistance or how it is brought about, whether by the tissues, cells, the serum, or intermediary organs. Organisms or their toxins when introduced into the body behave as antigens and stimulate the formation of antibodies which are specific for that particular bacterium. These antibodies are of the nature of antitoxins which neutralize the toxins; opsonins which lead to the ingestion and destruction of the organisms by the leukocytes; agglutinins which cause the organisms to adhere together and probably also bring about their destruction and bacteriolysins which cause their dissolution. From the contributions to this branch of research in lues the conclusions are that substances of a parasiticide nature do not develop in the course of the disease. At the most, says Neisser, we can reckon with complement binding and agglutinating substances of a specific nature. Levaditi, however, argues that since the spirochetes even before the evolution of the primary lesion may penetrate to the hematopœtic organs, they act like true antigens and their products of secretion stimulate the formation of antibodies. He assumes an analogy between these immune bodies and those of related diseases, where bacteriotropic substances and opsonins ensure destruction by phagocytosis. *Pari passu* with this antibody formation the skin acquires a refractory state to exogenous spirochetes, the biological changes being sufficiently advanced at the close of the second incubation period to determine the character of the reaction. He has offered two attractive hypotheses to explain why the skin which is resistant to exogenous spirochetes reacts to endogenous organisms, (1) by a generalized eruption, and (2) after a varying latency, by local and destructive lesions. His assumption is that for a time the immune bodies hinder the multiplication of the parasite, but with the enfeeblement or disappearance of the former the virus gains the ascendency, generalizes itself, and produces the secondary eruption. Or the spirochetes are vaccinated, so to speak, against the immune bodies, and, becoming resistant to these defensive substances, they succeed in multiplying and provoking the exanthem.

It is a well-established clinical fact that the early cutaneous

lesions are superficial and generalized, that with each relapse they show a tendency to localization and grouping with involvement of the deeper structures until we reach the tertiary stage with extensive destruction. Since it has been shown that these differences are not inherent in the specific virus but in the tissues of the host brought about by prolonged contact with the causal agent, the term allergy or, according to Neisser, Umstimmung has been proposed to explain the biological change which has taken place in the tissues. In the primary and secondary stage, when the organisms are numerous, the host is refractory; in the tertiary stage when they are few in number an anaphylactic state exists, the tissues are frail and more readily undergo necrosis. This is also seen in superinfection in tertiary syphilitics when the lesion corresponds to that type, and in the luetin reaction, which is especially applicable in congenital and tertiary syphilis, depending for its result on the hypersusceptibility of the tissues. In tuberculosis a similar condition is encountered. Erythema induratum, for instance, is caused by few organisms, and yet clinically presents extensive destructive lesions. Another clinical type is seen in large and deep ulcerations of the extremities in tuberculous subjects, all treatment, excepting surgical, being of little avail. The writer has recently had under his care a young man with glandular tuberculosis in whom the entire right leg was involved, necrosis extending through the musculature and laying bare the bone.

The immunity processes as outlined in the foregoing considerations are subject to modification under treatment. Where treatment is intensive and yet not sufficient to effect a complete cure it would appear that the anaphylactic stage is hastened, for it has been repeatedly claimed that specific remedies given early in the disease tend to produce relapses of severe local intensity. Herein we find the basis for the contention that salvarsan has changed the course of the disease, and when not given in sufficient doses to sterilize the patient, tertiary lesions appear much earlier than when the affection is permitted to run its course with the gradual establishment of a defensive mechanism, and consequently a longer refractory state. In so-called malignant syphilis we must also seek the cause in a precocious anaphylactic condition of the tissues rather than in the type of the invading organism, the reason usually evoked for this form of the infection. It has repeatedly been reported that spirochetes are numerically few in such lesions and that successful inoculations are relatively rare.

As accumulated evidence has shown that individual immunity is only relative, so racial immunity in the strict sense of the word does not exist. Lesser has said that neither race nor climate makes any difference in the receptivity of the virus of syphilis. Furthermore, it has been demonstrated that the children of syphilitic parents do not develop an immunity. Such children may be frankly

syphilitic at the time of birth or they may be in the latent stage for years (syphilis hereditaria tardiva). Or if they escape infection and acquire the disease later on, it has never been observed to have a milder course. Gluck reports that although syphilization is almost general in Bosnia, extra-uterine acquired lues is not rare. He noted 10 per cent. of cases of recent syphilis in children under fifteen years, one-third of whom were only five or six months old.

While complete statistics and comparative studies on the course of the disease in the different races are not available, the investigations made have revealed some interesting facts. Neisser found that in the Malays primary and secondary syphilis was insignificant. Treatment is therefore deferred and the percentage of cutaneous tertiary manifestations is proportionately large. He seldom met with visceral or nerve manifestations, and never encountered tabes or paresis. In Java and the tropics generally Europeans suffer more severely than the natives, which is attributable to unfavorable climatic conditions and changed mode of living. According to Quennac, Europeans, Hindoos, and Arabs in Africa suffer severely while the negroes only have mild attacks. In Central America, Rutschuh reported severe syphilis in the whites and negroes in contradistinction to the Indians and half-breeds who only suffered mildly. Among the Indians in the United States the infection is very destructive in some localities, as cited by Dr. Hrdlička, while it runs a mild course in certain other tribes. This authority also states that he has never seen tabes or paresis among the Indians, although they suffer from other forms of mental disease. As to the negroes in our country the writer has a personal communication from Dr. Green, of Milledgeville, Georgia, in which the statistics collected by him show that 5.27 per cent. of negroes suffer from paresis as against 2.12 per cent. of whites. Tabes is rare in this race.

It is often said that the European pandemic at the end of the fifteenth century was an exceedingly malignant one. This claim is now challenged by syphilographers that the disease was malignant in the present sense of the word, that is, ulcerating lesions in the early secondary period, but rather that many of the so-called cases were ordinary ulcerating tertiary forms. Instead of malignancy *per se* and a racial susceptibility, other factors are called into account, as the undeveloped treatment, wars, famines, etc. Neisser suggests that spirochetes in their continual passage through human beings lose in virulence, or that the treatment which the patient receives so modifies the virulence that when such modified spirochetes are transmitted they produce a modified disease.

Heredity. The question of the transmission of syphilis to the offspring is a very complicated one, and still far from clear. While the accession of serological knowledge has presented a partial solution, there still remain certain clinical phenomena for which no satisfactory explanation can be given.

The opinion is gaining on almost every hand today that germinal infection on the side of the father does not take place, but that the mother, infected by the father either before or at the time of conception, transmits the disease to the fetus through the placenta. Is this view tenable on the ground of our clinical and laboratory observations?

Disease of the testicles during the secondary stage is not common, although it has been demonstrated by animal experiments that this organ is one of the seats of election of the syphilitic virus. Later a diffuse orchitis is more frequent, and during the tertiary stage gummata are not uncommon. As to other lesions of the genito-urinary tract which might harbor spirochetes little is known.

In the transmission of syphilis the results depend upon the intensity of the infection, which intensity weakens with time.

In the secondary stage it is most active, so that a man is almost certain to infect his wife. If she becomes pregnant early abortion will result. Such a woman, if untreated may abort later, then have a stillborn child or a living child with active syphilis, and finally, after eight to twelve to twenty years, healthy children. Such women are obviously syphilitic. On the other hand, there is the group of women who have been free from the clinical manifestations of the disease but who have had several miscarriages or children with unmistakable signs of the infection. These women, according to Colles-Baumès law, have not syphilis but are immune to syphilis. What has taken place that prevents such a woman from developing a primary sore or a secondary rash and still has rendered her insusceptible to the disease? Is it because she has the infection or because Wassermann substances or antibodies are passed through the placenta? In other words, must we conclude in view of the positive Wassermann reaction that her tissues are harboring living spirochetes which without treatment are overcome by the defensive mechanism of the patient or does she simply receive Wassermann-producing substances?

Serological research has in the main overthrown Colles' and Profeta's laws. It has been demonstrated by a host of investigators that the majority of women apparently healthy who give birth to syphilitic children have a positive Wassermann reaction and are therefore in the latent stage of the disease. Furthermore, Baisch, Trinchese, and Weber constantly found spirochetes in the maternal portion of the placenta and in the intervillous spaces even in negatively reacting women. The claim then that Wassermann-producing substances pass over from the fetus to the mother had to be dismissed as the persistence of the reaction after birth was strong presumptive evidence of the presence of living spirochetes, their demonstration in the placenta supporting the contention. The transmission of organisms to the fetus by way of the placenta finds its analogy in other diseases, such as smallpox, relapsing fever, and

tuberculosis. In tuberculosis this takes place only in advanced and florid cases in contradistinction to lues, where no clinical evidence of the disease may be present, multiplication of the spirochetes probably taking place through the impetus given by pregnancy. It is interesting to note in passing that Uhlenhuth found typical testicular lesions in the young of a syphilitic mother rabbit, illustrating that the organisms pass through the placenta. Varying degrees of latency are met with. In some women a negative Wassermann in the blood is accompanied by a positive reaction in the colostrum of the breast, or the placental blood may be stronger than the rest of the serum. The evidence submitted in favor of maternal transmission is convincing, but the question as to how the mother received her infection is not so easy of solution. Is she inoculated prior to or at the time of conception or later? Do the organisms penetrate the ovum or do they enter the tissues of the mother without the production of the usual sequence of symptoms? It has been shown experimentally that the semen of latent syphilitic men may from time to time contain spirochetes. As many of these patients have had more or less treatment, it has been suggested that an attenuated form of the disease is transmitted to the wife. There are two ways in which paternal transmission could take place. In the one we may assume that the parasite is carried in the head of the spermatozoön and with it penetrates the ovum. As the organism is three times the length of the spermhead this possibility is dismissed by the majority of syphilographers. The other alternative is that the spirochetes are free in the semen and with it enter the egg cell. Such an event it is believed would have an untoward effect on the fertilized ovum, as it has been shown that the disturbance of a single blastomere in lower vertebrates is sufficient to arrest development or cause malformation, and the regenerative powers are greater in these animals than in the higher vertebrates (Weber).

Latency. What is our present conception of latency in syphilis? During these periods of apparent quiescence does the defensive mechanism hold the pathogenic agent in abeyance or is some pathological process insidiously undermining tissue in some part of the body? The application of the Wassermann reaction has materially changed our views since the demonstration in a large number of so-called latent syphilitics of involvement of the aorta and the central nervous system. It has been shown that such patients may have a chronic meningitis for years without producing obstrusive symptoms, and a limited aortitis may persist for a long time without making its presence known either subjectively or objectively. Aside from gummatous involvement of the viscera little is known of the effects of the infection on the various organs. Where must we seek the explanation of persistent Wassermann reactions in cases intensively treated in whom involvement of the central nervous system

and the heart and aorta can be excluded? A solution will probably be reached when the nature of the Wassermann reaction is fathomed, but on *a priori* grounds if a focus in the aorta or nervous system is capable of keeping up a positive reaction indefinitely, it is reasonable to assume that a similar process in one of the viscera may be provocative of a like result.

It is often asked where the spirochetes are lodged during the latent period. A number of investigators have urged that during this stage, resting forms of the organisms are harbored by the lymph nodes or blood-forming organs. Present knowledge does not support the theory of a cycle of evolution with the power to produce lesions according to the stage of its development. Spirochetes recovered from any source whatever—chancre, mucous patch, or gumma—the blood, nervous system, or viscera have all shown similar morphological and practically the same biological characteristics.

The relation of trauma to the localization of specific lesions has been so well appreciated by the medical profession that it is given a prominent place as an etiological factor. The query naturally arises as to whether the spirochetes in such cases have remained *in loco* since their primary deposition or are carried there by the blood after injury to the tissue. Pasini found spirochetes in an atropic and pigmented spot two years after the involution of a papular syphilide, while Hoffman demonstrated them in scar tissue of chancres long after their regression. Levaditi and Yamanouchi were able to recover them from the cornea of a rabbit one hundred and thirteen days after the keratitis had healed and at which time a recurrence took place. The so-called chancre redux is interpreted by many as the result of organisms which have escaped destruction rather than as a superinfection with a new strain. Neisser has demonstrated that spirochetes may be present in the skin without producing any macroscopic changes, and more recently Whartin has called attention to their presence in the heart without exciting tissue reaction.

Studies on the infectiousness of the blood in the various stages of syphilis have supplied us with the following data: In 19 cases of primary syphilis, Uhlenhuth and Mulzer obtained positive results in 16 rabbits injected with 2 c.c. of defibrinated blood into the testicle; in 36 cases of early secondary syphilis, 27 positive results, and in 15 cases of latent syphilis 2 successful inoculations. One of the latter was with the blood from a woman whose infection was four years old and who eighteen days before had given birth to a syphilitic child. Lieberman also succeeded with the blood from a woman whose primary lesion dated back four years and who six weeks before had given birth to a luetic child. Frühwald reports 2 cases: In one the disease had existed for one year, the Wassermann was positive and the patient had had two doses of

neosalvarsan, each 0.75 gm.; in the other the infection was one and a half years old, the Wassermann was positive, and the patient had received two doses of neosalvarsan of 0.6 gm. each.

Numerous attempts have been made with the blood of paretics and tabetics, but with little success. Levaditi demonstrated spirochetes in the blood of one patient with paresis, and Graves reported positive results with blood from two pareties. Ellis' experiments to confirm these findings gave constantly negative results.

The above facts are in accord with the clinical teaching that the blood of luetic individuals is infectious during the active primary and secondary stage, and that this diminishes with the age of the disease. Exceptions to the innocuousness of the blood of latent syphilitics are seen in the occasional infection of a surgeon in his operative work on an individual in this period of the disease. It is to be inferred therefore from clinical and laboratory experience that under conditions of which we are at present ignorant, spirochetes may reach the circulation from some focus in the body. In certain cases this may precede the cutaneous relapse, in others it is accompanied by no visible manifestations. Kraus has called attention to febrile attacks as the only symptom of latent lues, and suggests the spirochetemia as a possible explanation. An analogy is found in trypanosomiasis where the parasites may disappear spontaneously from the blood and reappearing give rise to an eruption and fever. Moreover, a latent period of three years may ensue before the nervous symptoms appear.

Pathological Anatomy. The predilection of syphilis for the vascular system is noted almost from the inception of the disease in the involvement of the cutaneous vessels at the point of inoculation. Here the pathological process consists of an endarteritis, later a panarteritis, with a characteristic inflammatory infiltration. Excepting the macule all the lesions succeeding the chancre show a marked affection of the vessels, especially those of the late secondary and tertiary stages. The formation of giant cells so frequently encountered in the secondary papule, the nodular syphilide and gumma may be traced to a vascular genesis, while the extension of serpigenous lesions may be explained by the progressive thrombosis of the vessels.

A study of the pathological anatomy of syphilis shows that fundamentally the reaction is on the part of the fixed connective-tissue elements, the labile constituents coming into play locally only secondarily. The chief cells are the lymphocyte and the plasma cell, the latter believed to be a derivative of the former and the antecedent of the fibroblast. It has been shown by Hazen that a circulatory leukocytosis is present in untreated secondary cases, sometimes as high as 20,000 white cells. The neutrophiles are absolutely and relatively increased and the percentage of eosinophiles is higher.

Under treatment there is a slight drop in the total count, with a marked relative increase in lymphocytes which under treatment may run as high as 65 per cent.

The syphilitic process is essentially a granuloma having its origin in the perivascular lymphatic spaces. In the primary lesion the main changes are found in the cutis, the very earliest of which are in the new formation of capillaries and the grouping about these and preëxisting vessels of lymphocytes and plasma cells. At first they mantle the vascular structures as a "coat-sleeve" infiltration, but as the lesion grows older, spread out and become diffuse. The endothelium of the capillaries is swollen and proliferated so that the lumen is narrowed or altogether occluded, and in the larger vessels with an external coat there is in addition evidence of inflammation and an increase in thickness. In some instances giant cells are found. From the newly formed granulation tissue, connective tissue is formed which later scleroses and leads to induration. Owing to interference with nutrition, regressive metamorphosis sets in. The epidermis presents a varied picture, depending on whether there is pressure from the infiltrate or retrograde changes with erosion and ulceration.

In the secondary stage the disease is characterized by a succession of eruptions and a general adenopathy. Ehrmann has said that the distribution of secondary syphilides is governed by the branching of the vascular stems. The roseola or macular syphilide under the microscope shows very few changes, being simply an erythema with dilatation of the vessels of the papillary body and adjoining corium and an infiltration of lymphocytes and plasma cells about them. In the papular or lenticular syphilide we find in the cutis a circumscribed lesion made up of lymphocytes, plasma cells, and proliferated fibroblasts, all in close relation with the vessels which show the characteristic changes. Lichen syphiliticus owes its peculiar features to localization, namely, distribution about the pilo-sebaceous apparatus. Here the process surrounds a hair follicle and extends deeply into the corium. Its structure is like that of other lesions, with usually abundant giant cells of vascular origin. The epidermis in all lesions of this stage shows only secondary changes. It may be thinned from pressure of the granulomatous tissue beneath or there may be edema with an increase in thickness and scaling. In condylomata papillomatous overgrowth is a marked feature. Pustular and suppurating syphilides usually signify extraneous inoculation with pus-producing organisms. The pigmentary syphilide, or leukoderma syphiliticum, according to Ehrmann, is due to chromatophores, the pigment passing from them to the basal layer of the epidermis.

As a rule, secondary syphilides undergo spontaneous absorption. Microscopic residua may, however, persist for a long time. Their connection with local relapses has been suggested.

The type of lesion of the tertiary period is the gumma. The process consists of an infiltration of lymphocytes, plasma cells, and proliferated connective-tissue cells about the vessels, newly formed and old, which are the seat of an endarteritis and panarteritis, and give rise to giant cells. Caseous degeneration usually begins in the centre of the granuloma, or in some cases it may be fatty or mucoid in character. The last mentioned is most often found in bones. The necrotic areas liquefy and are absorbed or discharged, the usual procedure being gradual absorption, with formation of cicatricial tissue, the contraction of which leads to deformity. It is believed by many that the fibrosis is not purely a process of repair or due to the irritating action of necrotic tissue, but that there is also a syphilitic element. The plasma cell thought to be the precursor of the fibroblast has been credited with being more than a passive participant. The late nodular or tubercular syphilide is in reality a gumma, situated more superficially in the cutis. The serpigenous lesions which also belong to this stage are made up of groups of nodules situated about the cutaneous vessels, the thrombosis of which probably explains the progressive character of the lesion.

Syphilitic phlebitis is relatively infrequent, occurs usually in the veins of the lower extremities, and is of minor importance. Arterial disease, however, is very common and of serious import, the vessels especially attacked being the aorta, the cerebral, pulmonary, subclavian, femoral, and popliteal arteries. Owing to disease of the walls, vasomotor response is impaired or lost, and where there are obliterative changes due to endothelial proliferation or secondary thrombosis, interference with the blood supply and impairment of nutrition. While the brain and the heart suffer more severely in this respect, other organs and the vessels of the extremities are not exempt. Several years ago the writer had under observation a case of gangrene of the leg consecutive to a syphilitic thrombosis of the femoral artery (Fig. 1). The patient was a colored girl, in the City Hospital, upon whom several amputations were made, after each of which the gangrenous process developed and spread. A picture closely simulating Raynaud's disease is also met with as the result of luetic involvement of the vascular supply of the extremities, and in several cases of symmetrical cutaneous atrophy which I have had under my care the syphilitic element was the predominant feature.

Aortitis. It is only within the last decennium that the syphilogenic nature of aortitis or mesaortitis has been generally recognized among internists and syphilographers. During this period the development of the Wassermann reaction and roentgenology, as supplementary to the physical examination, have shown us how widely prevalent the disease is among individuals who have had a syphilitic infection.

As to its frequency of incidence, Chiari found the condition present in 59 per cent., Fahr in 29 per cent., and Fraenkel fifty-three times

in 102 cases of constitutional syphilis. Stadler, whose statistics cover 256 cases, demonstrated the disease in 82 per cent., and of 211 of this number it was the cause of death in 117. Staub found an aortitis in 82 per cent. of paretics which came to autopsy, Buder in 84.5 per cent., and Alzheimer in 74 per cent. The findings of Rach and Wiesner show that in congenital syphilis, changes in the aorta or pulmonary artery are seen in 67.4 per cent. Lenz states that in large cities 25 per cent. of all syphilitics die from aortitis (angina pectoris, aortitic insufficiency, aneurysm) as against 3 to 4 per cent. from paresis, 1 to 2 per cent. from tabes, and 10 per cent. from all other syphilitic affections, as of the brain, liver, kidneys, etc.

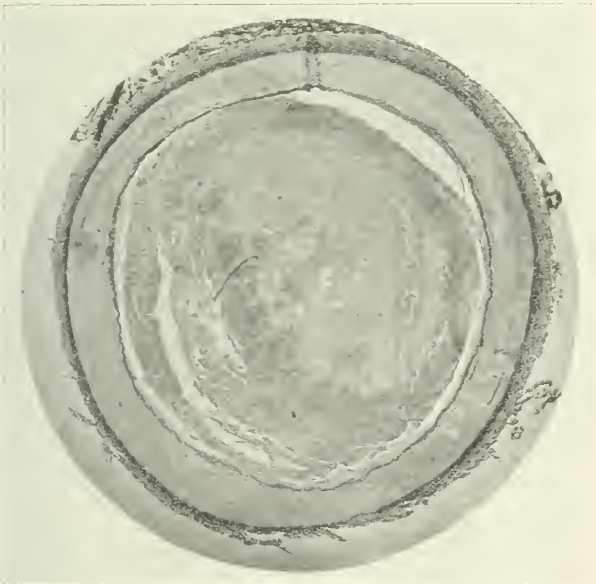

FIG. 1.—Syphilitic thrombosis of femoral artery. Transverse section of artery, showing thrombus and thickening of arterial coats.

Mesaortitis has been defined by Dochle, Heller, and others as a specific inflammation of the adventitia and media which terminates in cicatricial deformity. As a rule, there is a combination of processes so that cicatrization may be present in one part while active inflammatory lesions are found in another. The disease shows a decided preference for the ascending portion of the aorta and the arch, the explanation being that the impact of the blood is greater here than in the rest of its extent, following the well-known law that syphilis localizes where trauma has produced a *locus minoris resistentiæ*. In contradistinction, atheroma selects the lower portion of the aorta where the mechanical element is of slighter moment. Stadler could find no relationship between an increased

blood-pressure or marked variations in pressure. Strümpell favors a summation of injurious agencies, as the noxious influence of alcohol and tobacco, with consequent lowering of resistance of the vessels.

Grossly the aorta gives a characteristic picture (Fig. 2). The inner surface shows isolated or confluent elevated, wrinkled, grayish, and translucent sclerous areas, with puckering or cicatricial pitting, or again radiating ridges with depressed cicatrices between. The intima over the affected areas preserves its glistening appearance. The thickness of the artery varies in different portions, so that while indurated and sclerotic at one point it is thin and translucent at another. Depending on the extent of involvement, dilatation is present. This may be uniform throughout the length of the thoracic portion or appear as small aneurysmal pouchings or a true saccular aneurysm. All transitions are found. Ordinarily it is not difficult to differentiate this condition from arteriosclerosis in the absence of fatty degeneration and calcification. However, in old subjects there may be a combination.

Fig. 2.—Syphilitic aortitis, showing characteristic changes in the walls of the vessels, transverse rupture, and dissecting aneurysm into coats of the aorta. (Specimen of Dr. John H. Larkin.)

In the beginning the lesion is often confined to the vessel in proximity to the aortic valves. Later it extends to them and gives rise to insufficiency, which condition is very frequent. With the extension of the process the ascending aorta and the arch are involved. Not rarely changes are also noted about the mouths of the larger branches of the arch, causing narrowing of the left carotid, innominate, and subclavian arteries, which localization is significant from a clinical point of view. With involvement of the aortic ring the mouths of the coronary arteries are also considerably reduced.

The relation of syphilis to aortitis was for a long time disputed. On the one hand investigators classed it with parasyphilis because of the difficulty of demonstrating spirochetes, its indurative or

fibrotic tendencies, and indifferent results from treatment. On the other, which has the support of recent examinations, it was classed with active syphilis. The demonstration of spirochetes in the aortic wall by Reuter, Schmorl, Wright, Richardson, and others in acquired syphilis, and by Wiesner and Rach in congenital, together with the microscopic picture of gummatous lesions, and a positive Wassermann reaction in about 80 per cent. of cases, definitely places the affection in the category of active syphilis. It is difficult to demonstrate the organisms even in comparatively recent and active lesions. This, however, does not militate against their syphilitic nature, as they are equally difficult to demonstrate in cutaneous

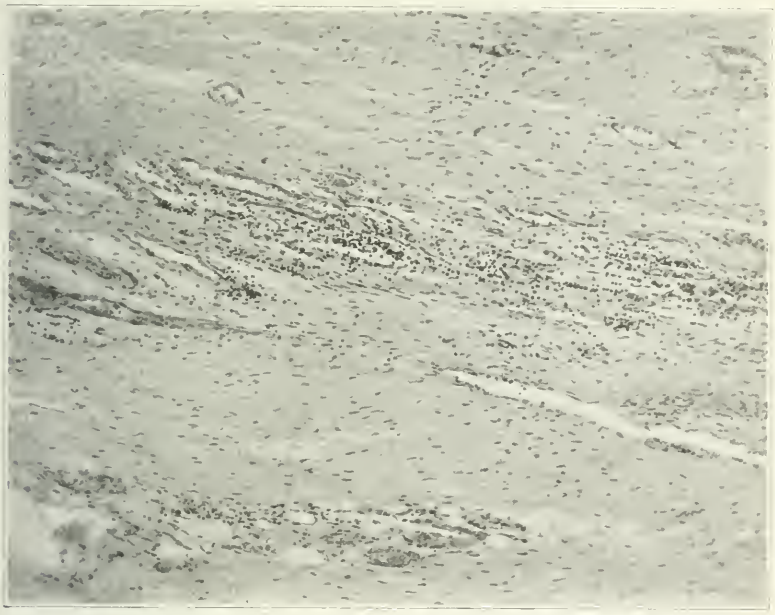

FIG. 3.—Early stage of aortitis, showing characteristic lymphocytic and plasma-cell infiltration about the small vessels in the adventitia.

gummata. In both the tissue is probably in a state of altered reactivity, so that numerically few organisms are capable of bringing about the necrotic change. The striking changes are in the media, although the disease begins in the adventitia. Miliary gummata undergo necrosis and are replaced by cicatricial tissue. In the adventitia in recent processes an inflammatory infiltrate of lymphocytes and plasma cells is localized about the vasa vasorum (Fig. 3), while in older ones only fibrotic changes may be left (Fig. 4), the nutrient vessels themselves being the seat of an obliterating endarteritis, such as is found in syphilitic lesions elsewhere in the body. The elastic tissue, and this is characteristic of luetic disease

of the larger vessels, is either fragmented or has entirely disappeared. The intima shows no change at all or various grades of a compensatory thickening. On the question of genesis of the early changes there is some dissonance of opinion. Doehle, Heller, Backhaus, Saathoff, and others trace the beginning of the disease to the vasa vasorum. They claim, primarily, a swelling of the endothelium of these vessels in the middle third of the media to large epitheloid cells, which lead to an obliteration with secondary regressive metamorphosis of the aortic wall. Marchand, Beneke, Arnsperger, and others not corroborating these findings incline to the view that the medial changes are primary, the virus so injuring the elastic lamellæ

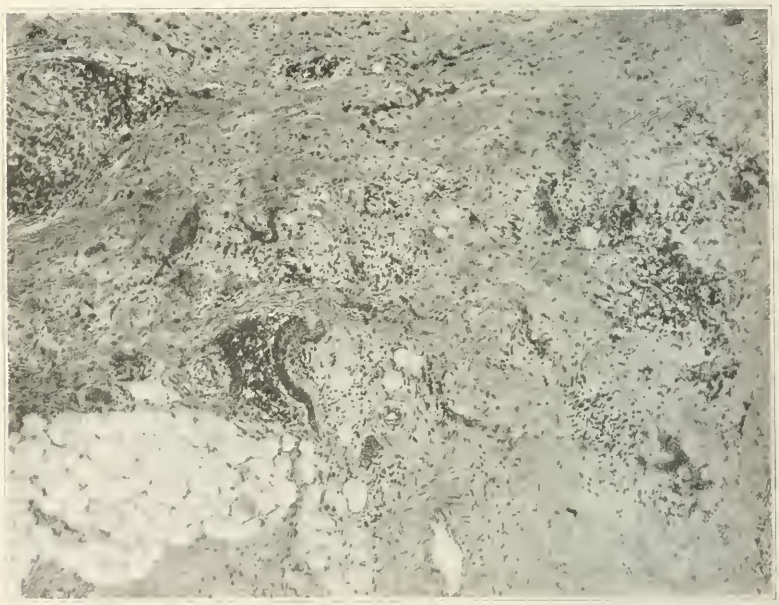

Fig. 4.—Later stage of aortitis, showing advanced sclerosis of the vessel walls.

that they succumb to the pressure of the blood. The difficulty of determining the genesis with positiveness even early is apparent, for, as Stadler points out, a simple infiltration of the vasa vasorum may also occur under the influence of the toxins of alcohol and other infections. Benda describes two forms of aortic disease. In the one submiliary lesions without necrosis which cicatrize and leave none or only a very slight deformity of the vessel wall, in the other typical gummata, with central necrosis, the scarring of which leads to typical sclerotic changes in the wall.

The clinical diagnosis of aortitis is often extremely difficult. Limited and circumscribed changes of the ascending portion without involvement of the ring are, as a rule, not accompanied by sub-

jective or objective manifestations. Such patients may be observed for a long time without eliciting signs pointing to the condition, Roentgen-ray examination also being negative. Only when a greater area is involved especially more or less of the circumference are there symptoms suggestive of disease, namely, pain, dyspnea, and tachycardia on slight exertion, increased blood-pressure, weakness, and easily induced fatigue.

The pain is often the primary and predominant symptom, although frequently it is lacking or indefinite. It is characterized as a dull aching or a feeling of pressure under the sternum, with pain radiating to the side of the chest, the back, and the arms. Disease of the innominate, carotid, and subclavian may be attended by a condition simulating intermittent claudication of the lower extremities, with weakness, radiating pain, and sensory disturbance. Periodic or continuous headaches, often with vertigo, accompany involvement of the mouth of the left carotid, and where the coronary arteries are the seat of disease the attacks are anginal in character. There appears to be no satisfactory explanation for the origin of the pain. Thoma referred it to injury of the larger and smaller nerve trunks as well as irritation of the Pacinian bodies in the aortic wall. Huchard attributes it to a peri-aortitis, and the neuralgic pains in the chest and shoulder to the changed relation of the subclavian to the brachial plexus. Longcope came to the conclusion that the anginal attacks were due to reflex disturbances set up by the syphilitic process involving the root of the aorta, the paroxysmal dyspnea being regarded as an acute bronchiospasm.

When does the aortic disease begin? Obviously this is difficult to affirm, as the disease in the majority of cases is insidious in its onset, the first symptoms appearing only when the affection has made some progress. In assuming that involvement takes place at the close of the primary stage when there is a general dissemination of the spirochetes, we are confronted with the same problem as when we endeavor to establish the time of infection of the central nervous system. Palpitation, arrhythmia, tachycardia, and disturbances in the pulse rate frequently occur in early secondary syphilis, which has been adduced as evidence that involvement takes place at the time the disease is a spirochetemia. The publication of fatal cases shortly after infection also inclines to the view that involvement takes place early. Brooks recorded perforation of an aneurysm before the secondary rash had fully appeared, and another case with a fatal aortic lesion within six months of infection. Longcope cites two patients who died from the effects of syphilitic aortitis four years after the appearance of the chancre. Stadler publishes two cases in whom death occurred five years after infection. The first patient, aged twenty-nine years, showed at autopsy a fibrous aortitis and aneurysm. The second, aged twenty-seven years, the objective and subjective signs of an aortitis.

He further studied 12 postmortem cases of severe secondary and tertiary syphilis in patients under thirty years of age. He assumed on account of the youth of the subjects that the infection could not have been of long standing, but in none were changes of syphilitic aortitis demonstrable.

The writer has recently investigated, in his private practice, all latent syphilitics, especially those with a persistent positive Wassermann, for the occurrence of cardiovascular disease, and in a large percentage has found the existence of such a lesion.

The average age at which the disease appears is forty-seven to forty-nine years, but it is not rare to find it in much younger patients. Aortic disease in general makes slow progress, for Weintraud, Stadler, and others give the average lapse of time as twenty years, the interval vacillating between five and forty years. The disease usually runs a fatal course in about two years after the development of the symptoms. The importance of early diagnosis is, therefore, apparent, especially in view of the fact that the affection is a manifestation of active syphilis and amenable to treatment. In 95 cases of aortitis collected by Benda the termination was as follows: In 9, coronary stenosis; in 22, aortic insufficiency; in 37, combined coronary stenosis and aortic insufficiency; in 27, aneurysm. In a total of 248 cases he found aneurysm forty-eight times.

The relation of cardiovascular affections to tabes has for a long time occupied the attention of clinicians. According to Lesser's statistics in 96 cases of tabes come to autopsy, aneurysm of the aorta was found eighteen times. A review of the literature shows that the coincidence of tabes and aortic insufficiency is most frequent. Rogge and Ruttner report the association in 6.5 per cent.; Rogge and Müller in 10 per cent.; Stintzing in 3.8 per cent., and Stadler in 6.2 per cent. of all cases of well-developed tabes. The latter did not include his cases of incipient tabes; in manifest tabes which came to autopsy, however, he found disease of the aorta in almost all. Rogge and Müller have called attention to the cause of sudden deaths in tabetics as being due to lesions referable to the central nervous system but to sudden cardiac insufficiency or rupture of an aneurysm. The so-called cardiac crises are in reality attacks of angina pectoris, due to changes in the coronary arteries.

Strümpell has emphasized the surprisingly frequent presence of rudimentary tabes in patients who seek medical advice for symptoms referable to the heart. Many of these cases show only pupillary changes, such as narrowing, irregularity, and fixation to light. Only one pupil may be affected, as in a case cited by him with severe endocarditis, myocarditis, and aortic insufficiency. The reflexes are only slightly altered or the Achilles reflex alone lost and the patellar reflex exaggerated. Observing these cases over a long period of time, weakening and gradual disappearance of the

reflex may be noted. In general, symptoms of aortic disease appear later than the earliest tabetic manifestations. Rogge and Müller are of the opinion that tabetic symptoms average four and a half years earlier than those of the circulatory apparatus. It is probable that it is not a later involvement, only that the condition has a longer latency and therefore manifests itself later.

The writer has under treatment at the present time several patients with tabes and concomitant aortitis. One of them, with optic atrophy, has an aneurysm. Five others, in whom the tabetic symptoms have existed on an average of eight years, show a marked sclerosis of the aorta. In a paretic, Roentgen-ray examination shows dilatation of the ascending aorta and in a case of cerebrospinal syphilis, with cardiac symptoms developing four months ago, a small aneurysm. In another patient, aged thirty-one years, who had had an attack of hemiplegia four years ago, signs of aortitis have developed within the past few months. The Roentgen-ray plate also show a marked sclerosis.

For the following interesting postmortem examination and also some of the illustrations which accompany this article I am indebted to Dr. John H. Larkin, Director of Pathological Laboratories, Department of Charities, New York City:

J. E., aged forty years. The patient was admitted to the City Hospital (service of Dr. Evan Evans) the latter part of 1913 for sciatica. After a few weeks he was discharged and five months later re-admitted, at which time in addition to the sciatic pains he complained of girdle pains. Lumbar puncture showed thirty-eight cells, an excess of globulin, and a strongly positive Wassermann. His serum was also positive. A diagnosis of tabes without clinical evidence, excepting the girdle pains, was made. Further examination, including Roentgen-rays, revealed an aneurysm of the ascending aorta. He was placed on salvarsan and mercurial treatment, which reduced his cell count and reversed the Wassermann in the fluid, but had no effect on that of the blood. The patient died suddenly from a rupture of the aneurysm into the thoracic cavity. Microscopically the aorta showed a characteristic picture with a round-celled infiltration in the adventitia. The interesting feature of the findings in this case was in the cord, which showed an involvement of the pia-arachnoid with a round-celled infiltration about the small vessels and an insular degeneration of the posterior nerve roots (Fig. 5). The posterior columns were unaffected.

Nervous System. With the acquisition of more exact knowledge our ideas concerning syphilis of the nervous system have undergone considerable revision. The present views based on clinical and laboratory investigations may be formulated as follows: Infection of the central nervous system probably takes place in the early stage of the disease with the generalization of the virus. Accumulated clinical evidence points to meningeal involvement during the first few

months, in some cases before the appearance of the cutaneous eruption. Lumbar puncture in the hands of different investigators has elicited varying results. Thus, Ravaut found the spinal fluid in secondary syphilis abnormal in 67 per cent. of cases, Altmann and Dreyfus in 78 per cent., Nonne in 40 per cent., and Swift and Ellis in 36 per cent. The writer's findings, based on the examination of cases in the secondary stage with and without cutaneous lesions, showed meningeal involvement in less than 20 per cent. Fournier's dictum that patients in whom secondary symptoms are overlooked or very mild later show involvement of the central nervous system has been reiterated again and again. This led Finger

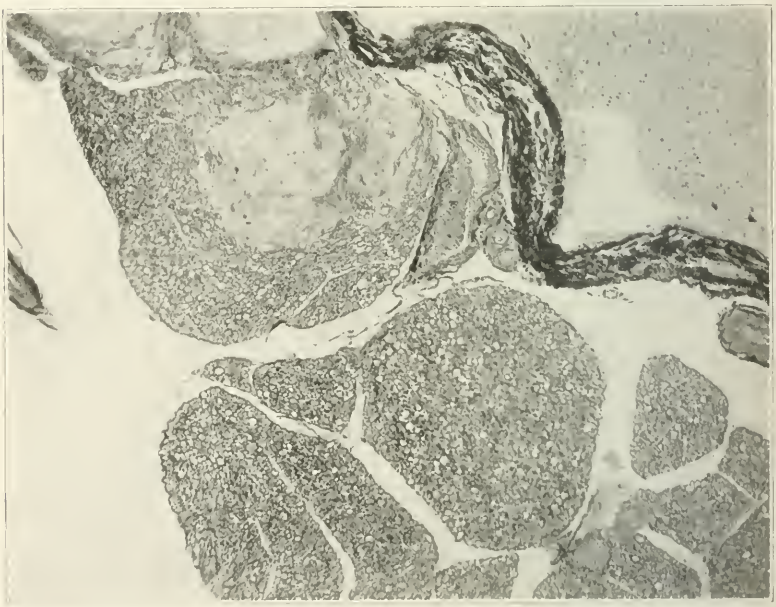

FIG. 5.—Insular sclerosis posterior nerve root, with accompanying meningitis. Posterior columns not involved.

to divide syphilities into two classes: those with manifest cutaneous lesions, and those with absent or mild skin lesions and meningeal involvement, which division is too arbitrary for many cases with severe cutaneous lesions as well as those which have been treated early later develop disease of the nervous system. The observation of patients over long periods of time has shown that a low-grade meningitis may exist for years without producing obtrusive nervous symptoms. Such lesions are comparable to the superficial lingual and palmar syphilides, which persist for years, produce little inconvenience, and are refractory to treatment. There has been a good deal of speculation as to whether the spirochetes producing lesions in the central nervous system are the remains of

those deposited during the spirochetemia or whether they later reach the nervous system from another focus. Head's work is perhaps suggestive. In seeking to explain the more frequent involvement of some areas in root affections over others he found that the roots most commonly subjected to irritation were those in connection by their visceral afferent fibers with certain organs known to be the seat of active spirochetosis in syphilis. Thus the second and third cervical contain afferent paths from the tonsil; the first, second, third, and fourth thoracic from the aorta, while those from the seventh thoracic to the first lumbar, the most frequently involved, carry afferent paths from the liver, kidney,

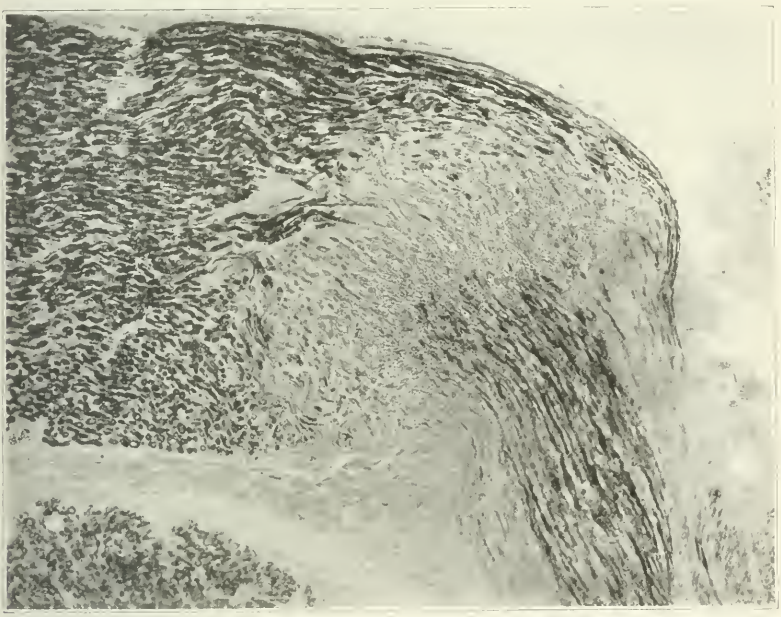

FIG. 6.—Degenerated posterior nerve root in tabes. Posterior columns involved.

suprarenal, and testicle, organs which are the sites of election of the parasite. Orr and Rows have shown in their investigations on the lymphogenous infection of the nervous system that organisms and their toxins travel along the perineural lymphatic space which surrounds every spinal nerve and extends along the roots to the pia mater. These spaces are not only in connection with the pia, but through the latter in communication with the adventitial lymph spaces of the perforating vessels. The rôle of these channels as distributors is therefore quite obvious.

The sharp distinction formerly drawn by clinicians and laboratory workers between cerebrospinal syphilis and parasyphilis is no longer tenable. Gradually the barrier has given way until we have come to regard these conditions as identical from an etiological

stand-point, though differing in reaction, which difference depends on localization and the tissue involved. By cerebrospinal syphilis

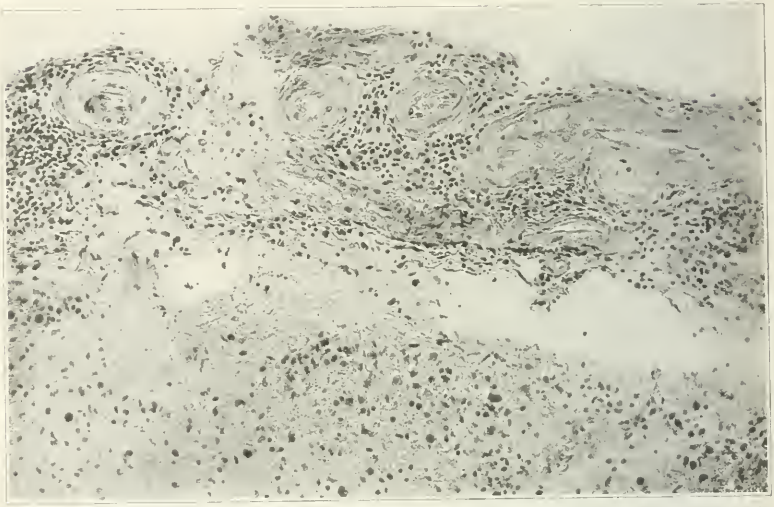

FIG. 7.—Syphilitic meningitis, showing various stages of obliterating endarteritis.

FIG. 8.—Mantling infiltration of lymphocytes and plasma cells about pial vessel in brain cortex.

we understand the exudative, vascular, and gummatous processes which involve the coverings of the nervous system and the blood-vessels within them (Figs. 7, 8, 9 and 10). These processes in the

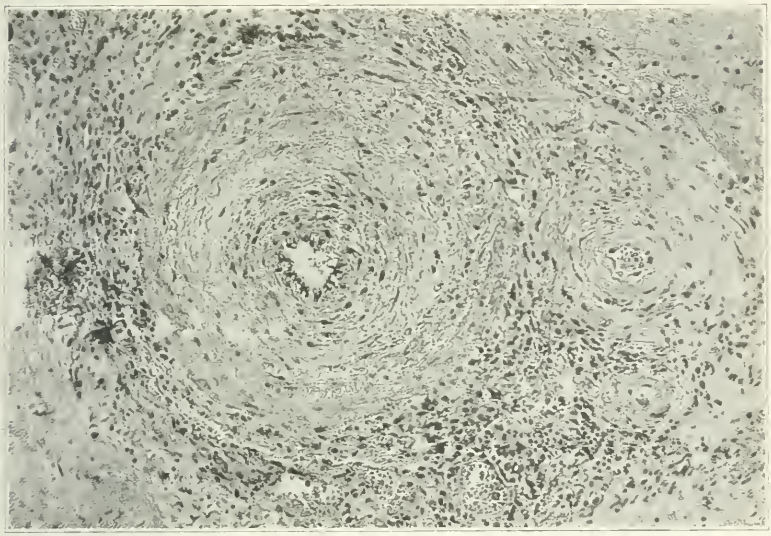

Fig. 9.—Heubner type of obliterating endarteritis in syphilitic meningitis.

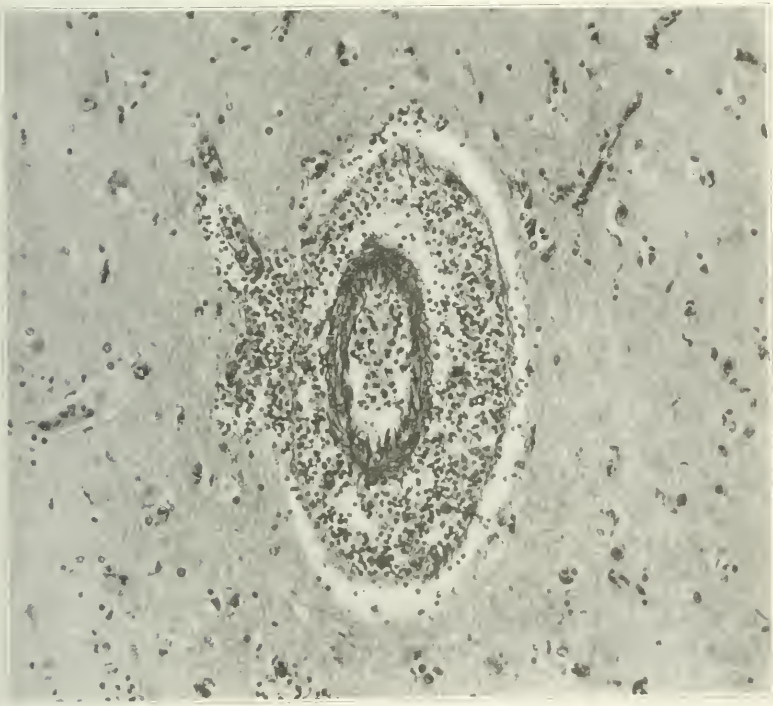

Fig. 10.—Small vessel in cortex of the brain, showing infiltration of perivascular spaces with lymphocytes and plasma cells.

great majority of cases remain superficial, but in some cases extend into the essential nervous structures along the pial or advential sheaths of the vessels, and give rise to the borderline cases of tabes and paresis.

It is proposed by Head and Fearnsides to divide luetic disease of the central nervous system into syphilis meningovascularis and syphilis centralis, the latter including all those cases where degeneration of nerve tracts or nuclei shows that the lesion must lie within the structure of the nervous system itself. As meningitis and endarteritis, however, are common to all these pathological states, this classification does not seem to the writer a tenable one.

What is the nature of paresis and tabes? In paresis there is a combined meningitis and encephalitis with a typical infiltration of lymphocytes and plasma cells in the adventitial lymph spaces (Figs. 11 and 12), the secondary degenerative changes probably depending on the primary vascular disease. Likewise we have a meningitis in tabes, but it is easier to comprehend the pathological condition and manner of invasion in paresis than the tract degeneration in the cord. The view that the genesis of both affections lies in a chronic meningitis now has a pretty wide acceptance. In tabes, Nonne believes it leads to disease of the roots and secondarily of the posterior columns. Nageotte was the first, in 1894, to describe a low-grade meningitis at the junction of the anterior and posterior roots on the proximal side of the ganglion, and in addition a neuritis, as shown by an inflammatory condition in the perineurium and a perivascular infiltration of plasma cells and lymphocytes in the posterior roots. This was confirmed by Dinkler, Dejerine, and others, but their views were not generally accepted, as the findings were interpreted as a combination. Again, in 1906, Schröder showed that collections of lymphocytes and plasma cells occur in the lymph spaces of the vessels in paresis and tabes, and that in the latter they are found not only in the pia and connective tissue about the vessels in the peripheral parts of the cord, but in the intramedullary portion of the columns as well.

Stargardt's findings in optic neuritis also have an important bearing. In a number of cases of tabes and paresis he found a true inflammation of the sheath and endoneurium. He also described an active inflammatory process in the joint structures of tabetic arthropathy, as evidenced by plasma cells and lymphocytes, with endarteritis of the small vessels. Steiner's studies on peripheral nerves in tabes and paresis also brought him to the conclusion that the process is an inflammatory one. The older view of a primary neuron degeneration in the light of present evidence would seem to have to be abandoned.

According to McIntosh, Fildes, Head, and Fearnsides, parasyphilis "depends upon an anaphylactic reaction in the tissues of the central nervous system which have been rendered hypersensi-

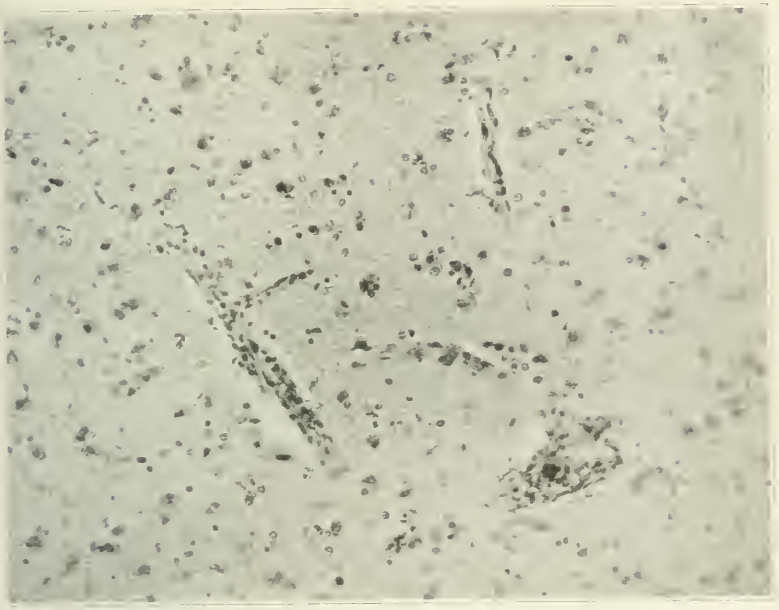

FIG. 11.—Showing the characteristic picture of paresis, with plasma-cell infiltration.

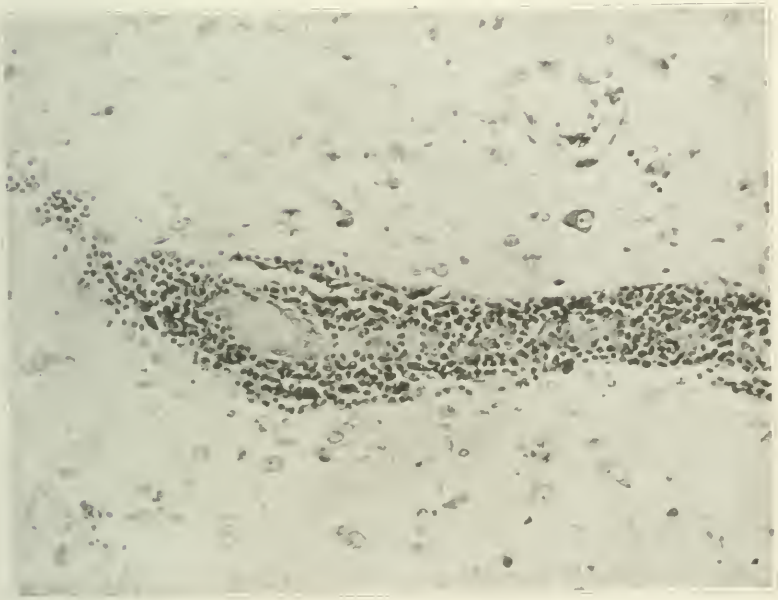

FIG. 12.—Paresis, showing the grouping of lymphocytes and plasma-cells about small vessels in cerebral cortex.

tive in accordance with their peculiar lymphatic distribution." Since it has been shown by Marie and Guillain, Orr and Rows, and others that the posterior columns are in direct lymphatic communication with the posterior roots, the aforementioned authors have evolved the theory that sensitization takes place during the secondary period by the spirochetes or their toxins ascending the afferent peripheral nerves. When spirochetes again become active in the posterior columns a violent reaction may ensue, injuring the nerve fibers and producing proliferation of the neuroglia and wandering cells. The injury of the nerve fibers will lead to degeneration, which will continue as far as the reflexion of the neurilemma. In the same way the cerebrum or isolated groups of cells in the anterior horns or other groups of fibers or cells alone or in combination may be affected, the particular region involved determining the clinical picture. Noguchi had previously shown by animal experiments that sensitization may be necessary before spirochetes can infect the brain. In both rabbits and monkeys he obtained negative results when the organisms were inoculated directly into the brain. He therefore injected rabbits with living and dead spirochetes intravenously, and after five months inoculated them subdurally with a particle of a scrotal syphiloma rich in spirochetes. They all remained well for two months, then became emaciated, and showed a slightly ataxic and spastic gait. The symptoms continued to increase, and after five months the animals were no longer able to jump. Microscopically some of these animals showed identical changes, with paresis, but the nerve cells were intact. In three an exudative meningitis was found and in one a unilateral atrophy of the frontal lobe. The control animals without previous sensitization remained well.

Analogies are frequently drawn between tabes and paresis and sleeping sickness. Spielmeyer, as the result of extensive investigations, came to the conclusion that in incipient cases the diagnosis between paresis and trypanosomiasis is not possible. He was able to produce in dogs with Trypanosma brucei an involvement of the central nervous system which was like human tabes. After nine to ten weeks the process was found in the posterior roots with beginning extension to the posterior columns, sensory trigeminus, and optic nerve. In trypanosomiasis, however, the central nervous system rarely escapes, whereas in syphilis only 1 or 2 per cent. develop tabes and 4 to 5 per cent. paresis.

Conclusions: Clinical observation and experimental work have shown that no true immunity exists in syphilis, but that an anergy develops during the first incubation period and is complete at the time of the general eruption. This refractory state usually persists as long as the body harbors spirochetes, and when it disappears, with the cure of the disease, the patient is again in a receptive state.

In the transmission of syphilis to the offspring the theory of spermatic infection has been abandoned in favor of placental infection, as the majority of mothers of congenitally syphilitic children have a positive Wassermann or show spirochetes in the intervillous spaces and maternal portion of the placenta.

The histopathology of syphilis is a uniform one. In all stages and in all organs the lesion begins in the perivascular lymph spaces as a lymphocytic and plasma-cell infiltration. The distribution of secondary lesions, according to Ehrmann, is due to a branching of the vascular stems. In the tertiary stage the ulcerative and destructive character of the lesions finds its explanation in a changed tissue reaction, the Umstimmung of Neisser, or allergy, in the sense of an increased susceptibility to the action of the organisms.

Syphilis produces a characteristic type of aortitis and is very common in individuals who have had the infection. It may be the only lesion present in so-called latent lues with a persistent positive Wassermann, and emphasizes the importance of examining all such patients for possible cardiovascular involvement. It is a frequent concomitant of paresis and tabes, especially the rudimentary form, occurring in about 80 per cent. of parasyphilitics.

Infection of the nervous system probably takes place during the secondary stage. A low-grade meningitis may exist for years or the spirochetes may remain quiescent for years until called into activity. In paresis a mantling infiltration of lymphocytes and plasma cells is found in the adventitial lymph spaces of the meninges and encephalon. From its pathological anatomy, which has been studied in all stages, it is much easier to comprehend this condition than the tract degeneration in tabes, as tabetics seldom die during the early period of the affection. The few pathological examinations which have been made, reveal, however, changes in the meninges about the posterior roots between the ganglion and the cord. It is not so difficult to understand how an infiltration in this region by pressure could produce degeneration of the afferent fibers extending to the posterior columns and leading to an ascending tract degeneration following the well-known law that a destruction of the neuron is followed by degeneration along its distribution. This explanation is a much more plausible one than a primary degeneration without inflammatory manifestations.

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THE VALUE OF CERTAIN TESTS FOR DIAGNOSIS AND PROGNOSIS IN CHRONIC NEPHRITIS.

By Channing Frothingham, Jr., M.D.,

BOSTON, MASS.

(From the Department of Medicine, Harvard University, and the Medical Clinic of the Peter Bent Brigham Hospital.)

Numerous tests have been devised from time to time in order to make an early diagnosis or prognosis in chronic nephritis. Also by a study of the responses to certain tests attempts have been made in recent years to classify the different types of chronic nephritis.

Of these different tests the examination of the urine for albumin and casts and the determination of the blood-pressure have been used pretty generally, especially for making a diagnosis of renal trouble. Recently, Rowntree and Geraghty[1] devised the now well-known test which depends upon the elimination of phenolsulphone-

[1] Jour. Pharm. and Exp. Ther., 1910, i, 579.

phthalein in the urine. Since its origin a considerable amount of work has been done on this test in regard to its ability to demonstrate chronic nephritis in the early stages or to make an accurate prognosis of the eventual outcome.

More recently Folin and Denis[2] have devised a technique for determining the non-protein nitrogen content of the blood which has given a fresh stimulus to this well-known method for studying renal disease and made it practical for clinical use. As a result, reports are coming from several clinics on the value of the non-protein nitrogen content of the blood in diagnosis, prognosis, and classification of chronic nephritis.

For years the study of the kidneys' ability to excrete sodium chloride and various forms of nitrogen has been carried on. Usually these studies have been made by a quantitative determination of the intake in the food and the output in the urine of sodium chloride and nitrogen. It has been found that the ability of the individual to put out in the urine salt and nitrogen varies in different types and stages of nephritis. Widal,[3] Müller,[4] Monakow,[5] and others have attempted to arrange the cases into groups according to the retention of one or the other of these substances.

In one group these authors place the cases with salt retention and normal nitrogen elimination. In another, the cases with nitrogen retention but fairly good salt elimination. Both of these groups present clinical symptoms according to these authors which are characteristic. Many of the cases, however, are a combination of the two types.

In order to test more rapidly the ability of the individual to excrete salt in the urine, Schlayer[6] suggested the addition of 10 grams of sodium chloride to the diet at one dose after the patient had reached a salt equilibrium by being on a known diet for several days. In a normal individual this added salt should appear in the urine in twenty-four hours according to some authors, or at most in forty-eight hours. Monakow[7] devised a similar test to show the ability to put out nitrogen, which consisted in giving 20 grams of urea at one dose under similar circumstances. The nitrogen content of this urea, approximately 10 grams, should also be excreted in twenty-four to forty-eight hours by a normal individual.

Of course, it is possible that an individual might excrete the full amount of salt and nitrogen contained in the daily diet and yet fail to put out properly the excess of these substances given at one time. Doll and Siebeck[8] have emphasized this point in some recent work. However, experience has shown that these two tests offer

[2] Jour. Biol. Chem., 1912, xi, 527.
[3] La Semaine Médicale, 1905, xxv, 313.
[4] Verhandl. der Deutsch. path. Gesellschaft, Meran, 1905.
[5] Deutsch. Archiv. f. klin. Med., 1914, cxvi, 1.
[6] Ibid., 1910–11, ci, 333.
[7] Ibid., 1911, cii, 248.
[8] Ibid., 1914, cxvi, 549.

a fairly good guide to the ability of the kidneys to take care of salt and nitrogen, and they have been used in recent years quite extensively for this purpose.

Recently, Ambard and Weil[9] have offered a method for determining salt and urea retention which consists in finding the blood content of these substances at a given time and their output in the urine at the corresponding time. It is hoped in this way the salt and nitrogen retention may be more readily determined.

Many other tests have been suggested for renal study, but those mentioned above seem to have received most attention in recent literature. Foremost among the workers on nephritis is Schlayer, who, with his assistants, has tried out many tests experimentally and clinically, including the lactose test of Voit[10] and the potassium iodide test of Duckworth.[11] More recently Hedinger and Schlayer[12] have been studying the work of the kidney by means of test meals, which are given for several days. The response of the kidneys at different periods of the day is carefully studied, and seems to be of both diagnostic and prognostic importance.

Since the opening of the Peter Bent Brigham Hospital the cases suspected of having chronic nephritis have been studied by a variety of tests. Up to the present time most attention has been paid to the blood-pressure, urinary examinations, phenolsulphonephthalein excretion, non-protein nitrogen content of the blood, and the ability to excrete in the urine added amounts of salt and urea given by the mouth. At the present time studies are being made on the cases of chronic nephritis by means of Schlayer's test diets, with modifications, and the Ambard and Weil method for determining salt and urea retention.

A sufficient number of cases of chronic nephritis have been studied by all of the six tests mentioned above to make a comparison of them of interest in order to decide on the value of these different tests for diagnosis, prognosis, and the purpose of classification. In all, over 100 cases diagnosed eventually as chronic nephritis have been studied by most of these tests. In only 40, however, have the tests been completed in all their details, and therefore this report will be limited to these 40 cases. It may be said, however, that the other cases in which some one or part of a test was lacking, apparently responded to the tests similarly to the forty reported.

The data collected in the accompanying table was obtained from the medical records of the hospital, and represent results obtained by a number of men on the staff either in their routine work or in some special study. The entrance blood-pressure is recorded, as it became evident that the pressure in most cases in

[9] Jour. de phys. et de path. gen., 1912, xiv, 753.
[10] Deutsch. Arch. f. klin. Med., 1897, lviii, 515.
[11] Bartholomew's Hosp. Rep., 1867, iii, 216.
[12] Deutsch. Arch. f. klin. Med., 1914, cxiv, 120.

which it was elevated fell after rest in the hospital. This reading also is probably nearer to that which would be found on meeting the patient in practice.

In the report on the urine the general impression from several examinations was recorded; for it is so well known that a single examination of the urine may not show albumin and casts which will be present on subsequent examinations.

The amount of non-protein nitrogen in the blood was determined by the method of Folin and Denis and the amount found on the first examination recorded; for in many of the cases attempts were made to change the amount by variations in the diet.

The phenolsulphonephthalein test has been done by the method originally suggested by Rowntree and Geraghty and the total excretion for two hours recorded. The first estimation after entrance was taken, and therefore it must be borne in mind that if passive congestion of a severe grade were present the output may have been considerably lower for that reason.

For several days before giving the extra amounts of sodium chloride and urea the patients were placed on a known diet and their ability to put out salt and nitrogen recorded until the amount became practically constant. The amount of salt or nitrogen in excess of that excreted on the day preceding the dosage was recorded for the first and second twenty-four-hour periods following the dose. In some instances the amount excreted on one or the other day was less than that on the control day. In such instances a minus sign is placed before the figure.

In order to group the cases according to their response to these tests the excretion was considered normal if 8.5 grams of the 10 grams of added salt or nitrogen were put out in the forty-eight hours. It was considered a slight retention if between 4.5 grams and 8.5 grams were excreted. If less than 4.5 grams were put out in the forty-eight hours the retention was considered marked.

Clinically the cases in the accompanying table varied from the edematous patients with normal or slightly elevated blood-pressures and considerable evidence of active renal disturbance without uremic symptoms, to the cases with high pressure, shortness of breath, marked uremic phenomena, pronounced eye-ground changes, and with or without edema.

The severest cases of nephritis are not included in this list because it was not considered advisable to give them added salt and urea, and because frequently it was impossible to feed them with enough regularity to find their normal elimination. It is interesting to note that cases with the same clinical course frequently showed at autopsy a form of chronic nephritis quite different from each other.

Of these 40 cases representing different types and grades of chronic nephritis, 37 showed a systolic blood-pressure of 150 or above, which is usually considered as abnormal. In 3 cases the pressure

Hospital No.	Systolic pressure.	Urine		Blood nitrogen per 100 c.c.	Per cent. phthalein in 2 hours.	Grams of NaCl above control.		Grams of nitrogen above control.		Complications.
		Albumin.	Casts.			1st day.	2d day.	1st day.	2d day.	
1443	225	+	Rare	27.2 mgs.	33	5.3	−0.3	9.6	0.0	Cardiac; no edema.
1358	145	+	+	46.0 mgs.	6	4.8	0.9	1.0	−1.2	None; no edema.
1340	225	+	+	35.2 mgs.	38	1.2	3.2	3.0	−0.8	None; no edema
1023	258	+	+	36.0 mgs.	30	1.0	1.0	3.0	1.0	None; edema.
1197	225	+	+	39.0 mgs.	54	0.0	2.0	2.0	2.0	None; no edema.
1139	210	+	Rare	38.2 mgs.	51	3.5	3.0	4.0	1.5	None; no edema.
1170	230	+	+	34.2 mgs.	50	6.0	2.0	4.0	2.0	Cerebral; no edema; arteriosclerosis.
1154	258	+	+	30.9 mgs.	45	−2.9	−1.8	12.0	2.2	None; edema.
1178	128	+	+	20.0 mgs.	54	1.5	2.0	2.0	−0.5	Cirrhosis of liver; edema; arteriosclerosis.
1072	200	+	+	31.0 mgs.	51	2.0	1.0	4.0	4.0	Arteriosclerosis; no edema.
1365	185	+	+	36.5 mgs.	33	2.0	−0.1	7.2	3 7	Cardiac; edema.
1490	270	+	+	26.8 mgs.	34	−0.3	−3.8	5 4	2.3	Cardiac; no edema.
974	190	+	+	54.1 mgs.	25	1.0	0.0	8.0	8.0	None; no edema
986	180	Rare	Rare	25.9 mgs.	36	2.6	−0.9	5.0	4.0	Cardiac; edema.
918	245	+	+	70.9 mgs.	14	0.5	−1.5	0.5	−6.0	None; edema.
1056	218	+	+	78.9 mgs.	0	1.0	−1.0	−2.0	3.0	Arteriosclerosis; no edema.
1075	192	+	+	23.8 mgs.	55	−1.0	3.0	8.0	1.15	None; edema.
1885	154	+	+	39.0 mgs.	24	0	2.1	2.0	2.0	Cardiac; edema.
1918	254	+	+	31.0 mgs.	49	0	2.5	3.0	2.0	None; no edema
1948	220	+	0	25.0 mgs.	65	4 5	5.5	9.0	−1.5	Cardiac; no edema.
2077	255	+	+	23.0 mgs.	52	2.0	−2.0	8.0	2.0	Myocarditis; no edema.
2074	164	+	+	40.0 mgs.	18	1.5	1.5	1.0	1.0	None; no edema.
1898	200	+	+	32.0 mgs.	43	2.5	1.0	6.0	9.0	Cardiac; edema.
1696	170	+	+	16.5 mgs.	54	0.0	3.0	4.0	−2.0	Cardiac; no edema.
1814	186	+	0	33.0 mgs.	42	0.0	−3.5	5.0	4.0	Cardiac; edema.
1661	190	+	+	38.0 mgs.	42	2.0	1.8	9.0	4.0	Diabetes; no edema; myocarditis.
1459	220	+	+	21.3 mgs.	48	0.0	3.0	3.0	1.0	None; edema.
1738	190	+	Rare	25.0 mgs.	50	3.0	1.5	8.0	2.0	None; no edema.
1804	260	+	Rare	33.0 mgs.	59	0.0	2.5	6.5	−1.0	Myocarditis; no edema.
1754	122	+	+	36.0 mgs.	28	−0.5	0.5	0.5	−0.5	None; edema.
1624	150	+	+	40.0 mgs.	28	1.0	2.0	6.0	2.0	None; edema.
1608	230	+	0	76.2 mgs.	15	−4.0	−2.0	2.0	0.0	Lead arteriosclerosis; no edema.
1821	188	+	+	33.0 mgs.	18	4.5	1.0	0.0	0.0	None; no edema.
1760	250	+	+	28.0 mgs.	30	−0.5	0.0	1.0	−1.0	None; no edema.
624	220	Rare	Rare	25.4 mgs.	45	−2.5	−4.7	3.9	3.0	Arteriosclerosis; edema.
684	210	+	Rare	25.0 mgs.	65	3.2	4.2	7.0	4.0	None; no edema.
762	180	+	+	50.0 mgs.	35	1.0	−0.5	4.0	1.0	None; edema.
782	185	Rare	0	33.2 mgs.	58	2.0	5.0	9.0	1.8	Acute rheumatism; no edema.
817	212	Rare	Rare	31.8 mgs.	56	1.8	1.6	5.0	2.0	None; no edema.
548	190	+	Rare	23.2 mgs.	45	3.3	−0.1	10 0	3 0	Cardiac; no edema.

was apparently normal. It seems fair, therefore, to decide that an elevated blood-pressure occurs with sufficient frequency to be a good aid in diagnosis. In another work, Smillie and Frothingham[13] have shown that the height of the blood-pressure is not a definite guide to the severity of the nephritis. Although it tends to be slightly higher on an average in the severer cases, the individual variation is so marked that very little aid for prognosis can be obtained from it.

The 3 cases with normal blood-pressure did not fall into any one clinical group, and cases with quite different clinical signs showed an elevated blood-pressure. Therefore, it is evident that the blood-pressure determination is not of much value in regard to the clinical classification of chronic nephritis.

In 36 of the cases albumin was present in varying amounts in all or most of the examinations; in 4 it was present so infrequently that its presence might have been overlooked even after several tests; 27 cases showed casts most of the time, 9 only rarely, and 4 not at all. It is evident that albumin is almost as common a sign in chronic nephritis as a high blood-pressure, but that casts do not occur so frequently. On account of the presence of albumin and casts in other conditions than chronic nephritis the occurrence of them in the urine is not of sure diagnostic value, but it offers a good guide for further study, and few cases would be missed by these tests alone if more than one examination were made.

It is well known that some of the most severe cases bordering on uremia show little or no albumin or casts in the urine, so that for prognosis these tests are of practically no value.

The number and character of the casts, however, are of considerable value as a guide to the amount of renal destruction actually going on at a given time. On the other hand, a large amount of albumin may mean a considerable amount of active renal destruction, or it may simply show a leakage through the kidney of serum albumin. Cases of a similar clinical type, namely, those in younger people with considerable edema, usually show considerable albumin and many casts in the urine, but other clinical types of nephritis also at times show much albumin and many casts. Therefore, for the purpose of a clinical classification of chronic nephritis, the presence or amount of albumin and casts in the urine is not of much assistance.

Thirty mgm. or less per 100 c.c. of blood was considered the normal content of non-protein nitrogen for the blood. With this as a standard, 26 of the 40 cases showed an increase over the normal of non-protein nitrogen. In 14 cases the amount fell within the normal limits. It is evident, therefore, that cases which are recognized as chronic nephritis may have a normal non-protein nitrogen content in the blood. Thus, for an early diagnosis of chronic nephritis this

[13] Arch. Int. Med., 1915, xv, 204.

test is not of great value. On the other hand, in patients whose unconsciousness is due to uremia the non-protein nitrogen is always elevated in our experience, and, therefore, in this type of case the test is of considerable value in making a differential diagnosis. For prognosis this test is of considerable value. There seems to be a fairly direct relation between the severity of the nephritis and the amount of non-protein nitrogen in the blood as was shown in a study of these and other nephritis cases by Frothingham and Smillie.[14]

The cases in this series with the same clinical type of chronic nephritis varied from a normal amount to a marked elevation of the non-protein nitrogen content of the blood, also some of the cases of all the clinical types included showed an elevated and others a normal blood nitrogen. It was felt, therefore, that this test would be of little value in the classification of chronic nephritis.

Fifty per cent. or more of the phenolsulphonephthalein should be excreted under normal conditions in two hours. Of these 40 cases 26 showed a diminished 'phthalein excretion and 14 put out a normal amount. This series showed, therefore, what has been found repeatedly, that certain cases of chronic nephritis have, especially in the early stages, a normal 'phthalein excretion. Therefore, for diagnosis in the early stages of the disease this test is not reliable. Furthermore, the diminished 'phthalein excretion in some of the cases may have been due to passive congestion.

For prognosis the test is more valuable provided that passive congestion is ruled out. This is specially true in the cases in which the 'phthalein elimination is markedly diminished. In this class of cases other tests and the clinical findings usually point to a severe nephritis. Occasionally for some unexplained reason in the severe cases of chronic nephritis the 'phthalein output may be practically normal. In some at least of all the clinical types of chronic nephritis studied the 'phthalein elimination was lowered, and so for the purpose of classification of chronic nephritis this test is not of value.

Of the 40 cases only 1 showed a normal excretion of the extra sodium chlorine; 8 had what has been arbitrarily called a moderate retention of the added salt, and 31 were very markedly unable to excrete it. Apparently, therefore, disturbance in the ability to eliminate salt is a common occurrence in all types of chronic nephritis and may be considered a good diagnostic sign. For prognosis this test is not of much value, because the kidneys apparently lose the ability to excrete the added salt in appreciable amounts before the other tests suggest that the nephritis has become severe. Although other authors have attempted to group the cases of chronic nephritis somewhat in their relation to sodium chloride excretion, it was not possible to do so in this series, because practically all the cases, including a variety of clinical types, showed the inability to excrete it.

[14] Loc. cit.

Fifteen of the 40 cases excreted the added urea well, 9 fairly well, according to the set standard, and 16 showed a marked inability to excrete it. This test, therefore, can not be depended upon for making an early diagnosis. For prognosis the test is more useful, as in all but 3 of the 16 cases, which showed a marked retention, the other evidence pointed to a severe grade of nephritis.

This test has not been of value for classifying chronic nephritis, for in cases which are apparently of the same type the excretion of the urea varies considerably. In all but 3 of the 16 cases with marked urea retention the salt retention was also marked. In these 3 cases the salt retention was moderate. Therefore, although there were some cases with what might be termed pure salt retention, there were none in which there could be said to be a pure nitrogen retention.

Twenty-five of the 40 cases showed edema at entrance. Of course, it cannot be definitely determined in how many of these cases the edema was due to cardiac disturbance. A list of the important complications to the chronic nephritis is also added in the table.

From this study it seems fair to conclude that the blood-pressure determination, repeated urinary examinations, and a study of the ability of the kidney to excrete extra sodium chloride are the most reliable tests for making an early diagnosis of chronic nephritis.

For prognosis in chronic nephritis the determination of the non-protein nitrogen in the blood, the excretion of phenolsulphonephthalein in the urine, and the ability to excrete extra nitrogen in the urine are the most useful tests.

By means of these tests it is not possible to group the cases of chronic nephritis in relation to their clinical appearance. Further study on the relation of these tests to the pathological lesions in the kidney is being carried on.

PRACTICAL IMPORTANCE OF EXAMINATION OF STOOLS IN INFANTS.

By H. M. McClanahan, A.M., M.D.,
PROFESSOR OF PEDIATRICS, UNIVERSITY OF NEBRASKA,
AND
J. Clyde Moore, A.B., B.S., M.D.,
CLINICAL ASSISTANT, UNIVERSITY OF NEBRASKA, OMAHA, NEBRASKA.

The subject of infant feeding involves many problems. Every physician of experience meets with cases that baffle his skill and try his patience, although great progress has been made during the last few years. Percentage feeding as developed by the late

Professor Rotch has certainly led to a more careful study of the problem and has helped in lifting it out of the chaotic state. The estimation of the caloric value of food is another step in advance, however. As the caloric needs of an infant may be met with a diet lacking in important food elements, it cannot in itself be considered a system. It is, however, of practical value in checking up any cases of overfeeding or underfeeding.

Fortunately many infants will do well on any reasonable modification of milk. The feeding of the infant may be considered satisfactory if it is comfortable, if there is a steady gain in weight and increasing strength, and if the gain in weight is properly balanced. Every physician has observed infants with a feeble musculature, soft bones, and often evidence of rickets, make a steady gain on condensed milk and water. Such a gain is not satisfactory. If in the ordinary case the stools appear normal, that is, a proper color, smooth and free from offensive odor, while the child is gaining in weight, then such a case requires no further consideration. On the other hand, there are cases where the examination of the stool is a valuable practical aid. In these cases mere inspection does not give sufficient information. One of us (Dr. J. Clyde Moore) made 125 examinations in the manner to be described. We feel that as a result of these examinations we have been able to treat our cases more intelligently and to obtain better results. In all of our feeding cases we use the following plan of obtaining the necessary facts: First we make an analysis of the milk, human or cow's milk. We examine for specific gravity, reaction, fat, carbohydrates, and proteid. Occasionally we make bacteriological tests when it seems desirable. The Babcock method is used for determination of the fat in both human and cow's milk. For the human milk we use a Babcock tube specially designed for the medical centrifuge. On account of the smallness in quantity of milk we always make four tests and take the average. For sugar we precipitate the lactalbumin and casein by acetic acid and heat and titrate with Fehling's solution. For estimation of proteids in cow's milk we use the formula of Bowditch and Bosworth. The fat is determined by the Babcock method, the specific gravity is taken with the ordinary lactometer and corrected for temperature, and the sugars and proteids calculated according to the following:

1. Total solids: L/4 + (1.2 × F) = total solids.
2. Casein: (F. — 3) × 0.4 + 2.1 = casein.
3. Total proteins = (F — 3) × 0.4 + 2.8.
4. Sugars: total solids — (F + total proteid + 0.9.)

L = reading of Quevenne lactometer.

F = per cent. fat as determined by Babcock method.

This gives a formula exact enough for clinical purposes. The next point of consideration is the baby itself as to age, previous

feeding, weight curve, energy quotient, and clinical symptoms, such as colic, vomiting, regurgitation, and number and character of stools. The latter often gives important information, and should be carefully followed in every case. The methods used by us are as follows:

The stool is collected on the diaper or square of gauze and then put in a small vaselin jar with a screw top, so as to prevent drying before examination. The following outline is used in the examination: Number of stools; color; reaction; odor; consistency; blood; mucus; curds; neutral fats; fatty acids; soaps; total fat; reaction to Lugol's solution; Gram-negative bacilli; Gram-positive bacilli.

The reaction is determined by moist litmus paper, being careful to take the specimen from the centre of the stool. The mucus is determined macroscopically, and if in doubt, by staining with iodin solution. Partially digested starch, which is sometimes confused with mucus, stains bluish pink, while mucus is unaffected. In one case thought to contain mucus, examination revealed starch. The use of a dextrinized gruel instead of cereal gruel caused complete disappearance of apparent mucus from the stool. Curds are always determined macroscopically. The simplest method for determination of the character of the curds is to treat them with formalin, the casein curds hardening in this while the fat curds are not affected. Fat curds will float in water. Casein curds sink. For some time there has been contention over the composition of curds. Meyer and Leopold have contended that all curds are really fat curds, but Talbot, Morse, and others have proved conclusively, by biological and chemical experiments, that the large, tough, citron-colored curds occasionally found in infant's stools are casein curds. The small flocculent curds found very often are fatty acid or neutral fat curds. The significance of these curds will be discussed later.

For estimation of fats we use the methods advocated by Morse and Talbot and by Cowie and Hubbard. The former is of value in giving a quick, general idea of fat digestion. The method is as follows: From a thoroughly mixed stool a small fragment is taken and put on a slide, a drop of the saturated solution of Sudan III is added and thoroughly mixed in; cover with cover-glass and examine under low power with No. 1 objective; fat appears as bright-red droplets scattered through the field; fatty acids also stain, but are of an orange hue; soaps do not stain. To another fragment a drop of dilute carbofuchsin is added. This does not stain the neutral fat, but does stain fatty acids and soap splinters. A comparison of this slide with the previous one gives a rough estimate of the neutral fats and fatty acids and soaps. To the Sudan III slide then a drop of glacial acetic acid is added and the slide heated until bubbles begin to appear under the cover-glass. This changes all of the fat into the fatty acids which show up as red-

stained droplets. If there is a large increase in the number of drops after adding the acetic acid it is known that a large amount of the fat has been present as soaps. A comparison of the number of drops with the residue on the slide gives a rough estimate of the total fat. Dr. Talbot has devised a scheme for more accurate estimating by counting the drops in the field. Since, however, this is simply a rough, comparative method, and as we have found that different fields on the same slide differ so materially, we conclude that the general appearance of the slide is sufficient without counting the drops in any certain field. Much information can be obtained by this simple method of examination, which is very satisfactory in our work. For a more accurate study of the total fat in the stool we have recently been using the method suggested by Cowie and Hubbard, of the University of Michigan. One-half gram of moist stool or 0.25 gram of pulverized stool is carefully weighed out and rubbed up in a beaker or thin-lipped mortar with 20 c.c. of warm water and then transferred to a Babcock milk bottle graduated in fiftieths. The water is added little by little to the specimen so that the entire portion can be transferred to the milk bottle with the first 10 or 15 c.c. of water, using the last 5 or 10 c.c. to wash the mortar and pestle. The sample is thoroughly mixed and 17.5 c.c. of H_2SO_4 (1.84) added slowly. Mix by shaking vigorously and then add 1 c.c. of amylic alcohol. Counterpoise and centrifuge for three minutes at a rate of about 1500 revolutions to the minute. Add hot water to bring the fat into the graduated stem of the bottle; centrifuge for one minute and then read with bottle immersed in hot water. If 0.25 gram of stool has been used, multiply percentage on stem of tube occupied by fat column by factor 7.2; if 0.5 gram sample of stool is used, multiply by the factor 3.6; the result is the percentage of fat in sample examined. To estimate total of fat in twenty-four hours, weigh each stool as passed and multiply by percentage obtained in sample examined. This work can easily be done within fifteen to twenty minutes. The apparatus necessary is an ordinary prescription balance, a 2 bottle Babcock hand centrifuge, and Babcock skimmed milk bottles. The latter are graduated in hundredths instead of fiftieths, but the same result is obtained.

Sugars. The examination of sugars is limited to the examination for lactic acid. Uffelman's test is fairly satisfactory. Clinically, however, the odor and reaction of the stool gives all information necessary. Babies with excess of sugar have distended abdomens due to excess of gas.

Proteids. This is limited to examination macroscopically for casein curds.

Bacteriological Examination. In this work we have only tried to determine the predominance of either Gram-negative or Gram-positive bacteria. No cultural methods are used except

for particular study of some case. Sterilized milk is the culture most frequently used. We have followed the methods outlined by Vincent, of London, in this work.

Significance of Data. *Color.* The normal breast milk stool is golden yellow, sometimes becoming greenish in tinge on standing. The color of the stool of artificially fed babies depends upon the food given and condition of digestion. The normal stool is a light yellow. Malt feedings give brown stools. Condensed milk light yellow. Skimmed milk, very pale stools. Excessive soap whitish stools. In various infections stools may be green. The green color of the stool, however, is not of so much importance as usually considered. Always ascertain if the stool was green when passed or changed in color on exposure to air. The color is due to the change of bilirubin to biliverdin, and may be caused by excessive acidity or alkalinity of intestinal contents or by the presence of some oxidizing ferment. A greenish color may also be due to the Bacillus pyocyaneus. This latter color disappears when the stool is treated with nitric acid, while that due to biliverdin gives the characteristic bile reaction. A gray stool may be due to the absence of bile, as in congenital obliteration of the bile ducts or certain diseases of the duodenum or biliary tract, or it may be due to soap. Various drugs may color the stool. Blood may color the stool black.

Reaction. A highly acid stool is usually due to relative excess of carbohydrate. We also get a very acid stool with fatty acid. A relative excess of proteid gives an alkaline stool. Soap stools are alkaline.

Odor. The normal stool has a slight sweetish odor. Stools with excessive putrefaction, as when there is a relative excess of proteid, have a musty or cheesy odor, sometimes taking on a distinctly fecal type. When there is fever the odor is that of decayed egg. The fatty acid stool or that due to excessive carbohydrates gives the sour odor of butyric or lactic acid.

Consistency. The normal stool of a breast-fed baby is thin and mushy. That of a baby on cow's milk is usually thicker and more pasty. The stool with excessive neutral fat or fatty acid is usually soft and oily, with excessive soap hard, or dry and crumbly, with excessive carbohydrate varies from mushy, foamy type to thin and watery. Excessive proteid seems to make but little difference in the consistency of the stool unless causing a diarrhea. Occasionally foamy stools are found with excessive proteid. Malt soup nearly always gives a salve-like stool of a characteristic brown color. A watery stool indicates either some irritable condition of intestine which causes its contents to be hurried through without allowing absorption of water, or else the presence of some substance which by osmosis draws the water from the vascular system into the intestines. The associated history and clinical symptoms usually reveal the nature of this substance.

Blood. Blood is occasionally found in infant stools. Black blood, macroscopically visible or as occult blood, in a marasmic baby in nearly every case points toward duodenal ulcer or blood swallowed from a fissured nipple. An infant breast fed, aged five months, gave us serious concern because of blood in the stool, until it was discovered that the infant was getting the blood from the mother's nipple. Fresh blood is often caused by a fissure in anus or lesion in colon or by a proctitis. In cases with fresh blood, careful inspection of rectum should be made.

Mucus. Mucus always indicates some irritation of the intestinal tract, either chemical, bacteriological, or mechanical, as often noticed in cases of dry constipation.

Curds. Small, flaky fat curds in the stool of a newborn breast-fed baby have no significance. We do not consider them of any marked significance even later in infancy unless accompanied by other clinical signs of an indigestion. The large fat curds occasionally encountered indicate some disturbance of fat digestion and absorption, and may be due to excessive fat in the feeding, lowered tolerance for fat, or a proteid or carbohydrate high enough to cause irritation of intestine and thus interfere with fat absorption. Which of these factors come into play must be decided after a study of the diet in the individual case.

The casein curd when accompanied by clinical signs of disturbed digestion, such as colic, either diarrhea or constipation, restlessness, etc., usually point to poor proteid digestion. The casein curd, however, may appear in the stool and be of no significance. Heating the milk or the addition of some protective colloid, such as barley water or sodium citrate by preventing the firm coagulation of the milk in the stomach, stops the appearance of curds in the stool. The value of sodium citrate was strikingly proved in two cases, 1 grain to the ounce of milk preventing curds.

Neutral Fats. The excess of neutral fat as shown by the staining method indicates either a lowered tolerance for fats, that is an inability to digest and absorb normal amount of fat, or it indicates an excess of fat in the food.

Fatty Acids and Soaps. An excess of these indicates that the neutral fat has been broken up by the digestive processes, but that for some reason or other there has been a failure of absorption. This condition should always lead to suspicion of tuberculosis. There are several theories advanced as to the reason for soap stools. Meyer, Stolte, Usuki, and others have shown that the three requisites for a soap stool are a moderate amount of fat, casein, and calcium in considerable quantity, and the absence of sufficient carbohydrate. A case under our observation recently showed this very clearly. The food was, approximately, fat 2 per cent., sugar 2 per cent. proteid 1.7 per cent., with about 5 per cent. of lime water. The stools were alternately of the foamy, putrefactive

type, and the hard, soap type. Addition of sufficient carbohydrate brought immediate change in the stool. Excessive fatty acid in intestinal contents often produces a diarrheal stool. Accompanying this is a marked loss of sodium and potassium, and a relative acidosis is developed. We believe this is a practical point worthy of consideration in cases of cyclic vomiting. In the soap stool mentioned above there is a positive sodium and potassium balance, but a negative calcium and magnesium balance.

Total Fat. So far we have only used the Cowie and Hubbard method in observing cases in which we were trying to increase the fat tolerance. We occasionally find cases which seem unable to digest the smallest quantities of fat. These cases may, however, have their fat tolerance gradually increased by carefully increasing the fat content of their food as they are able to digest it. In these cases an increase of the total fat in the stool, especially if persistent and rising, is an indication for lowering the fat percentage of the food. We find fat tolerance is usually reëstablished by withdrawing fat for a few days then slowly increasing.

The Reaction to Lugol's Solution. The presence of blue-staining particles means undigested starch. It is very common in cases on barley water to find partially digested vegetable cells staining blue with the iodin solution. Certain bacteria accompanying disturbances of carbohydrate digestion stain blue with Lugol's solution.

Bacteriological Examination. As mentioned above, we only determine the preponderance of the colon or lactic type, that is, the Gram-negative or Gram-positive type. A marked preponderance of the colon type indicates a change from normal fermentation to putrefaction. This is shown particularly when the colon bacilli take the methylene blue stain poorly. Vincent says that this indicates a change in the colon bacillus from fermentative to proteolytic type. We have seen this type very markedly in two recent cases of apparent colon toxemia. We wish to emphasize that the examination of the stool is a very important point in feeding cases, and should be made in all cases of bottle-fed infants. There should be repeated examinations of both milk and stools during the whole course. In this way the feeding can be made definite and well balanced. It is, however, only one means of watching the case, and should not be relied on to the exclusion of the weight curve and energy quotient.

Conclusion. Chemical and microscopic examination of stools has passed the experimental or laboratory stage. In any well-worked-up case the procedure ranks with blood counts and urinalysis in importance. Indeed, in infants with intestinal indigestion, it is the only accurate method of determining the food element that causes the disturbance. The conclusions drawn from the examination of the stools give information of practical value.

IMMUNITY IN TUBERCULOSIS: WITH SPECIAL REFERENCE TO RACIAL AND CLINICAL MANIFESTATIONS.[1]

By Edward R. Baldwin, M.D.,

ASSISTANT DIRECTOR SARANAC LABORATORY FOR THE STUDY OF TUBERCULOSIS, SARANAC LAKE, NEW YORK.

Nine years ago Professor Theobald Smith[2] delivered an address before this body on the subject of tuberculosis, with especial reference to the parasitic properties of the tubercle bacilli. He gave a most illuminating view of the bacillus from the biologist's point of view as well as a working theory of the reciprocal action of the tissues and parasite.

I refer to his hypothesis that the bacillus forms a protective envelope or capsule which permits it to retain vitality in a latent focus. He further explained the mechanism of infection and immunity, and presented the problem for clinical medicine as developed up to that time.

I fear that my selection for a similar task is inadequate; certainly I am deeply conscious of the responsibility and honor in offering the Harvey Society this effort to supplement that of our most distinguished American worker in tuberculosis.

It appeared to me better suited and more useful at the present time to treat the subject of immunity in its clinical aspect, and, while discussing some of the recent laboratory researches, to take also a broad survey of tuberculosis from the racial and epidemiological view-point. We may in this way discover a proper attitude toward the complex problem of prevention and treatment of tuberculosis, a matter fraught with frequent misunderstandings and wide differences of opinion. Only by this combination of experimental and clinical experience have we any claim to judicious decisions. Too often we encounter confusion and perplexity in the face of the frequent contradictions met with in tuberculosis from the clinical side. The deceptions and fallacies of laboratory experiments have also led us astray to the discouragement of many. It must be admitted to be a difficult field, yet not barren of encouraging results to the patient worker.

To begin the theme of immunity, one must at once discard the meaning of absolute protection usually conveyed by it and employ the expression "relative immunity," or, better, "heightened resistance." We know, so far as tuberculosis is concerned, that in man no absolute immunity has been observed, meaning by this, *effective resistance throughout life*. The actuality is quite otherwise;

[1] Harvey Lecture, New York Academy of Medicine, January 16, 1915.
[2] Ibid., 1906, Jour. Amer. Med. Assoc., April 28, 1906.

yet many individuals unquestionably attain it in a practical sense in that no disease follows infection with tubercle bacilli.

From the pathologist's view-point few escape the formation of tubercles from the introduction of the bacilli. Even the nearly refractory animals, like the goat, cat, or dog, form primary foci. The immunity is thus not against infection but against its further spread. On the other hand, by the extensive observations of Harbitz,[3] Bartel,[4] and many others we know that living tubercle bacilli may lodge in the lymph glands for a considerable time without producing infection or tuberculous tissue. Doubtless many are disposed of before they have a chance to multiply. Nevertheless, given the proper conditions for multiplication and a bacillus of sufficient virulence or adaptability, it is perfectly conceivable that a single bacillus may suffice for infection. We must keep in mind the reciprocal relations between host and parasite, so well emphasized by Professor Smith, to understand why an infection may be balanced by the defenses and fail to make headway beyond the primary focus or port of entry.

Some of the conditions favorable to immunity are fairly defined; others elude our search or can only be stated in vague terms. Inoculated bacilli will at least act as irritant foreign bodies, unlike most bacteria, owing to their waxy substance; yet we can be certain that small numbers of bacilli, for example, or those of low virulence for the species, will hardly produce a focus at all, or if such is formed it will soon be encapsulated or absorbed.

On the part of the body, maturity of tissues, freedom from trauma (including such as is produced by inoculation), normal nutrition, and the absence of any exhausting malady or other toxic influence, constitute factors of safety of first importance.

On the other hand, right here we must remember that whatever balance or adjustment may take place *after* tubercle bacilli have established a lodging place in the tissues, no *specific* natural defenses existed so far as we know when they entered. The bacillus undoubtedly has an advantage here, because, given virgin soil and a race of bacilli already adapted to the species, an initial infection takes place with little hindrance from the non-specific defensive powers. The further history of such infections depends in part, at least, upon the amount of specific resistance aroused.

Natural Immunity. It has always been easier to define disposition to tuberculosis than immunity. Volumes have been written and an enormous literature has accumulated on the subject of disposition, yet something can conceivably be said for natural or acquired immunity in the qualified sense here used.

Certain species are relatively immune to strains of bacilli occasionally pathogenic for them. The horse and mule, for example,

[3] Jour. Infect. Dis., 1905, ii, 143.

[4] Cent. f. Bakt. (orig.), xxxviii, 154.

are rarely infected by the bovine bacillus that occasionally may produce disease in them under constant exposure and sufficient dosage. Likewise, swine and sheep are ordinarily resistant to human infection. It does not seem difficult to explain these instances on the ground of non-adaptability of the parasite to races other than those forming its usual habitat.

The tubercle bacillus, especially the mammalian type, has, however, shown a rather widespread parasitic power as compared with other pathogenic organisms. It adapts itself also to many kinds of culture media in the laboratory, and there is practical agreement as to the existence of modifications of the two main divisions, human and bovine, Hence when any individuals of a race can be infected we can hardly speak of a natural immunity to all strains of tubercle bacilli.

Some ingenious explanations of the immunity of certain races and species have been propounded. As an example, a plausible theory for the immunity of a certain caterpillar of the bee moth is given by Metalnikoff[5] as the digestive power for wax with which the insect is endowed. Considerable experimental work is adduced by the author to support this idea of the mechanism of protection.

That cellular ferments of lytic character play a prominent part in natural resistance to bacterial infections is a convenient assumption. Otherwise there are temperature conditions, chemical and physiological differences, that can conceivably interfere with the growth of tubercle bacilli in highly resistant animals. We are obliged to leave the question unanswered by any formula capable of demonstration.

So far as man is concerned no race has been discovered that exhibits high natural resistance. The true explanation of any observed differences is quite different, as will be referred to later.

Some observations have been made tending to show a natural resistance in the Zulu natives of Natal, South Africa,[6] also of certain French families.[7] Such instances may be dismissed on the ground that opportunities for infection were limited.

Inherited and Acquired Immunity. A consideration of inherited and acquired immunity is more important in its practical results.

Some experimental work has been directed to the solution of the problem as to whether a susceptibility or immunity can be transmitted to offspring of tuberculous animals. No conclusion favorable to immunity to my knowledge has so far been made. The universal observation is that during an active stage of the disease a tuberculous mother has borne weak offspring, which if not, as a rule, tuberculous, often succumb to marasmus or are maldeveloped.

[5] Zeit. f. Immunität. (orig.), 1914, xxii, 235.
[6] Allen, J. F., Lancet, 1901, clxi, 198.
[7] Dubousquet-Labordoree, La Sem. Méd., 1897, xvii, 307.

If any form of specific resistance is conveyed from mother to young it is too much masked in these cases to be discovered.[8]

The toxic influences on the fetus from maternal disease are added to those affecting the germinal cells before fertilization. Consequently the anti-infectious or antitoxic principles if present are overshadowed.

In point of fact, as stated by Adami,[9] an actual specific immunity acquired by inheritance must be proved through the male parent. "It is essential to immunize the male parent alone, and that through a series of successive generations; and what is to be expected under these conditions is a Mendelian inheritance, certain of the progeny being immune, others not."

From the maternal side we know that substances derived directly from the bacilli can pass through the placenta in one form or another, together with antibodies produced in the mother. The results are disastrous to the young as in the experiments of Carrière,[10] and Maffuci,[11] who injected healthy guinea-pigs with extracts of tubercle bacilli. More than two-thirds of the offspring were either stillborn or died in two weeks. Schenk[12] claims to have demonstrated antibody by means of complement fixation in the offspring of normal and tuberculous guinea-pigs treated with bacillen emulsion. In my own experiments, in association with Dr. A. K. Krause,[13] the inheritance of anaphylactic sensitiveness was demonstrated by injecting pure tuberculoprotein into young guinea-pigs.

These experiments do not, of course, directly relate to the problem of most interest, and that is whether individuals who recover from tuberculosis can transmit any specific resistant quality, be it humoral or cellular. Several authors have assumed the presence of antibodies in the milk of vaccinated cows, which may fairly be considered as recovered animals while their immunity lasts. Von Behring, in 1903, suggested this, and because of the known secretion in the milk of antitoxins for other diseases (tetanus) considered the possibility of a transient passive immunity obtainable in this way. No experiments were published to my knowledge, nor has it been claimed that the calves born of the vaccinated cattle have shown unusual resistance to natural infection.

The only published work that I have found showing either an active or passive resistance in tuberculosis conveyed by milk is that of W. L. Moss,[14] and S. H. Gilliland.[15]

[8] The theory of inherited and acquired "lymphatism" expounded by Bartel comprehends an inherited resistance, though exhibited by a changed form of tuberculosis. Bartel, J., Probleme der Tuberkulosefrage, Deuticke, 1909.

[9] Principles of Pathology, 1910, 2d edition, i, 194.

[10] Arch. d. méd. exp., 1900, xii, 782. [11] Baumgarten's Jahresb., 1902, xxviii, 471.

[12] Folia Serol., 1909, ii, 343.

[13] Studies from Saranac Laboratory, Jour. Med. Res., 1910, xxii, 189.

[14] Transactions National Association for the Study and Prevention of Tuberculosis, 1914, x, 221.

[15] Ibid., p. 228

The former reported on a few calves fed on milk from vaccinated cows. There was a slightly favorable influence. Gilliland mentions a similar experiment with pigs fed on the milk of immunized cows in 1904–5, also suggestive of some protection. Neither experiment was very satisfactorily controlled.

So far no evidence of an experimental nature has shown any form of active immunity to be transmissible. It is quite true, too, that a truly specific disposition, acquired by inheritance, lacks an experimental basis. Here again the bovine race gives a negative to the assertion that tuberculous infection necessarily involves a transmitted weakness or susceptibility. On the contrary, breeding from tuberculin-reacting cows is actually practiced as of eugenic value in preserving the best stocks. The well-known Bang system has been on trial long enough in Denmark to have demonstrated its value, and is, I believe, the approved method of procedure in valuable dairies where tuberculosis is a serious menace.[16]

The observations on cattle here mentioned will not be conclusive that either resistance or susceptibility are stamped on the calves in one generation, but after the lapse of time the future generations should give an answer. They seem to me of great potential value at least in deciding whether the future generations will continue to be affected with the mild form of tuberculosis now prevalent and only discoverable by the tuberculin test.

Then, too, the non-inheritance of tuberculin sensitiveness as such leaves an opportunity for the discovery of some other hereditable quality, specifically adapted to favor or oppose the bacillus. (I shall again refer to the relation of tuberculin reactivity to immunity in connection with the clinical aspect of the problem.)

To make the assertion, finally, that there is no experimental basis for an inherited immunity or disposition does not mean that it is wholly impracticable to reach results of value, though admittedly difficult and wearisome to carry on such work successfully.

We must turn for the present to the biologist, the hygienist, or the statistician, as well as the historian, for further information. Immediately we find opposing views and many facts adduced to support each position. The matter is complex when inquiry is applied to families and races, and not less so in individuals.

Martius[17] took this view, and considers the statistical method inadequate to decide for or against a specific inherited predisposition or immunity. Hueppe[18] believes that both may be inherited, also certain organs show inherited predilection or the opposite for the tubercle bacillus. The latter, at least, has clinical observations to support it.

[16] A recent contribution by Harlow Brooks (Amer Jour. Med. Sci., 1914, cxlviii, 718) testifies that no defects were inherited from a tuberculous cow of unusual milk capacity.

[17] Berlin. klin. Woch., 1901, xxxviii, 814.

[18] Harben Lectures, London, 1903.

Turban[19] showed what he considered an inherited *locus minoris resistentiæ* in the large proportion of pulmonary cases where the morbid process began in the corresponding lung in parents and children. I was able to corroborate this observation in sixty-three families.[20]

I can only mention here some more recent noteworthy works on the subject of heredity in tuberculosis.

Cornet,[21] as is well known, has always scouted any belief in disposition.

Schlüter,[22] in a monograph of considerable size and value, concludes that there is no well-defined specific disposition.

Boeg[23] in studies on the Faroe Islanders gives no support to hereditary disposition.

Grunberg,[24] in a study of 568 families also found no specific heredity.

On the opposite side stands Karl Pearson,[25] the statistician, who by means of strictly mathematical rules applied to 384 families proves a clearly marked family inheritance of diathesis. It is impliedly a specific inheritance, though this appears an unnecessary assumption to me, considering that physical defects from other causes probably form an equally weak resistance and should be considered in estimating the specific element. Practically I think we must accept his conclusion that tuberculous families carry along more of the factors regarded as predispositions, and comprehended under the vague term "diathesis" than the average non-tuberculous family." Insurance interests must necessarily make their rules on the basis of such methods of study. But for the purpose of this lecture, I have only considered evidences of specific resistance, inherited or acquired, and therefore we can hardly confine the study to family groups and a few generations.

In passing, however, it may be of interest to note that such an eminent clinician as Herman Weber,[26] who believed in the heredity of tuberculosis, accepted insurance risks among the fibrous and so-called gouty tuberculous persons, thus recognizing their staying powers in the wrestle with the bacillus.

Leaving the question of family and individual inheritance for the moment, I will briefly mention the racial question. Reibmayr,[27] in an interesting monograph twenty years ago made a fair argument that a gradual process of immunization was taking place in the white race under civilized conditions. His reasoning was that owing to greater care, more weakly children survived to become tuberculous. The disease was consequently more widely spread,

[19] Zeitsch. f. Tub., i, 30, 123.
[20] Yale Medical Journal, 1902, p. 215.
[21] Die Tuberkulose, 2d Auf., 1907.
[22] Die Anlage zur. Tub., 1905.
[23] Zeitsch. f. Hyg., 1905, xlv, 161.
[24] Inaug. Thesis, Paris, 1912.
[25] Draper's Company Memoirs, 1907, ii; also Coring, Charles, ibid., 1909, v.
[26] Medical Examiner, 1898, p. 122.
[27] Die Ehe Tuberculosis u. Ihre Folgen, Wien, 1894.

but it developed chronicity as a sign of increasing resistance. Uncivilized races by contrast exhibited only acute forms of the disease of short duration. The infection is thus limited in extent. This theory admitted the paradox of a disposition and immunity (only relative, to be sure) in the same individual, and in my opinion has much to support it in clinical observation.

Many reports about tuberculosis in late years establish the fact that uncivilized races and those isolated for centuries from the chance of infection, develop acute forms of the disease when exposed. An excellent review of this subject was recently made by Maurice Fishberg,[28] whose well-known studies on the epidemiology of tuberculosis in the Jewish race have shown a decreasing mortality for many years in spite of their ample opportunities for infection. No doubt other factors—indeed, almost countless reasons other than a specifically acquired resistance—may tend to minimize the important conclusion that past generations of Jews have passed on an increasing resistance.

Enough evidence remains, I think, to accept the principle involved which Fishberg elucidates in his recent article, namely, that "the fatality of tuberculous infection depends on the length of time the ancestors of the affected people have been acquainted with the disease."

This principle is accepted with reference to other diseases, such as syphilis, malaria, and yellow fever, and is a rational inference from the known facts about tuberculosis.

There are, however, such marked exceptions to such a generalization that one must consider large groups rather than individuals. There are also other explanations of the relative mildness of epidemic diseases (as mentioned by Professor Theobald Smith) due to the disappearance or weeding-out process of the weaker individuals and races, both of host and bacillus.

I am more impressed, however, with the variability in resistance shown by man than by that of the bacillus. We may leave the subject of racial immunity, in my judgment, with a feeling of hopefulness that some progress has been made in the history of mankind, however slow, toward a self-protection. In this epoch, at least, the bacillus has not appeared to keep pace as an increasingly dangerous parasite.

Artificial Immunity. If the question of inherited predisposition or immunity is so difficult of answer, we yet have evidences of an artificially acquired immunity in the life of the individual. An endless amount of work has been done in laboratories and clinics to demonstrate this. A review of even the most important work would not be appropriate here;[29] it is enough to declare that

[28] New York Med. Jour., September 12 and 19, 1914.

[29] A most satisfactory review may be found in the Kolle-Wassermann Handbuch, 1913, 2d Aufl., Bd. v.

up to now no satisfactory method of active or passive protection has been discovered which applies to man. Nevertheless, I should like to discuss some of the recent contributions to the subject, and especially the reasons for failure as well as partial success. Finally, the application of the knowledge is of value in interpreting clinical tuberculosis.

Since the disappointment with the vaccination of bovines and serotherapy for tuberculosis the conviction was borne in upon us that only transient protection could be attained, and this chiefly by a vaccine in which the vital spark was not quenched.

Since the time human bacilli were ruled out for use in vaccinating cattle, owing to the short duration of immunity, and their ability to get into the milk, other races of acid-fast bacilli have been put forward for protective inoculation. The feeble resistance obtained in this way merely confirmed previous experiments with them.[30]

McFadyean,[31] of Edinburgh, has more recently advocated avian bacilli for cattle vaccination because non-infectious for human kind, a doubtful assumption considering the occasional presence of such bacilli in tuberculous patients.

Webb[32] even ventured living human bacilli, trusting to small numbers gradually increased in children to avoid infection. This was found impracticable.

The results also with bacilli killed with very gentle heat[33] or devitalized by soap,[34] glycerin,[35] sugar, etc., have been but slightly encouraging thus far.

Vaccines made from the different elements of tubercle bacilli (von Ruck[36]) or from solutions of their substance (Deycke and Much[37]) have also failed to show any advantages over previous tuberculins used for immunization.

The significance of a living vaccine as compared with all substitutes has at present a close parallel in the now much-discussed *immunity from infection*.

The opinion is justified that mild infections are responsible for the considerable immunity hitherto observed in animals inoculated with weak-virulent living bacilli. These mild infections are closely comparable to those spontaneous ones from which the large proportion of our urban population recover. The results of bovine vaccination further justify the opinion that such protection as is con-

[30] Weber and Titze, Tub. Arb. a. d. Kais. Ges.-Amt., 1907, No. 7; Klimmer, M., Beit. z. Klin. d. Tub., 1910, Bd. xvii; Friedmann, F. F., Berlin. klin. Woch., 1912, xlix, 2214.

[31] Jour. Comp. Pathol. and Therap., 1913, xxvi, 327.

[32] Jour. Med. Research, 1911, xxiv, 1.

[33] Klimmer, M., Beit. z. Klin. d. Tub., 1910, Bd. xvii; Smith, Theobald, loc. cit.

[34] Noguchi, H., Jour. Exper. Med., 1910, p. 235; Zeuner, Cent. f. Bakt. (orig.), 1909, l.

[35] Levy, Blumenthal, and Marxer, Cent. f. Bakt. (orig.), 1906, p. 42; 1908, p. 48.

[36] New York Med. Record, August 31, 1912.

[37] Beit. z. Klin. d. Tub., 1910, xv, 277.

ferred depends on the presence of living bacilli or tuberculous tissue in the animal. This protection gradually wanes or disappears with the absorption of the bacilli or the tuberculous tissue.

The above statement being granted as based on experimental grounds, we may first observe that a spontaneous vaccination of human beings is in progress owing to wide-spread opportunities for infection. Many slight infections must be effective if we will interpret the healed tubercles in that light when found at autopsy. Unfortunately, neither the virulence nor the dose is controlled; hence progressive infections will occur in a considerable proportion of people. If both factors were under control and repetitions of mild infections obtainable at proper intervals it is imaginable that much good would result. Since we cannot assure a stability of virulence for inoculated bacilli, such a dream is far from realization. But we may again inquire, Why is the living bacillus necessary? Cannot the dead bacillus persist a long time in the body and produce tubercles (as we know to be true)? If tuberculous tissue is needed why not use dead bacilli?

The answer is difficult, but it is not likely that the dead bacilli persist long (except when shut off in the form of encapsulated nodules where large clumps may lodge). The tissue changes are also probably less pronounced and certainly more transient. I will also venture the theory that ferments in the living bacilli play a part. Until recently the presence of any function of ferment nature in the tubercle bacillus failed of demonstration. Through the studies of Wells and Corper[38] and those recently published of Kendall[39] and his associates, the presence of a lipase or fat-splitting ferment in the bacillus appears certain. Reciprocal and antagonistic ferment activity on the part of the bacillus and tissues is doubtless a better means of producing an immune reaction than when the ferment action is one-sided.

The studies of Opie[40] in this country, and later those of Manwaring,[41] support the belief that cell ferments combat the tubercle bacilli. Furthermore, the antibodies such as specific lysins are not readily demonstrable in the blood, yet their presence both in the leukocytes and fixed cells cannot be questioned. During a short period following inoculation the blood may contain some specific lysin, though it has not been fully recognized *in vitro*.

Roemer[42] was able to protect two sheep with the serum of another inoculated sheep; later this transferred immunity failed, probably because no serum lysin was left in the vaccinated sheep (some months after inoculation).

The "partial" serum antibody theories of Much[43] and others, while plausible in theory, seem to lack well-controlled experimental

[38] Jour. Infect. Dis., Chicago, 1912, xi, 388.
[39] Ibid., 1914, xv, 443–471.
[40] Jour. Exper. Med., 1908, x, 419.
[41] Ibid., 1912, xv, 1; 1913, xvii, 1.
[42] Deutsch. med. Woch., 1914, xl, 533.
[43] Ibid., xl, 554.

demonstration. In truth, no serum antibody[44] in tuberculosis has been definitely associated with immunity; in all experiments the cellular influences appear predominant.

A most interesting confirmation of this veiw was obtained by Manwaring and Bronfenbrenner,[45] who demonstrated lytic properties in the fixed peritoneal cells of animals. On the other hand, with the serum of vaccinated horses, Ruppel[46] obtained evidence of protective substance of antitoxic nature.

Hypersensitiveness or Allergy. There is another phenomenon intimately associated with immunity from tuberculous infection with which much speculation and many experiments have been made. This is the hypersensitiveness to tuberculin and especially to reinoculated tubercle bacilli, to which the term "allergy" was given by von Pirquet. It appears to be an important protective mechanism and probably a specific ferment action called forth from the leukocytes and fixed tissue cells by the presence of the invading bacillus or its derived substance.

The similarity and difference between the tuberculin reaction and the tissue reactions following inoculation are being much discussed at the present time; also the analogy to the anaphylactic reactions.

Reviewing the work on the artificial immunization of animals and the attempts to transfer anaphylaxis in tuberculosis, I think we can conclude that the mechanism is the same for all these phenomena. The differences in the manifestation of the reactions are chiefly explained by the presence of focal deposits of tubercle bacilli which can be regarded for comparison in the light of solid particles of foreign protein peculiarly difficult for digestion by the cellular ferments.

It is difficult to understand the cutaneous reactions, and most authors do not consider them anaphylactic manifestations. Unlike the majority of the latter, the skin sensitiveness as well as that of other tissues in a tuberculous animal is dependent upon the presence of tuberculous tissue or tubercle bacilli. Remove the bacilli or the tubercles and one finds that this form of sensitiveness disappears, and with it apparently all specific immunity to the disease is soon lost. The same thing happens when tubercles become thoroughly fibrous or calcified. In the changed reactivity, or the allergic inflammation, therefore, we have the essential features of the relative immunity of whatever grade, acquired in tuberculosis.

It is plain from these facts that a special form of sensitization is produced in tuberculosis by the cellular activities about the bacilli

[44] The "anticutines" of Loewenstein and Rappoport (Deutsch. med. Woch., 1904), and the hypothetical antitoxins of Sahli (Tuberculin Treatment, 1912) are too uncertain for demonstration, if indeed such exist.

[45] Jour. Exper. Med., 1913, xviii, 601.

[46] Zeits. f. Immunität. (orig.), vi, 344.

which radiates gradually to distant tissues not necessarily touched by the bacilli as such. Dead bacilli will act temporarily in this way, but pulverized preparations and extracts appear too fleeting in their effects to arouse it. They do nevertheless cause a true anaphylactic sensitiveness without skin manifestations, but unaccompanied by any recognizable immunity. The inflammatory reaction following inoculations of immune animals is the prominent feature, and is conspicuously absent in the others. Hence, we are justly entitled to the opinion that the cell accumulations about the bacilli are performing the duty of dissolving them or restricting their growth. The lymphocytes and endothelial cells have thus received much attention in connection with the tubercle bacillus inasmuch as they show lipolytic activity. The former are especially the reacting cells about the actively spreading foci of disease. Bartel[47] was one of the first to recognize the import of the lymphocyte reaction, and many facts have since tended to confirm it. (Opie,[48] Manwaring,[49] Kling,[50] Bergel,[51] Webb.[52])

No less important are the endothelial cells in connection with the fixation and absorption of the bacilli as histological studies show, by vital staining methods.

Some recent contributions are noteworthy. Lewis[53] found by the removal of spleen in white mice that a considerable increase of resistance was created to bovine bacilli. A rapid increase of lymphocytes following the removal of the spleen, due to hypertrophy of lymphoid tissue, is a possible explanation. On the other hand, Murphy and Ellis[54] of this city have exposed white mice to Roentgen radiation to destroy their lymphoid tissue and cells with the result that a tuberculous septicemia could be produced as compared with focal disease in control animals.

Much more may be said in relation to cell reactions and hypersensitiveness as a measure of resistance as well as the participation of humoral antibodies or ferments in the reactions.

These may be mentioned in connection with clinical observations.

Clinical Evidences of Immunity. We will now direct attention to a somewhat modern, possibly to some a novel, interpretation of tuberculosis in the symptomatology of the patient.

If our knowledge by experimental methods and observations is to be of value, we should expect to find signs of specific resistance under natural conditions of infection. This term "immunity" is seemingly too strong when used in describing such signs, but when we can discern that life is possibly conserved, and surely

[47] Cent. f. Bakt. (orig.), xl, 48.
[48] Jour. Exper. Med., 1914, xx.
[49] Loc. cit.
[50] Zeits. f. Immun., 1910, vii, 1.
[51] Zeits. f. Tub., 1914, Bd. xxii, 343.
[52] Transactions of the National Association for the Study and Prevention of Tuberculosis, 1910, Sixth Annual Report).
[53] Jour. Exp. Med., 1914, xix, 187.
[54] Ibid., xx, 397.

prolonged, by the defensive functions, it may not be amiss to employ that word.

Tuberculosis from the standpoint of the immunologist is possibly the best illustration of auto-immunity to an infectious agent. From this position we may divide tuberculous infections into four classes:

1. Those which recover without spreading or metastasis of the bacilli.
2. Those which continue to spread acutely, unresisted.
3. Those which progress in a slow chronic form.
4. Those which intermittently progress, becoming arrested in the intervals.

Each form may pass into another in all possible variations.

The types of each are recognized by symptoms except the first. This may only reveal itself by the various tuberculin tests or at postmortem.

It is most important from the point of view above taken, *i. e.*, from that of immunology, that the white race, at least, has for many centuries found a way to recover from repeated infections. We know that the chance of recovery increases from the second year of life to puberty in childhood infection,[55] depending on numerous factors, such as frequency of exposure, amount and virulence of the bacilli, intercurrent diseases, trauma, etc.

We also know that the majority of first infections involve the deeper lymphatic glands, not being resisted at the path of entrance. The course of events from this time forth is of exceeding interest from every standpoint.

We can then trace the path of infection thus far with fair certainty whatever the path of entry. But owing to the allergic state now induced, and which is known to be almost universal in ages over fifteen years (in greater or less degree with exposed families), we find it difficult to associate future disease with a new, exogenous infection. This is a problem about which discussion continues, and which is an important hygienic question.

Exposure to danger of massive infection without disease development in some instances can be ascribed to auto-immunity from earlier slight infections. In other instances it appears to be the cause of later pulmonary tuberculosis of the open ulcerated form occasioned by surface infection.

Both experimental and statistical studies have been brought to bear on this problem of reinfection, the first notably by Hamburger[56] and Roemer.[57] Pathological studies have seemed to give

[55] Hamburger, F., (Wien. med. Woch., 1914, No. 15) considers all infections in infants under one year develop into progressive disease and 50 per cent. of those in the second year. In ages over four years infection is rarely followed by progressive disease. Only 2 per cent. are found between eleven and fourteen years with an active form of tuberculosis.

[56] Beiträge z. Klin. d. Tub., 1910, xiii. [57] Ibid., xvii, 383.

rather uncertain results with reference to the question of new exogenous infections. Recently, however, a few cases have been found where the bovine type of bacillus has been isolated from one part of the body, usually a healed gland, and the human type from a fresh lung focus (Rabinowitsch).[58] Orth,[59] therefore, considers that such early bovine infections predispose to later human infections, yet the link is difficult to fit between them. Naturally, the question of changed type or virulence also comes into this problem.

Since old foci can break down and cause autogenous reinfection, there is reason to doubt the possibility of new exogenous infection in most cases. The acquired resistance to such a subsequent infection in adult life may be feeble after the complete healing of the old infections, which are usually confined to the lymph glands at the lung hilus or in the near vicinity. In those individuals, while the specific changes in reaction to tubercle bacilli seem to have been lost, when measured by a tuberculin test, we know the old allergy is latent, because in animal experiments reinoculations will arouse it even though no tuberculin reaction can be obtained. This is experimentally shown by intravenous inoculations, a rather extreme method, though we have a human parallel to it in the outbreak of an old focus suddenly rupturing into the blood stream, which is not uncommon in clinical experience. It is generally regarded inevitable that progressive miliary tuberculosis must follow this, and yet it is not necessarily true.

No doubt many of these cases occur, but the number of bacilli, their virulence and frequency in the blood stream, may confine the disease to the upper lobes of the lungs, where complete encapsulation may soon follow the acute febrile reaction. This is not usually regarded as a bacillemia, but we may readily consider it as such in the onset.

The commonly observed exacerbations or relapses in the course of tuberculosis follow the well-known "immune period" of two weeks in so many cases, that we may readily compare them to animals who overcome intravenous inoculations after a protective vaccination. In these it has been found that clumps of agglutinated bacilli are likely to lodge in some other organs, normally resistant to the germ (see Roemer[60]). The parallel may be carried yet further, for in the case of man some bacilli are apt to survive and form new sources of danger in other organs, later emerging as open ulcerations or latent in a soil of less resistance, that is, the lung.

Experience with cattle, sheep, and goats has demonstrated this in various ways, yet in cattle, adult pulmonary tuberculosis is regarded as a new infection from without, obtained in adult life for the most part.[61]

[58] Deutsch. med. Woch., 1913, xxxix, 105.
[59] Berlin. klin. Woch., 1913, l, 429.
[60] Beit. z. Klin. d. Tub., 1910, xvii, 287.
[61] Smith, Theobald, Harvey Lecture, 1906.

The grafting of new exogenous bacilli in the human lung in adult life nevertheless requires especially lowered health or enormous doses of bacilli. Specific resistance may run down to zero and yet the adult tissues seem naturally prepared for ordinary exposure to infection. Therefore, it is difficult to ascribe the immunity to any allergic state. This seems especially true after the lapse of tuberculin allergy due to complete healing of former foci.

Some inquiries have been made to determine the frequency of adult infection from new sources. In Breslau an investigation of sources of infection by Bruck and Steinberg[62] led to the opinion that both autogenous and exogenous infections caused the adult disease. Hillenberg[63] in a thousand tuberculous cases in the city of Leitz agreed with the above-named authors. He thinks it safe to say that those patients who develop the disease after the age of forty-five years, are due to later infection than childhood unless the disease was in the family. The relative infrequency of the disease in married partners he suggests as being due to a continuous process of immunization due to increasing exposure. The proportion of new infections among sanatorium and hospital staffs is so small that we may use the same explanation to account for it.

The facts anyway appear to show that frequent contact with the bacillus can occur without harm in adult life, and this is a comforting thought. This idea may be new to many who have become phthisiophobic, but a little reflection must arouse curiosity as to the vital resisting powers of many persons in constant contact with tuberculous patients!

As already noted, the absence of resistance in non-infected races ("virgin soil") is of some significance. Nor is it confined to uncivilized peoples, as many instances of acute tuberculosis are seen among healthy adults, particularly from rural districts.

I am not aware that the virulence of the bacillus in these cases is unusual, except for the individual involved. This is shown by the many instances of family infection of all grades of severity. In these the age and amount of infection at the time of primary infection are of great importance.

Whatever the immediate exciting cause of metastatic or fresh reinfection, the result is a higher degree of allergy unless miliary or acute pneumonic disease supervenes. We may note the symptoms of such resistance by the fever, stronger cutaneous reaction and hyperemia about the foci, as, *e. g.*, in the larynx. That the disease now continues to progress is not necessarily because of failure of the immunizing mechanism to act. There may be mechanical reasons, such as trauma and overexercise that cause the bacilli to spread, bringing new foci to the lungs, or elsewhere into the system of tuberculous tissue, thereby heightening the

[62] Zeitsch. f. Hyg., 1912, lxxi, 177.

[63] Zeitsch. f. Hyg., 1914, lxxvii, 101.

allergy until it reaches a maximum point. From this time a paradoxical state may prevail. The hypersensitiveness now causes a chronic poisoning by its constant activity, or rapid exhaustion occurs from the toxemia. On the other hand, we have reason to believe that but for this protective function miliary tuberculosis might occur oftener in a fatal form.

In recent years we have learned the fact that tubercle bacilli wash into the blood stream more frequently than was formerly considered possible, unless an acute miliary disease was present. It is highly probable that many such bacilli are weakened and dissolved by lysis without producing lesions—only causing anaphylactic fever. They may even aid in immunization if intermittently received, so that the dose at any given time can be overcome readily. For example, it is alleged that a tuberculin reaction can produce a bacillemia, which seems to me quite probable to a small extent, yet such a violent reaction as would lead assuredly to loosening bacilli from their moorings has been known to promote a rapid healing. It is not unknown to have other causes lead to strong reactions followed by improvement in the course of a progressive tuberculosis. Such stimulations to the immune reactions are obviously dangerous and unsafe when repeated often, and no experience is so disastrous as an "auto-inoculation" pushed too far, whether by natural means or by tuberculin treatment, artificially applied. It is significant, however, that physical and nervous exhaustion are the most dangerous sources of auto-inoculation.

Moreover, we are familiar with the healing of sluggish ulcers as the result of irritants directly applied, and even intercurrent disease causing the absorption and disappearance of tuberculous foci in the skin, glands, and occasionally elsewhere. The method of Bier by producing alternate passive and active hyperemia has much value and a correct rationale in the light of immunology as applied to tuberculosis.

Stimulation of foci in the lungs, however, requires clinical experience and judgment, for a highly vascular moving organ with, as we have seen, a possible selective affinity for cultivating the tubercle bacillus is to be treated cautiously.

There is often a delicate adjustment or balance in tuberculous disease after it has become arrested. Regarded as a problem in maintaining immunity, the tuberculous individual must be taught to patiently await the time when cicatrization can change the highly sensitive foci to fibrous tissue, before danger of relapse is lessened for those who retain the two-edged sword of hypersensitiveness in an active form.

Here we may refer to the strong contrast between a recently active tuberculosis and one of chronic, fibroid type. In the first there is need of strong lytic action to prevent dissemination of the bacilli. In the fibrous form the bacilli may be abundant in the

sputum, but so shut off from the blood that little allergy is present. These latter patients are true "carriers" of tuberculosis, but have no longer any symptoms of absorption from the focus, and consequently low capacity for reaction. They recover very slowly, if at all, but bear stimulation of all kinds more safely. I mention these contrasts for their suggestiveness in treatment.

Interesting examples of the healing of a tuberculous focus in one part of the body while an acute outbreak is in progress elsewhere can be mentioned as auto-immunity phenomena. This is occasionally observed in the larynx during a pulmonary exacerbation, and *vice versa*. The influence of pleural effusion in arresting intrapulmonary disease of the opposite lung is another illustration. The laryngeal swellings often diminish without reactive indications. Likewise, pulmonary ulceration may heal in the course of pleurisy, apparently with no increased inflammation. Immune bodies circulating in the blood best account for these cases, but I cannot offer a satisfactory explanation.[64] The use of autoserotherapy from pleural effusions has been considered rational, on the presumption that immune substances are present, but with what experimental proof I am uninformed.

Many other manifestations of auto-immunity could be cited, including all forms of surface ulceration in advanced tuberculosis, also the various cutaneous affections. These can only be grouped as consequences of the life-protecting functions but not happy in effects.

It remains to emphasize some of the points from which I may draw conclusions.

1. There is no natural immunity to tuberculosis in warm-blooded animals to the types of bacilli found in the bovine or human race.

2. There is a considerable variation in resistance in some species probably due to the chemical effect of their secretions or physiological differences in the animals, but chiefly to the fact that the bacillus has not become adapted to long-continued parasitic existence in them.

3. In the human species no natural immunity is found in any race. All uncivilized races long removed from infection are very susceptible, but the white races, especially the European Jews, have acquired a certain degree of immunity by inheritance and almost universal infection. The rapid increase of intercourse between all lands and races facilitates the universal spread of tuberculosis, which is certain to occur through the medium of numerous bacillus "carriers."

[64] A few cases of completely arrested advanced tuberculosis following artificial pneumothorax with marked purulent pleurisy have suggested anew to me the importance of the cellular reactions in tuberculosis. The pus which contained tubercle bacilli alone, was repeatedly withdrawn and striking improvement in the intrapulmonary disease accompanied the effusion after it became full of leukocytes.

4. The ultimate survival of those who acquire a relative immunity will tend to diminish the severity of the disease, but many generations may be required to accomplish this.

5. The opportunities for infection, now universal in cities, will diminish gradually in civilized lands by lessening the danger from advanced cases, also from bovine sources. For many years, however, the number of "carriers" will increase owing to improved care, longer life, and higher standards of living among the people.

6. The best degree of resistance against tuberculosis that has been attained by experiments on the lower animals involves inoculation of living bacilli. This is of little value because of short duration of the protection and the danger of sequestered bacilli.

7. The natural infection of human beings takes place largely in childhood and increases the resistance to subsequent disease in a large measure. Under improved care of the tuberculous and better hygiene the amount and frequency of severe infections should diminish, while the number of those with slight, relatively harmless infections should relatively increase.

8. Adults withstand exogenous reinfection under extreme exposure, partly on account of slight infections in earlier life and favorable occupations, environment, and nutrition.

9. The specific immunity acquired from natural infection is largely due to cellular reactions of bacteriolytic nature, which take place outside the blood stream for the most part.

10. The interaction between the ferments of the body cells and those of the bacillus, lead to heightened activity of the lytic power, both lipolysis and proteolysis.

11. The tuberculin sensitiveness or "allergy" is the chief indication of specific resistance. In the patient most of the inflammatory symptoms are due to the actively working immunity functions.

12. In the therapy of tuberculosis this principle should be applied:

To avoid interference with Nature's powers of resistance when she is attempting to localize the infection with apparent success.

FEVER IN TUBERCULOSIS.[1]

By H. A. Bray, M.D.,

NEW YORK STATE HOSPITAL FOR THE TREATMENT OF INCIPIENT PULMONARY TUBERCULOSIS, RAY BROOK, N. Y.

The contributions of physiology relating to heat production and heat dissipation, and the factors responsible for the mainten-

[1] Read before the Saranac Lake Medical Society, Saranac Lake, New York, Dec. 30, 1913.

ance of body temperature, are of special value for the correct interpretation of the pathology of fever. The special role of bacteria in the production of fever and the more recent work by Vaughn showing the part played by the toxic radicle of the protein molecule in the etiology of fever are also pertinent to the elucidation of this subject, and of paramount importance to the further development of a more comprehensive understanding of the basic factors in relation to fever. However, in the present paper, it is desired to emphasize only the clinical aspect of fever as observed in pulmonary tuberculosis.

Since temperature and fever are so closely related, it might be of interest to precede the discussion by a brief historical sketch of the thermometer. From earliest times the body temperature has occupied a place in the scale of heat measurements, and physicians have long recognized an increase in the blood temperature as a cardinal symptom of fever, although the degree of fever was measured by the pulse acceleration.

About 1610 Galileo constructed the first thermometer. This consisted of a glass bulb containing air, connected to a glass tube of small bore, dipping into a colored fluid. Owing to changes resulting from atmospheric pressure, this style of thermometer proved unsatisfactory. Some years later Galileo introduced a second type of thermometer, familiar to us at the present day, containing a liquid hermetically sealed in a glass bulb with a fine tube attached. In 1710 Isaac Newton proposed a scale, divided into twelve parts, in which zero represented the freezing-point of water and twelve the body temperature. Gabriel Daniel Fahrenheit, in 1714, in devising the scale now in general use, also employed the temperature of the human body as one of the major divisions of his scale. Traub, Baronsprung, and Wunderlich established the value of the clinical thermometer to medicine. From this period, about 1850, the clinical thermometer has become an important part of the physician's accoutrement.

Methods of Taking Temperature. The first requisite in taking temperature is a standard thermometer. Out of a series of eighty-three certified thermometers tested in a water-bath, seventeen showed a variation of from 0.3° to 0.6°. Comparative rectal readings approximated closely the discrepancies obtained by the water-bath. To corroborate these tests, six thermometers showing marked error were forwarded to the Bureau of Standards at Washington, D. C. The letter here reproduced needs no comment: "The Bureau begs to state that the five clinical thermometers which exceeded the limits of allowable error were in error by from 0.4° to 0.6° at different points. The readings of the thermometer which retreated were not recorded. As these instruments were so badly in error the sign of the correction was not carefully noted."

A further series of fifty-five were examined by the Bureau; thirty-five passed and twenty were rejected. To obtain an accurate reading irrespective of type of thermometer, demands a period of from five to ten minutes. Many authorities, including Walther, Nordrach, Penbold, and King, advocate rectal temperatures on account of greater accuracy. However, parallel determinations by Schroeder, Bruhl, and others have shown that the discrepancies between oral and rectal readings are so slight that they can be ignored. Conditions regulate the choice at times. Thus the rectum or axilla is preferable in children, the weak or acutely ill, patients suffering from marked dyspnea, oral or throat inflammations, and nasal obstruction. When fever is suspected, but not revealed by oral reading, rectal reading is indicated as control.

The disadvantages of rectal readings are obvious. The manipulations are distasteful, and in ambulant cases, necessitates the patient retiring to his room. Care must be taken that the rectum

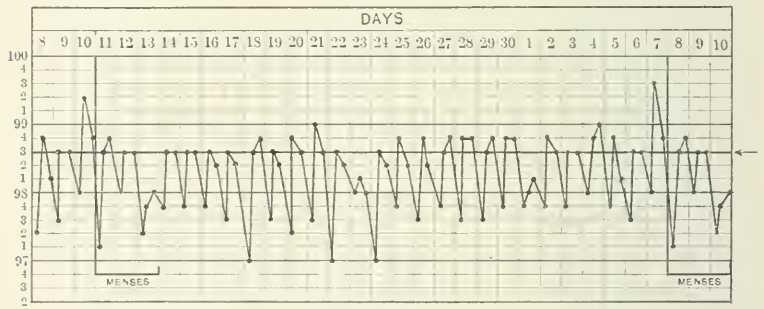

FIG. 1.—Case 2977. Female, aged nineteenyears. Premenstrual fever in an afebrile case of incipient tuberculosis.

is free from fecal matter. It has been shown that exercise has a decided influence on the rectal temperature, due presumably to the close approximation of the large muscles in this region. A preliminary rest is therefore especially indicated before rectal readings, as this method does not record the actual body temperature after exercise. The axilla still remains in high favor, especially in certain European centres. Cornet favors rectal temperatures and prefers axilla to mouth readings. Franck concludes that the axilla method of taking clinical temperature observations no longer meets the requirements of diagnosis on account of possible inaccuracies and the time required. He regards rectal measurements as the quickest and most accurate means. So good an authority as Turban is satisfied with oral temperatures, and he voices the consensus of opinion, at least in this country.

WHAT IS NORMAL TEMPERATURE? Since in no other disease are minor fluctuations of temperature of greater import, the establishment of the normal temperature range is the first essential in

determining the significance of fever in tuberculosis. A detailed study of the literature shows obvious disparities among authors in their ideas regarding normal temperature. The following tabulation by different authors gives the maximum normal:

Wunderlich: Axilla, 98.94° F.; mouth, 99.3° F.

Vierordt: Mouth, 99.6° F.

Turban: Mouth, 98.9° F.

Stewart: Axilla, 99.5° F.; mouth 99.1° F.

Foster: Axilla, 36° to 37.5° C.; mouth, 0.25° to 1.5° C. higher than axilla.

Finlayson: Mouth, 98.6° F.

Sahli: Mouth, 99.32° F.

Meyer states that oral readings exceeding 37.3° C. represent fever.

Schneider and Weise concur with this view.

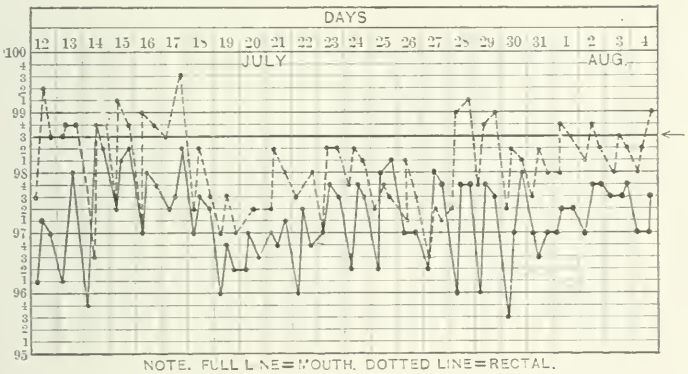

FIG. 2.—Case 3042. Female, aged thirty-seven years; stage three; progressive type. Comparative oral and rectal readings showing subnormal temperature.

Turban considers 99.3° F., if frequently recurring, as fever. Sahli says 99.32° F. is within physiological limits. This, in consumption, would correspond to a rectal temperature of 100.4° F., and so indicate fever.

The above discrepancies can hardly be accounted for by errors in technique. Sex, time of day, and season are not mentioned, and the possible inclusion by the older authorities of cases of early tuberculosis might offer a partial explanation. Notwithstanding these facts it is reasonable to suppose that normal temperature has a considerable range, and is of some moment in estimating the degree of temperature in tuberculosis.

The diurnal range is approximately 1.8° F. Any definite increase beyond this limit is considered by some as indicating fever. Thus we may have the paradoxical condition of a patient with fever and apparently normal temperature. The normal diurnal curve is

modified by exercise, food, seasonal change, the ingestion of hot or cold liquids, and psychical conditions, such as, anger, grief, and mental concentration. A physician of my acquaintance could, by matching himself against a worthy chess opponent, regularly raise his temperature over 100° F. Care must be taken to avoid misinterpretation of the slight premenstrual increase in temperature normally present in some cases. When slight fluctuations are present it has been suggested to take readings over a lengthy period, and by this means the normal range for any certain individual can be approximately obtained.

The Bacteriology of Fever. In the bacteriology of fever in tuberculosis we are confronted by a complex problem which has not yet been completely solved. The toxins of the tubercle bacillus

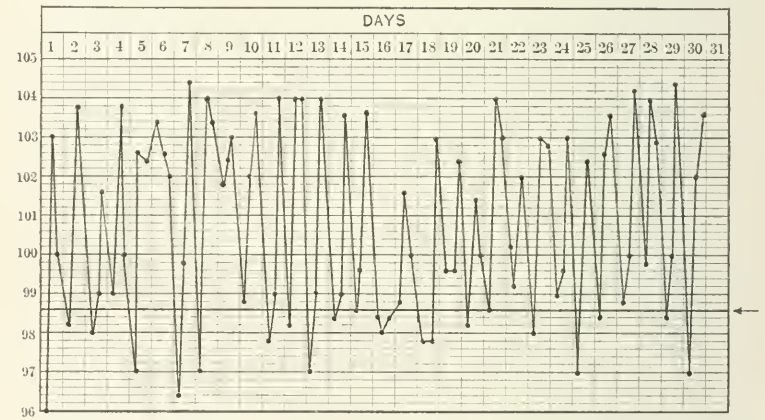

Fig. 3.—Case 2189. Female, aged twenty-six years; stage three. That the above hectic type of fever exhibiting such wide temperature variations is compatible with life for a period of months is clinically of decided interest, indicating that the prostrating action of the fever is more kindly borne in tuberculosis than in most other infections.

are capable in themselves of inducing fever. This is well exemplified in the tuberculin reaction, where the question of mixed infection is certainly excluded, and in the fever accompanying an exacerbation of a tuberculous process. For many years the exact role played by secondary organisms in the production of fever in tuberculosis has caused lively discussion; among such organisms may be mentioned the various streptococci, Staphylococcus pyogenes aureus, Friedländer's bacillus, influenza bacillus, and pneumococcus. They may be readily demonstrated in tuberculous sputum, and can be recovered at autopsy directly from the involved tissue. The question is one of indecision in individual cases, but we may, on clinical grounds, with some degree of certainty, assume that in certain cases, especially those in the terminal

stages, and exhibiting a hectic type of fever, are suffering from a mixed infection.

Character of Fever in Tuberculosis. Patients exhibit marked differences in their reaction to fever and to the clinician; the striking contrast between the apparent comfort of the patient and the temperature record forms one of the most marked peculiarities of the fever in tuberculosis. On the other hand, some patients, especially those with a neurotic tendency, are notably affected. The apparent selective action of the toxin is evident in some cases and may lead to error in diagnosis. The pulmonary lesion may remain latent, or apparently so, and yet evidence of intoxication appears in many cases. Thus we may see cases where the gastro-intestinal symptoms dominate the clinical field, obscuring

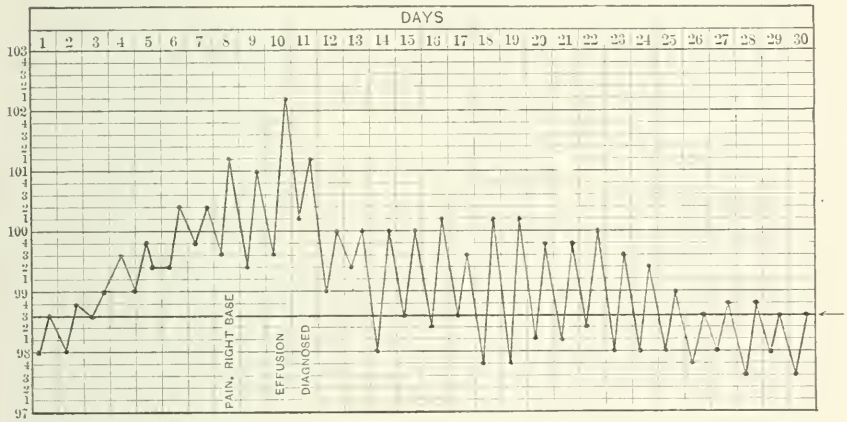

Fig. 4.—Case 2281. Male, aged seventeen years. After a gradual rise in temperature for a few days, onset of base pain; two days later effusion detected. The temperature reactions in cases complicated by pleural effusion are variable, but the above chart expresses, in a fairly typical manner, the reaction in those cases terminating favorably.

the real nature of the infection. At other times the condition may be masked by an accompanying neurasthenia. Disturbances of the circulatory system may lead to false conclusions, especially when anemia is present. A profound weakness may be the sole complaint for which the patient is unable to give an explanation. Finally, fever may be present in some cases with such slight constitutional symptoms that it escapes even the patient's notice.

Unfortunately no typical temperature curve exists in tuberculosis as in some other infectious diseases. The fever occurring at the onset can so closely simulate the typical temperature curve observed in certain other diseases, notably pneumonia, typhoid, and malaria, that error not infrequently arises, the further course of the disease alone suggesting the true nature of the causal agent. A certain type of initial fever, however, is worthy of mention, because

of its frequent association with beginning tubercle formation. It is distinguished by a slight post meridian temperature ranging from 99.2° F. to 100.2° F., evanescent, showing marked fluctuation and requiring two-hour readings for proper interpretation.

In a study of the temperature curve of pulmonary tuberculosis over a period of months the alternating febrile and afebrile states and the extreme irregularity of these intermittent periods, form one of the most striking characteristics. The curve also represents in some cases, fairly typically, the actual clinical course. In the progressive type the afebrile periods become shorter, the febrile correspondingly longer, with increase in the temperature range, and toward the end the fever generally assumes the hectic form, A reversal of the above picture in cases with a favorable outlook commonly occurs.

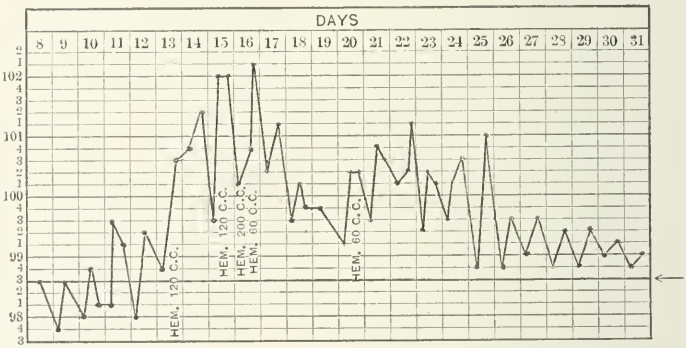

Fig. 5.—Case 2731. Male, aged twenty-one years. Hemoptysis with temperature. The frequent rise in temperature preceding hemoptysis is noted. Following the hemoptysis a considerable rise occured. On account of bacteriological difficulties the role of secondary organisms in the production of hemorrhages and their relation to the different types of fever has in our hands received no definite confirmation.

Williams, Minor, and others have drawn attention to the frequently accompanying subnormal temperature to which they attribute much importance. The temperature is extremely labile, oscillating readily to slight stimuli. Exercise can induce a decided rise in temperature, the reaction being more pronounced when little or no exercise has been previously allowed. Eating and mental excitement often lead to an increase in temperature.

The fever is arbitrarily divided into three parts, the divisions depending on the degree of temperature: First, from 99.2° F. to 100.2° F.; second, from 100.2° F. to 102.2° F.; third above 102.2° F. The fever may be continuous or remittent, but intermittent fever is the rule in tuberculosis.

The following tabulation of the temperatures of 223 cases admitted to the Ray Brook Sanatorium consists of two hourly readings from 7 A.M. to 9 P.M. for a period of eight days subsequent

to admission. To separate the febrile from the non-febrile cases it was necessary to establish some arbitrary rule in the following tabulation: all cases that presented a temperature of 99.2° F. or above on three separate days were classified with the febrile group:

Incipient, 107; febrile, 45 or 42 per cent.; non-febrile, 62 or 58 per cent.

Moderately advanced, 76; febrile, 44 or 58 per cent.; non-febrile, 32 or 42 per cent.

Advanced, 40; febrile, 32 or 80 per cent.; non-febrile, 8 or 20 per cent.

Average maximum temperature of 45 incipient cases, 99.8° F.

Average maximum temperature of 44 moderately advanced cases, 100° F.

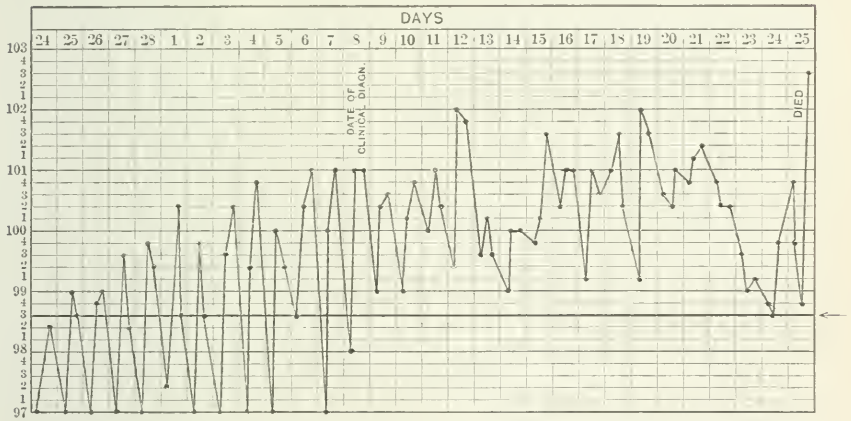

Fig. 6.—Case 1665. Male, aged twenty-one years. Pulmonary tuberculosis; stage two. Symptoms quiescent, excellent nutrition. Diagnosis of meningitis two weeks after onset of fever. The effect produced on the temperature curve by the meningeal complication is well illustrated.

Average maximum temperature of 32 advanced cases, 100.4° F.

The selection of patients for sanatorium treatment probably exercises a decided influence on the above figures, since the acutely ill are excluded. Nevertheless, these figures indicate that the percentage of febrile cases and the degree of temperature increase with the stage of the disease.

An endeavor has been made to establish a connection between fever and the stage of the disease, and, *a priori*, there would seem justification for this classification, since the degree of temperature should be closely related to the amount of lung infiltration. However a considerable number of cases cannot be so classified. The degree of saturation of the blood and tissues with toxin is in direct proportion to the absorptive powers of the contiguous tissues

surrounding the focus. Their ability or inability to impede peripheral absorption is one of the factors which determine the degree of fever present. Concerning a second factor the protective substances generated by the tissues, nothing definite can be said, but clinical experience would lead us to believe that fever is also definitely influenced by these agents. Furthermore, individual susceptibility of the heat-regulating centre must be remembered. These factors, peripheral absorption, the presence of protective substances, and the condition of the heat regulating centres offer some explanation why certain cases with a slight initial lesion show grave constitutional symptoms, while others with gross pulmonary lesions may remain afebrile.

Miliary tuberculosis requires special consideration, in that a considerable degree of temperature is usually present at the onset and may be ushered in by chills, with rapid rise in temperature to 104° F. or above. The pyrexia may persist in the form of a continued fever, can assume an irregular remittent character, or, for short periods, be intermittent. The entire course of the disease may be characterized by moderate or even slight elevations of temperature. The typus inversus morning temperature with afternoon decline, according to Brunnechi, is characteristic of this type of tubercle invasion.

Factors which Influence the Temperature. Sudden relatively high temperatures of short duration are commonly the result of non-tuberculous complications, throat inflammations, gastro-intestinal disturbances, etc. Tuberculous meningitis often has a depressant influence on the temperature and may give rise to decided fluctuations. Profuse hemorrhages and continued diarrhea often cause a fall in temperature. The temperature invariably registers higher after an exacerbation of the local inflammatory process, pleurisy, aspiration, following hemorrhages, etc. The anatomical position of the lesion has apparently no direct bearing on the temperature. The favorable effects resulting from cardiac insufficiency has been pointed out by many observers, and is explained on the basis of pulmonary stasis.

Diagnosis. The determination of fever is of great clinical value, forming, as it does, the cardinal index of the constitutional symptoms in tuberculosis, and one of the earliest and most reliable indications of tuberculous implantation. Since slight fluctuations of temperature are of great diagnostic value the question arises, at what point on the thermometer does normal temperature end and fever begin? Owing to the variability in the normal temperature as above mentioned, only an approximate estimate can be made in a given case; roughly, the maximum normal temperature ranges between 98.6° F. and 99.4° F.

Experience would seem to indicate that a mere transitory rise of temperature can be ignored in diagnosis, as various obscure

factors may play a part in its cause. Slight elevations of temperature, 99.2° F. to 99.4° F., however, if persistent or recurring frequently, become of diagnostic value.

The extreme variability of the temperature curve in pulmonary tuberculosis materially decreases its value in diagnosis. Cornet says, "A temperature of 99.8° F., which is intermittent but obstinate, and which increases upon the slightest exertion, indicates tuberculosis unless some other etiological factor can be discovered." This is a satisfactory rule, but must be applied with caution, since not infrequently the other etiological factors can be excluded only with difficulty. The forwarding of patients to sanatoria because of an unexplained temperature, which later proves itself to be non-tuberculous, is not infrequent.

There are a few diseases in which the temperature curve so closely simulates that of pulmonary tuberculosis that a differential diagnosis is of extreme importance. These diseases may be classified as pulmonary and extra-pulmonary. In the first group the disease most frequently leading to error is influenza. The bacteriological examination is often the only available means for differentiation. Other conditions of less frequency are lung abscess, syphilis, actinomycosis, bronchiectasis, occasionally mediastinal tumor, and malignant disease. In the extra-pulmonary group may be included Graves' disease, gastro-intestinal conditions, syphilis, certain cardiac conditions, Hodgkins' disease, cryptic suppurations, malaria, and typhoid. The differential diagnosis of Graves' disease is of special importance, and not infrequently cases are admitted to sanatoria with this mistake in diagnosis. Gastric dilatation, intestinal toxemia, and chronic appendicitis are confusing, in that functional changes of the digestive tract are frequent in pulmonary tuberculosis. The anemia, the loss of weight, the malaise, and even the fever of secondary syphilis, in the absence of rash, sore throat, etc., may strongly suggest the presence of tuberculosis. An irregular intermittent fever extending over a period of months in a certain group of cardiac cases has of late received attention, since the diagnosis of these cases has frequently been confused with that of tuberculosis. The fever that occasionally precedes the glandular enlargement of Hodgkins' disease, and which is so frequently accompanied by weakness, anemia, loss of weight, and anorexia extending over many weeks, has led to the erroneous diagnosis of concealed tuberculosis in more than one case. Local pus pockets, especially in the nasal sinuses, with latent local symptoms, are often confusing. In malarial districts the malarial type of fever in tuberculosis renders differential diagnosis difficult. The fever of miliary tuberculosis is similar in many respects to that of typhoid, and the differential diagnosis forms one of the most difficult problems in clinical medicine.

Prognosis. In the prognosis of pulmonary tuberculosis, fever is a most reliable index of the ultimate course of the disease. Fever that resists treatment always speaks for an unfavorable outcome. The height and duration of the fever affect the prognosis correspondingly. The absence of fever does not, as is often accepted, necessarily imply improvement. Progression of the disease in the absence of fever can be clinically demonstrated.

Conclusions. 1. There is a necessity for testing the accuracy of certified thermometers.

2. Normal temperature may vary within considerable limits.

3. The selective action of tuberculo toxin in pulmonary cases may directly affect other systems than the respiratory, and thus lead to error in diagnosis.

4. The temperature curve in pulmonary tuberculosis is protean in character, and may simulate that of many other diseases.

5. Fever is the cardinal symptom of incipient tuberculosis: its nature and persistence are of diagnostic import.

6. The persistence of fever bears a definite relation to prognosis.

The appended temperature charts are presented to illustrate types of fever in tuberculosis.

EXUDATES IN ARTIFICIAL PNEUMOTHORAX.

By Earl Sprague Bullock, M.D.,
physician-in-chief,
and
David Cushman Twichell, M.D.,
associate physician, the new mexico cottage sanatorium,
silver city, new mexico.

When one has had the experience of seeing a Lazarus rise from the dead, the incident will never be forgotten, and the procedure which enables this to be done will not be abandoned even though such dramatic successes are but few in comparison with the whole number of cases in which artificial pneumothorax is performed. This method is still in the experimental stage, and many more years' experience will be required to more truly indicate its limitations as well as the type of case in which it is likely to prove most successful. The mechanical conditions met with in advanced tuberculosis, as, for instance, adhesions, consistency of the lung to be compressed, thickness of cavity walls, metabolic reactions to compression, the state of the other lung, the effect upon complications, particularly those of tuberculous character, the alteration of circulation, position of the heart, and the effect of pressure upon

the digestive organs, compose a picture of great complexity with an endless variety of factors introduced into the problem presented by each and every case.

One thing seems certain, compression has come to stay, and the problem facing phthisiotherapists is the delimitation of the method —to use it for the greatest good of the greatest number of consumptives applying to us for help. The purpose of this paper is to assist in a measure toward the elucidation of the problem of the application of artificial pneumothorax.

We thought at first that our cases were too few to enable us to draw any conclusions from our own experience in clarifying the problems of this treatment, but we find upon studying the literature that the number of cases in which we have employed this method during the past three years will compare favorably with those of other clinicians. To date we have had fifty cases. In 50 per cent. it was impossible to obtain an efficient pneumothorax on account of the mechanical conditions encountered, such as adhesions, etc. In a small number, even though a certain degree of compression could be induced, it was not effective as regards compression of the essential lesion—the cavity, etc. There has been about the proportion of really successful cases that other observers have noted. From our experience we do not hesitate to draw two conclusions; one of them is that in certain of these cases in which a clinically effective degree of compression is impossible the procedure must be supplemented by surgery, and we think that the time will come shortly when a qualified surgeon will be necessary as an adjunct to the staff of every large institution for tuberculosis. The other conclusion is this: admitting, as we all do, that in something like 50 per cent. of the cases we cannot obtain an artificial pneumothorax on account of the mechanical conditions presenting, it seems to us very plain, indeed, that our efforts should be directed toward the anticipation of these extensive adhesions; in other words, that when a case presents the unqualified evidence of progression, especially in the presence of a relatively sound or arrested process in the good lung, that we should not wait until pneumothorax is forced upon us, but should perform this operation when it is not only mechanically possible, but when the organism is still capable of withstanding the effects of compression.

During the past year we have been trying to do this, and from the results already achieved we have little doubt that in a few years we will be able to prove, if it has not already been done, that the most successful pneumothorax cases will be those in which this method was applied in the comparatively early stages of advanced disease or in a progressive lesion not far advanced, when the conditions are of our own choosing and not relatively or wholly beyond our reach. It is all very well and gratifying to save an occasional far-advanced case by this method, but infinitely more useful to

prevent them in a larger proportion of cases from ever becoming far advanced, for under such conditions, as we all know, the method is grossly handicapped, not only by the 50 per cent. of instances in which it is no longer possible on account of the adhesions, but by the failure of the good or relatively good lung to withstand the effect of the pneumothorax, as well as by the unfavorable conditions presented by the body in far-advanced tuberculous disease, and also the possibility that complications, such as laryngeal or intestinal tuberculosis, the existence of which may have been previously unsuspected, may immediately become flamboyant in their manifestations upon the induction of a pneumothorax, though, as we all know, such complications, are as likely to be benefited as aroused to activity.

During the past year or two, as experience with this method has matured, we have heard more and more of the occurrence of exudates following pneumothorax; in fact, it is claimed by a consensus of opinion in Europe and America that in at least one-half of the cases in which pneumothorax is mechanically possible that ultimately an effusion will occur. It is but natural to suppose that the more extensive the involvement the more the pleura has been invaded by a tuberculous process; in other words the longer we wait the more likely we are to witness this phenomenon of effusion. An examination of the cases abroad definitely proves that this statement is true, and further substantiates our opinion that pneumothorax has other applications than are found in so-called hopeless cases. When we first read of the occurrence of these frequent effusions it was astonishing to us, for in but one of our 26 cases in which gas could be introduced effectively have we had a large effusion, and in but 4 an insignificent quantity of fluid, which in 1 was subsequently resorbed, and in 3 a small quantity still persists. Our physical examinations were controlled by fluoroscopic inspection. We asked ourselves, Is our experience unique? and if so, to what is it due? We communicated with the medical authorities at the United States Army General Hospital at Fort Bayard, New Mexico, and it proves that their experience has been as follows: of 19 cases in which artificial pneumothorax was induced there were 3 relatively large effusions, and in 3 cases there was a demonstrable quantity of fluid which did not increase or was subsequently resorbed. Webb, in Colorado Springs, reports "85 cases for pneumothorax in which we met with success more or less in the collapse of 63. Nine of these had moderately large effusions which we drew off part, and then they disappeared. I do not know how many we had with small effusions, as we did not Roentgen-ray them all." Shortle, of Albuquerque, New Mexico, reports "50 cases in which a satisfactory degree of compression was produced. Among these cases 9 developed an exudate, as shown by physical signs. No examinations of patients were made with

Roentgen-rays." We may take it then as probably true that on the high, dry plateau of the Rocky Mountains we do not have effusions in our pneumothorax cases with the frequency witnessed elsewhere, and when they do occur the tendency is to remain small and be reabsorbed. This phenomenon cannot be due to altitude, for von Muralt, at Davos, Switzerland, who has made a most exhaustive study of exudates, a report of which he presented last September before the eighth meeting of the Society of Sanatorium Physicians at Freiburg, states that at Davos they have the same percentage of exudates following artificial pneumothorax observed in other places. He observes without equivocation that general injury, such as cold, exertion, fatigue, intercurrent infections, account in a large measure for the occurrence of effusions. The reason why we do not apparently have quite so many effusions on the Rocky Mountain plateau may lie in the fact that we do not have colds and intercurrent infections among our tuberculous patients with anything like the frequency observed in less favorable climatic environments. It is only fair to observe, however, that in Europe this method has been employed much longer than in the United States, where it has only been used about three years to any extent, and that after longer experience we may see more effusions, though in the East the experience corresponds to that of Europe, even though they have employed pneumothorax a much shorter time.

Von Muralt, in common with most observers, thinks that the effusion in pneumothorax is directly parallel with the common exudative pleuritis; in other words, to use his exact language, "it is to be ascribed to a going over of the tuberculosis to the pleura." With this statement we do not wholly agree. The secretion of a fluid by the pleura is as natural a phenomenon as that of tears by the conjunctiva. If the tear duct is occluded the tears will overflow upon the cheeks. When the mechanism of the pleura is in perfect working order as to secretion and absorption an excess of fluid is never found; but we certainly know that as pneumothorax is protracted the absorption properties of the pleura become more and more impaired; that as time goes on refillings are required at longer and longer intervals, and in the presence of this impaired function on the part of the pleura it may be true that it will become less and less possible for it to take care of the excessive secretion. Exudate in the beginning may be a response to irritation, and the mechanical condition induced by pneumothorax, as well as a abnormal substance, such as nitrogen gas in contact with the pleura, certainly furnishes the factors of irritation. This theory will not apply to those exudates the result of pus infection, or of true tuberculosis of the pleura, in which tubercle bacilli are found in the exudate. However, these forms of exudate von Muralt states are in the minority, but we believe that this theory may be

the true explanation of the small serous and lymphocytic exudate. In contradiction to such a theory is the experience of Shortle, who has made it a practice to withdraw all exudates on their appearance in any quantity and replace with gas. It has been his observation after such a removal of exudate that it does not tend to return. Under our theory it would seem most likely to.

It has been proved that the choice of operation, whether Forlanini or Brauer, does not influence the occurrence of exudates. It also seems true that the more serious the case the more extensive the tuberculous pleuritis is or has been the more likely they are to occur. It is perhaps needless to say that the small and, as we think, mechanical effusions are of no importance and do not require treatment. In one of the four instances we have observed it was promptly resorbed, and in the three in which it persists there has been no tendency to increase. However, in the East and in Europe the large percentage of exudates observed becomes a factor of real importance in artificial pneumothorax. These exudates are said to gradually increase and more and more approximate pus in character, becoming first cloudy; later containing polymorphonuclear neutrophiles, and lastly tubercle bacilli. They finally lead to gross thickening of the pleura. It seems to be the common practice under such conditions and in the presence of pressure symptoms to remove a portion of the exudate and replace it with gas. All observers are practically a unit that washings and the injection of antiseptics are little worse than useless under these conditions.

We do not know when it first occurred to one of us, independent of artificial pneumothorax, in fact, years before we knew anything about this method, that nothing could be more favorable, especially in far-advanced tuberculosis, than an extensive effusion into the pleura. We are certain that independent of the practice of any other physician one of us (Bullock) distinctly conceived the idea that such effusions should never be disturbed except for pressure symptoms, and then only enough removed to relieve the circulation. Often after an effusion these patients would take on weight, present a normal temperature, slowing of the pulse, and a general feeling of well-being. The observation of a few of these cases in which effusion occurs naturally will prove to anyone that in such an exudate there is something, or a combination of things, which we suppose we can safely class under the generic term antibody or antibodies, which are vastly beneficial to the affected individual. There has never been a time during the past seventeen years when one of us has not had such a person under his observation, and we have a clear-cut conviction that as long as the fluid remains the individual is relatively safe, and that it is usually only upon its complete resorption that the tuberculosis resumes its course. As soon as Röhmer and Hamburger showed that the already tuberculous

animal could not be reinfected with tuberculosis, this, of course, being in line with Koch's original observation of the injection of tubercle bacilli into already tuberculous guinea-pigs, one of us (Bullock) felt safe in removing small portions of these natural effusions and injecting them into other and seriously ill consumptives. He did this several times, but to his surprise there was neither local nor general response. Why this fluid which partially protects the individual having it will not benefit others is difficult to understand. One reasonable explanation is, we think, that the quantity injected or possible of injection is too small or too infrequently employed, or both. The individual with the exudate, however, has a large reservoir of antibodies in the fluid upon which he can draw continuously.

Extensive exudates in artificial pneumothorax may produce, through vast pleural thickening, a marked shrinking of the pneumothorax, and, according to von Muralt and others, there occurs, in spite of refillings under high pressure, a retraction of the thorax with an expansion of the compressed lung before we are ready for any such functional mobility. Right here we must call in the surgeon and have him do a plastic operation, a Wehlm or some of its modifications, or better yet a Schede. We have never seen a pus infection of the pleura follow artificial pneumothorax. Such an accident must occur from infection from without by means of the needle or from perforation of the lung. All observers agree that they are very rare, and should be treated by thoracotomy, drainage, frequent washings, etc.

Von Muralt holds that on account of the great uniformity in the occurrence of pleural exudates in artificial pneumothorax that their cause must be wholly interior, and whatever the actual cause, whether a true tuberculous effusion (or, as we hold, the small mechanical effusion), he is undoubtedly right in attributing their causation to internal conditions and not to methods of procedure.

Von Muralt classifies the effusions as follows: (*a*) True serous or light sanguinolent exudates which remain small and show only a slight tendency to increase in quantity, and which generally disappear in the course of a few weeks or months. Of his 35 exudate cases 14 were in this category. Of our 5 exudates 4 were of this type (this is the character of exudate which we ascribe to mechanical causation). (*b*) Exudates which begin like (*a*) but have a greater inclination to increase and retain their character for a long time. (These also may be ascribed to a mechanical causation.) If, however, tubercle bacilli make their appearance in the effusion it is probable that a true tuberculous pleurisy has become superimposed upon the original effusion. As a rule, tubercle bacilli can only be demonstrated in these effusions by means of animal inoculations. Von Muralt has had 16 cases of this type which continued over a period of years, and in the later stages contained plentiful cell detritus. (*c*)

Virulent infections of the pleura with mixed organisms originating either through wound infection or rupture of the lung. Von Muralt has had 5 such cases. In one of our patients a natural was superimposed upon an artificial pneumothorax, with subsequent exudate, which examination proved to be sterile under the microscope. The fluid also proved negative when injected in a guinea-pig. Von Muralt makes it plain that the seriousness of the cases has a distinct influence upon the occurrence of an exudate. Of his 29 cases without exudate, 20 were moderately advanced, 7 very serious chronic, and 2 acute tuberculosis; while of his 35 exudate cases, 13 only belonged to the moderately serious class, 19 to the very serious chronic class, and 3 to the acute. With the first group exudates of the (*b*) type have been mostly observed by him. In his moderately serious cases exudate generally occurred later; in some cases not until a year after the first operation, and were usually small and serous. Von Muralt's experience corresponds to and may well be said to be a reflection of that of others. Therefore if it is so that the more serious the case the more likely the effusion is to occur it constitutes a most important reason for anticipating the use of pneumothorax and not waiting until the procedure is forced upon us. The microscopic examination of these exudates as well as animal experiments rarely shows anything, with the exception of the (*c*) type, but tubercle bacilli, if they are not wholly sterile, as is true of the (*a*) exudate.

According to von Muralt, Gratz, and Saugman it should be kept in mind that when a pneumothorax is present the pleura is unable to prevent a tuberculous focus from extending by means of the adhesion of the two membranes, parietal and enteral, but rather tuberculous foci are able to develop and spread on the surface of the pleura. The stimulation of such foci is in fact favored by tearing adhesions and stretching the pleura. In our opinion this accounts for some of the acute febrility manifested during the early stages of compression in some instances.

Saugman further states that we should remember that the pleura, through the steady contact with gas, is placed in a wholly unphysiological relation, which, as Kaufmann has demonstrated in dogs, produces an anatomical change of the serosa with a decreased ability of gas resorption, and as we would like to interject once more for the sake of emphasis, probably a decreased ability to absorb its own secretion. Von Muralt states that one has the right to accept the principle that the tuberculous pleura is particularly prone to exudative inflammation under these changed conditions. He also emphasizes that in addition to the causative factors already mentioned certain individual ones should be considered. In his 35 exudate cases, 11 had had marked pleuritis before the pneumothorax, and in these, in 6, exudate had occurred; to quote exactly, "doubtless, therefore, it is just the patients

which are individually disposed to exudates who take a pretty large share in pneumothorax exudates." Von Muralt, Forlanini, and Brauer all protest against the use of the term transudate as an explanation for the occurrence of fluid in pneumothorax. The reason for this seems to lie in the fact that the exudate does not appear in the beginning when the circulation changes are most marked. Faguoli, who has made a study of the character of exudates, has found them of not only high specific gravity, but with a high albumin content, which he states is good evidence in favor of their inflammatory origin.

Of course, on account of the extremely few exudates that have been observed in our work to date, it has been impossible for us to make any exhaustive study of their character; but in the 4 cases with small exudate that we have observed the exudate has been sterile even upon passage through animals. In the large exudate case the fluid is purulent and tubercle bacilli are present. For the same reason the insignificance of our exudate material, we are unable, from our own experience, to discuss the therapy of these exudates; notwithstanding which, as the result of a long and extended experience with natural exudates, we have very positive convictions regarding their treatment. From the point of view of treatment we can see no reason for differentiating natural effusions from those which follow artificial pneumothorax. We believe they should be handled the same, and that is, with certain qualifications to be explained later, let severely alone. If, however, upon gradual thickening of the pleura there is reëxpansion of the compressed lung before it is clinically desirable and by refilling with nitrogen it becomes impossible to prevent this premature expansion, or, as in some instances, even upon withdrawal of a portion of the fluid more nitrogen cannot be introduced, then, providing the patient is in a position to withstand the operation, the desirability of a plastic should at once be considered. Under these conditions our conviction would be that a Schede should be performed rather than the tentative and less complete procedure of Wehlm. Von Muralt and others agree that in the presence of inflammatory symptoms and an exudate that positive pressures cause more inconvenience than the same pressure previous to the appearance of the exudate. Under these conditions, lowering the pressure to zero may at once reduce the fever. This is in line with the observation that all of us should have made that there are patients without exudates who must always have a zero or a bit of negative pressure in order to be free from fever. It is well at this juncture to state pointedly tht every gas case is an individual matter, and that a theoretic degree of pneumothorax may practically prove undesirable. As one of us (Bullock) stated before the American Sanatorium Association in 1913, the least pressure that will accomplish the result clinically is the pressure to be maintained.

It now occurs to us that possibly one reason why we have seen so few effusions is because we have always used warmed nitrogen. The lack of this precaution may account in part at least not only for some of the effusions but also for the so-called pleural reflexes of which personally we have seen none. We have no doubt that von Muralt is correct in his observation that in small saculative, pocket-shaped, or indented pneumothorax, in which a compressing effect is only possible with high pressure, clots and progressive adhesions are easily formed. Several times we have been able to find a pocket which we could refill, using relatively high pressures, for a certain length of time, then, much to our surprise before we understood this phenomenon, we would never be able to find the pocket again. In such cases, if we are to accomplish anything with pneumothorax, high pressures and frequent refillings are essential.

It is advised in the presence of an exudate and inflammatory symptoms that the pressure should be kept neutral until the fever period is passed, high fever itself being treated by means of counter-irritation (the acutal cautery), the use of pyramidon, aspirin, etc. A small quantity of the fluid should be withdrawn for examination, and if pus and pyogenic organisms are found, energetic surgical measures should at once be instituted. If, however, the fever remains low in type we should employ all our supporting measures and patiently await an amelioration of the condition before resorting to radical surgical procedures. We will then have time to adequately study the situation, and if surgical intervention becomes necessary, know best just what sort of operation is likely to meet the situation. From von Muralt to Saugman and Brauer every observer is agreed that antiseptic injections into the exudate are worse than useless. In this connection von Muralt observes, in making his plea for the conservative management of exudates, that the removal of even a small portion of the exudate may exacerbate the symptoms. We have observed this phenomenon in natural effusions when we have been forced to remove a portion on account of pressure symptoms. In the absence of mixed infection in an exudate in which fever continues from one to two months or longer, von Muralt would not ascribe the fever to the exudate, but to a tuberculous focus either in the lungs or another organ. The same observation undoubtedly holds good in the absence of an exudate with the presence of a complete pneumothorax when fever persists.

All observers are agreed that in the presence of fever the removal of the exudate and cleansing of the pleural cavity—when the exudate has been sterile, or simply tuberculous and free from mixed infection—is more likely to accomplish harm than good. It should be remembered that it is in just such cases that with patience we are likely to witness the most happy sero-immunizing effect. To employ von Muralt's forceful observation, "whoever has been able to observe these remarkable beneficial changes will not do

things which do not bring any benefit anyway." In other words, to further follow von Muralt, the fact that an exudate is present does not indicate the use of surgery even if the test puncture looks ugly, grayish, and contains tubercle bacilli. He puts it very happily when he states "one must learn to consider the tuberculous pyopneumothorax as well as the dry pneumothorax as a pathological-physiological condition." When the temperature returns to normal in one of these exudate cases it is no longer necessary to keep the pressure low, and most observers are agreed that the individual indications can be followed as before the onset of the fever. It is as true of a large exudate as of a large pneumothorax that they may act unfavorably on the stomach, liver, and heart through the pressure exerted. Such conditions must be met either by lowering the pressure or partially removing the exudate. These large exudates are slowly resorbed, as is true in natural effusions, and the end result is the same in both instances, an enormous pleural thickening, which helps to permanently maintain the lung in a state of physiological rest. Nearly everyone who has to do with a large number of consumptives has observed this termination in natural effusions, and some of the most brilliant results in far-advanced cases we have ever seen have fallen in this category.

True empyemas with marked clinical manifestations are amenable only to plastic operations. Von Muralt thinks, however, that if they are small in quantity that large antiseptic injections, for instance, 20 to 30 c.c. electrargol in repeated doses, if necessary, are often sufficient to arrest the process. According to him this is particularly true of pneumococci infections. In his opinion, however, if improvement does not soon follow this measure, the exudates should be reduced through puncture; but the plastic operation for the reduction of the pleural cavity should not be done until the abscess has been drained by a thoracotomy, thus lessening the chance of infection of a large plastic wound. Forlanini states that the imposition of a natural pneumothorax upon an artificial one is an absolutely fatal catastrophe. We have had one such case in which all the classical symptoms of rupture of the lung were present, which were subsequently followed by an effusion of clear sterile serum, and in which instance up to the present time (eleven weeks after the rupture) the patient is either holding her own or improving a little.

A phenomenon which occurs in pneumothorax of very great interest, for it is still unaccounted for, is the preliminary marked loss of weight which occurs in many of these cases no matter how completely the clinical symptoms are relieved. We have endeavored to account for it specificially, but so far have had to content ourselves with the generalized explanation of altered metabolism and circulation following the unphysiological relations of artificial pneumothorax. It has been observed, however, that should effusion

occur the loss of weight stops promptly and the patient begins gaining in weight.

In this country it is too early to permit of adequate discussion of end-results. In Europe they are just beginning to do so, but it seems reasonable to expect that in time our end-results will approximate theirs. This will prove notably true providing the measure is reserved in the future, as it has been in the past, in large measure, for otherwise hopeless cases. If, however, as we advocate, the method is applied in all suitable cases that are progressive in type the story may read more happily. There is one point to be borne in mind which was especially marked in the experience of one of us in the earlier use of pneumothorax, and which we have not seen mentioned by other workers. It is this: It requires relatively a higher pressure and a larger pneumothorax to relieve the clinical manifestations in a lesion confined to one lobe than it does in more extensive disease of the lung. Under these conditions we more often observe the phenomenon which European operators designate as "puffing up of the mediastinum." In several instances in which we have performed this procedure in one-lobe cases we have had the physical signs and sounds of pneumothorax impinge upon the sound lung as much as three inches from only a slight positive pressure. On the reduction of such a pressure the former signs and sounds returned to the area in question. We have never seen any harm come from such a dislocation of the mediastinum.

For many years the workers in the Rocky Mountain plateau have tried to impress upon their Eastern confrères that under our climatic conditions the picture of tuberculosis is altered and ameliorated as compared with the manifestations of the disease in many other localities; that patients do not have night sweats; that hemorrhages are less often observed; that fever is less often in evidence, and patients apparently acquire sooner, and in greater number of cases, a toxic immunity; that the circulation is improved; that the red blood cells are increased in number; that the percentage of lymphocytes tends to increase; that tubercle bacilli disappear sooner from the sputum; that the lesions are drier; and, in fact, that we get better results. We would furthermore like to impress upon our Eastern confrères that we apparently do not have exudates, or such serious exudates, with the same frequency as they do in the East and many other localities.

PELLAGRA IN CHILDHOOD.[1]

By Frank Crozer Knowles, M.D.,

INSTRUCTOR IN DERMATOLOGY, UNIVERSITY OF PENNSYLVANIA; CLINICAL PROFESSOR OF DERMATOLOGY, WOMAN'S MEDICAL COLLEGE OF PENNSYLVANIA.

Pellagra was first described by the Spanish physician Casal in 1735, although Frapolli gave the appellation to the affection in 1578. The importance of the disease cannot be overestimated, as in the year 1884 Italy reported the appalling total of 104,067 cases, which fortunately decreased to 60,000 in 1903, and since then has exhibited a still further abatement. Our own country is showing an increased epidemic, since the disease is becoming more generally recognized, particularly by the physicians of the South. C. H. Lavinder made the calculation that from 1907 to 1911 a total of 25,545 cases of this affection were observed in the United States; 15,870 of these occurred in the States of North Carolina, South Carolina, Georgia, Kentucky, Alabama, Mississippi, and Louisiana. The Northern States have been afflicted with comparatively few cases, and therefore those of us who have desired to study the affection have been compelled to visit the neighborhoods where the disease is endemic.

During the last four years I have had the opportunity of studying about a dozen cases of this affection in Philadelphia and in the neighborhood of forty in the South and Southwest. Two of the cases observed in Philadelphia occurred in childhood, one of which has already been reported by Dr. Hartzell. Although very little has been written exclusively on pellagra in childhood, the further one delves into the disease the greater becomes the conviction of the frequency of this affection in children.

Age. Lavinder found in a statistical study of 15,870 cases of pellagra, 412 under five years of age and 1719 between the fifth and twentieth year. Merk tabulated 4836 cases of the affection, of which 46 were observed under five years of age (0.9 per cent.) and 406 between the fifth and fifteenth year (8.3 per cent.). R. M. Grimm made a study of 323 cases from Kentucky (three counties), South Carolina (seven counties), and Georgia (fifteen counties) and discovered 15 cases under five years of age, 23 from the fifth to the tenth year and 23 aged ten to fifteen years. Sambon states that pellagra is quite a frequent occurrence in children, particularly after two years of age. There have been, according to Rohrer, 31 cases of this affection in Maryland up to September 25, 1912, 4 of which occurred in children aged six, nine, ten, and eleven years respectively. Mizell observed 15 cases of this affection under fifteen years of age out of a total of 100 cases. Potarca collected

[1] Read before the Philadelphia Pediatric Society, January 12, 1914.

17,027 cases of pellagra and found 13 per cent. under twenty years of age. Calderini, in Italy, observed, in 1844, 352 cases of this affection and found 83 of them under three years of age. Siler and Garrison discovered in a series of 254 cases, 21 under six years of age, 22 from six to nine years, and 28 from ten to nineteen years. Mason has seen 20 instances of the affection under the age of twelve years. Snyder sent a circular letter to sixty physicians of the South who had had extensive experience with pellagra and the consensus of their replies placed the prevalence of the disease in childhood at 10.5 per cent.

According to Snyder the youngest case observed by any of these sixty physicians developed at the age of two months (Savage). Chrisoferetti records instances of the affection at forty days, five, seven, ten, and seventeen months respectively. Sambon has seen cases at three, four, and five months, and states that while such early cases are rare the disease is quite frequent in children from six to eighteen months. The latter considers puberty in boys a vulnerable time for the pellagrous attack. Roberts has studied 2 cases of the affection at the age of four and five months respectively.

Sex. It is a well-known fact that the female sex in the adult is very much more apt to be attacked than are males. Siler and Garrison found in a study of 282 cases there were 191 females showing the affection and but 66 males. They found from one to six years of age, ten males and eleven females attacked, and from six to eleven years, twelve males and the same number of females. Rohrer reported that 3 out of 4 cases under fifteen years of age attacked by pellagra were of the male sex. Mizell recorded 15 cases under fifteen years of age, 5 were females and 10 males. Of 85 cases of this affection seen by Rice in two orphanages, 45 were females and 40 males. Tucker recorded 4 cases under fifteen years of age, 3 were males and 1 a female.

Race. Lavinder analyzed the sex and the race in 15,870 cases without separating the adult and the childhood cases. He found in the white race 2924 males attacked and 6857 females, and in the negroes, males, 931, females, 3117. Siler and Garrison compared the frequency of attack in the white and negro races. They found in the community where pellagra was endemic out of 282 cases, 257 occurred in the white race while but 25 were found in negroes; of these 25 cases but 1 was observed under six years of age, 1 also between the sixth and the tenth years.

Pellagra in Families. Sambon makes the statement that in families with numerous children living in districts where pellagra is endemic he has often found the parents and all of the children attacked. Siler and Garrison report that in one-half of the cases observed the disease occurred singly in one family, about one-quarter were noted two in one family, and the remaining one-quarter in groups of three, four, or five in one family.

Preceded or Associated with Other Diseases. Of the 43 cases observed by Siler and Garrison, infantile paralysis preceded the pellagra in one instance, chicken-pox in another, and whooping-cough in two others. Measles occurred before the pellagrous outbreak in 12 instances; 11 of these were under twelve years of age (approximately 23 per cent.). In most of these the attack of pellagra occurred shortly after recovery from measles (Siler and Garrison). Sambon recorded a case in a child of three years which developed shortly after an attack of pneumonia.

Because of the frequent occurrence of hookworm in the South the association of this affection with pellagra is often observed. Rice in order to determine the relative frequency of hookworm in the pellagrous and the non-pellagrous examined microscopically the stools of all the inmates of an orphanage and found that 26 per cent. of the total population were infected. Hookworm was found in association with pellagra in 29 per cent. of the cases.

Differences in Symptomatology between the Adult and the Child Pellagrin. *Cutaneous Manifestations.* Snyder found in his investigations that the skin outbreak in children was more prominent than the other manifestations of the disease. According to Wood, children, as a rule, are not seriously affected, the cutaneous outbreak being the most prominent feature. Sambon believes the malady is frequently overlooked in childhood because it is often very mild and of a short duration; the parents not infrequently believe their children only sunburnt.

In the cases observed by Rice in the orphanages of the South all of the eruptions were of a dry type, usually on the dorsum of the hands and the feet, in some only on the former; in certain instances extending up the backs of the legs, some only on the backs of the forearms and calves. He found the covered portions of the body attacked in but two instances; a mask form was present in one instance; Casal's necklace in one case; and the face and the neck were involved in a few. After desquamation in these cases the affected surface was smooth and of a lighter color than the adjacent unaffected skin. A few complained of burning of the affected areas. Thirty-three of his 43 cases had the dermatitis on the dorsa of the feet and the calves of the legs; these were the barefooted children. In the larger children who wore shoes the dermatitis was on the backs of the hands alone or the backs of the hands and the forearms.

Merk analyzed, in children and adults, 1679 cases of pellagra; 77 per cent. had an erythema on the backs of the hands alone; 282 cases (13 per cent.) had the eruption on the backs of the hands and the neck; 164 (7.5 per cent.) had the outbreak on the neck; 53 (2.4 per cent.) had the dermatitis on other portions of the body. In only 5 per cent. of Wood's 189 cases were the lesions lacking on the backs of the hands, and most of these patients were children

who were accustomed to go without shoes and stockings, thus exposing these areas as much as the hands.

Gastro-intestinal Symptoms. Rice in a study of 43 pellagrous children found that 16 had frank sore mouth, 8 had diarrhea, and 22 a denuded and fissured tongue. The mucous membrane of the mouth was redder than normal, but did not have that fiery redness which is seen in the severe types of the disease. Some had "geographical" tongue.

Nervous System. Rice found but few changes in the nervous system in his series of pellagrous cases with the exception of the patellar reflexes. In 54 cases in children he found the reflexes exaggerated in 28; decreased in 10; absent in 6; normal in 8; and unequal on the two sides in 2. Snyder found after comparing his statistics with fifteen other authorities on the subject that the nervous manifestations of the disease were very much less marked in childhood than in adults. Such also was the experience of Mason in his 20 cases in children.

Other Manifestations. The hair is not usually affected in those developing pellagra during adult life, but in children it is often short, thick, and course, lacking the usual amount of sebaceous matter, and feels rough (Roberts).

Comparative studies of the blood findings in adults and children with the disease have not been made in a sufficient number of cases to determine the resemblance or difference. In a considerable number of these cases there is some anemia present; the small lymphocytes are relatively increased, and the large mononuclear cells normal or diminished in number.

Indicanuria is very common and oftentimes a constant accompaniment of pellagra. Rice found in 42 cases of pellagra in children an excessive amount of indican in the urine in 50 per cent. of those attacked. The interval between the active attacks gave the reaction as markedly as during the stage of activity.

Rice made a comparative study of pellagrous and non-pellagrous children and found, at the same age, they were approximately the same weight and height. A large proportion of those attacked seemed to be in excellent physical condition.

Etiology. The conflicting views on the cause of the condition will not be discussed in the present article, with the exception of the question of heredity.

Snyder received eleven replies to his interrogation upon this phase of the subject; 9 had seen pellagrous mothers who had been or were nursing infants without any manifestations of pellagra being present in the latter; 13 babies were represented. None of Grimm's observations have led him to believe that the affection is hereditary. The latter reported 58 children whose mothers had developed pellagra within one year after the birth of the child, 9 were dead (cause undetermined) but none was pellagrous; of 18

children whose mothers had developed the disease within one year before the birth of the child, 2 were dead but none of the living were pellagrous. Grimm found that of 30 infants who were being nursed by pellagrous mothers, none were pellagrous at the time of his visits, 6 were not well, and 24 were healthy.

According to Sambon, he has never seen or heard of a single case of congenital pellagra, neither has he been able to find in literature any first-hand and authentic record of a case. Roberts states that pellagra is not inherited, but the ravages in the parent is inherited and appears in the child in the form of dwarfism, deficient development, anemia, various malformations of the skull, asymmetry, badly set ears, mental weakness, slow growth, an unusual lack of resistance, and a frailness out of all proportion to the age. Boudin prepared a paper on this phase of the subject: The first three groups with pellagrous parents give 443 pellagrous children, while the last two groups with the parents well give 297 pellagrous children; an excess in favor of pellagrous degeneracy and predisposition of only 20 per cent.

Agostini believes that the disease is not inherited, but that a certain weakness is present which makes the affection more easily acquired and tends toward the "gravest syndrome of somatophysical degeneration such as dystrophic cretinoid and myxedematous infantilism."

Case Report. Harry E., aged five years, came to the skin dispensary of the Children's Hospital July 10, 1914, because of an eruption on the face and the hands. A marginated dermatitis, dull red in color, was observed on the hands, ending abruptly at the sleeve line, and on the face extending half-way up the forehead to the hat margin. The same condition was noted on the rims of the ears. He has had several attacks of this dermatitis, beginning in the early spring and extending during the summer. Its occurrence is apparently independent of sunlight. The face is more or less red even in winter, but much less so than during the spring and the summer; desquamation of the affected areas occurs several times during each of the latter periods.

The tongue is partially denuded of mucous membrane and quite red. Other portions of the mouth likewise show this redness. The bowels move on an average of three times daily, usually after meals. The patient is quite thin, very small for his age, and is exceedingly nervous. The knee-jerks are diminished, the gait sluggish, incoordination poor, speech hesitating, pupillary reaction lessened, and there is a decided hebetude. His gait is decidedly ataxic, walking like a child with spastic paraplegia of the toxic multiple neuritis type. The urine examination was negative excepting for an excessive amount of indican.

During the two months the case was under observation the eruption became of a typical dark brown, mahogany color, and exfoli-

ated, leaving the skin dry and atrophied. The diarrhea continued and the nervous symptoms remained the same. The history insofar as it is obtainable apparently shows an attack of infantile paralysis; shortly afterward the present symptoms developed. The gastro-intestinal symptoms started at six months of age; the dermatitis appeared shortly afterward. The mother is healthy while the father has always been delicate, and is an inveterate cigarette smoker. The mother was born in Italy while the father is Irish. The child has always lived in the suburban portion of the city. While the case was under observation, quinin, salol, and mercury and chalk were given internally. The child when last seen was in much the same condition as when he originally came under observation, excepting that the active dermatitis was not present, as it was in the autumn.

Prognosis. Lavinder found the death rate in 15,870 cases of pellagra between the years 1907 and 1911 was 39.1 per cent., both adults and children being represented in these figures. Rice records 103 cases in children from 1907 to 1913, and but three deaths have occurred during this period. Snyder found that nineteen other authorities on pellagra considered the mortality in children either much less or less than in adults. The two cases I have seen in children one is dead and the other is still living.

In conclusion I wish to emphasize the importance of the pellagrous eruption. In communities where very few cases of pellagra are seen there seems to be a distinct tendency to diagnose every symmetrical eruption as a case of this disease. The color of the eruption should be particularly emphasized; a marginated, symmetrical dermatitis of the exposed parts of a deep mahogany shade, as if the skin had been painted with iodin, could scarcely be mistaken for any other affection, particularly if associated with gastro-intestinal and nervous symptoms. A considerable amount has been written on pellagra without eruption, "pellagra sine pellagra."

A paper on this disease could scarcely have a better ending than to quote two recent articles: Roussel, who first employed the term "pellagra sine pellagra," states: "The expression pellagra sine pellagra can only be applied to a temporary absence of the cutaneous eruption, either at the beginning or during the course of the malady."

Siler and Garrison start their instructive paper, "An Intensive Study of the Epidemiology of Pellagra," with the statement, "In view of the essential importance of diagnosis in our work the conservative position was taken that a positive diagnosis would be made only when the characteristic skin lesion was evident or its earlier presence could be definitely ascertained by the testimony of patient and physician."

Conclusions. Pellagra is of rather frequent occurrence in childhood. In endemic neighborhoods approximately 10 per cent.

of the cases occur in children. The disease is rare under two years of age.

The affection is almost evenly divided between the two sexes in childhood.

The negro is far less susceptible to the disease than is the white individual, particularly in early life.

In endemic neighborhoods in about one-half of the cases two or more members of one family are attacked (Siler and Garrison).

In a considerable number of cases in children, pellagra follows shortly after the exanthemata, particularly measles. In the South, pellagra in children frequently develops in those with hookworm.

The skin eruption in childhood is quite marked, while in a considerable proportion of cases the gastro-intestinal and nervous symptoms, particularly the latter, are comparatively mild.

Although formerly the death rate in children was rather high, at present, the disease occurs in a much milder form and the mortality is low.

Heredity plays no part in pellagra, excepting by lowering the general resistance of the child, the disease is more readily contracted.

The typical cutaneous outbreak or an accurate history of its former occurrence is essential in making the correct diagnosis of pellagra.

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THE BORDERLAND BETWEEN MEDICINE AND SURGERY IN RELATION TO CHRONIC PROSTATITIS.[1]

By Joseph R. Wiseman, A.B., M.D.,
INSTRUCTOR IN MEDICINE, COLLEGE OF MEDICINE, SYRACUSE UNIVERSITY.

Chronic inflammation of the prostate gland is one of the commonest diseases with which the adult male is afflicted. Out of approximately 500 adult men seen by the writer in medical practice, 36, or 7 per cent., were suffering from this disease. Chronic prostatitis is often overlooked, particularly when the symptoms do not point directly to the pelvic organs as the possible site of trouble; yet many symptom-complexes depend directly upon this condition, and their cure is well-nigh impossible without recognition and treatment of the primary prostatic disturbance.

This paper is not intended to be a treatise upon chronic gonorrhea, but to take up briefly a class of cases which presents general medical symptoms, particularly of a nervous character, caused by inflammation of the prostate gland. This may in turn depend upon a previous gonorrhea, perhaps long forgotten, or may have been induced by other causes. In discussing this subject I wish at the outset to express my great debt to the late Dr. Nathan Jacobson. Through his influence I was led to take an interest in this branch of medicine, his knowledge of which far exceeded that of any physician or surgeon I have ever known. The cases upon which this study is based are taken largely from Dr. Jacobson's records, partly from my own.

The normal prostate gland resembles a horse-chestnut in size and shape. It lies just below the neck of the bladder, and is penetrated from base to apex by the prostatic urethra. The structure of the prostate is comparatively simple, consisting of a connective-tissue capsule, from the inner aspect of which numerous muscular and connective-tissue bands run inward to form the stroma of the organ. In the interstices of the stroma, and supported by it, lie the prostatic glands. They are of the compound tubular type, and end in ducts which empty by fifteen or twenty openings into the prostatic urethra along the sides of the veru montanum. The two ejaculatory ducts pass through the substance of the prostate and empty upon the summit of the veru montanum, a small but important muscular structure which forms part of the floor of the prostatic urethra.

The prostate gland is provided with a free blood supply, and is surrounded by a plexus of veins so large and so closely interwoven

[1] Read before the Seventh District Branch of the Medical Society of the State of New York, October 1, 1914.

as to suggest the cavernous spaces of an erectile tissue. The veins of the prostate form one of the connecting links between the portal and inferior caval systems. The nerve supply shows an extraordinary wealth of nerve fibers, ganglion cells, and nerve end-organs. It is conceivable that the unusually rich blood and nerve supply of the prostate may determine on the one hand the readiness with which the gland undergoes congestive changes, and on the other hand the numerous local and general nervous manifestations associated with prostatic inflammation.

After studying the structure of the normal prostate it becomes easy to understand some of the changes which chronic inflammation brings about. If, for example, there is an increase of the connective tissue sufficient to compress some of the numerous tiny ducts the secretion of the tubular glands becomes dammed back, dilatation of the glands follows, and often small cysts are formed. The inflammatory changes may involve principally the stroma which increases in density, thereby producing a hard prostate, or the glandular structures may bear the brunt of the inflammatory changes and become distended with purulent secretion. In the latter instance an enlarged but soft or adenomatous prostate results. As a rule, both the glands and the interstitial tissue are involved, although often in unequal degree. Cases of long standing with much sclerosis show contraction or even obliteration of many glands.

The most common cause of chronic prostatitis is, of course, gonorrhea. "For practical purposes," as Hugh Cabot says, "chronic gonorrhea is chronic posterior urethritis, and in the same way chronic posterior urethritis is chronic prostatitis." Inasmuch as the posterior urethra is probably involved in from 70 to 90 per cent. of all cases of gonorrhea, it goes without saying that chronic gonorrheal prostatitis must be a very common disease. It is not so generally recognized that there is an important class of cases in which chronic prostatitis exists with no antecedent gonorrhea. The etiology of non-gonorrheal prostatitis is not entirely clear. Young believes that the prostatitis is of bacterial origin and that the organisms are probably conveyed to the prostate by the blood stream or from contiguous structures, notably the rectum. Of underlying factors the most important appear to be prolonged sexual excitement without gratification; excessive masturbation or sexual intercourse; irregular sexual practices, as coitus interruptus; and occasionally bicycle- or horseback-riding. Lydston states that when the periods of rest between the acts of ejaculation are so short that the circulation cannot regain its normal equilibrium, disturbances of the prostate are likely to follow. He considers that any masturbator who has practised the habit for any considerable length of time may be regarded as having a more or less swollen and tender prostate. Keyes lays stress upon cases where

there is association with a person of the opposite sex who permits dallying, even though coitus is not indulged in, thereby producing excessive dilatation of the prostatic vessels. Any or all of the above-mentioned factors probably pave the way for later bacterial invasion.

The symptomatology of chronic prostatitis is exceedingly varied, and, as Young says, may involve any of the organs in the various regions between the diaphragm and the toes. Pain is one of the most common complaints, usually dull and aching in character. It may involve the abdomen, back, external genitals, rectum, perineum, or be referred down the legs even to the toes. Among the conditions simulated may be renal calculus, lumbago, varicocele, sciatica, disorders of the abdominal viscera, and neurasthenia. Young has reported a number of cases in which there was strong resemblance to renal colic, even to the appearance of blood in the urine. In some instances the symptoms very closely simulate those of prostatic hypertrophy. Here it is exceedingly important to recognize the true condition, as proper treatment will save the patient from catheter life or an operation. McCrae mentions cardiac symptoms, such as anginal pains, palpitation, and tachycardia, accompanied by feelings of anxiety and distress. A common complaint is a sensation of fulness just within the anus, even though the rectum may be entirely clear of feces. With reference to urination there may be pain before, during, or after the passage of urine, or inability to expel the last drops of urine. Among the sexual symptoms may be mentioned diminution or loss of sexual power, premature ejaculations, and nocturnal pollutions.

The mental effects of chronic prostatitis are of great importance. Dercum states that there is apt to be difficulty in the performance of mental acts which require concentration, and a distinct disinclination for mental work. The sleep is often distrubed and true insomnia may result. The well-known picture of sexual neurasthenia or hypochondria is familiar to all. The patient has his mind constantly fixed on his sexual organs, believes that he is afflicted with severe or incurable maladies, and falls a ready prey to the quack, who knows best how to play alternately upon his hopes and fears.

The diagnosis of these conditions is simple. It depends upon rectal touch and the examination of the expressed prostatic secretion. The prostate usually feels enlarged, and may be irregular and indurated, or soft and boggy. Often it is nodular or shotty, due to dilated or cystic glands, and in many cases areas of softening and infiltration are irregularly encountered over the surface of the gland. Old inflammatory adhesions may extend from the prostate to the sides of the pelvis, making the organ more fixed than normal, and usually involving the seminal vesicles, with obliteration of the furrow between the upper margin of the prostate and each seminal

vesicle. Inflammatory changes in the substance of the vesicles may coexist. Tenderness of the prostate is frequently met with, and in some cases the patients can hardly endure the lightest touch.

Normal prostatic secretion is a thin, milky fluid containing principally lecithin bodies (round, refractile structures the size of a red blood cell), granular phosphates, mucus and an occasional leukocyte, epithelial cell or amyloid body. In chronic prostatitis the secretion is increased in amount, and is yellow and thick. Occasionally it is tinged with blood. The characteristic feature of the microscopic examination is the presence of pus. Young states that in some cases pus is not found at the first examination, and the prostate may have to be massaged several times before pus appears. This, however, is not the usual occurrence. The amount of pus gives a rough estimate of the degree of inflammation. In cases which are progressing toward cure the polynuclear cells are gradully replaced by mononuclear elements. The constant absence of pus excludes active prostatic inflammation.

Investigation of the expressed secretion for bacteria is of some assistance. The finding of the gonococcus, of course, gives positive information, but as most of the cases are of long standing this organism is either very hard to find or has entirely died out, its place being taken by secondary invaders. Occasionally cases are reported in which the gonococcus has persisted in the prostate for a great many years, but many competent observers believe that it is exceptional for the organism to be found after three years. In the non-gonorrheal cases various bacteria have been encountered, such as the staphylococcus, streptococcus, or colon bacillus.

Inflammatory changes in the posterior urethra usually accompany prostatitis, and particularly affect the veru montanum or colliculus seminalis. Expert endoscopic examination is likely to reveal congestion, infiltration, or enlargement of this structure, with perhaps dilatation of the ejaculatory ducts. In many cases the prostatic urethra is extremely hyperesthetic.

The sheet-anchor of treatment is prostatic massage. Although a simple procedure, it is one that requires a considerable degree of skill when scientifically performed. The patient stands with his legs apart, the knees held stiff, and the trunk bent well forward. The physician is seated behind the patient and rests the elbow of the examining hand against his thigh for additional leverage. If preferred he may stand with one foot upon the seat of a chair and the elbow resting against his knee. In some cases it is necessary to press very firmly against the perineum in order to reach the upper part of the prostate. The free hand of the examiner may exert counterpressure over the lower abdomen if this is needed. The gland should be methodically and slowly stroked from above downward and inward, and the entire organ systematically covered. Two or three minutes are usually sufficient. Haphazard rubbing

of the rectal mucosa is to be avoided. At the first treatment it is well to err upon the side of gentleness, as with some patients massage seems to produce powerful reflex effects. They become pale and faint and are covered with profuse perspiration. At subsequent treatments the degree of pressure used can be gradually increased. It is desirable for the patient to have the bladder moderately full of urine or, perhaps even better, for the physician to distend it with a mildly antiseptic solution. Failure to observe this precaution is said to occasionally result in infection of the urethra from the expressed prostatic secretion, although in our experience this has never occurred. In case no glove is worn on the examining hand, but only a finger-cot, additional protection is afforded by thrusting the finger through a small opening in the centre of a piece of gauze eight inches square. The value of prostatic massage lies in periodically emptying the dilated prostatic tubules of their retained secretion, and in promoting absorption of the inflammatory infiltration of the prostatic tissue. Ordinarily it should not be repeated oftener than once in three to five days, the latter interval usually being the most satisfactory.

Instillations into the posterior urethra by means of a drop syringe are often very helpful in overcoming the associated posterior urethral inflammation or irritability. We have had the best results with a 30 per cent. solution of Argyrol. In some cases hot or cold rectal irrigations with a two-way rectal tube help to stimulate the gland and promote resolution. In suitable cases additional urethral instrumentation may be needed, such as irrigations, dilatations, the passage of sounds, etc.

Every effort should be made to improve the patients' general health, and various tonics and sedatives may be needed. Sometimes, in intractable cases, a complete change of scene, with suspension of all treatment, will bring about a cure. Psychotherapy should not be forgotten. Most of these patients are introspective, and have a tendency to magnify their symptoms. Many of them become discouraged at the length of time necessary for cure. It is only too true that the most important element in the treatment of chronic prostatitis is time, and the longer treatment is continued the better are the chances of cure. An absolute anatomical cure can never be expected, as the pathological changes in the gland are usually too far-reaching for complete resolution, but a symptomatic cure can, as a rule, be obtained.

This paper is based upon the analysis of 161 cases of chronic prostatitis seen during the past twelve years. Of this number 100, or 62 per cent., gave a history or other evidence of the presence of gonorrhea; 61 cases, or 38 per cent., gave no history of gonorrhea. Even granting that a few of the patients may have been unwilling to admit a previous venereal infection the proportion of non-gonorrheal cases, fully one-third, is fairly large.

CASE I.—*Close simulation of lumbago; relief afforded by prostatic treatment.* J. M., aged forty-six years, miller, seen February 2, 1903. Denies venereal disease. Nearly a year ago was seized with a "crick in the back." At first it was intermittent, lately it has become constant. At times he cannot bend his back. The pain affects principally the lumbosacral region. He has been treated by cauterization of the back and also by static electricity.

The prostate was found to be enormously congested, and after massage there was a very free discharge of prostatic secretion. Treatment by prostatic massage was continued at irregular intervals for two months. The prostate became much reduced in size and scarcely any discharge appeared after massage. The pain in the back disappeared save at rare intervals and the patient felt greatly improved in strength and vigor.

CASE II.—*Symptoms suggesting prostatic hypertrophy; patient saved from catheter life by treatment of neglected prostatitis.* C. V. W., aged sixty-two years, manufacturer in metal trade, married, seen September 21, 1907. Patient had a mild attack of gonorrhea about forty years ago, and syphilis thirty or thirty-five years ago. Four or five years ago he began to have painful urination. The pain seemed to come on when the bladder was full of urine and persisted until urine was passed. At first the desire to urinate was not very pressing, but during the past year he has had periods of marked disturbance. As a rule, he urinates five or six times a day, and until lately has not been up at night. These periods of aggravation of the trouble recur every two or three months, and last four or five days. At such times he is obliged to urinate every two hours and the desire to pass urine during the time is increased. For the past three or four days he has urinated more frequently than usual. He is up three or four times at night and has distress at the end of urination. The urine is clear and he has never passed any blood. At no time has there been retention. A physician advised him to use a catheter, and he has done so for four or five days.

Examination showed the right lobe of the prostate to be sensitive and much larger than the left; both were of soft consistency and easily reduced by massage. Three ounces of residual urine were found in the bladder. At the end of two and a half months' treatment the prostate had lost its tenderness and was nearly normal in size. The patient experienced marked relief from symptoms, was able to sleep all night in comfort, and had no disturbance of urination by day.

CASE III.—*Urinary symptoms depending upon old gonorrheal prostatitis.* V. K., aged forty-seven years, tailor, married, seen February 28, 1907. Patient denies venereal disease, but in 1890 had an internal urethrotomy performed for stricture. Five or six years ago he began to suffer from burning during urination and a sense of pinching of the bladder. As soon as the urine enters

the bladder there is a desire to urinate. This desire begins to manifest itself within fifteen minutes after he has emptied his bladder. He is then in great distress until he can void urine. The longest period that he can hold it is one and a half hours. At night he does not awaken until five in the morning, and is then obliged to urinate several times in succession. He feels the irritation and pressure mostly at the head of the penis. The bladder holds, he thinks, about three ounces. He is very comfortable after urinating. If he holds the urine too long it is apt to dribble away.

The prostate was normal to touch, but the right seminal vesicle was tender. Upon massaging the prostate a gleety discharge occurred which contained gonococci. No evidence of urethral stricture or bladder stone was found.

Treatment.—Prostatic massage, with deep urethral injections of 2 per cent. silver nitrate solution at five-day intervals, tonics, urinary sedatives, and antiseptics. Improvement began almost immediately, and at the end of ten months the urinary symptoms had almost completely disappeared. The patient was able to hold his urine many hours by day, was not disturbed at night, and felt stronger and better in every way.

Case IV.—*Unusual sexual symptoms depending upon chronic prostatitis.* T. D., aged sixty-five years, miller, seen February 17, 1906. Denies venereal disease. Has been married twice. Prior to his first marriage he suffered a great deal from seminal emissions. During the early years of his first marriage he did not have proper control of his sexual organs during intercourse, but of late there has been no trouble in this direction. For a period of several years he has been awakened at night, from one to three or four times a week, with a series of painful erections. Each time it is associated with an urgent desire to urinate. Sometimes this occurs four or five times a night. The next day he feels completely tired out. He suffers from a feeling of pressure and bearing down in the left side of his scrotum and over his left hip. Other nights he is apt to be awakened two or three times to urinate. During the day he urinates about four times. He is apt to urinate oftener on the days following the erotic nights. He never has had any failure of sexual power, but feels nervous and broken down in health.

The prostate was found to be moderately enlarged, soft, and easily reduced by pressure. Two drachms of residual urine were present. The patient was somewhat improved by repetition of the massage, but did not come regularly for treatment.

Case V.—*Headaches induced by sexual intercourse, and caused by chronic prostatitis.* R. R., aged forty-five years, farmer, married, seen April 1, 1911. Two and a half years ago he had an obstinate attack of gonorrhea. A year ago he began to have attacks of pain in the forehead and back of his head, lasting about twenty-four

hours. Each time the attacks would be brought on by sexual intercourse. While engaged in the act he would be seized with intense pain in the back of his head, which would extend to the forehead. These seizures do not occur every time he has intercourse, but have become more frequent of late.

The urethra was found to be very sensitive, and the prostate exceedingly tender, enlarged, and soft, with greater involvement of the right lobe. Under massage it was considerably reduced in size.

Treatment consisted of prostatic massage, instillations of Argyrol into the prostatic urethra, and suitable medication. The patient was advised to abstain from sexual intercourse as much as possible. He was under observation for two and a half months, and showed great improvement. The attacks of pain during intercourse entirely disappeared, his sexual vigor became greater than for many years past, and his general condition decidedly better.

Case VI.—*Sexual neurasthenia relieved by treatment of the prostate and urethra.* M. M., aged thirty-nine years, married, railway mail clerk, seen June 8, 1910. Patient had gonorrhea twelve years ago and again three years ago. For several years has worried excessively over trifles. Six months ago he had an attack in which he began to tremble and felt as if he would collapse. He has had frequent spells of this kind since. For three months has been troubled with insomnia. He has what he calls shivers and seems to tremble inside. He is weak and tired and has pains in the heels after standing. Blood rushes to the head at times and there is ringing in the ears. He is particularly anxious about his sexual organs and his mind is constantly occupied with sexual matters. The patient admits excessive indulgence in sexual intercourse, but states that of late his sexual vigor has diminished and he fears that he is losing his vitality. After urinating he frequently feels as if he had not fully emptied his bladder, and there is apt to be a stinging sensation with some dribbling of urine.

Nothing abnormal was found in the urethra, but it was exceedingly sensitive to the passage of a sound. The prostate was very large, and after massage there appeared a great quantity of mucopurulent secretion streaked with blood.

The patient was under observation for over a year and was treated by massage of the prostate, the passage of sounds, and suitable internal medication. The urethral sensitiveness entirely disappeared, but when last seen the prostate was still large and considerable secretion could be expelled by massage. The symptomatic improvement, however, was very marked. The numerous nervous manifestations largely disappeared. The insomnia was replaced by restful sleep, the sexual life became more nearly normal, and the ability to do better work and to enjoy life were greatly increased.

Case VII.—*Sexual hyperesthesia causing excessive sexual excitement.* H. M., aged thirty-two years, married, seen July 3, 1911. Patient never has had any definite illness. States that he began to masturbate when he wore dresses, and has always been exceedingly passionate. For years his sexual desire has been most violent, and he sometimes has intercourse with his wife as many as six or eight times in a single night. He is thoroughly aroused over his condition and tries very hard to control himself, but seems unable to do so. He is very nervous and has a great deal of indigestion. He has pain in the back and a feeling of irritability in the rectum.

The prostate was found to be greatly enlarged and soft. A large quantity of prostatic secretion was forced out by massage. Immediately the patient had a series of hysterical convulsions. He jerked, twitched, and was greatly agitated. He afterward stated that many years ago he had been similarly affected by having sexual intercourse. After three and a half weeks of treatment by prostatic massage an attempt was made to pass a sound, but the mere introduction of it into the meatus again threw him into convulsions. The influence of massage, however, was little short of wonderful. The nervous symptoms showed great improvement, the stormy sexual desires lessened, and after a time he could endure the passage of a sound without difficulty.

In this case the excessive masturbation of early life probably led to congestion of the prostate, which was later followed by true prostatitis. The inflamed prostate still further stimulated the patient's sexual desires, which were always unduly strong, until relief was obtained by suitable treatment.

Case VIII.—*Painful seizures of obscure origin; stone suspected; relief afforded by treatment of the prostate and deep urethra.* J. M., aged fifty years, druggist, seen April 30, 1912. Patient never had any acute illness, although he has never been vigorous. Ten years ago he broke down nervously, and since then his power of endurance has been much diminished. Two years ago he was taken with pain to the left of the navel, which extended into the groin. The next day he vomited and had a continuance of the pain. Three weeks later he had a similar attack of pain which extended to the end of the penis and up his left side into the back. For a year he had recurring seizures of pain about every three weeks. He never passed any gravel. Roentgen-ray examination for stone was negative. The urinary tract was carefully investigated on several occasions, including ureteral catheterization, but nothing abnormal was found save a small swelling on the veru montanum. This was treated with silver nitrate and the patient had no attack of pain for a whole year. Lately he has had a constant desire to urinate and an uncomfortable feeling after urinating. The pain extends to the head of the penis, but if his bowels move freely the pain disappears. He complains of smarting in the perineum, with

pain in the right groin and right hip. For the past week he has had pain shooting up and down the penis, and the desire to urinate has been very urgent.

The prostate was found to be considerably enlarged, especially the right lobe, and the seminal vesicles were swollen. Under massage considerable reduction in size was apparent.

Treatment by massage of the prostate and the injection of 30 per cent. Argyrol into the deep urethra gave the patient considerable relief, but he remained under observation only a short time.

Case IX.—*Attacks of abdominal pain of obscure origin caused by chronic prostatitis.* R. B., aged thirty-five years, farmer, married, seen October 12, 1911. Patient has never had any serious illness. Two or three years ago, in midwinter, when it was very cold, he was drawing logs and had an attack of what was called inflammation of the bladder. It was attended with a constant desire to urinate and some difficulty in passing urine, together with pain across the lower abdomen. In a day or two he was well again. About a year ago, while milking a cow, he was seized with severe pain in the right inguinal region. The pain was so intense that he could not get to his house. It lasted an hour and was followed by tenderness which persisted for a week. At times he has had a creeping and trembling sensation throughout the abdomen. Six days ago he began to have pain in the left side of the abdomen below the level of the umbilicus. The pain extended into the left testicle and lasted half an hour. Two days ago the pain recurred in the left groin, extending into the left testicle, and was associated with a cramping of the muscles on the inner side of the thigh. The pain was so severe that he was forced to lie down in the field. At no time was there difficulty in passing urine. At present he has so much tenderness that he is unable to work.

On examination a left-sided varicocele was found. The prostate was considerably enlarged and tender, the right lobe more than the left. The urine contained no blood. The patient was under treatment for only six weeks, but during that short time showed definite improvement, with no return of the painful seizures from which he had suffered.

Case X.—*Attacks of pain in lower abdomen definitely relieved by treatment of prostate and deep urethra.* E. C., aged fifty-six years, farmer, married, seen January 6, 1910. Four years ago he began to have attacks of dull pain across the lower abdomen. If he became constipated the pain was likely to come on. At first the attacks were of a few hours' duration and occurred about once in six or eight weeks. Recurrence of pain has lately been more frequent. The seizures are usually associated with an increased desire to urinate, but he has no pain associated with urination. For the past three weeks he has been obliged to pass urine once during the night. Frequently the pain is relieved by movements

of the bowels. If he can have sexual intercourse when an attack appears to be impending he can usually avoid its occurrence.

The prostate and seminal vesicles were moderately enlarged and quite a little secretion appeared after massage. Catheterization showed half an ounce of residual urine in the bladder. Treatment consisted of massage and deep urethral instillations of 30 per cent. Argyrol. The patient showed steady improvement. During the early months of observation he was obliged to have fairly regular treatments in order to keep in good condition. If there was an interval of ten days between treatments he began to have an uneasy sensation about the prostate, perineum, and rectum, and if two weeks elapsed he was very certain to have a bad attack. Gradually he was able to take the treatments less and less often, until finally he could wait several months without suffering any evil results. The patient was seen last on June 27, 1914. He had not been treated for ten months, but stated that he had been very comfortable until within a few weeks. He had then experienced a recurrence of his old trouble, with severe pain in the lower abdomen, lasting two or three hours, and compelling him to lie down. The prostate was only a little enlarged, but was tender, hard, and nodular.

Case XI.—*Symptoms of general neurasthenia with no indications of disturbance of the prostate; chronic prostatitis discovered in course of routine examination.* T. L., aged thirty-five years, stenographer, single, seen September 30, 1913. Denies venereal infection. Has never been strong, but has had no serious illness. Patient has been nervous for about ten years. Complains of a full feeling in the ears and does not sleep well. Head gets tired after he works hard. He has a throbbing sensation in various parts of the body and the legs feel weak. Finds it hard to concentrate his mind. Is easily annoyed by trifles. Has frequent headaches and dizziness, and a cough which he considers of nervous origin. Urinates once or twice at night and rather frequently by day.

Examination revealed no organic anomaly save for the condition of the prostate. This was found to be moderately enlarged, soft, succulent, and very tender. After massage a profuse, purulent, yellow secretion literally poured from the penis. The patient has been under treatment for a year, and was last seen on August 15, 1914. The prostate was smaller but much firmer, and presented areas of softening alternating with small nodules. There was no special tenderness. The secretion expressed by massage was thinner and less abundant. The patient stated that his general health and nervous strength have been greatly benefited. He is able to endure more, can concentrate his mind more easily, sleeps better, and rarely has headaches or dizziness. The cough has disappeared.

These cases are illustrative of some of the common types of disturbance produced by chronic prostatitis. In many of them certain urinary or sexual symptoms might make one think of the

prostate as a possible source of trouble, but in others absolutely no indications are present to lead the diagnostician to the region of the pelvis. Young very aptly says that if the systematic and complete physical examination, so thoroughly emphasized today, were extended regularly to the prostate, many obscure conditions would be readily made clear. "The locality of symptoms is not of necessity the seat of disease" (McCrae), and the area to which the patient refers his complaints may be far from the primary source of trouble. It is well understood that pelvic disturbances in women may cause a great variety of reflex symptoms, often in distant parts, but it is not so commonly believed that similar conditions are encountered in disease of the male pelvic organs. Finally, a diagnosis of neurasthenia in the male is never justified unless a thorough examination of the prostate gland has been made.

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PRACTICAL OBSERVATIONS DRAWN FROM ONE HUNDRED AND SIXTY-ONE CASES OF HYSTERECTOMY.

By William Edgar Darnall, A.M., M.D., F.A.C.S.,

ATLANTIC CITY, N. J.

The subject of hysterectomy has been so thoroughly investigated that there seems to be little more left to be said as to its indications, its technique, or its results. Yet sometimes the retreading of the well-worn paths of experience may be productive of practical ideas and improved methods. We each develop our own ways of doing things, and we each may have experiences that are not common to all.

The development of this operation, which but a few years ago was considered one of grave danger and high mortality, to the point which has made it one of the safest procedures of abdominal surgery is a matter of history. Formerly the greatest dread of the surgeon was of infection or of hemorrhage, and many cases were lost from these complications. In the earlier operations each bloodvessel of the broad ligament was separately tied, making the operation tedious and difficult. Then the other extreme was reached in mass ligatures, which were productive of large necrotic stumps and insufficient care was taken in covering the raw places. It was not until we learned that ligatures applied to the six main trunks of the circulation adequately controlled all bleeding and made a safer operation with less danger of the ligatures slipping and less danger of morbidity from the raw areas left uncovered.

The technique of the modern operation for subtotal hysterectomy is simple, and simplicity should be the constant effort of all good surgery. When the average operation is well done it should leave a clean field and no raw surfaces. Panhysterectomy with its wide dissection often in a vascular and diseased field is by no means so easy of accomplishment.

A point somewhat neglected, but one which we have found to make the supravaginal amputation much easier, is that the appendages on both sides should be thoroughly freed of all adhesions and impediments, so that they are movable and can be brought up into the field before the clamps are applied or the broad ligaments divided. The writer recently observed a prominent surgeon doing a hysterectomy, start his dissection and removal beginning at the right side and working to the left in removing the uterus. When the mass had been removed a large part of a diseased ovary and tube was left on the left side still adherent to its bed, and the result was far from neat and satisfactory. If the appendage on that side had been thoroughly enucleated first, the removal would have been easy instead of difficult.

After everything is free, clamps are placed on the broad ligament. The infundibulo-pelvic ligaments on both sides are tied as well as the round ligaments. This is a necessary precaution, because if the clamp is depended on to hold them until the mass is removed, it is frequently found that they have slipped through the bite of the clamp, and that the vessel has retracted and is hard to find. The broad ligament is now divided on each side down to the uterus. The bladder is pushed down on front, revealing the course of the uterine artery. The artery is tied securely. Our custom is usually now to cut across the cervix carefully until the opposite side is reached, then to clamp the tissue containing the right uterine artery and with one stroke finish the amputation. The right uterine artery is now tied with a suture ligature. Three interrupted sutures close the cervical stump. The cervical stump is not usually disin-

fected in cases of simple fibromyomata, or unless there is an active acute infection present. In such case swabbing it out with iodin or iodin and carbolic acid seems to be all that is necessary. We have not had any bad results from this practice in the way of infections. As a rule the cervical canal need not be touched. A long running suture now carefully approximates the two layers of the broad ligament, starting at the right infundibulo-pelvic ligament, running down to the cervix, covering the cervical stump over with the reflected bladder peritoneum, and ending at the left infundibulo-pelvic ligament. Thus the field of operation is left as clean and as smooth as the face.

In view of the studies of recent years, showing that 60 to 80 per cent. of fibromyomata undergo some form of degeneration sooner or later, and are more or less associated with cardiovascular changes, whether they actually cause them or not, we are inclined to remove all palpable growths of any size, particularly if they are productive of symptoms. In the majority of cases they will eventually make trouble for the possessor of them.

Whenever it becomes necessary to extirpate both tubes and ovaries for any cause, conservative surgery would demand that the uterus be removed also. The only known function of this organ is that of an incubator for the fetus, a resting place where it may remain for nine months under proper conditions of temperature and nutrition. If there is no chance of its being used for this purpose, it only remains as a focus of infection, particularly if the appendages have been removed for pyogenic disease, or it may become the seat of carcinoma.

For the cases of simple fibromyomata without complications the mortality in competent hands should not be over 2 per cent. In those cases presenting pyogenic degenerations, severe complications from badly adherent pus tubes or cystic ovaries associated with extensive plastic exudate and infections the mortality is, of course, higher, the patients usually dying from peritonitis, septicemia, or shock in proportion to the difficulties and extensiveness of the complications that have to be attended to. The highest direct mortalities, as a matter of course, accompany the extensive Wertheim operations for carcinoma.

The difficulties of the operation are less frequently found in the large, movable fibromyomata. They are usually the easiest to remove. The easiest case perhaps in my series was that of a woman presenting an eighteen-pound tumor which could be rolled right out of the abdomen. Oftentimes the most difficulty is experienced with a rather small tumor located in a funnel pelvis, where the space for work is narrow and the tumor cannot be displaced upward. This is particularly so if the tumor is in the lower uterine segment posteriorly or under the bladder anteriorly or between the layers of the broad ligament. In one of the difficult cases met with by

the writer the tumor by pressure against the pubis divided the bladder into an upper and a lower chamber. Although the lower chamber was emptied by catheter before operation, the upper chamber was so distended that it could not be emptied so that the operation could proceed until the tumor mass was forced backward, allowing the urine to flow into the lower chamber and be catheterized.

The really difficult cases of hysterectomy are those in which one has to deal with extensive inflammatory affections of the appendages; cases in which there have been repeated attacks of pelvic peritonitis, leaving everything in the pelvis matted together with layer after layer of inflammatory exudate and associated with pus tubes, ovarian abscesses, or inflammatory cysts. The difficulties here are the difficulties of the complications involving adjacent organs, such as devitalized bowels from the separations of adhesions, injury to ureters or bladder, and the presence of large raw necrotic areas that have to be left because there is no way to cover them over. Ureters may have to be implanted, bowel may have to be repaired, resected, or covered over with omental grafts to avoid fecal fistulas, one of the most trying complications to be encountered. It is these cases that give the highest mortality outside of the carcinomata and present the greatest morbidity. They often suffer much pain afterward, but in many cases they ought to be thankful that they survive.

The following is a table of the indications for which hysterectomy was done in this series:

Simple fibroids	37
Submucous fibroids	4
Fibromatosis of the uterus	2
Fibroids and double pyosalpingitis	20
Fibroids and cystic ovaries	16
Fibroids, cystic ovaries, and pyosalpingitis	6
Double pyosalpingitis and infected uterus	38
Double pyosalpingitis and cystic ovaries	19
Infected uterus	3
Cesarian section with infected uterus	4
Carcinoma	11
Complete procidentia	1
Total	161

In the complicated cases those associated with many crops of old organized adhesions due to repeated attacks of pelvic peritonitis and the matting of everything together with plastic exudate it is the proper "clean up" after the operation *per se* that makes for the safety of the patient. Sometimes all anatomical relations seem to be lost in the mass of pathology, and the tangle must be carefully and patiently unravelled. If in doing so the bowel is denuded of its peritoneal layer the raw place must be turned in and stitched over. If this is impossible from the thickened and friable condition of things a piece of omentum may be grafted over the area, and in my

experience this has been found to be one of the most reliable methods of covering sometimes a hopeless area that would otherwise demand resection of the bowel. If the gut is too badly involved then indeed resection is at times necessary. Failure to take care of these details in a painstaking way and to look out for every raw and injured area may result in a fecal fistula, an ileus, or some other trying and at times fatal complication. Nowhere in the human body is it more necessary to make every detail of the operative technique perfect than in the abdominal cavity, for when once the work is finished and sewed up there is no way to take a daily look at what is going on, as might be done with an amputation or other external operation. The careless placing of a suture that might leave a fecal leak, or the omission to cover over a weakened place in the gut, or the slighting of what may sometimes seem a trivial detail, may destroy the work of an otherwise brilliant operation and cost the patient her life, and this is true of all abdominal surgery.

CEREBRAL EDEMA (WET BRAIN) IN CHRONIC ALCOHOLISM.

By C. E. Sceleth, M.D.,
DIRECTOR, HOUSE OF CORRECTION HOSPITAL,
AND
Arthur F. Beifeld, Ph.B., M.D.,
CLINICAL ASSISTANT IN MEDICINE, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL; ATTENDING PHYSICIAN, TUBERCULOSIS, COOK COUNTY HOSPITALS; CONSULTING INTERNIST, HOUSE OF CORRECTION HOSPITAL, CHICAGO, ILLINOIS.

Our paper concerns itself with a phase of chronic alcoholism, to which the pathologically prominent change has given the name cerebral edema, or wet brain.

The clinical complex, which we purpose elaborating has been given scant place in the literature upon complications of alcoholism; only the most cursory mention of it, in fact, is made in any publication, with exception of two American texts. Dana[1] seems to have been the first to recognize the condition. His description is very complete in most details, and it is only because of our considerable experience with wet brain at the House of Correction Hospital, Chicago, and because we presume to add to the picture both from the point of view of clinical manifestations and differential diagnosis, that we reopen the subject.

Lambert[2] is the other American who describes cerebral edema

[1] Text-book of Nervous Diseases and Psychiatry, 7th edition, p. 444 et seq.
[2] Modern Medicine (Osler), I, p. 186, et seq.

at some length. He, too, lays stress upon the meagerness of literature relative to the subject, and credits Dana with the first recognition of this phase of alcoholism. Standard works, such as Oppenheim,[3] Lewandowsky,[4] and Curschmann,[5] speak only of a serous meningitis which may be traced, in some cases, to chronic alcoholism. This type of meningitis, however, we would emphasize at the outset, is something quite distinct from the condition which is the topic of our paper. It is true that long-continued alcoholic overindulgence may be associated with serous meningitis; the latter, however, may be secondary to a number of factors, toxic, infectious, traumatic, and mechanical, and presents clinical features indicative of gross nervous changes, such as pareses, pathological cerebrospinal fluid and the like. Alcoholic cerebral edema, on the other hand, is, to all appearances, a toxic vascular phenomenon, and its correlated clinical manifestations are not similar to those of inflammations of the brain or its coverings.

Wassermeyer,[6] in his exhaustive monograph on delirium tremens, gives no place to the train of symptoms which we look upon as characteristic of wet brain and the general absence of reference to the subject in foreign literature, brings up the question whether we may not see alcoholics under conditions differing from those generally obtainable elsewhere. About 2500 cases of alcoholism come under our observation annually. They include patients of every age, sex, and social condition; as to the last, however, the great majority are from the lowest stratum of society. Some have been subjected to trauma of one kind or another; others are suffering from an infection, acute or chronic. Most of the patients are naturally enough accustomed to the cheapest alcoholic beverages. All of these factors are present in practically equal degree in most American public hospitals, and, so far as our personal knowledge goes, in German and Austrian institutions, too, so that we feel justified in assuming that we are working under no unusual conditions.

Wet brain, dissected out from the network of alcoholic complications and sequelæ regularly associated with it, is definitely delimited in nearly every respect, particularly as to classification, symptomatology, and prognosis.

Our view as to its place in the phase of chronic alcoholism has undergone change from time to time. Certain etiological factors deserve emphasis: (1) the longer the history of alcoholism and the more frequent the attacks of delirium tremens the more likely is the patient to develop wet brain, and one attack predisposes to a second; (2) some patients regularly go over into the wet-brain state from each attack of delirium; (3) cerebral edema always

[3] Lehrbuch der Nervenkrankheiten, Berlin, 1908, II, S. 1087.
[4] Handbuch der Neurologie, Berlin, 1911, II, S. 1903.
[5] Lehrbuch der Nervenkrankheiten, Berlin, 1909, S. 524.
[6] Archiv. f. Psychiatrie und Nervenkrankheiten, 1908, xliv, S. 861 et seq.

follows, never precedes, delirium tremens; (4) an unambiguous instance has never come under our observation of edema occurring independently of an immediately preceeding delirium, though Dana mentions the possibility of such an occurrence.

The close relationship to delirium tremens is evident, but whether wet brain is a sequela of *mania a potu*, an equivalent of the same, or an independent phase of chronic alcoholism has not been an easy problem to solve. We are strongly of the opinion, however, that delirium tremens in its classic form and wet brain represent merely successive time events in the alcoholic cycle, and that the pathological condition, wet brain, might aptly be called, clinically, comatose delirium tremens.

A long period—seven to ten years—of overindulgence in alcohol precedes the onset of the condition. This is the incubation period of delirium tremens. For some reason, as yet quite unknown, the individual develops delirium. Hypotheses are not wanting, however, to explain the transition. Among other causes suggested have been auto-intoxication, that first-aid explanation in so many doubtful conditions. According to the views of E. Meyer,[7] Ganser,[8] Ziehen,[9] and others the long alcoholic abuse renders the gastro-intestinal tract and liver incapable of destroying toxins or renders them susceptible to pathogenic organisms, with the result that the poisons accumulate and at a given time overwhelm the individual. The same view is held by some to explain the origin of liver cirrhosis in alcoholics, a theory supported by experimental work.

The hypothesis of Wagner V. Jauregg[10] is an ingenious one. It, too, is based on a toxic theory, namely, alcohol gives rise to a toxin and an antitoxin which neutralize each other as long as alcohol is exhibited. When the drug is withdrawn the antitoxin is no longer formed, with a consequent preponderance of the poison. This view is surely untenable, however, as many of our patients developed delirium after a prolonged spree, not after withdrawal of the alcohol. Starvation with its sequelæ, as seen in other conditions, is also advanced as an explanation, and has much in its favor, for it is well known that the alcoholic can take practically no food while he is drinking and, further, that the taking of nourishment goes hand in hand with improvement.

We shall not tarry longer on this interesting topic, as it does not concern itself immediately with the wet-brain condition. The predisposing factors of delirium tremens—pneumonia, trauma, especially fractures of the long bones, mental shock, combined with with a period of excessive alcoholism or a sudden withdrawal of the drug, these are all too well known to be dwelt upon.

[7] Ursachen der Geisteskrankheiten, Jena, 1907, S. 138.

[8] Zur Behandlung des Delirium Tremens, Münch. med. Woch., 1907, No. 3., S. 122.

[9] Psychiatrie, Leipzig, 1902, 2 Aufl.

[10] Quoted by Wassermeyer, q.v.

Delirium tremens shows itself in several forms. In the undeveloped type, or *forme fruste*, the so-called "touch of the horrors," the patient exhibits a vague uneasiness, starts at slight noises, may have ill-formed hallucinations of sight and hearing, is restless, loses sleep, has disturbed dreams, paresthesias, marked tremor of the hands and tongue, and a constant fear that some evil will overtake him.

The incipient period has a variable duration, usually two to three days, yielding to appropriate therapy—a good hypnotic, followed by sleep—or going over into the fully developed delirium tremens. The latter with its well-known features we shall not dwell upon except to bring to your attention a further subdivision into types which we observe with unequal frequency. These types are more or less comparable in their manifestations to the two ways in which excessive heat affects men, namely, heat exhaustion and thermic fever. In the first form, occurring in about one-fourth of all, and showing the highest mortality, there is profound asthenia, pallor, cold skin, a rolling of the eyes from side to side, and often subnormal temperature; whereas in the more frequent second type there is observed a flushed face, a full-bounding pulse, great mental and motor excitement, and possibly fever. The former requires heat and analeptica, the second cold packs and sedatives; both demand strychnin to replace the alcohol. The deciding factor as to which of these sub-types of delirium will occur is possibly the previous integrity of the cardiovascular system.

Delirium tremens, when treated, ordinarily lasts three to eight days, perhaps oftenest five, though some cases tend to continue, with clear intervals, for several weeks. In about 10 to 15 per cent., however, there is an entirely different outcome and the condition called wet brain or, better, comatose delirium tremens supervenes.

The transition from delirium to edema is fairly well marked. Striking is the semicoma succeeding the active delirium. The latter is now of a low muttering type, the individual lies with his eyes closed and is aroused with difficulty. Supraorbital pressure and rubbing of the knuckles briskly over the chest in the mid-axillary line bring about a momentary lifting of the stupor, but questions will not elicit intelligent answers. During the early stages he will swallow food and still retain consciousness enough to have delusions and hallucinations resembling a low typhoid delirium. The pulse is rapid and weak; the temperature elevated a degree or more. Conjunctivitis is common, the tongue and teeth are sordes-covered, the breath is foul, and albumin is usually present in the urine.

The train of symptoms peculiarly indicative of wet brain are essentially those of meningeal irritation and of cerebral compression. Hyperesthesia is one of the most marked and constant features; the integument is ultrasensitive, and pressure on the muscles causes

the patient to grimace and moan and try to draw himself away. Photophobia, however, is absent; as the individual does not complain we can form no judgment as to the presence of headache. Vomiting is not observed.

Rigidity in its various manifestations is always prominent, occupying with hyperesthesia the centre of the wet-brain picture. The degree to which it is present is significant of the severity of the particular case; thus Dana remarks that when the neck becomes stiff the outlook is hopeless. Kernig's sign is always present to some extent; toward the end it becomes marked.

The deep reflexes are early increased, as is the rule in delirium tremens; later, with the increase in the edema, they are lost. The pupils are usually small, equal, regular, responding sluggishly to light; they dilate somewhat if the patient can be aroused, narrowing down once more as he relapses into coma. In a small percentage of cases we have observed one or all of the criteria of the Argyll-Robertson phenomenon—usually the reflex rigidity—a condition which other observers, notably Nonne,[11] Uhthoff[12] have described in long-standing alcoholism. It is a mooted question whether this pupillary condition is permanent or not.

We are not yet prepared to express ourselves definitively as to the cerebrospinal fluid in wet brain. Cytoanalysis gives normal results; globulin and Wassermann reactions, in frank cases, are negative. It is in regard to the pressure under which the fluid exists that we withhold our opinion. Dana in his cases seems to have found a high tension the rule. He does not state, however, the means he employed to determine the pressure. As will be brought out later, there was no indication at autopsy in our cases that the cerebrospinal fluid *intravitam* was under increased tension. Clinically we have made no manometric obervations, judging the pressure only by the velocity of flow accurate enough, perhaps, in a relative way. The fluid does not spurt out, as in meningitis, for example, but comes out drop by drop, with a rapidity not much different from normal. The many pathological changes recorded as characteristic of the fluid in the hybrid serous meningitis are regularly absent. In brief if the fluid is not free from abnormalities an uncomplicated case of wet brain is not present.

Side by side with the meningeal picture, except in very rare instances, to which we shall refer below, is another, not an integral part of the wet brain, but pointing rather to one of the infectious complications so regularly accompanying alcoholism. The commonest of these by far is pneumonia, usually patchy in character,

[11] Klinische und anatomische Untersuchung eines Falles von isolierter echter reflectorischer Pupillenstarre Ohne Syphilis, bei alcohol chron. gravis-Neurolog, Zentralblatt, 1912, xxxi, 60.

[12] Graefe-Saemisch-Handbuch der Augenheilkunde, Leipzig, 1901, 2 auf. Band xi, abt. 2a. S. 24.

and accounting for the temperature, tachycardia, tachypnea, leukocytosis and the like. This associated infection clouds the wet-brain picture and demands extreme caution in making a diagnosis. Neither Dana nor Lambert has dwelt at any length upon this interweaving of conditions, and it has taken us several years to feel assured that there is a meningeal phase of delirium tremens, and that it is not a manifestation of the co-existing infection.

In six instances no gross pathological lesion was found to account for the symptoms of some infection in the wet-brain complex. It has occurred to us that these may be examples of what Magnan[13] has called delirium tremens febrile. The possibility, however, of a microscopic bronchopneumonia or of some unrecognized septic condition must be admitted. Temperature and other signs of infection are hardly compatible with an uncomplicated wet brain.

All of our deaths are made "coroners' cases." Since July, 1911, in practically all instances, Dr. E. R. Le Count has performed the postmortem examinations, and to him we are indebted for the following:[14]

"As a rule, edema of the brain in delirium tremens is characterized by two features, which, although they do not serve to distinguish it invariably as to etiology, are, nevertheless frequently helpful in determining the cause of death; for without knowledge of the clinical conditon, it may be difficult to conclude from any postmortem examination that death was due to delirium tremens.

"The pia-arachnoid membranes are lifted away from the brain over the vertex, both in front and behind, but principally anterior to a line passing over the head between the external auditory meati. The fluid, as it is seen under these transparent membranes, appears slightly yellowish. In a glass pipette it is quite clear and colorless; naturally the fluid is most abundant opposite the sulci, but in many instances it is so plentiful that the arachnoid, or the outermost portion of the pia-arachnoid is lifted away from the surface or highest part of the convolutions.

"The fluid is, strictly speaking, in the loose meshwork which connects the arachnoid with the pia, for when the outer layer is broken or torn away and the fluid released there still remains the vessel-bearing part of the pia covering the brain.

"The other feature is more noticeable after the brain is removed. It is a widening of the sulci and a narrowing of the convolutions, principally of the frontal and parietal lobes. This may be general for these regions, but often there are places where pits with dimensions of 2 to 3 cm. and 0.5 cm. in depth occur—pits into which

[13] Alzheimer, Das Delirium alcoholicum febrile Magnan. Centralblatt f. Nervenheilkunde und Psehyiatrie, 1904, S. 437.

[14] Personal communication.

about one-half of the terminal phalanx of the little finger may be laid. These pits, or more marked and localized regions of atrophy, are at the meeting-points of the sulci.

"There is a more or less prevalent idea in medical literature and circles that a fibrous lepto-meningitis in patches, may result from the long-continued use of alcoholic beverages. I have not found it with any regularity in the brains of persons dying of delirium tremens, and it certainly is not as characteristic as the two features emphasized.

"Another change is a softening or increased moisture of the brain tissue; but this, too, is inconstant and in some measure probably connected with cadaveric decomposition. In some instances the finer arterioles of the pia are more engorged with blood than in others; this apparently is associated with a type of active or maniacal delirium rather than with those showing a lethargic or semicomatose delirium. The atrophy of the cerebral cortex and the accumulation of fluid have impressed me as an edema *ex vacuo;* and, certainly, there is no indication at the postmortem examination that the fluid during life is under an increased pressure."

Wassermeyer nowhere makes mention of a cerebral edema similar to the above. Dana, on the other hand, who has autopsied twenty of his own cases of wet brain, found such a condition, and from it coined the name. It is most marked, according to him, in the arachnoid and subarachnoid spaces, and may penetrate into the brain substance for a variable distance. An increase in the ventricular fluid content is also not infrequent, with consequent dilatation of the ventricular spaces. As for the remainder, Dana's findings are not different from those of delirium tremens. The picture of the latter, we digress to say, is by no means a constant one, as Wassermeyer points out. He emphasizes the hyperemia, the frequent capillary, less often extensive, hemorrhages; the occasional thickening of the meninges; and in some instances the presence of a condition indistinguishable from the poliomyelitis acuta hemorrhagica superior of Wernicke and in others from a pachymeningitis hemorrhagica interna. Finally there may or may not be evidence of degeneration in the nerve cells or a growth of the glial tissue.

It would seem, therefore, that the more or less extensive fluid accumulation in the arachnoid, with the widening of the sulci and the narrowing of the convolutions, constitute the salient autopsy findings of wet brain. As there is no evidence of the fluid's having existed under increased pressure, it might be urged that the primary change is cerebral atrophy and that the fluid is secondary, much like the *vacatwucherung* about the kidneys when the latter atrophy and the space they formerly occupied is filled with a compensatory fatty deposit.

The diagnosis of alcoholic cerebral edema may be extremely

easy or, on the other hand, impossible. When there has been opportunity to observe the patient through the phases of incipient and fully developed delirium tremens there is, as a rule, no difficulty; the same is to a great extent true in cases which are brought into the hospital already suffering from frank delirium tremens, especially when there is no history of trauma. At times the comatose form of delirium tremens may have to be distinguished from the ordinary form (especially from the sub-type we have called asthenic); the semicoma in the former, the hyperesthesia and rigidity, the absence of the rolling of the eyes, etc., usually serve to differentiate the two; in addition following wet brain there is usually a total amnesia, while after delirium tremens the individual commonly recognizes part of his hallucinations, as such, or he may jumble hallucinations and facts.

A history of, or the possibility of, trauma may cloud the diagnosis almost beyond the possibility of solution. With us basal skull fracture is the condition above all others to be kept in mind, as bitter experience has shown time and again. The following points have been of the greatest value in the diagnosis of basal fractures, in the absence of cerebrospinal fluid or blood from the ear or nose; delayed ecchymoses over the mastoid and about the orbit; eye-muscle palsies; paretic involvement of one or more extremities; and blood in the spinal fluid.

A number of other conditions must likewise be taken into account. The meningitides can, usually, be ruled out by the negative bacteriological, serological, and chemical cerebrospinal fluid tests, according to the type present. Uremic coma, which may present great difficulties both because of a marked similarity to wet brain on the clinical side and also because most alcoholics show renal changes, is recognized by the associated cardiovascular phenomena, retinal changes, by the exaggerated knee-jerks usually present, the absence of hyperesthesia, and the occurrence of convulsions and vomiting. Cerebrospinal lues is distinguished by the Wassermann and globulin reactions, by cyto-analysis in the spinal fluid, and by the presence of definite organic changes in the nervous system Cerebral hemorrhage, thrombosis, and embolism are suggested by etiology and by the organic nervous findings. Finally, pachymeningitis, hemorrhagica interna, and polioencephalitis acuta superior of Wernicke must be thought of because of the common etiology—alcohol. In these, however, gross nervous changes are distinguishing characteristics.

The duration of wet brain is variable, the condition lasting from two to twelve weeks, usually about three. The mortality is nearly 75 per cent.; death may occur at any time, oftenest from a bronchopneumonia, which frequently can scarcely be diagnosed in view of the paucity of physical signs. Unfavorable symptoms, indicative of an increase in the edema, are augmented muscular rigidity

especially of the neckmuscles, diminution in the size of the pupils and more marked sluggishness in their response to light, and deepening of the coma. The pulse finally becomes rapid and feeble, there is incontinence of urine and feces, and death occurs.

As to treatment, aside from symptomatic measures, little can be done. The death rate would indicate this. Cardiac stimulants are in order. The nutrition of the patient suffers markedly consequent upon the long state of coma; persistent effort should be made to force liquids; and in the severer cases it may be necessary to give alimentation by the nasal tube. Elimination must also not be neglected. Ergot we have found harmful as compared with its usefulness in the asthenic type of delirium tremens. Lumbar puncture has been of no service in our hands, contrary to favorable reports by Dana. Scientific hydrotherapy, now not available to us may prove an important addition to our therapeutics.

Resumé. After long-continued overindulgence in alcohol an individual, for reasons as yet undetermined, develops delirium tremens. The latter usually manifests itself in three stages: incipient, fully developed (classic), and comatose (wet brain). The symptoms of wet brain are essentially meningeal, semicoma, generalized hyperesthesia, and muscular rigidity (Kernig and neck rigidity) standing out prominently; the more marked are the latter two features, the graver the prognosis. The cerebrospinal fluid is, to all appearances, normal. The mortality is nearly 75 per cent. Necropsy reveals no gross lesions aside from the more or less marked fluid accumulation in the pia-arachnoid space, a widening of the sulci, and a narrowing of the convolutions to account for the symptoms of changes in the brain. Associated with the cerebral edema complex there is very often bronchopneumonia, which clouds the diagnosis and usually is responsible for death. The differential diagnosis must concern itself particularly with the possibility of a concomitant skull fracture which may easily be obscured by the nervous manifestations of comatose delirium tremens.

THE STUDY OF TWO HUNDRED AND FIFTY STAINED BLOOD-FILMS IN PYORRHEA ALVEOLARIS.

By F. Hecker, B.S., D.D.S., A.M., M.D.,
KANSAS CITY, MISSOURI.

The object of this paper is not to discuss the etiology or the prognostic value of the stained blood-film. It is written for the purpose of informing the reader that tinctorial changes and an increase of the large lymphocytes are common findings in the stained blood-films made from patients affected with pyorrhea alveolaris.

Six years ago, by chance, a stained blood-film from a patient affected with pyorrhea alveolaris was examined microscopically. The picture which this stained blood-film presented was a very interesting one. On close observation it showed a wide variation tinctorially of the stained leukocytes. Thinking that a mistake had been made in the technique of preparing and staining the blood-film, a second blood-film was made. The technique employed to prepare and stain the second blood-film was the same as had been used to prepare and stain the first blood-film. Microscopically the second blood-film showed that the stained leukocytes were tinctorially and in number a duplicate of the first stained blood-film examined.

Having observed the tinctorial changes of the stained leukocytes, the next step was to determine if the differential blood-count of the stained films showed the normal proportion of the different varieties of leukocytes. The differential count when finished presented an interesting picture. The large lymphocytes and the irritation forms of Ehrlich were increased in number, while coincident with this change the polymorphonuclear neutrophiles were diminished in number, as were also the small lymphocytes. At the time of this observation the author was busily occupied in the study of the growth rate of some of the pathogenic bacteria of the mouth associated with pyorrhea alveolaris, and as a result thereof further study was deferred.

Two and a half years ago the author commenced to make it a matter of regular routine to make a blood-film from all patients consulting him relative to pyorrhea alveolaris, and also from all patients treated for pyorrhea alveolaris. The findings of the differential blood-count of each case were recorded with the other clinical findings.

To avoid the possibility of error in the staining of the blood-films the following precaution was taken: Wright's blood-stain was made as described by its originator. After being made it was allowed to dry thoroughly, then it was dissolved in methyl-alcohol made by C. A. F. Kahlbaum. The reason this alcohol was used was because it was neutral when titrated. By observing the above step one can, we believe with safety, exclude the possibility of error which might have entered if different batches of Wright's stain had been used.

The interesting features of the stained blood-films are: the wide variation of the stained nuclei and cytoplasm of the leukocytes; the morphological changes of the nuclei and cytoplasm; the increase of the large lymphocytes and the irritation forms of Ehrlich; with the coincident decrease of the polymorphonuclear neutrophiles, and small lymphocytes. The following summary shows the variation in the number of the different varieties of leukocytes: polymorphonuclear neutrophiles, 45 per cent. to 60 per cent.; large lymphocytes, 15 per cent. to 30 per cent.; small lymphocytes,

5 per cent. to 15 per cent.; eosinophiles, 1 per cent. to 3 per cent.; mast cells, 1 per cent. to 2 per cent.; transitionals, 1 per cent. to 3 per cent.; irritation forms of Ehrlich 3 per cent. to 10 per cent.; degenerates, variable in number.

At a glance one notes that on comparing the above figures of the differential count of the blood-film of a patient affected with pyorrhea alveolaris to the normal number of the different varieties of leukocytes that the large lymphocytes and the irritation forms of Ehrlich are in excess and that the polymorphonuclear neutrophiles and the small lymphocytes are diminished in number. The excess of the large lymphocytes, which together with the small lymphocytes brings the total number of the lymphocytes far above the number of these cells contained in the normal blood, in the condition presented, is known hematogically as lymphocytosis.

Returning to the study of the stained blood-films and beginning with the large lymphocytes, there is noted a wide variation of the intensity and shade of the stained nuclei. They vary tinctorially from an intense reddish-violet to a pale reddish-violet or from an intense blue to a very pale blue. Sometimes there appears in the same field a variably stained reddish-violet nucleus and a variably stained blue nucleus. Other specimens present a nucleus which is faintly stained, and at times it is scarcely descernible.

Contained in the substance of the nucleus of the large lymphocytes there are present granules which are variable in size and in shape, and have no definite arrangement. In some of the nuclei of the large lymphocytes they are reduced to a dust-like fineness. As a rule the granules of the large lymphocytes are stained the same, but a slightly darker color than the nuclus. When the granules are reduced to a dust-like fineness they are stained a dirty shade of reddish-violet or blue. In some specimens the nuclei may be well stained and the granules are poorly stained, while in other specimens the nucleus is poorly stained and the granules are distinctly stained.

The cytoplasm surrounding the nucleus of the large lymphocytes is also subject to a wide variation tinctorially. The cytoplasm of one large lymphocyte may be stained a reddish-violet, while that of another one in the same field is stained a pale blue. Or it is stained a quite intense reddish-violet, and that which surrounds the nucleus of an adjacent large lymphocyte is stained a delicate reddish-violet. Or that which surrounds the nucleus of another large lymphocyte is stained a sharp, well-defined blue, and that which surrounds the nucleus of another leukocyte, this variety is stained a pale blue. Occasionally the nucleus of a large lymphocyte is stained a beautiful shade of reddish-violet and the cytoplasm surrounding it is stained an excellent shade of blue, which stands out in bold contrast to the color of the nucleus.

Morphologically the large lymphocytes vary in size and in shape. The nucleus may be located centrally or excentrically in the cyto-

plasm. The nucleus varies from a round to a semilunar shape; its margins are, as a rule, smooth and regular in outline, but occasionally they are quite rough and irregular in outline. The margin of the cytoplasm surrounding the nucleus is, as a rule, smooth and regular in outline, but occasionally it is irregular and rough in outline. The cytoplasm of this variety of leukocyte varies from round or square to a semilunar shape.

The nuclei of the polymorphonuclear neutrophiles, like the nucleus of the large lymphocytes, are variably stained. Some of them are stained a reddish-violet, which varies in intensity from a dark shade to a light shade of this color. The nuclei of other specimens of this variety of leukocyte are stained blue, which varies in intensity from a dark shade to a light shade of this color. In some of the blood-films there appear in the same field a nucleus which is stained a variable reddish violet and the nucleus of another leukocyte of this variety which is stained a variable blue. Many times one notes that the nuclei of the polymorphonuclear neutrophiles are found free from any cytoplasm. These nuclei are stained a variable reddish-violet or blue. They should not be classed as degenerates, but should be tabulated with the other polymorphonuclear neutrophiles. The absence of the cytoplasm does not necessarily indicate that it is not present, for in all likelihood it is, and its apparent absence is the result of some chemical reaction which prevents it from taking the stain.

Contained in the substance of the nuclei of the polymorphonuclear neutrophiles are granules which are variable in size and in shape, and which are scattered without any definite arrangement in it. Sometimes the granules are reduced to a dust-like fineness. As a rule they are stained several shades darker of the same color as the nucleus. When the granules are reduced to a dust-like fineness they are stained a dirty reddish-violet or blue of varying intensity.

The cytoplasm of the polymorphonuclear neutrophiles like the nuclei has a wide variation of color. The cytoplasm surrounding one nucleus is stained a dark reddish-violet, while that which surrounds the nucleus of a neighboring cell is a light shade of this color, or it is stained a variable blue, or it may be stained a blue which has a reddish tinge, or it may be stained a delicate pinkish red. Any of the colors may be the predominating color of a stained blood-film, or, as is sometimes observed, any two or them or all of them may be noted.

Contained in the cytoplasm of the polymorphonuclear neutrophiles are round granules which vary in size from dust-like fineness to round bodies about the size of a small pinhead. The granules are variably stained, some of them are a reddish blue, others a reddish-violet; others are a dirty pale blue, while others tinctorially vary from a pale pinkish-red to a sharp red.

The irritation forms of Ehrlich found in the blood-film of a patient

affected with pyorrhea alveolaris are, as a rule, distinctly stained a reddish-violet or blue, the variation tinctorially of this variety of leukocyte being very slight.

The shape of this variety of leukocyte is variable: some of them are uniformly elongated, others are irregularly elongated, one extremity being much larger than the opposite one, or they may be somewhat round in shape. The margins of the stained nucleus may be irregular and smooth in outline, while others are irregular and rough in outline. In some of the nuclei of this variety of leukocyte, granules are noted which are irregular in size and in shape and have no definite arrangement. The granules are, as a rule, stained darker than the nucleus, but are of the same color which it is stained. In other leukocytes of this variety there are found in its substance vacuolated spaces which when present are variable in size and in shape and have no regular arrangement. At present the stains which are used to stain blood-films do not demonstrate a cytoplasm surrounding the nucleus of this variety of leukocyte.

The small lymphocytes observed in the stained blood-films from patients affected with pyorrhea alveolaris are more constant tinctorially. The color which they are stained is a rich reddish-violet or sharp, well-defined blue.

Contained in the nucleus of the small lymphocytes are granules which are variable in size and in shape and have no definite arrangement. They are stained several shades darker than the nucleus, but are of the same color that it is stained.

The cytoplasm which surrounds the nucleus of the small lymphocyte is scant in amount when compared to the quantity which surrounds the large lymphocyte, in some instances it being so very small in amount that it is quite difficult to find it. The stained cytoplasm of this variety of leukocyte is quite uniformly a deep reddish-violet or deep blue.

The small lymphocyte morphologically is quite uniform, showing little if any deviation from the normal.

The degenerated polymorphonuclear neutrophiles also present a very interesting picture. The nuclei of the degenerated cell are widely separated when compared to their normal position in the cytoplasm when the cell is intact. The granules likewise are scattered over a considerable area. The position of the nuclei and the granules of the degenerated cell suggest an explosion of it. The nuclei of the degenerated cell are variably stained; some of them are reddish-violet or varying intensity, others are stained various shades of blue, while the nuclei of others are scarcely stained at all. The granules are stained many shades of reddish-violet, blue, and red.

From the foregoing description of the many varieties of the tinctorial changes and the changed proportion of the different varieties of leukocytes observed in the studied blood-films it may well be

asked what practical significance has all this? The answer is that the study of the stained blood-films in this paper emphasizes the importance of a better understanding of the blood changes and their significance which occur in the blood of patients affected with one of the greatest plagues with which the body of civilized man is at the present cursed, pyorrhea alveolaris.

Many diseases are at the present time identified by the changes observed in the differential blood-count, namely, chlorosis, pernicious anemia, myeloid leukemia, acute and chronic leukemia, etc. One cannot overlook with discretion the possibility that the changes observed in the differential blood-count in pyorrhea alveolaris may be of value.

No doubt much will be done in the future to interpret the meaning of the changes in the staining properties of the leukocytes and the relative changes in number of the different varieties of leukocytes observed in the differential blood-count of patients affected with pyorrhea alveolaris. The findings perhaps will be interpreted etiologically and also prognostically; perhaps not by the dentist, but by his colleague the trained medical man. One cannot at the present forecast what tomorrow or a year from now may have in store for the investigator as to the relation of the change in staining and the lymphocytosis observed in pyorrhea alveolaris. These changes may be the key which will open the long-locked chest in which is hidden one of the causes of pyorrhea alveolaris.

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REVIEWS

A Text-book of the Practice of Medicine for Students and Practitioners. By Hobart Amory Hare, B.Sc., M.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital. Third edition, revised and enlarged. Pp. 969; 142 illustrations and 16 plates in color. Philadelphia and New York: Lea & Febiger, 1915.

The appearance of the third edition of Dr. Hare's text-book of medicine will be received with pleasure by those who have studied the former editions of this volume and those who have become acquainted with the other text-books of the distinguished author. The wide popularity of Dr. Hare's other publications demonstrates the worth of the matter that comes from his pen, and this present book presents no exception to the character of his previous work. The book is written in a remarkably clear, smoothly-expressed style, so that he who reads, acquires knowledge of medicine and enjoys at the same time the ease and grace with which the subject is put forth.

The contents follow the following order: first the infectious diseases are discussed, then the diseases of the several systems and organs of the body, the intoxications, the disorders of the nervous system, and finally the functional nervous diseases and diseases of disputed pathology. Each disease is discussed under the sub-heads of definition, etiology, morbid anatomy, symptoms, prognosis, and treatment. Of these sub-heads in general it is found that the sections dealing with symptomatology and treatment are splendid, as would be expected; the sections upon etiology are fairly complete, but greater interest would be added to them by a more complete exposition of the pathogenesis and mode of action of the various diseases; and the section upon pathology would be benefited by the addition of comments upon the pathological-physiology of the disorder under discussion.

Here and there throughout the book are found, occasionally, a few points which seem open to criticism. It hardly seems necessary to include various laboratory procedures in a book of this type; epidemic sore throat might be classified properly in the infectious diseases; pellagra, though still a subject of dispute, with beri-beri;

the several arrhythmias could be more completely discussed and several types that are omitted should be included; no mention is made of vagotonia and sympathicotonia; only the phenolphthalein test of kidney function is mentioned, and no reference is made to its application in the various nephropathies; the statements regarding the wiring of aneurysms are, most properly, quite conservative; lastly, it may be questioned if women of a "lean, lank type" should be compared to a "hunting dog in training."

J. H. M., Jr.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M.D., Professor of Therapeutics, Materia Medica and Diagnosis in the Jefferson Medical College; Physician to the Jefferson Hospital, etc. Assisted by Leighton F. Appleman, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. III, September, 1914. Pp. 339; 41 illustrations. Vol. IV, December, 1914. Pp. 413; 102 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

Continued experience with this quarterly has convinced us that for a work of its kind it is unequalled in English. The contributors are all men of distinction in their respective fields, their articles are invariably carefully compiled, and their comments and criticisms are always illuminating and helpful.

In Vol. III, William Ewart discusses diseases of the thorax and its viscera, paying particular attention to tuberculosis, physical examination of the chest, and the organs of circulation. Dermatology and syphilis are taken up by William S. Gottheil, who particularly emphasizes the new serum treatment in dermatology. Obstetrics is covered by Edward P. Davis, who includes obstetric surgery and conditions of the newborn in his complete review of the entire subject. A really excellent article on diseases of the nervous system, by William G. Spiller, concludes the volume.

The last volume for 1914 opens with a long contribution by Edward H. Goodman on diseases of the entire digestive tract. John Rose Bradford follows this with a few pages on diseases of the kidneys, whereas genito-urinary diseases are taken up at length by Charles W. Bonney. One of the most interesting contributions is that by Joseph C. Bloodgood, who takes up a wide range of important subjects, namely: The surgery of the extremities, shock, anesthesia, general and local infections, fractures and dislocations, and tumors. As usual, one of the most practical contributions for the entire year is H. R. M. Landis' therapeutic referendum, in

which he discusses critically many of the most important questions of modern therapeutics.

We cannot refrain from reiterating an opinion already expressed in these reviews, that whoever desires to be well informed about the advances that are continually taking place in the medical sciences, cannot do better than to become well acquainted with the admirable contributions for which *Progressive Medicine* is conspicuous. G. M. P.

The Commoner Diseases: Their Causes and Effects. By Dr. Leonhard Jores, Professor of Pathology and Pathological Anatomy, University of Marburg. Authorized English Translation by William H. Woglom, M.D., Assistant Professor in Columbia University, Assigned to Cancer Research. Pp. 424; 250 figures in the text. Philadelphia and London: J. B. Lippincott Company, 1915.

The presentation of a familiar subject in a new form is always interesting and often valuable because it gives a new point of view to the reader and tends to impress him by its very novelty. It is this element which gives particular value to the collection of a series of articles upon special pathology by Dr. Jores, which were just presented as lectures to his students at Marburg. Each article deals primarily with gross pathology, omitting entirely questions of morphology or of differential diagnosis and showing in what way anatomical changes can produce physiological upsets and complications. It is the newer conception of disease, which has spread so rapidly in the past few years, that the clinical manifestation of any disorder are due almost entirely to disturbances of function of the diseased organ, or organs in close relation to the diseased one. Jores assumes this to be true, but throughout his work endeavors to show that pathological changes are the real basis of disease, while at the same time demonstrating the functional derangements that are produced by the morbid processes. This method of presentation of pathology, considering it largely from the viewpoint of disturbed physiology is a novel one and one that can not help being interesting to those accustomed to the long description of morphological changes and minute anatomy that are found in the usual text-book of pathology.

To consider the book more in detail, it may be said that the various chapters follow no consecutive order but skip from subject to subject and by no means include descriptions of all disorders that may occur. The discussion of etiology and pathogenesis is particularly good, so that in many cases one wishes that it might be even fuller and more complete and detailed than it is. The illustrations are

superb and are really valuable in showing and emphasizing what the author wishes to teach. The references are quite complete, but very graphically illustrate the present-day attitude of the German mind. There are hundreds of references to German works, but the work of investigators in other countries is almost completely ignored. Their work, not having been done in Germany, is of course, not comparable to that which has been produced by the Germans. J. H. M., Jr.

Operative Surgery: The Head and Neck, the Thorax and Abdomen. By Edward H. Taylor, Professor of Surgery in the University of Dublin. Pp. 505; 300 figures from original drawings, many printed in colors. New York: William Wood & Co., 1914.

The author confines himself almost entirely to the discussion of operations performed or preferred by himself. He has aimed to present in convenient form a description of the operations most frequently required in general surgical practice. The general appearance of the volume makes a favorable impression. The print is large, the paper excellent, and the illustrations profuse and admirable. In many of the illustrations several colors are employed to show the anatomical structures and their relations to each other in the field of operation, and the various steps of the operations. The space given to anatomy in the text is very limited but this is more than made up for by the excellent illustrations. They emphasize to better effect what anatomy is important and exclude the unimportant. An error has crept into Figure 254, on page 415, which illustrates the operative approach to the kidney through the loin. The latissimus dorsi muscle does not overlie the posterior portion of the external oblique as shown here, but the two lie in the same plane, forming together a single layer of muscle, as shown in Figure 256 on page 423. The general excellence of the illustrations permits also a justifiable restriction of text descriptive of many of the operations. That the book is intended for the active general surgeon is shown well in the section on intracranial surgery. If the twenty-four pages allowed, only four apply to radical procedures on brain tumors and none to the surgery of the pituitary body. The remaining sixteen pages are confined almost exclusively to the general subject of craniotomy and craniectomy and their employment for middle meningeal hemorrhage, fractures of the skull, and decompression for brain tumors.

As one would expect, the practise of British and American surgeons does not always coincide. In this country the biniodide of mercury (potassio-mercuric iodide) has not "largely supplanted

corrosive sublimate in general use." Nor is iodoform any longer extensively employed. Newer methods of general anesthesia receive rather full attention, but local anesthesia is barely mentioned and spinal anesthesia not at all. General anesthesia by ether is preferred to that by chloroform, as it always has been in Dublin, and the preference thus coincides with the prevalent practice in this country. The majority of American surgeons have probably discarded most of the restrictive indications for operation on inguinal hernia enumerated by Taylor, and few will employ a drainage tube for twenty-four hours after operation. Pyelotomy for the removal of renal calculi deserves more attention than it receives, and the 'phthalein method of estimating the functional capacity of the kidney appears to be more highly esteemed by American surgeons than by Taylor, who does not mention it, and prefers Luy's urine segregator for the purpose. Aside from such differences in practice and thought, however, this work deserves, and in all probability will obtain, an encouraging reception in this country. T. T. T.

Mendelism and the Problem of Mental Defect. A Criticism of Recent American Work. By David Heron, D.Sc., Galton Laboratory, University of London. Pp. 62; 4 diagrams. London: Dulau & Co., Ltd.

As is seen by the title this is a criticism of the work done chiefly by Dr. C. V. Davenport, Director of the American Eugenics Office, either alone or in collaboration with Dr. D. F. Weeks, head of the Skillman Colony for Epileptics in New Jersey, of a paper by A. J. Rosanoff and Florence I. Orr, and lastly of a paper by A. H. Estabrook and C. V. Davenport. All these papers have been issued from the Eugenics Section and its record office, which is part of the Carnegie Institution at Washington, by its Director C. V. Davenport in the shape of bulletins by the above-mentioned authors. The criticisms are at length and go over the papers quite thoroughly. Perhaps the conclusion will best express the point of view held by the author.

"We believe that those who dispassionately consider the papers discussed in this criticism must conclude with the present writer that the material has been collected in an unsatisfactory manner, that the data have been tabled in a most slipshod fashion, and that the Mendelian conclusions drawn have no justification whatever. The authors have, in our opinion, done a disservice to knowledge, struck a blow at careful Mendelian research, and committed a serious offence against the infant science of eugenics. We shall be told, no doubt, that it is idle jealousy of the work of another laboratory. The public have common sense, and when they see

such statements as those propounded in some of these recent American papers, followed by such advice as Dr. Davenport's: 'Let weakness in any trait marry strength in that trait, and strength marry weakness,' they will apply the test of experience to such doctrine, and end by condemning wholly a science which proclaims such absurdities. Shall the stocks tainted with tuberculosis, with insanity, with epilepsy, with every defect and deformity of hereditary nature be directly encouraged to taint socially valuable stocks, healthy in mind and body, and the latter be directly told to marry weakness? When we find such teaching—based on the flimsiest of theories and on the most superficial of inquiries—proclaimed in the name of eugenics, and spoken of as 'entirely splendid work,' we feel that it is not possible to use criticism too harsh, nor words too strong in repudiation of advice, which, if accepted, must mean the death of eugenics as a science. We are confident that Dr. Davenport's advice would have been as heartily repudiated by the founder of eugenics as it is by all members of the laboratory that bears his name. The future of the race depends upon the strong mating with the strong, and on the weak refraining from every form of parenthood. Nothing short of this rule will satisfy the true eugenist."

A careful perusal of this book leaves no doubt in one's mind that the author is quite correct in his criticism. T. H. W.

The Prevention of Common Diseases in Childhood. By J. Sim Wallace, D.Sc., M.D.L.D.S., Dental Surgeon and Lecturer on Dental Surgery and Pathology, London Hospital, Hon. Dental Surgeon, West End Hospital for Nervous Diseases. Pp. 103. London: Ballière, Tindall and Cox.

The "motif" of the book is a plea for a diet which will stimulate physiologic mastication with all its attendant and subsequent benefits, both dental and gastric. The two main objections are that the prescribed dietary—like Fletcher's far-famed chewing—is sure to prove irksome to many; and that nutrition and digestion are liable to suffer in others. The value of the teaching could easily be tested in any institution of permanent or lengthy residence for children, where opportunity for complete supervision is afforded. With regard to other diseases than dental decay, the author's theories may be described as suggestively interesting, but it seems probable that his inferences are drawn from an insufficient medical experience. The book serves the very important function of a stimulus to thought, lest we rest too securely upon the basis of self satisfaction. J. C. G.

THE ANATOMY OF THE BRAIN. By J. F. BURKHOLDER, M.D., Professor of Ophthalmology in the School of Medicine of the Loyola University. Pp. 206; 40 plates. Chicago: G. P. Engelhard & Company.

THE purpose of this book, as set forth on the title page, is that of a "manual for students and practitioners of medicine, the brain of the sheep being selected, because of its availability and its practical identity with the human brain for laboratory use." Of the 206 pages, 113 contain the text, while the rest compose an atlas of 40 full-page plates, together with the legends.

The text consists of a running description of the parts of the brain as they are exposed, with frequent guiding references to the plates. The book is therefore a dissector and an atlas, rather than a text-book. The structures should be considered more in their relation to morphology and development. Thus, it should be explained that the lateral ventricle is but an outpouching from the third, which, in turn, is the remains of the cavity of the prosencephalon.

The plates represent with diagrammatic clearness most of the structures referred to in the text. Their artistic effect is mutilated by the guide-letters and numerals, which are of heavy black-faced type, at times a quarter of an inch in height, and by the initials of the artist, which are written in bold script.

The chief differences between the sheep's and the human brain are pointed out by Prof. Henry H. Donaldson in the introduction. The study of the architecture of the pallium of the sheep's brain can be of but little value to the medical student, except insofar as it emphasizes the greater development of the rhinencephalon in quadrupeds.

The book is of value first to comparative anatomists, and second when a study of the sheep's brain is intended as an introduction to, but not as a substitute for, that of the human brain.

P. G. S., JR.

THE SENSORY AND MOTOR DISORDERS OF THE HEART. THEIR NATURE AND TREATMENT. By ALEXANDER MORISON, M.D., F.R.C.P., Senior Physician to the Great Northern Central Hospital. Pp. 261; 12 illustrations and many tracings. New York: William Wood & Co., 1914.

THIS extremely interesting work stands as a protest against the modern tendency to base cardiac diagnosis and prognosis upon sphymographic or electrocardiographic tracings. In the 50 pages of Part I, the author gives a most satisfactory discussion of the nature of cardiac action in which he tends to emphasize the impor-

tance of the nervous system. Part II, 115 pages, concerns itself with the sensory disorders of the heart and in this discussion of the pathology, clinical history, diagnosis, prognosis and treatment of cardiac pain, the author is at his best.

The remainder of the book is taken up with a *resumé* of the disorders of cardiac motion in which the author advances a nomenclature of his own for the various varieties of arhythmia. He admits in the preface that he does not expect this nomenclature to meet with the approval of all and to the reviewer this acknowledged fault is the chief one of the book. In style and typography the book is pleasing and the illustrations are good, but the pulse tracings are certainly poor examples of the mechanical methods against which the book protests. That such a protest is not ill-timed today will be agreed in by many clinicians to whom this book will be especially interesting. O. H. P. P.

Isolation Hospitals. By H. Franklin Parsons, M.D., Ph.D., Cambridge University Press, 1914.

This well-written book will undoubtedly be very useful to the medical profession, bacteriologists, municipal engineers, and architects, health officers, sanitary inspectors, teachers, and students.

The uses of isolation hospitals are put down as:

1. "The cure or relief of persons suffering from such diseases."

2. "The separation of such persons from the rest of the community with a view to prevent the spread of disease."

3. "To obviate the disabilities, inconveniences and primary losses which the presence of infectious sickness might entail." There value is proved by the gradually decreased death rate of the infectious diseases in the last twenty-five years.

Substitutes for hospital isolation are fully considered and advised against. "With the improvement in recent years of means of communication, with the increasing readiness to make use of hospitals in infectious illness, and with the demand for better and therefore more costly accommodations than the primitive structures and arrangements of former days, the tendency has been toward enlarged areas of combined instead of small separate hospitals." This is proved more advantageous in economy and efficiency.

The selection of a suitable site for and the design of isolation hospitals are exhaustively treated, many good suggestions made and numerous plans shown. The varieties such as movable and temporary hospitals are considered and not recommended.

Sanitary administration and extramural isolation were shown to have reduced smallpox in London from 332 per 1,000,000 to 5 per 1,000,000 in one year. T. G. A.

Genito-urinary Diseases and Syphilis. By Edgar G. Ballenger, M.D., Adjunct Clinical Professor of Genito-urinary Diseases, Atlanta Medical College; Assisted by Omar F. Elder, M.D., and Edgar Paullin, M.D. Second Edition Revised. Pp. 527; 109 illustrations and 5 colored plates. Atlanta, Ga.: E. W. Allen & Company.

The author has presented as concise a review of the subjects treated as is possible in a volume of its size and displays throughout the text the fact that he is thoroughly conversant with all the modern aspects of genito-urinary diseases. Perhaps the most notable content of the book is the "sealing-in" cure for the abortion of gonorrhea. The author claims to have cured 750 patients or 90 per cent. of cases in three to six days. This should be chronicled as *important, if true.* We are pleased to note the author's partiality to the importance and application of "vaccine therapy," but do not agree that the use of "phylacogens" is so commendable. The extent of space and discussion devoted to urethroscopy and cystoscopy we feel is disproportionate to other subjects of lesser importance. A number of misspelled words or typographical errors attracted the attention of the reviewer. We feel that the publishers have not done justice to the illustrations, which certainly are not up to the standard of a modern text-book. B. A. T.

A Manual of Medical Treatment or Clinical Therapeutics. By I. Burney Yeo, M.D., F.R.C.P., Emeritus Professor of Medicine in King's College, London; Consulting Physician to King's College Hospital; Hon. Fellow of King's College. Edited by Raymond Crawford, M.A., M.D. (Oxon.), F.R.C.P., Physician and Lecturer on Clinical Medicine to King's College Hospital, Fellow of King's College, etc., and E. Farquhar Buzzard, M.A., M.D. (Oxon.), F.R.C.P., Physician for Out-patients to St. Thomas's Hospital and to the National Hospital for the Paralyzed and Epileptic, etc. Fifth Edition; Vols. I & II; pp. 834 and 846; 24 illustrations. New York: William Wood & Co.

The author looks upon therapeutics as a study of sick people and not simply as the application of remedies to disease, and consequently prefaces his discussion of treatment in every case by an outline of the etiology, symptomatology, pathology, and clinical course of the disease insofar as these have a bearing upon the therapeusis. From these considerations he deduces his rational indications for treatment, and these he considers in turn, emphasizing only those measures which are of proved value, and not neglect-

ing the hygienic and dietetic management. For the more questionable things he states his authority without in most cases giving an expression of personal opinion.

The two volumes are divided into nine parts and fifty-eight chapters. Each chapter has at its beginning a brief outline of its contents, and important words throughout the chapter are in bold type. In addition to numerous prescriptions throughout the text there are appended to most of the chapters additional formulæ copied from various authors. In the first volume alone there appear 461 prescriptions. The last fifty-eight pages in each volume are taken up with a general index and a list of authorities for the two volumes. Taken all in all this publication is of convenient size, systematically arranged, well indexed, concisely written, and thoroughly practical. T. G. M.

Treatment of Neurasthenia. By Dr. Paul Hartenberg. Translated by Ernest Playfair, M.B., M.R.C.P. Pp. 283. Edinburgh and London: Henry Frowde & Hodder & Stoughton, 1914.

This volume reveals the author's grasp of the whole subject of neurasthenia. The site of fatigue is no longer regarded as peripheral, a conclusion reached after much investigation with the writer's own apparatus; he at least has convinced himself that the fatigue is central.

The rest cure is heroic and only given to neurasthenics with grave debility. Diet is carefully but somewhat surprisingly treated. Milk is spoken against. Meat is highly recommended. "The neurasthenic being a weakling, requires meat to build up his blood and muscle." The amount is reduced only in the gouty, in Bright's disease and in enteritis with putrid stools. Sugar is given in considerable quantity. The best drug is strychnin in large doses and by preference hypodermically.

The management and treatment of the sexual neurasthenic is admirable and a feature is the elaborate psychotherapy. One phase of treatment is neglected: That of exercises to strengthen and tone up the abdominal muscles and organs, supplemented by abdominal support.

The book is an excellent translation of the methods employed by a successful Parisian neurologist. N. S. Y.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

CHIEF OF THE DEPARTMENT OF INTERNAL MEDICINE, CLIFTON SPRINGS SANATORIUM AND HOSPITAL, CLIFTON SPRINGS, NEW YORK.

The Effect of Nucleic Acid on the Normal Antibody.—Observations made some years ago showed that there is an increase in the natural immunity to infection following the injection of substances of the class of nucleins or nucleoproteins derived from tissues or bacterial cells. This increase was thought to be due to marked leukocytosis produced by these substances but more recent work has shown that such an explanation must be considered as incomplete. The present study of Bedson (*Jour. Path. and Bact.*, 1914–15, xix, 191) deals with an attempt to determine what affect if any, these substances have on the normally occurring immune bodies. The first experiments confirmed the work of Leddingham in that it was found that a yeast nuclein when injected intravenously, produced a marked rise in the phagocytic index. This rise was detectable within an hour after the injection but had completely disappeared within the course of twenty-four hours. Several other preparations were similarly tested with reference to their power to raise the opsonic index. These included: (1) sodium nucleinate (Merck), (2) a yeast nucleic acid (Boehringer), and (3) a preparation of pure tissue nucleic acid supplied personally. Following the use of some of these, no rise in the phagocytic index was obtained, which tends to confirm the idea advanced by Gay and Robertson, who believe that these preparations of nuclein and nucleic acid, which act as antibodies, are able to do so owing to the presence of some protein impurity obtained in the first instance from the tissue or bacterial cells from which the acid was derived. The increased opsonic activity of the serum is readily determined by heating for thirty minutes at 56° C. and by diluting with normal salt, from which it would appear that there

is no increase in the thermostable opsonin normally present in the serum. If this is the case, it may be possible that the injection of these substances results in an increase in the complement content of the serum and that this is responsible for the increased opsonic power of it. Some evidence in favor of this view has already been advanced.

The Pressure Curves in Cases of Auricular Fibrillation.—Wiggers (*Arch. Inter. Med.*, 1915, xv, 77) describes the instruments which have been used by him to study in detail the pressure changes in the auricles, ventricles and aorta during auricular fibrillation. The instruments used are essentially optically recording manometers of high vibration frequency and a photokymograph by means of which records of any length can be obtained. In experimental animals it was found that the auricular contractions in themselves produce no intra-auricular pressure waves. The intraventricular pressure curves show that the ventricle contracts at a very irregular rate, the height of the pressure being determined largely by the interval between the contractions. Thus, when the pace is set too rapidly, there results a series of inefficient systoles which may result in a fall of the arterial pressure and dilatation of the ventricles. These contractions are often not strong enough to open the aortic valves and hence such contractions are not accompanied by any audible sound. This is of importance in the clinical auscultatory explanation of the ventricular rate. The aortic pressure is influenced only by these systoles which are capable of raising the intraventricular pressure above the arterial diastolic pressure and hence it follows that the amplitude of the arterial waves depends upon the strength of the ventricular contraction and the diastolic pressure. The amplitude, therefore, of the arterial pulse is not a suitable criterion of the strength of the heart beat in these cases. The curves show that the vigor of the ventricular systoles is largely governed by the time relation between contractions.

Studies on the Oppler-Boas Bacillus.—This bacillus was first described in 1895; since then practically no work has been done to determine its exact place in the bacteriological world. Numerous observations have confirmed the fact that these bacilli are essentially associated with malignant conditions in the stomach, but they may occur in benign ones. The bacillus doubtless belongs to the so-called "acidophile" group, the members of which produce lactic acid and are capable of growth in media which are detrimental to most other organisms. The best known representative member of this group is the B. bulgaricus, which was first described in 1905. The present work of Galt and Iles (*Jour. Path. and Bact.*, 1914–15, xix, 239) consists of the study of three strains of Oppler-Boas bacillus which were isolated from three cases of cancer of the stomach, which showed the presence of lactic acid and the absence of hydrochloric acid. Cultures were best obtained by sowing them in whey with subsequent transplantation for three days' incubation to plates from which characteristic colonies could be transferred to litmus milk. These strains were then compared under standard conditions with a known culture B. bulgaricus, to which the resemblance on morphological and cultural grounds is so close that the description of one applies equally well to

the other. Full details of these characteristics are given. True dichotomy was observed in both organisms which strongly suggests that the B. bifidus is also identical with them. Galt and Iles conclude from their evidence that the Oppler-Boas bacillus is not an organism *sui generis*, but is identical with the B. bulgaricus and that in cases of cancer of the stomach it is the absence of hydrochloric acid that permits of the growth of the bacillus and that lactic acid is formed as a result of the activity of this organism.

A New Malaria Parasite.—J. W. W. Stephens (*Annals Trop. Med. and Parasitol.*, 1914, viii, 119) describes what he believes to be a new species of malarial parasite, which he designates Plasmodium tenue. His observations were made from one stained smear sent to him from Pachmari, Central Provinces, India. The parasite is (1) extremely ameboid (judging from the stained specimen). Thin processes often extend across the cell or occur as one or more long tails to more or less ring-shaped bodies, giving the parasite peculiar fantastic shapes, like an irregular web or mesh, when the processes are multiple; (2) the cytoplasm is always scanty, the pseudopods being delicate or thin. The parasite has but little bulk or density. While forms resembling "rings" do occur, yet, owing to the abundance of all kinds of irregular forms, it is difficult to find typical signet rings. Laterally applied parasites also occur, but in them the chromatin is not dot-like, as is usual in the malignant tertian, but practically always rod-like; (3) the nuclear chromatin is out of proportion to the volume of the parasite. It takes the form of rods or bars, strands, curves, forks, patches; the occurrence of chromatin in dots, as in the ring forms of other species, is rare. In the web-like protoplasmic processes mentioned above, there may be seen several chromatin strands, and not uncommonly one observes a minute dot of chromatin some way from the parasite, or between two processes, of the parasite, though the protoplasmic process connecting it with the main mass or masses is so thin as to be invisible. The chromatin masses are frequently angular, the angles jutting into the points at which an ameboid process is given off. Abundance of, and marked irregularity in the distribution of, the chromatin masses are characteristic of this parasite. (The value of the description is much enhanced by a beautiful colored plate, showing numerous parasites.) The new parasite differs from the malignant tertian parasite (Pl. falciparum) in the following particulars: (1) Its ameboid activity. In the case of the malignant tertian parasite a certain amount of ameboid activity is observable, giving rise to "star-fish" shapes and to somewhat irregular or even bacillary forms; but the activity is not comparable to that of Pl. tenue, which has for this reason a most strange and peculiar appearance; (2) in the abundance and irregularity of nuclear matter. Signet rings are rare. From Pl. vivax it is distinguished (1) by the fact that its bulk is much less (*i. e.*, it is a smaller parasite); (2) its ameboid processes are far more delicate; (3) the chromatin shows a relative abundance, an irregularity and a peculiarity of arrangement (*e. g.*, strands, bars and rods) not seen in Pl. vivax; and (4) typical signet rings are exceedingly rare or absent. The author was unable to determine definite swelling of infected erythrocytes; in some instances it was present, in others the infected cells were

diminished in size. There seemed to be no rule. Schuffner's granules were found in one infected red cell, which contained a parasite considerably larger than any others encountered. Although Stephens could detect no pigment in this particular parasite, it was otherwise indistinguishable from a simple tertian parasite.

Naso-oral Leishmaniasis (Espundia) Originating in the Anglo-Egyptian Sudan.—J. B. Christopherson (*Annals Trop. Med. and Parasitol.*, 1914, viii, 485) reports two interesting cases of leishmaniasis originating in the Anglo-Egyptian Sudan. Naso-oral leishmaniasis, known as espundia, has hitherto been described only in South America (Peru and Brazil). The case reported by Christopherson corresponds clinically with the descriptions of espundia. In the ulcers typical Leishman-Donovan bodies were found, though they were very few in number. Media on which the kala-azar organisms grew readily were inoculated with scrapings from the ulcers, but no growth occurred. The case of cutaneous leishmaniasis (Oriental sore) reported also originated in the Sudan, the first recorded from this district, in which kala-azar is of frequent occurrence.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Observations on Myeloid Sarcoma with an Analysis or Fifty cases.—Stewart (*Lancet*, Nov. 28, 1914, 1236) says that there is no subject in the whole range of surgical practice where the coöperation of surgeon and pathologist is more necessary than in the case of myeloid sarcoma. Not only the extent of the operation but the ultimate prognosis depends finally on the histological diagnosis, although in most instances it is possible to say, from the naked-eye characters alone, whether or not one is dealing with a case of this kind. On the other hand, a perusal of the literature shows that errors in diagnosis may be made even where the growth is submitted to microscopic examination, and this is generally due to mistaking a malignant giant-celled for a myeloid sarcoma. Although it is the usual teaching nowadays that these growths (myeloids) are of very low malignancy, there still seems to be an unwillingness on the part of many surgeons to treat them by local excision, and this is undoubtedly due, as already indicated, to the fact that in the past, cases of so-called myeloid sarcoma have been reported

in which death with visceral dissemination occurred at a longer or shorter period after operation. These 50 cases have been investigated from both the clinical and pathological stand-point, but special attention has been paid on the one hand to the question of prognosis, and on the other to the minute anatomy of the growths. Stewart divides giant-celled sarcomata into: (1) the myeloid sarcomata, myelomata of some authors; and (2) the malignant giant-celled sarcomata. Myeloid sarcoma is locally malignant only and does not undergo dissemination. It is to be clearly distinguished, both clinically and pathologically, from malignant giant-cell sarcoma, in which death with visceral dissemination is the rule, even after the most radical operative treatment. The histological diagnosis is based on the morphological characters of the giant cells, especially as regards their nuclei. In myeloid sarcoma the latter are numerous, uniform, small, and without mitoses; in malignant giant-cell sarcoma they are few, sometimes single, irregular, and often very large, while mitotic figures are frequent. After investigating this comparatively large series of cases, and from a study of the literature, Stewart feels bound to advance a strong plea for the conservative treatment of myeloid sarcoma. Especially would he advocate thorough curettage as the operation of choice in the first instance in suitable cases; failing this, a local resection of the growth. Amputation should be the last resort, and only after the failure of less radical measures. An accurate histological investigation of the tumor is in all cases essential.

Acute Emphysematous Gangrene.—Swan, Jones and McNee (*Lancet*, Nov. 14, 1914, 1160) say that since the commencement of the war some 2000 cases have been admitted to the Royal Herbert Hospital, but this disease has only appeared in the last fortnight. In the three cases reported were found spore-bearing organisms identical morphologically with the bacillus of malignant edema. The diagnosis of "malignant edema" in these cases, however, rests as much on the clinical appearances as on the bacteriological findings. The following diagnostic points are emphasized: (1) The blackish-brown, almost charred appearance of the wound; (2) the abundance of a thin, brown-colored serous discharge, in which microscopically much granular debris but comparatively few pus cells could be recognized. Great numbers of other pathogenic organisms were present in all three cases in addition to the spore-bearing bacilli; (3) the curious heavy, penetrating odor from the wound; (4) the skin surrounding the wound became of a slate-blue color. Blisters containing brownish fluid were present over the area of dark skin in the case in which the gangrene had spread; (5) fine emphysematous crepitations could be made out in the tissues surrounding the wound; (6) marked toxemia accompanied the disease in the two fatal cases, but it is noteworthy that in both of these consciousness was unimpaired until a minute or two before death. With the occurrence of the disease active measures must be adopted as soon as the bacteriological evidence is forthcoming, first to isolate the patient from other surgical cases and then to attack the wound. In the first cases the condition was hopeless from the onset of the spreading gangrene, and in the second amputation well above the wound was performed at once owing to the extensive injury to the knee-joint. In the

third case the patient's general condition was such that it was decided to attempt in the first place to save the limb, especially as any operation would have to be performed through infected tissue. When it can be carried out, free and extensive incisions into the area with thorough swabbing with peroxide of hydrogen and permanganate solution should be used, and the writers are inclined to recommend this in preference to carbolic acid, because the organisms are anaërobic. Dressings soaked with hydrogen peroxide were applied very frequently. At the same time large quantities of saline should be given by the rectum and subcutaneously.

The Treatment of Osteomyelitis: Observations on Ninety-seven Cases, with the End-results.—Simmons (*Surg., Gynec., and Obst.*, 1915, xx, 129) says that in children with pain in a limb and evidence of toxemia, always consider osteomyelitis. Operate early even if the symptoms are rather vague. If the diagnosis is incorrect practically no harm is done while if correct a great deal of suffering may be avoided. In acute cases, open to the medulla and pack the wound. The prognosis is good. The treatment and prognosis varies of necessity somewhat in these early cases but in general the earlier the operation the better the prognosis. In cases where bone destruction has taken place, seen less than three months after the onset of the disease, perform subperiosteal resection when possible. The prognosis is good. In chronic cases of bone abscess of less than one year's duration, drain and pack. The prognosis is good. In chronic cases with bone destruction of less than one year's duration, remove the sequestrum and pack. The prognosis is good. In old chronic cases, either with bone destruction or of the bone abscess type, remove necrotic areas and drain. Try to obliterate the cavity with flaps of living tissue. If this cannot be done either use bone wax, pack or sterilize the cavity, allow it to fill with blood-clot, and close without drainage. The prognosis, if the cavity can be obliterated, is fair, otherwise poor. The treatment when such bones as the pelvis are involved is unsatisfactory and the prognosis problematical. When in old chronic cases the shaft of a long bone is badly diseased the possibility of resection of the entire shaft with bone transplantation is resorted to.

Experiences with Nail Extension.—Grabowski (*Deutch. Ztschr. f. Chir.*, 1915, cxxxii, 529) reviews the experiences of various surgeons wtih this method of extension and reports 19 fractures of the lower extremity treated by nail extension in Garrè's clinic at Bonn. They were for the most part simple fractures, a number having united with deformity. The following technique was observed: After thorough disinfection and painting of the skin with iodin, a nickel-plated nail or gimlet was driven into the bone. The free ends were wrapped around with iodoform gauze, covered by a sterile metal cap and the whole protected by a gauze bandage. For extension from the calcaneus a single perforating nail is employed and for the femoral condyles a nail is used on each side, because it diminishes the danger of tearing away the bone at the epiphyseal line. In fractures the nail is passed near the junction of the epiphysis and diaphysis and in fractures of the leg through the calcaneus, in order to avoid danger to the joints. Control during the treatment is maintained by the Roentgen-ray and measurements.

In most cases local anesthesia was employed, light general anesthesia being employed only in especially painful cases. The experience at the Bonn clinic is favorable to nail extension and shows it to be very effective. Its superiority over other methods of extension, especially in complicated and old fractures with deformity, is beyond doubt. It cannot be considered, however, as the method of choice because of the dangers associated with it. Grabowski considers it as an open operation with its possibilities of danger. One case resulted in a severe infection extending from the nail. In the Bonn clinic nail extension is reserved for especially appropriate cases, those in which the Bardenheuer method fails or its employment seems without hope of success. Nail extension has given brilliant results in advanced consolidation with considerable shortening and bad position of the fragments. It is valuable in complicated fractures with marked overlapping of the fragments and extensive injury of the soft tissues. The extension can be applied immediately with proper treatment of the wound, with far better prospects than formerly of good functional results. A third indication for nail extension is to be found in very severe fractures of the leg near the ankle-joint, in which there is not sufficient room for the application of the adhesive plaster extension. The indications for this method of extension, however, were very limited in the Bonn clinic. The technique should be observed closely and infection guarded against carefully. Only under these circumstances with a proper choice of cases and in experienced hands, should the method be used.

The Gross Anatomy of the Human Prostate and Contiguous Structures.—Lowsley (*Surg., Gynec., and Obst.*, 1915, xx, 183) says that this report is based upon a study of two hundred and twenty-four prostate glands from patients varying in age from one month to seventy-nine years, most of which were obtained from routine autopsies conducted by the pathological department of Bellevue Hospital. These specimens have been studied in gross, in sections, and microscopically, both in serial sections and in sections taken at random. It has seemed wise to consider in this communication only the gross characteristics of the structures at the neck of the bladder, as relationships at this complicated area are of the utmost importance to the genito-urinary surgeon. The following interesting facts are deduced from the study: The width of the prostate in every instance is greater than the height, always less than the length. The prostate develops very slowly until puberty, at which time it increases enormously in size, assuming proportions which are twice those previous to this period. It reaches a maximum size during the third decade. One out of every four specimens observed shows an obstruction of greater or less extent at the orifice of the bladder. Asymmetry of the trigonum vesicæ frequently occurs (26.3 per cent. of Simmons' cases). The upper portion of the posterior urethra continually lengthens from birth until death. The seminal vesicles and the lower end of the vasa deferentia are enveloped in a triple-layered fascia, which is of great importance surgically. Enlargement of the seminal vesicles occurs in one-third of the cases over twenty years of age, the right being affected three times as often as the left. The ejaculatory ducts rarely, if ever, open into the utriculus prostaticus.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Treatment of Pyorrhea Dentalis and Alveolaris.—Bass and Johns (*Jour. Amer. Med. Assoc.*, 1915, lxiv, 553) say that pyorrhea dentalis and alveolaris is practically a universal disease, which leads to the loss of the teeth by a long suppurating process. All people have it sooner or later. It begins in early adult life or earlier. They believe that the specific cause of the disease is Endameba buccalis and possibly other species which infect and destroy the peridental membrane. The pyorrhea results largely from the secondary infection. The demonstrable endamebas can be destroyed by giving $\frac{1}{2}\frac{1}{4}$ grain of emetin hydrochlorid hypodermically for three to six successive days. Apparently equal endamebacidal effect is produced by two or three alcresta ipecac tablets taken by mouth three times a day for four to six successive days. This form of ipecac does not cause nausea, but there is frequently more or less abdominal discomfort produced by it and also some looseness of the bowels. The lesions require variable lengths of time to heal, but many could not reasonably be expected to heal in less than several weeks or months. The treatment must be repeated from time to time until the lesions all heal. Injecting ipecac or emetin into the worst lesions ought to be of service and can be carried out by patients in many instances. Rinsing the mouth thoroughly with a solution of fluid extract of ipecac is believed to protect, to some extent, against reinfection, and actually cures the disease in its earliest stage in some instances.

The Effect of Intravenous and Intraspinal Treatments on Cerebrospinal Syphilis.—Draper (*Arch. Int. Med.*, 1915, xv, 16) reports a series of 25 cases of syphilis of the cerebral nervous system grouped with especial reference to the predominating symptom or symptoms. These twenty-five patients were all treated intensively for active syphilis. All but one received combined intravenous and intraspinal injections. Mercury and potassium iodin were also used, but the chief reliance and interest were centred on the action of salversan, neosalvarsan, and salvarsanated serum. Most of the patients were treated intravenously at weekly intervals with doses of salvarsan varying from 0.3 to 0.6 grams, or neosalvarsan in full doses. Salvarsan was the drug of choice and was changed for neosalvarsan only when the patient had an anaphylactic reaction. The usual technique in the preparation of doses was observed. Intraspinally most of the cases received 30 c.c. of 50 per cent. or from 20 to 25 c.c. of full-strength serum, separated by centrifugalization from blood withdrawn forty minutes after the intravenous dose of salvarsan. The serum was heated to 56° C. and was introduced intraspinally the same day. Lately

several patients have been bled before the intravenous dose, and then salvarsan up to a milligram added *in vitro* to the serum. This mixture was heated to 37.5° C. for forty minutes, and then 56° C. for half an hour. No serious symptoms followed any of the injections. Clinically, very marked improvement occurs in all groups of cases. In the spinal types pain is usually relieved; ataxia helped in most instances, and not very markedly in a few. The bulbar types and those with fairly pronounced psychic disturbance depending perhaps on meningeal irritation, show marked improvement in symptoms as well as in spinal fluid. The more definite psychic disturbances also may clear up completely, but their spinal fluids cannot in every case be brought to normal. The cell-count has almost always been reduced in them but the Wassermann test rarely disappears below 0.3 c.c. In some cases, especially those treated with serum salvarsanized *in vitro*, transient numbness in the feet has appeared; in other cases a slight failing in general robustness which may be an arsenic effect; and in several instances rather severe pains following the intraspinal injection have been seen. In two cases there has been a sudden increase in ataxia following a period of definite improvement. Notwithstanding these undesirable features, the improvement in symptoms in almost all cases is of such striking nature that the method should be given a most careful and thorough study by numerous observers. It is, however, a procedure which must be carried out with the greatest attention to the detail of technique in all its steps, otherwise serious symptoms may be induced. At present there is sufficient evidence to show that it is unsafe to give more than two, or at most three, consecutive injections of serum to which salvarsan has been added directly. In no case should more than 0.0005 gram be added. On the other hand, apparently any number of intraspinal injections may be given with impunity when serum salvarsanized *in vivo* is used. In those cases which do well the rapid and satisfactory improvement may lead to a premature cessation of treatment. But with our present knowledge of the significance of syphilitic serological reactions, so long as the spinal fluid or blood gives a positive Wassermann test, the case must be looked on as one potentially capable of relapse. Consequently, no matter how well the patient feels and seems to be, treatment must be continued unremittingly until the laboratory tests are persistently negative.

Sensitized versus Non-sensitized Typhoid Bacteria in the Prophylaxis and Treatment of Typhoid Fever.—Garbat (*Jour. Amer. Med. Assoc.*, 1915, lxiv, 489) reports a series of 17 consecutive cases of typhoid fever treated with sensitized vaccine. In the majority of instances treatment was begun in the second week of the disease when the diagnosis was definitely established. Of this series only one patient died who developed a large, deep spreading abscess of the thigh and scrotum requiring operation. Four patients had relapses. Only in two of the 17 cases did the temperature subside acutely, reaching normal forty-eight to seventy-two hours after the vaccine inoculation; in the great majority the temperature did not go any higher but began to show remission, coming down to normal gradually. On the whole, the impression was gained that the inoculated patients ran what might be termed mild courses with comparatively few complications.

Garbat believes that the treatment of typhoid fever by sensitized typhoid bacteria offers a more rational therapy from an immunologic point of view that by the ordinary non-sensitized vaccine. The repeated inoculation of large doses of sensitized vaccine even in very sick patients, was not attended by any harmful effects or a distinct negative phase; the general course of the disease seemed milder and the complications less; the occurrence of a crisis in the infection took place in a small percentage of cases, the improvement usually being gradual. He also suggests that perhaps more striking results will be attained by a larger number of smaller doses more often repeated.

Splenectomy in Primary Pernicious Anemia.—Roblee (*Jour. Med. Assoc.*, 1915, lxiv, 796) in the summary of his article states that primary pernicious anemia is probably due to a toxin of bacterial, chemical or parasitic origin, and in some cases there is an increase of the unsaturated fatty acids. The spleen seems to exercise an influence favorable to the elaboration of these substances. These toxins appear also to cause a hyperemia of the splenic pulp because of changes in the blood-vessels, which cause the blood to be poured directly into the pulp. The presence of the spleen seems to cause a diminution in the amount of the total fats and cholesterins of the blood which are antihemolytic. For these theoretical reasons, and because of the numerous cases on record in which a cure has been obtained in Banti's disease, which is closely related to pernicious anemia, splenectomy appears to be indicated in these and the closely associated anemias. Removal of the spleen either in sickness or in health does not effect the patient injuriously. The operative mortality is not high even in very weak patients. A rapid and striking remission of all symptoms appears, the change in the blood picture coming quickly and quite certainly. It is as yet too soon to know whether or not any patients will be permanently cured, but it is quite probable that a large percentage will succumb to the disease within a few months after operation. Other methods of treatment should be combined with splenectomy, as more than one factor is doubtless at work in these cases. It will certainly prolong life, and in our incomplete knowledge of the etiology of this disease and the certainty that death will come under every other method of treatment, he believes that these patients should be offered this additional chance of recovery. We must remember that some patients have been reported symptomatically well at the end of nine months, even though the blood still showed the characteristics of pernicious anemia.

The Treatment of Syphilis with Copper Salvarsan.—Fabey and Selig (*Münch. med. Wchnschr.*, 1915, lxii, 147) write concerning copper salvarsan which is a combination containing about 24 per cent. of arsenic and 11.6 per cent. of copper. According to the authors this preparation has certain advantages over salvarsan and neosalvarsan. They claim that smaller doses of arsenic are required to cause disappearance of the symptoms and in consequence of these smaller doses of arsenic the injections can be given more frequently. They found that patients bore the injections well and no untoward symptoms were noted. The chief objection to its use is that the preparation of

the solution is very complicated and can be carried out only in the hospital, therefore cases cannot be treated on the ambulatory plan which is the aim of salvarsan therapy. They claim that copper salvarsan is efficient in all three stages of syphilis and influences syphilitic symptoms quickly and positively. The effect on the Wassermann reaction, however, is not so marked as with the older preparations of salvarsan.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND FREDERICK O. WAAGÉ, M.D., OF PHILADELPHIA.

Subcutaneous Injections of Antitetanic Serum.—J. Comby (*Brit. Jour. Child. Dis.*, 1915, xii, 1) describes three cases of tetanus in children cured by the subcutaneous injection of antitetanic serum. He reviews much of the literature pertaining to the intracerebral and intraspinal methods of administering the antitetanic serum, and shows numerous successes following each of the different methods. The first case of the author's series was a boy, aged eleven years, in whom tetanus developed nineteen days after the injury. Two hundred c.c. of antitetanic serum were used subcutaneously in eight days followed by recovery and by serum arthralgia and urticaria eight days after the last injection. This case serves to show the harmlessness of large and repeated doses of antitetanic serum and the success of large doses in young persons. The author, however, prefers preventive serotherapy, and believes that all wounded in the streets or in battle should be given a preventive dose of from 10 to 20 c.c. of antitetanic serum. The second case occurred in a boy, aged thirteen years. Eighteen days following injury tetanus made its appearance. Recovery occurred after subcutaneous injection of 10 c.c. of serum daily for five successive days, showing that success may follow when relatively moderate doses are given. The third case occurred in a boy, aged twelve years, in whom the tetanus did not appear until three weeks after the injury. Recovery followed one subcutaneous injection of 40 c.c. serum. With a long incubation period the course of the disease is long and the prognosis good. With a short incubation period the course is short and the prognosis almost always fatal, irrespective of the serum therapy usually.

Blood-pressure Estimation in Children.—Melvin and Murray (*Brit. Med. Jour.*, 1915, No. 2833, 669) offer an excellent discussion of the technic and results in blood-pressure estimation in children. Blood-pressure, clinically is a more or less constant pressure—the diastolic pressure—on which is periodically imposed an additional pressure—the systolic pressure. Any instrument is inaccurate which is indefinite in this indication it is designed to give, such as maximum oscillation,

etc. The auditory method is simple, determinate and accurate, especially in children. The apparatus consists of an ordinary mercury manometer, an armlet about 8 cm. broad, some form of filler and an Oliver tambour with strap attachment which leaves the observer with both hands free. With the armlet snugly fitted to the upper arm, the tambour strapped lightly over the artery at the elbow and the ear pieces fitted to the ears, one hand palpates the radial pulse and the other manipulates the compressor. As the pressure is being reduced the observer hears the onset of the first, sharp, clear sound. This indicates the systolic pressure on the manometer and occurs before the pulse is felt in the radial artery. The point at which the loud clear sound becomes dull and diminished in intensity is the indication of diastolic pressure. Investigations were made on 40 children of an average age of 9.5 years. These were all normal children. The average systolic pressure was found to be 108.1, only slightly lower than in adults which was found by the same method to be 111.8. The diastolic pressure in the children was 72.4 as against 65.7 in the adults, and the pulse pressure was 35.7 as against the adult pressure of 46.0. These readings for children are definite and reliable and constitute a sound basis for the study of pathological variations.

Bacteriology of the Urinary Tract in Children.—Ross (*Lancet*, 1915, clxxxviii, 654) gives the results of a bacteriological examination of 106 catheter samples of urine. A series of 19 catheter specimens from normal children were also examined and 11 were found sterile after seventy-two hours incubation and 8 grew an organism which was invariably a white staphylococcus. This coccus is probably present in that part of the urethra inaccessible to outside cleansing. In the infections by the Bacillus coli Ross divides the cases into those entirely latent or with mild symptoms only, such as slight pyrexia, and showing a few leukocytes in an acid urine and the class of cases with frank pyuria with symptoms of cystitis or pyelitis. Most of the cases investigated belonged to the first class. Out of 43 cases of this type of infection 36 were females and Ross favors the view that infection is from without and due to a direct passage of organisms from the anal orifice to the vulva and thence upward. This view will not cover all cases, most of which were suffering from acute summer diarrhea. Given an impaired resistance the colon bacillus might easily gain entry to the bladder by direct extension in the female. The colon carrier is distinct from the pyuria cases with their very abundant leukocytes. Out of 40 cases of colon infection examined, only one showed a true pyuria. The autogenous vaccine treatment on three cases of pyuria showed a diminished amount of pus and some clinical improvement but the bacilluria persisted. In certain cases of acute enteritis complicated by edema the majority had a colon bacilluria but there was no obvious connection between the bacilluria and the edematous state. Staphylococci alone were isolated twenty-five times from pathological urines. Their value as etiological factors in pathological conditions is discounted by the fact that they can be cultivated from control urines, their low degree of virulence and the great diversity of pathological states in which they are found.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

The Absorptive Power of the Genital Tract During the Puerperal Period.—Ahlfeld (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) cites a classic case of Walthard, where a woman, aged forty-two years, whose last labor had been nineteen years previously, stated that she had suffered from fever on this occasion during the puerperal period. She suffered greatly from an adherent retroflexed uterus, and was operated upon. No fever developed after the operation, but peritonitis occurred, with death on the fifth day. At autopsy, bacteriological examination of the interior of the uterus, and also of the pus from the abdominal cavity, was made, showing the presence of Streptococcus pyogenes, Bacillus coli communis, and the bacillus of malignant edema. There was every reason to believe that these germs had remained in this patient's uterus for nineteen years, in the form of spores, and that they had developed at the time of operation. The writer has also reported a case where a primipara gave birth to a child of very moderate size, after an entirely normal labor. The placenta was delivered by expression, when it was found that the vagina was closed by a hematoma as large as a fetal head. The pulse during labor had been 64, the temperature 97.5°. A record was made of the temperature for fourteen days, morning and evening, and on the evening of the fifth day the temperature rose to 103°. A vaginal douche was then given daily. As every precaution had been taken in labor, the blood retained in the vagina became infected from germs in the body of the patient not introduced from without. Ahlfeld concludes from his observations that at no time in pregnancy, labor or the puerperal period, does the absorption of pathogenic material go on simultaneously from the vagina to the uterus. Independently of the size of the uterine cavity absorption from the contracted uterus is lessened and from a relaxed uterus increased. On the third, fourth and fifth days of the puerperal period absorption from the inner surface of the uterus is most active. From the sixth day on this steadily diminishes, especially when the uterus undergoes prompt involution. The most rapid and abnormal absorption is seen in cases where after the sixth day the uterus remains unusually large. These observations evidently have a practical bearing of considerable value on the occurrence of puerperal septic infection.

Purulent Peritonitis at the End of Pregnancy from Infection of a Placenta Previa.—Frank (*Monatsch. f. Geburtsh. u. Gynäk.*, 1915, Band xli, Heft 2) describes the case of a multipara who, during her last pregnancy, suffered greatly from disturbance of the stomach, with tenderness over the epigastrium. Examination by a physician showed pregnancy at five months. Life was felt naturally, but the

patient suffered from severe pain in the right side which extended up to the right breast. About a month later the amniotic liquid escaped, followed by symptoms of peritonitis, chills, and pain in the abdomen, for which the patient was sent to hospital. Examination showed that the cervix had not been obliterated, but could be found high in the right side of the pelvis, and very thick and dense. The tip of the finger only could be introduced through the external os. The uterus was contracted tetanically. No fetal tear could be felt. Heart sounds could be heard on the level of the umbilicus. As there was no active pain the patient was given morphin to secure rest. Pain gradually developed, accompanied by vomiting of bile-stained material. After some hours there was sudden vaginal hemorrhage so severe that the patient collapsed. On examination the vagina was full of blood and the cervix unaltered, but one finger could be introduced through the cervix. When the finger was carried, with difficulty, through the cervix it came upon a mass of rather tough tissue which could scarcely be made out. Fetal heart sounds could no longer be heard. On opening the abdomen purulent peritonitis was found, and Douglas's cul-de-sac was filled with purulent fluid. The intestines were adherent and greatly injected. The child was still living and was quickly extracted. The heart sounds were weak, but the child could not be revived. The appendix was removed, the uterus encircled by a constricting band, and the peritoneum closed around the stump. Although the patient was severely shocked she made a final recovery. On studying the specimen it was seen to have been a central placenta previa, with masses of fibrin and thrombi, showing that infection had occurred at the site of the placenta previa and in its tissue.

Malaria Complicating the Puerperal Period. — Solomons (*Jour. Obst. and Gynec. Brit. Emp.*, September, 1914) describes the case of an apparently healthy primipara with normal pelvis, and the fetus in breech presentation. The patient had lived for some time in India. Labor developed with the breech impacted high in the pelvis. It was necessary to extract the child, which was done with great difficulty. There was extensive laceration of the perineum into the rectum. The lacerations were immediately closed. The temperature rose to 102°, and a pulse of 120 developed on the fourth day. Bacteriological examination was negative, so far as the contents of the uterus was concerned. The urine contained a slight amount of albumin but no pus, and the chest sounds were normal. Blood was taken from a vein in the arm, and another examination was made for the malarial parasite, which was present. Quinin bisulphate, 10 grains three times daily, was given, which brought the temperature to normal after six days. It so remained for nine days, and the patient had been up for two days, when on the thirtieth morning the temperature again arose, and on the following day was 103°. Quinin was again given, and the final recovery of the patient followed. No mention is made of the fetus, and evidently the blood of the child was not examined to determine the presence of the malarial parasite. The reviewer has observed severe malarial intoxication occurring after spontaneous labor in the wife of a coal miner, who had contracted malaria when living in the vicinity of a semi-stagnated creek and pool. On the fourth day after

labor the temperature rose to 104°, accompanied by severe chills. Microscopic examination of the blood showed the characteristic parasite. The free use of quinin was followed by the patient's gradual and complete recovery. During the height of the malarial paroxysm the child was not allowed to nurse, the breasts were evacuated by the breast-pump, and the child was fed artificially. When the mother became convalescent the child was able to resume nursing, and the mother and child ultimately made a complete recovery.

A Case of Adeno-cystoma of the Labium Majus, of Fetal Origin.—Gerlich (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, Band xli, Heft 2) from the hospital in Przemysl reports the case of a women, aged twenty-four years, who gave a history of three spontaneous births. During the first confinement a small tumor in the right labium was noticed which had grown slowly but steadily since that time. It had evidently become sufficiently large to cause inconvenience, and its removal was desired. On examination, the pedicle of the tumor extended the length of the right labium majus. The tumor was covered with unaltered integument, and over it passed some large veins. On examining the tumor with a detached light, it seemed to contain an almost clear fluid resembling that in hydrocele. There was no fluid in the labium itself, and on pressure the cystic tumor did not diminish in size. There was no abnormality in the surrounding tissues. The operative procedure consisted in dissecting out the cyst under anesthesia and in uniting the borders of the wound by stitches. Primary union occurred in eight days. On microscopic study of the tumor it was found to be a papillary adenoma with a sufficient mixture of fetal tissue to show that it was of fetal origin. Similar cases have been reported by Weber, Ludwig Meyer, Veit, Bluhm, and others. Illustrations showing the microscopic study of the tumor are included in the paper.

The Diagnosis of Uno- or Duovular Twins Before and During Labor.—Ahlfeld (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, Band xli, Heft 2) believes that the question as to the origin of twins from one or two ova can be settled by diagnosis during labor. When after the birth of the first child the second engaging in breech presentation is of the opposite sex to the first, the twins are du-ovular. It is observed that twins of different sex are never produced from one ovum only.

The Etiology of Chorio Gravidarum.—Albrecht (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) describes the case of a young primipara who during pregnancy was taken with disturbance of the nervous system. Choreic movements were present in the upper extremities, without pain, becoming worse at evening and ceasing during the night. An examination of the patient showed the muscles to be poorly developed and the fatty tissue in moderate quantity. There was no edema. Sensibility was intact. The movements of the right hand and also of the right lower extremities, the facial muscles, and the muscles of deglutition, were irregular and incoördinate. The reflexes were fairly active, and a diagnosis of chorio-gravidarum was made. For sixteen days the patient was treated with bromides, quinin, and antipyrin, without result. A trial was then made of normal preg-

nancy blood serum, given by injection into the gluteal region, the dose being 20 c.c. Immediate improvement followed, and there was no relapse during the pregnancy. He also describes the case of a girl, aged sixteen years, in whom menstruation had not yet been established, who had well-marked chorea, with difficulties in speech and in swallowing. After the patient had been in hospital for a few days menstruation appeared and the chorea became intensely violent. When the period gradually ceased the patient began to improve and made a good recovery. There seemed to be a definite relation between the function of menstruation and the chorea.

GYNECOLOGY

UNDER THE CHARGE OF
JOHN G. CLARK, M.D.,
PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA

The Coincidence of Gall-stones and Gynecologic Diseases.—In a paper presented before the Southern Surgical and Gynecological Association, PETERSON (*Surg., Gyn., and Obst.*, 1915, xx, 284) takes up the questions of the frequency, significance, and treatment of gall-bladder conditions occurring coincident to some pathology of the lower abdomen or pelvis, for which latter the patient has primarily come to operation. He said that the day of the small incision in dealing with intra-abdominal pathology is a thing of the past, since through such an incision it is often impossible to discover important subsidiary conditions, which may subsequently give rise to more trouble than the one for which the operation was performed. He thinks, therefore, that unless special conditions contra-indicate it, every abdominal incision should be large enough to permit the introduction of the operator's entire hand, for thorough exploration of the abdominal cavity. It has come to be pretty well recognized, Peterson says, that under ordinary circumstances the appendix should be routinely removed when the abdomen is opened for any purpose, in order to stall off the possibility of future trouble in that organ. He now wishes to raise the question, whether the gall-bladder does not offer as important an organ for at least routine examination during every pelvic or abdominal operation, in the absence of pus, adhesions, or other special contra-indications. Personally, he firmly believes that it does, having been gradually brought to this viewpoint by the relatively large number of cases in which he has found stones, or other distinct pathological conditions in the gall-bladder, in patients whose primary symptoms were located in the field of strict gynecology. His paper is based on a series of 1066 such cases, in all of whom the gall-bladder was palpated during the course of a gynecologic laparotomy, and in something over 12.5 per cent. of whom gall-stones were discovered, although in no instance has a gall-stone history been in the foreground. As Peterson

very justly says, if we are going to really cure the greatest possible number of our patients, such a frequent coincidence of what in many cases certainly amounts to a major pathologic condition must be met by a recognition of its importance, and a consciencious attempt to remove this pathology wherever it appears feasible. In somewhat less than half (57 out of 135) of the cases in which gall-stones are palpated in Peterson's series, were they actually removed, in the others the condition of the patient, or other conditions, rendering it apparently inadvisable to extend the original operation. Peterson has been able to trace a large proportion of cases of both classes, and has found that about 90 per cent. of those from whom stones were removed have remained since operation free from any symptoms referable to the gall-bladder, whereas only about 60 per cent. of the patients in whom stones were palpated, but not removed, have remained free of such symptoms. Peterson therefore concludes that if we do not consider the gall-bladder in our routine gynecologic operating, about 30 per cent. of our patients will be left with a symptom-producing residuum of pathology, from which in many cases they could have been relieved. Especially in this attention to the gall-bladder important, he has found, in women who have borne children, and who are of advancing years, both of which conditions are apparently important factors in the production of stones.

New Medium for Pyelography.—After citing a number of cases, reported in the literature, in which damage to the kidney tissue has followed the use of collargol or similar substances in order to obtain a Roentgen shadow of the renal pelvis, Young (*Boston Med. and Surg. Jour.*, 1915 clxxii, 537) says that all soluble preparations of silver are more or less irritating to mucous surfaces, and are therefore bound to cause a certain amount of irritation when applied to them in any degree of concentration. In the attempt to find a perfectly harmless, non-irritating substance for use in pyelography, he therefore turned his attention at once to the insoluble silver salts. Kelly and Lewis suggested silver iodide some time ago, but various attempts with it proved unsatisfactory, because of the difficulty of getting a medium which will hold the salt well in suspension, and at the same time be sufficiently fluid to be easily introduced into the kidney pelvis and drained out again. In conjunction with the pharmacist to the Massachusetts General Hospital, Young says that he has succeeded in evolving a menstrum which satisfactorily fulfils these requirements. It consists primarily of a thin quince-seed mucilage, with which is incorporated a definite amount of "argentide," an easily obtainable commercial product, consisting merely of a saturated solution of silver iodide of constant composition. (The details of the formation of the emulsion are given in the original article.) The resulting emulsion is a thin, clear fluid, which flows readily through a ureteral catheter, and which remains good for use for several weeks after manufacture. Young says that this substance has now been in use in the Massachusetts General Hospital for about three months, and has given entire satisfaction. No untoward after-effects have been encountered, and in a few cases in which nephrectomy has been performed subsequent to the pyelography no trace of the material could be found in the substance

of the kidney, and mere traces adhering to the pelvic wall. In no case was an injection of more than 3 c.c. necessary to produce a good shadow, although in some instances the capacity of the renal pelvis was 20 c.c. or more, so that the silver emulsion must have been greatly diluted. The author employs the barrel of a 10 c.c. syringe as a container, from which the solution is allowed to flow by gravity through the catheter. After the picture has been taken, the piston of the syringe is inserted, and as much as possible of the solution sucked out of the kidney pelvis, the larger part being thus recovered in most instances. The pelvis is then washed out once or twice with boric acid or salt solution.

Results with the Percy Treatment for Uterine Cancer.—For the past few years, Percy has been advocating a modified form of treatment of inoperable uterine cancer by heat, employing what he terms the "cold cautery," *i. e.*, an iron heated to a point not sufficient actually to char tissue, but only to disseminate through it an amount of heat which will kill cancer cells without affecting those of normal tissue. Percy claims that malignant cells can be destroyed by a temperature of 50° to 55° C., whereas normal cells require from 55° to 60° for their destruction. His endeavor, therefore, is to maintain the temperature of the cautery at about the lower of these figures, and to keep it in place for fifteen minutes to half an hour, in order that the heat may be thoroughly disseminated throughout the entire mass of malignant tissue, the vaginal walls being protected by a water-cooled speculum. In a recent paper, Clark, of New Orleans (*Surg., Gynec. and Obst.*, 1915, xx, 558), reports some excellent results from this procedure, and especially emphasizes its usefulness as a preliminary to radical operation. He reports two cases which when first seen were considered entirely inoperable, but after a series of heat applications they were transformed to such a degree that radical operation was possible. Examination of the removed uteri, even by repeated serial sections, failed to reveal any cancer cells in either specimen. He says that he has two other cases in his hospital service which, after five and three treatments respectively, show such marked improvement, both constitutionally and locally, that it is believed a radical operation may be done. "In the border-line operative cases," continues the author, "the application of this extensive heat has a most gratifying result, making many operable that otherwise would have been declined. Whenever there is a definite ulceration with bleeding, having as a rule an associated local infection with slight infiltration, the Percy cautery should be employed as a preliminary measure, since it not only acts in destroying the infection, but stops bleeding and toxemia, and the case will in three weeks be a far better surgical risk than when first seen." Clark does not advocate the use of the cautery and the performance of a radical operation at one sitting, but thinks it is better to divide the procedure. He firmly believes, however, that a judicious combination of these two methods of attack will yield a higher percentage of permanent cures than either alone. In very early cases, where the patient is a good risk, he sometimes applies the cautery for about twenty minutes immediately before proceeding to a radical extirpation, with the idea of killing off the cancer cells, at least those near the uterus and within the vault of the vagina, thus avoiding the danger of grafting cancer cells when the abdomen is

opened. Clark emphasizes that this paper is merely in the nature of a preliminary report, since his experience with the method is barely two years old, but his results with it so far have been so encouraging that he wants to get others interested in it. With regard to technique, Clark follows that described by Percy himself, with a few minor modifications. He has had two cases of severe hemorrhage following the treatment, one of these ending fatally, and now ties the internal iliacs in order to avoid the possibility of this.

Artificial Impregnation.—Prochownik (*Zentralbl. f. Gynäk.*, 1915, xxxix, 145) says that in the course of a practice covering several decades he has made upon 13 individuals 21 attempts at artificial fertilization, with 3 successes. He emphasizes strongly the necessity for a thorough examination of both husband and wife, not only from the point of view of their general physical and sexual development, but also entering somewhat into the psychic field. Having determined the presence of apparently living spermatozoa in the seminal fluid of the husband, and the absence of mechanical obstructions to conception in the wife, Prochownik says that he now always demands permission for at least two attempts before undertaking artificial fertilization. The best time for this he considers between the fifteenth and twenty-second day after the beginning of the preceding menstrual period. He lays great stress on the importance of carrying out all procedures quickly, deftly, and without undue fuss and elaboration. He uses the ordinary Braun intra-uterine syringe, which should be warm and dry. Coitus is permitted with a condom; immediately following this, the semial fluid is drawn into the syringe from the condom, and not more than 0.5 c.c. injected into the *uterine cavity* (not merely into the cervix), the remainder being placed upon a sterile tampon against the external os. The woman is kept in bed for about an hour and a half, after which the tampon is removed, and she is allowed to resume her normal activities. Prochownik thinks that the mental attitude of the patient is of equal or greater importance than refinements of technique, hence the importance of a second trial if the first does not succeed, since the patient is apt to be much less nervous and frightened than at the first attempt.

Dysmenorrhea Associated with Ovarian Hemorrhage.—Whitehouse (*Jour. Obst. and Gynec. Brit. Emp.*, 1914, xxvi, 152) reports a rather interesting case of dysmenorrhea, in which the only demonstrable lesion was in the ovaries. The patient was forty years of age, unmarried, and had suffered throughout her entire mentrual life with severe pain at each period. This pain always began a few days before the onset of the flow, first over the sacrum, gradually extending to the flanks and hypogastrium. A dilatation of the cervix and curettement had been performed nine years previously, without relief. Physical examination was negative, but all medical measures failing to give relief, it eventually became necessary to remove the uterus, tubes, and ovaries. No inflammatory or other lesions were found, but on section both ovaries, which were about normal in size, appeared dark red in color, and studded with minute punctiform hemorrhages. The blood was entirely in the stroma tissue, none being found in the Graafian follicles or corpora

lutea. The hemorrhages did not appear to be all of the same age, the blood cells in some of the apparently older collections not staining well, and being partly absorbed. The operation was done in the premenstrual period. The author suggests for the condition the term "ovarian purpura;" as no inflammatory reaction was present, such a term as "hemorrhagic oöphoritis" would be inapplicable. The clinical association of the condition with acute menstrual pain is, he thinks, clear. He suggests that perhaps the cause of the hemorrhage may lie in a local developmental defect in the capillaries of the cortex, by which they are unable to resist the congestion taking place at each menstrual period, and says he is quite convinced that whereas in cases of severe dysmenorrhea, attention is generally directed to the uterus rather than the ovaries, the latter are frequently the seat of menstrual pain. He considers, therefore, that when drugs and other measures applied to the uterus fail to relieve, exploration of the ovaries appears to be justifiable and indicated.

OTOLOGY

UNDER THE CHARGE OF

CLARENCE J. BLAKE, M.D.,

EMERITUS PROFESSOR OF OTOLOGY IN THE HARVARD MEDICAL SCHOOL, BOSTON.

Treatment of Chronic Suppurative Disease of the Middle Ear by Means of Lactic Acid.—Eitelberg (*Wien. med. Wchnschr.*, 1914, 22) recommends the lactic acid treatment in cases of a moderate degree of engorgement of the tympanic mucosa with the presence of small polypi which either speedily shrink or come away as necrotic masses in the subsequent syringing of the ear. The result of the treatment is speedily apparent in the more favorable cases and the resultant pain from the application is usually slight, of short duration, and unaccompanied by prejudicial results. The application of the lactic acid is made, after thorough syringing and drying of the middle ear by means of a cotton tipped probe, dipped in a warm solution of equal parts of lactic acid and allowed to remain in contact with the affected parts, the head of the patient being so inclined as to bring the ear under treatment uppermost for a period of three minutes, after which the ear is dried by means of absorbent cotton and boric acid powder insufflated. This application may be repeated on alternate days and, as the suppuration decreases, the preliminary syringing may be dispensed with.

Treatment Consecutive to the Mastoid Operation.—In cases of uncomplicated acute mastoiditis Delsaux (*Presse. Méd.*, 1914, xiii, 2) regards the primary stitch closure of the postaural wound as allowable only when there is a large perforation of the drumhead with ample assurance of drainage through the external canal and when, moreover, the post-operative treatment can be properly supervised, otherwise the post-operative treatment by packing is to be preferred. In chronic uncomplicated mastoiditis, after thorough

evacuation and removal of diseased tissues and completion of the plastic portion of the operation in the external auditory canal, the postaural wound is to be primarily closed and a light sterile gauze wick inserted into the external canal for the purpose of keeping the canal flap in place, this dressing being renewed every second day, or at longer intervals, until it is possible to dispense with it altogether and substitute insufflation of boric acid, or of lactol in powder form, or the insertion of a light gauze wick soaked in neutral vaseline or in albolene. In event of caries of the ossicles these should be removed as a precedent to the radical operation and, even in cases of cholesteatoma the author deviates but little from the postoperative procedure outlined for the cases of uncomplicated mastoid disease except that the, surgically provided, lumen of the external auditory canal should be made larger and that, as a provision against relapses, no islands of epidermis should be allowed to remain within the operation cavity. A persistent and, especially, a firm packing is prejudicial; in its place there should be the boric acid insufflation, but always carefully supervised, the accumulated powder being removed from time to time by means of syringing and the surface, which it has covered, minutely inspected, the tympanic end of the tympanopharyngeal tube carefully cleansed, granulomata cauterized, and all epidermal accumulations removed. Under these conditions the author has been able to discharge his cholesteatomatous patients to the out-patient department in from eight to ten days with resultant complete healing in from twenty to fifty days, an average period of after-treatment much shorter than that under the formerly customary firm packing.

Otitis Circumscripta Externa Simulating Mastoiditis.—Botella (*Archiv. Internat'l*, xxxvii, 3) makes distinction first between the circumscribed inflammation of the external canal and the more defined furunculosis, which is limited to the inflammation of a hair follicle and its immediate environment, and then draws attention to the superficial simulation of a mastoiditis due to extension of the dermatitis of the canal to the postaural space, originating in an infection in the canal, from a scratch wound for example, and implicating the subcutaneous connective tissue which constitutes the medium of communication from the external canal to the skin of the mastoid region with resultant edema, tenderness and localized abscess formation with fluctuation, suggestive of an inflammatory and suppurative process of deeper origin. As differential evidences the author draws attention to the fact that in the circumscribed inflammation of the canal the pain is severe but more superficial and increased by movement of the auricle, while pressure upon the mastoid surface, without touching the auricle, is unproductive of pain, that there is distinct evidence of swelling, redness and tension in the external canal confined to its cartilaginous portion and only secondarily implicating the dermoid surface of the bony canal wall and that the drumhead is not a participant in the congestion and inflammation. In mastoiditis the pain is more constant and more deeply seated, pressure upon the mastoid surface evokes a sensation of internal, as well as of external, tenderness and the swelling of the canal is principally upon the posterior superior wall and is evidenced

particularly in the bony portion of the canal, while the drumhead gives evidence of the implication of the middle ear. In the matter of treatment of the circumscribed inflammation of the canal the author recommends early and free incision and dressing with plain sterile gauze in perference to iodoform gauze because of the effect of the latter upon the usually accompanying eczema.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL,

AND

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

Leukocytic Bacteriolysins and Their Relation to the Alexin.—Levaditi (*Bull. de l'Institut Pasteur*, 1914, xii, p. 481) has given a very comprehensive review of the work upon this subject. For many years active discussion has surrounded the problem of the origin of the bacteriolytic substances of the serum. Buchner contended that the leukocytes liberate them by active secretion, while Metchnikoff believed that the active substances were only liberated on the death of the leukocytes. Each of these views has had its followers. The problem has not alone an academic interest but, because of the newer suggestions for the therapeutic application of some of the principles involved a definite knowledge of the nature of the leukocytic enzymes is desirable. Levaditi has discussed the subject from various view-points. He compares the experimental results upon the bactericidal action of leukocytes *in vitro* and *in vivo*. Baumgarten claimed that the phagocytosis in the absence of a specific serum was an incomplete process in that the bacteria were not actually destroyed within the leukocytes. On the other hand, the majority of authors agree with Hektoen that the *in vitro* experiments upon phagocytosis demonstrate a definite destructive activity and that the experiments closely simulate the reactions of the body. Some *in vivo* experiments also establish a destructive process by the leukocytes of many forms of bacteria. Moreover, a definite relation has been established between the protective power of an individual and the height of a leukocytosis. From these observations the Metchnikoff school wish to contend that our immunity in general has a direct bearing to the leukocytic response. Many studies have been undertaken to determine the anti-microbic substances in leukocytes. For the most part, the substance is of a common kind, acting against a variety of bacteria. It has some similarities with alexin, but is more heat resisting than that body. The active substance of leukocytes is not of a lipoid nature, but is soluble

in water and has the character of a ferment. It appears from a number of experiments that the active substance can be preserved for considerable periods of time when kept in the dry state. Ordinary fresh leukocytes rapidly dried show bactericidal powers for several weeks. An interesting observation is recorded that the leukocytes of immunized animals are consideraby more active against the specific bacteria than normal leukocytes. The work is very suggestive and stimulates interest to follow the therapeutic application of leukocytic extracts as was suggested in Opie's work.

The Cellular Reactions Induced by Local Deposits of Cholesterin.—Recently much interest has been displayed in the significance of cholesterin in health and disease. It is a not uncommon finding during the routine examination of human tissues under pathological conditions to observe some form of cholesterin. Stewart (*Jour. Path. and Bact.*, 1915, xix, 305) has noted that cholesterin may appear in different physical forms, as well as give rise to different reactions in human tissues. Thus, both under normal and pathological conditions, cholesterin often appears in a peculiar type of cell, the foam cell, which deals with the cholesterin in combination with lipoids. True crystals of cholesterin are not to be observed unless the fatty compounds have been disturbed by the preservative. On the other hand, cholesterin also appears in tissues in the pure state as rhomboid crystals, bunches of fine needles or prisms. Such free cholesterin is not readily handled either by the cells or the tissue fluids. The crystals stimulate the production of foreign body cells and their presence in sections is distinguished by the clefts seen in the tissues. Frequently large cells surround these crystals and render them physically inert. At other times the cholesterin forms a rosette-like deposit. Many spicules radiate from a center producing curious masses. Here again giant cells commonly surround the deposit. Such deposits are found in the breast.

Symmetrical Cortical Necrosis of the Kidney in Pregnancy.—Since the first report of Rose Bradford and Lawrence 1898 of symmetrical cortical necrosis of the kidney, eleven more cases have been reported by the English and American authors. The condition is such a serious one that each new case assists in bringing to light new facts concerning the disease. Glynn and Briggs (*Jour. Path. and Bact.*, 1915, xix, p. 321) record another in a primipara of 29 years. In the eighth month of pregnancy she aborted. There was almost complete suppression of urine for the next week and she died in coma. There were, however, no convulsions. At autopsy the kidneys were found to have the characteristic appearance described in this disease. The outer portion of the cortex was found to be of a lemon yellow color while the medulla was somewhat congested and a hemorrhagic zone demarcated the necrotic layer from the underlying tissues. The main vessels of the kidney were uninvolved but in the zone of demarcation a widespread thrombosis of blood plates was observed. The nature of this thrombosis has been the point mainly in question by the various authors. Some have described them as of fibrin, others of red blood cells, others of debris, while now a new suggestion of

platelets is offered. They believe that the condition may begin with injury to the vascular endothelium followed by thrombosis of the interlobular arterioles. It is not clear why this particular group of vessels should be picked out.

Teratoma of Anterior Mediastinum.—The unusual finding of a mediastinal teratoma is reported by Prym (*Frank. Zeit. f. Path.*, 1914, xv, 181). The tumor mass, the size of a flattened orange, was removed at operation from the anterior mediastinum of a girl of eleven years. The mass was attached by a pedicle to the inner wall of a cyst which was clothed by epithelium. Incomplete removal of the cyst wall led to a recurrence of the cyst. The tumor mass was amorphous, covered by epithelium and long hair, and having several teeth on one surface. Bony structures were contained within it. There are seven other reported mediastinal teratomata in which teeth were found, while in only two did the bony structures resemble the mandible. On account of the similarity between the mediastinal tumors and those of the ovary the author believes that the blastomere theory of Marchand is best adapted. By this it is suggested that in the early history of the embryo polypotential blastomeres become misplaced.

Myocotic Aneurysms of the Aorta with Perforation into the Œsophagus.—New cases are constantly being added to the relatively long list of mycotic aneurysms and with the new reports attempts are being made to classify the nature of the process and the manner in which the serious outcome is brought about. There have been at least five suggestions as to the mode of localization of the infection upon the aortic wall: (1) extension of an inflammatory process from an external neighboring infectious process; (2) a metastatic deposition upon the aortic intima from valvular endocarditis; (3) a lymphatic distribution into the wall of the aorta; (4) infection of the media by an invasion through the vasa vasorum; (5) infection of the surface of the intima from a distant focus. Edenhuzien (*Frank. Zeit. fur Path.* 1914, vol. 16, H. 1) reported two new cases of this disease, in the first of which he suggests another mode of infection. The case was one of an acute septic process in diabetes which led to the localization of the infection in the arteriosclerotic plaques of the aorta. It is suggested that the invasion took place upon the intimal surface and then progressed deeply into the wall of the aorta. Perforation without the development of a sacular aneurysm took place into the œsophagus. In the second case a tuberculous process extended from the outer portion of the aorta until the weakened wall ruptured into an erosion of the œsophagus. The tuberculous process progressed relatively rapidly in its destructive lesion of the aorta and the neighboring tissues.

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All communications should be addressed to—

Dr. George Morris Piersol, 1913 Spruce St., Philadelphia, Pa., U. S. A.

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