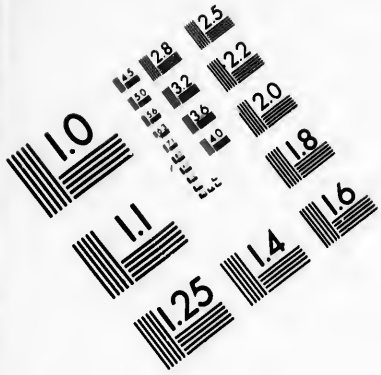

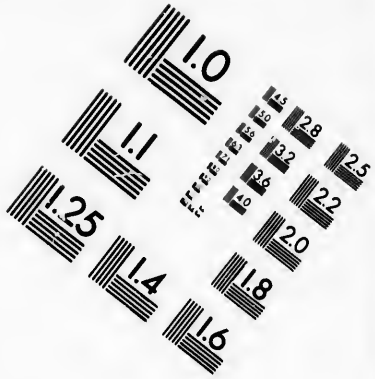

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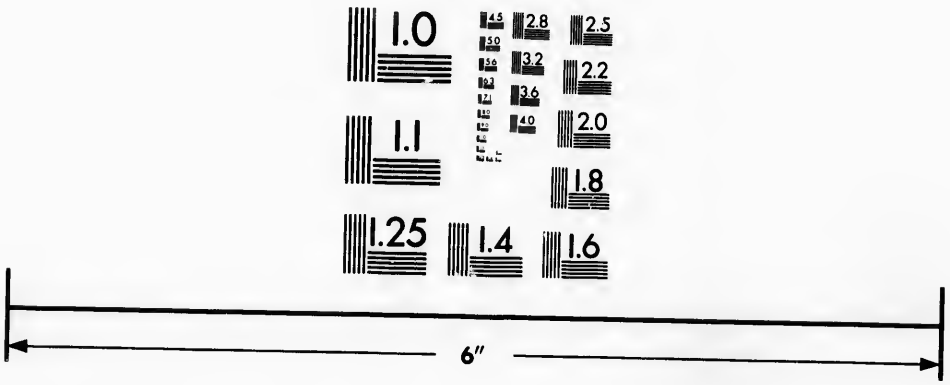

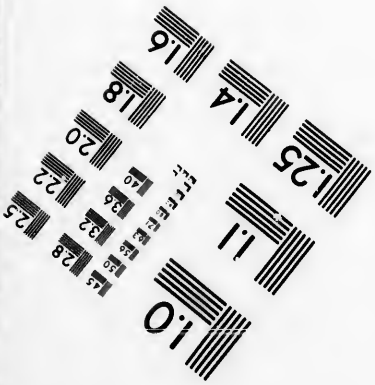

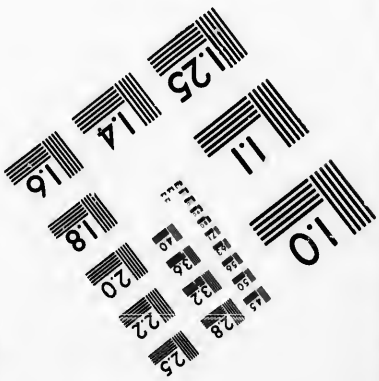

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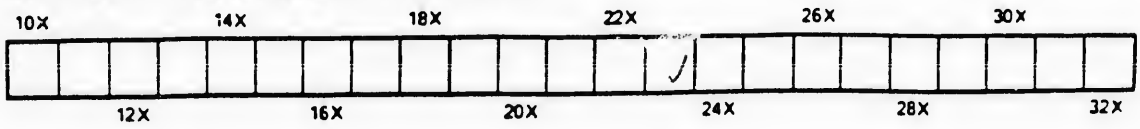

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WILLIAM OSLER, M. D., F. R. C. P., LOND.,

Professor of Medicine in the Johns Hopkins University, and Physician-in-Chief to the Johns Hopkins Hospital, Baltimore.

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ON SOME POINTS

IN

THE ETIOLOGY AND PATHOLOGY

OF

ULCERATIVE ENDOCARDITIS

BY

WILLIAM OSLER, M.D.

MONTREAL

LONDON

J. W. KOLCKMANN, 2, LANGHAM PLACE

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ON

SOME POINTS IN THE ETIOLOGY AND PATHOLOGY OF ULCERATIVE ENDOCARDITIS.

Ulcerative, infectious, or diphtheritic endocarditis is an affection of unusual interest to the profession, both on account of the serious nature of the malady which it excites and of the illustration which it offers of many points in the pathology of infective processes.

Ulceration, loss of substance, on the endocardium occurs under a variety of conditions. Clinically we should, I think, recognise three classes of cases. *First*, those in which the disease appears without any obvious cause, either spontaneously or in connection with rheumatism or some other affection, as pneumonia, chorea, &c. These cases present a remarkable set of symptoms, very variable in character, but of which two chief types have been recognised—the typhoid and the pyæmic. This is the preliminary form of some writers. *Second*, those cases which arise during the existence of some local inflammatory process, as puerperal endometritis, acute necrosis of bone, &c., and in which the endocarditis is usually regarded as part of a pyæmic state and secondary to the local disease. And, *third*, the cases of ulcerative affection engrafted upon valves the subject of chronic sclerotic changes. In this latter variety no special symptoms necessarily accompany the process; the patients are usually in the last stage of chronic valvular disease.

I propose to consider briefly in the following paper some of the conditions under which the disease arises, some points in the morbid anatomy, and, lastly, make a few remarks on the supposed relation of micrococci to the disease.

Of the conditions under which the disease is met with.—(*a.*) *Rheumatic fever.*—It is very generally stated by writers on the subject that the "great majority" of the cases of the ulcerative form of endocarditis occur during the course of this affection. While it undoubtedly holds good that the verrucose or plastic variety is met with most frequently in patients the subjects of rheumatism, my own experience, as well as an examination of the literature, leads me to believe that the above statement requires reconsideration. Of twelve cases of the acute primary form which have come under my observation, in only three was there any history of rheumatism, and in all only as indefinite painful conditions of the joints, not as acute rheumatic fever. Of sixty-seven cases of the primary form, the reports of which I have gone over, in only nineteen was there any mention made of acute rheumatism or of previous rheumatic attacks. It may be

I think, safely stated that ulcerative endocarditis does not occur frequently in rheumatic fever.

(*b.*) *Pneumonia.*—A very considerable number of cases are associated with this disease. Thus, in seven of the twelve cases which have fallen under my notice this obtains, and in twenty-four of the sixty-seven cases which I have analysed. As this relationship has not, so far as I know, been specially noticed by any other writer, I append condensed reports of these cases.

I.—Mary D., aged twenty-nine, admitted October 22nd, 1878, in an unconscious state. No history of onset of attack. Dulness and blowing breathing at right apex; systolic murmur at left nipple. Temperature range from 104° to 107°. Death on the fifth day in hospital.

Autopsy.—Ulcerative endocarditis of anterior segment of mitral; red hepatisation of upper half of right lung; purulent meningitis; infarcts in spleen, which was enlarged.

II.—James B., aged thirty-eight, a healthy man, admitted January 1st, 1880. Had pneumonia ten years before. On evening of 4th, got feverish, had pain in the side and cough. On admission all the signs of consolidation of right lung, lower three-fourths. During first week in hospital delirium set in with prostration. Patient lived for forty-two days, during which time he was in a low typhoid state, had chills, profuse sweats, and a parotid abscess. The temperature range was from 100° to 104°. After the second week the lung symptoms subsided, though the dulness never quite disappeared.

Autopsy.—Extensive ulcerative vegetations on mitral segments; tissue of right lung firmer than that of the left, but not granular; infarcts in spleen, which was enlarged.

III.—M. W., aged forty-three, a well-built man, the subject of syphilis, admitted February 26th, 1880. In October, 1879, he had had a severe attack of inflammation of the right lung. On February 23rd, had a severe rigor, followed by fever, pain in left side and cough, and examination showed signs of pneumonia of lower half of left lung. Up to March 3rd, patient, though delirious at times, appeared to be doing well. Temperature on that date was normal. On the 4th he had a chill, and became feverish and delirious. From this time until his death on the 14th, the chief symptoms were prostration, delirium, occasional chills, and profuse diarrhœa. Temperature range from 101° to 104°. Lung never became clear.

Autopsy.—Small vegetations on mitral segments; large vegetations in right posterior aortic cusp, with destruction of tissue; base of left lung airless and solid; purulent meningitis; spleen large; small infarct in kidney.

IV.—Robert L., aged twenty-nine, admitted June 4th, 1880, with a history of diarrhœa of several days' duration, chills, fever, and cough. Signs of consolidation at left base, with blowing breathing. He was known to have aortic valve disease, and there was a double murmur at the base. The inflammation extended and involved nearly the entire lung. It did not run a typical course, but a low typhoid state supervened, with chills and sweats. Temperature range from 99° to 105°. Death on July 1st.

Autopsy.—Old sclerotic endocarditis with fusion of two segments of aortic valves; small ulcerative vegetations; extensive ulcerative disease of aorta with vegetations and four aneurisms; lower lobe of left lung showed signs of a resolving pneumonia; infarcts in spleen and kidneys; superficial meningeal hæmorrhages.

V.—M. G., a young girl aged nineteen, jumped during a fire from a three-

story window, and sustained a fracture of both legs and of the lumbar vertebræ. She did very well for a week, when the temperature rose, and she had cough, shortness of breath, and pain about the heart. Delirium came on with prostration, and death occurred on the sixteenth day after admission.

Autopsy.—No suppuration about the fractures, which appeared to be doing very well; a large endocardial outgrowth, with destruction of substance on anterior curtain of mitral valve; hepatisation of central portion of right lung; infarcts in spleen and kidneys; patches of membranous (diphtheritic) colitis; purulent meningitis.

VI.—Edward B., aged sixty-three, admitted to surgical wards March 31st, 1881, with carbuncles on buttocks. They were freely lanced, and though he was much debilitated and had an irregular temperature, he improved considerably, and on April 27th the wounds were doing nicely, and the temperature was normal. Then signs of inflammation of left lung were detected; temperature rose, and there were rapid breathing, cough, and rusty expectoration. The whole organ became involved, and the patient became greatly prostrated. Death on May 8th.

Autopsy.—Body wasted; bed-sore on sacrum; carbuncles had almost healed; grey hepatisation of three-fourths of left lung; ulcerative and suppurative endocarditis of top of one of divisions of anterior papillary muscle with exudation in contiguous chordæ tendineæ; numerous infarcts in the kidneys.

VII.—James H., aged forty, drayman, large and powerfully built. Admitted May 13th, 1881, with pneumonia. Had had two previous attacks of inflammation of the lungs. Rigor on the 11th, followed by fever, cough, and pain in right side. When admitted, consolidation of lower two-thirds of right lung was determined. Delirium set in early. Resolution did not supervene and the fever did not abate at the usual time. Patient fell into a low typhoid state, with delirium and free diarrhœa. Temperature range from 102° to 105°. Petechiæ appeared in the skin. Death on the thirtieth day. There was no heart murmur.

Autopsy.—Extensive ulcerative endocarditis of mitral segments and of two of aortic cusps; lower top of right lung airless, heavy, firm, and on section granular; spleen large; infarcts in kidneys; numerous infarcts in intestines; purulent meningitis.

Of these seven cases, in five the endocarditis came on during the course of simple pneumonia. Cases V. and VI. were complicated by surgical disease. In the girl with fractured legs the endocardial mischief appeared to develop with the inflammation of the lung, and not to be secondary to the fractures. The patient with carbuncles was much debilitated and succumbed to an extensive pneumonia. Whether the endocarditis was present before the onset of the pneumonia remains doubtful, but I think it scarcely could have been, as the general condition of the man was improving before it came on. The association of these conditions in such a large proportion of cases is very striking, but the relationship between the processes is not easy to trace. So far as one may judge, the pneumonia in the above cases was the primary morbid change. In all it was of the ordinary lobar variety. Cases of ulcerative endocarditis of the right heart have been described, with extensive secondary changes in the lungs, but in none of my cases was the pulmonary process of a pyæmic character. I have not specially stated it in the condensed reports of the cases, but it is worthy of remark that all the patients were either debilitated at the time of the attack, or were hard drinkers. Many constitutional affections predispose to endocardial inflammation, notably rheumatism, less frequently some of the exanthems, and to these we may

now add pneumonia, which is regarded by many as a constitutional disease. Unfortunately the form of endocarditis which accompanies it appears to be more often of a serious nature, judging at least from the evidence before us. With our present knowledge, the most, I think, that can be said on this point is, that in certain cases of inflammation of the lungs there is a tendency to ulcerative endocarditis. In a former paper * on this subject I called attention to the fact that inflammation of a diphtheritic character had been observed in other organs in pneumonia, particularly in the colon, in which region Dr. Bristowe met with diphtheritic exudation in four out of sixteen cases. There was purulent meningitis in four of the seven cases above reported, which was doubtless secondary to the endocarditis.

(*c.*) A very considerable number of all the cases of ulcerative endocarditis occur in connection with local inflammatory processes of an unhealthy type. In this group the *endocarditis puerperalis* of Virchow is most conspicuous, and not unfrequently complicates the endo- and peri-metritic disorders following parturition. It is further met with in acuto necrosis of bone, occasionally in gonorrhœa, and in pyæmic states. In some cases it is very difficult to say whether the pyæmia has excited the endocarditis, or whether the former has not been determined by the latter; indeed, the relation may be reciprocal. This form is often referred to by writers as "secondary," the exciting cause being, in most instances, obvious. There are some peculiarities in the endocardial lesions, which will be referred to later.

(*d.*) The valves of patients who die of chronic heart disease present very diverse anatomical pictures. There may be—(1.) Simple sclerotic changes with great deformity; (2.) the same with small bead-like vegetations; and (3.) sclerotic and deformed valves with recent ulcerative changes, destruction of tissue, and valvular aneurisms. Probably the great majority of ulcerative processes on the valves occur in this connection. These cases usually proceed as ordinary examples of heart disease, with little or no fever, in fact, none of the severe typhoid or pyæmic symptoms so striking in other instances. In one or two cases I have seen slight, irregular fever, or signs of extensive embolism, which may indicate the nature of the process going on, but the clinical picture is not that of the primary infectious form. It has long been recognised that ulcerative changes appear with special proneness on damaged valves. In two of the cases of pneumonia with this complication, the valves were the subject of that peculiar malformation by which two of the segments had fused together; and in two instances of chronic heart disease, with extensive ulcerations and aneurisms, the same condition of the segments was met with. Interference with the vessels and consequent defective blood supply may, as Virchow suggests, have something to do with this tendency in sclerotic valves to ulcerative changes.

It occasionally happens that ulcerative endocarditis arises as a complication of one of the acute exanthemata. According to Lancereaux † chronic malaria is also a predisposing cause.

Morbid anatomy.—I shall only deal in this place briefly with a few points in the cardiac lesions. In the great proportion of cases the affection is valvular and confined to the left side. The changes met with are by no means uniform, but a remarkable variety prevails. There may be—(1.) Superficial losses of substance, not extending much deeper than the endocardium, the surface rough, without

* *Archives of Medicine*, Feb. 1881, New York.
† *Archives Générales*, 1873.

much exudation, nothing deserving of the name of a vegetation. My experience has been that this variety is most common in the puerperal state and in pyæmia. Sometimes it is difficult to make out the erosion, particularly when post-mortem staining of the membrane has taken place. In only one of the twelve cases of the primary form was the lesion of this nature, and in this there was also a good deal of swelling and infiltration about the base of the ulcer. It is natural to suppose that lesions of this kind would prove more dangerous by the rapid infection of the blood with small emboli; and in the case just referred to, the infarcts were more numerous than in any other instance, scarcely an organ being free. (2.) For the great majority of the cases of the primary form, the term "ulcerative" hardly expresses the precise anatomical condition. The expression used by French writers is more correct, "*l'endocardite vegetante ulcereuse*," for there are both loss of substance and vegetative outgrowths. The affected valve presents irregular nodular excrescences of a greyish-white colour, often fissured, cauliflowerlike; the surface either quite smooth and covered with a thin fibrinous lamina or granular from exposure of the texture of the mass. On section the cut surface may be uniform and fleshy, or broken and granular. The consistence is not very great, the masses crumbling on firm pressure. They are intimately united with the tissue of the valve, which, if the vegetation is large, is usually indistinguishable at the site of attachment; indeed, the whole thickness of a segment may be involved and the mass spring from both sides. In two instances the vegetations were of a fleshy character, not friable. The ulcerative outgrowths, which develop on the sclerotic valves of patients the subject of chronic heart disease, resemble closely in coarse features those met with in the more acute process. Small calcareous concretions are not uncommon in them, and they are, I think, more frequently accompanied by perforations and aneurisms of the valves. (3.) In a small group of cases the endocardial process is suppurative and the tissue is bathed with pus corpuscles. An abcess may be formed, and after discharging, leave an ulcer. In Case VI. of the group of cases occurring in pneumonia, the tip of one chorda tendinea was soft and bathed with pus; in another case there was a purulent deposit at the base of a large vegetation in a sinus of Valsalva.

In my previous paper I have dealt with the histological characters of the vegetations, and would here simply state that the micrococci have been present in all the cases examined by me. A peculiar arrangement of them was noticed in a specimen obtained from a cow. In addition to the usual forms there were definite spherical bodies of various sizes, looking like aggregations of micrococci enclosed in capsules.* In two specimens from man I have met with somewhat similar appearances. I have not seen the chain-like filaments described by some writers.

In this connection I may state that micrococci are not peculiar to the vegetations of the ulcerative form of endocarditis, but exist in the small bead-like outgrowths of the rheumatic and other varieties of the disease, as Klebs was the first to point out. My experience tallies with his; in seven specimens of verrucose or plastic vegetations which I have examined, all contained micrococci.

The relation of the micrococci to the disease has been very fully discussed by Virchow, Eberth, Klebs, and others, most of whom hold that they are the specific elements which account for the peculiar malignancy of the disease, and that they stand in the same position in this affection as the baccillus in anthrax. There

* *Vide* plate illustrating my previous paper already quoted

are some points which should, I think, make us hesitate to accept this view without further evidence. Micrococci abound in all forms of endocardial vegetations —in the warty outgrowths of rheumatic endocarditis, in the vegetations of old sclerotic valves, as well as in the excrescences which develop in the acute ulcerative form. This latter is a malady which runs the course of an infective disease and may destroy life in four or five days. The micrococci are supposed to gain access to the blood and to excite in some way endocarditis; at any rate they flourish in the vegetations which are regarded as centres for the distribution of the germs throughout the body. In the majority of cases emboli are carried away from the vegetations and infarcts produced in the different organs. In other cases, equally malignant, the vegetations may remain unbroken and no emboli are found in the viscera. So far as my observation goes, the micrococci do not exist in the blood during the course of the malady. Nor are they constantly found in the infarcts. The occurrence of micrococci in the warty vegetations of rheumatic endocarditis and in the extensive ulcerative outgrowths so frequently met with in old sclerotic valves are facts strongly opposed to the view of their specific poisonous nature. The micrococci appear to be identical in these cases, though Klebs states that those of rheumatic endocarditis are larger and have a brownish tint. I cannot say that these differences have been constant in the specimens which I have examined. It seems a pertinent question to ask, if in the malignant form of endocarditis, the micrococci are so potent, why in other cases in which they are equally prevalent, should they be inert? Of course it may be urged that the micrococci may be of different kinds or possess diverse qualities, or that the resistance offered by the tissues to their penetration varies in different cases, or that it is only in weakened and debilitated states that these little bodies thrive. There is, I think, something worthy of attention in this latter view. If we study the conditions under which endocarditis develops, we find almost invariably that the patients are the subject of some other constitutional affection which, as we say, predisposes to it. What determines the precise form of the endocarditis, we do not know, but the soft endocardial vegetations form a suitable nidus for the development of micrococci. They appear in fact to be just as much normal components of endocardial outgrowths as the fibrin fibrils which are usually deposited and among which the micrococci abound. It is evident that these structures are common elements in a series of endocardial processes which display totally different symptoms and arise under different conditions. How far they are responsible either for the development of the endocarditis or for the subsequent characters which, in the grave form it assumes, the evidence does not, I think, warrant as yet a very positive opinion.

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ON THE BRAINS OF CRIMINALS.

WITH A DESCRIPTION OF THE BRAINS OF TWO MURDERERS.

(PLATES I. AND II.)

BY WILLIAM OSLER, M.D., M.R.C.P., LOND.
Professor of the Institutes of Medicine in McGill University, and Physician to the Montreal General Hospital.

[*Read before the Medico-Chirurgical Society of Montreal.*]

Mentally and bodily, we are largely the result of an hereditary organization, and the environment in which we have been reared. The child of a bushman nurtured in the family of a philosopher will not be able, with favourable surroundings, to rise much above his race level; the child of a philosophor, reared among the bushmen, will not reach his paternal standard, but the grossness of the savage natures around him will have weight to pull him down, and what is fine will learn to sympathize with the clay. In the former case, the individual cannot transcend his organization; and in the latter, he cannot burst the iron bars of his environment. That the mental and moral status of a man is determined by the conformation and development of his brain is an axiom with the school of physiological psychologists. The conformation is a matter of inheritance; the development, of education (in its widest sense). The different mental conditions of individuals are the expression of subtle differences in cerebral structure, just as the diversity in the features of men is the result of minute variations in the arrangement of the tissues

of the face. That a faulty physical basis can have no other sequence than a faulty mental and moral constitution is acknowledged and acted upon by every one, so far as idiots and imbeciles are concerned, but that mental and moral obliquity is invariably the outcome of an ill-conformed or ill-developed brain is a doctrine novel and startling, though logical enough from the standpoint of modern physical fatalism. Endeavours have recently been made to put this theory on firm grounds by showing that in a large number of criminals the type of brain differs from that in the law-abiding members of the community.

Anatomists and physiologists have of late paid much attention to the conformation of the brain surface, and the convolutions and fissures are now studied with care and minuteness. In a typical European brain, the cerebellum is completely covered by the cerebrum, and the general arrangement of the gyri and sulci is such that there is rarely any difficulty in mapping them out and assigning their proper names to each. Thus on the external surface of each hemisphere we recognize two fissures which are constant and invariable in position—the *fissures of Sylvius and of Rolando*, (*central sulcus.*) Other fissures constantly present, but less definite in their arrangement, are: the *inter-parietal*, which passes through the parietal lobe, the *parieto-occipital*; separating the parietal and occipital lobes, best seen from the median surface, the *superior* (1st), *inferior* (2nd), and *ascending* (3rd) frontal sulci and the 1*st* and 2*nd temporal.*

On the median surface, the *calloso-marginal*, the *parietal-occipital*, the *calcarine* and *collateral* are well marked and distinctive.

The convolutions or gyri separated by these fissures are remarkably uniform, and, though often intersected by subsidiary sulci, can usually be determined without difficulty. Of these, the only ones which need be now mentioned are the three frontal, 1st, 2nd and 3rd, the general direction of which is parallel to the longitudinal fissure and the two central gyri which bound the fissure of Rolando on either side.

In the typical brain the main fissures are unconnected with each other; thus the fissure of Rolando is isolated and does not

unite with the Sylvian fissure below, or the ascending frontal or ascending parietal sulci on either side. The Sylvian fissure does not join with any of the sulci above or below it.

Prof. Benedikt of Vienna has made a special study of the brains of criminals,* and believes that he has met with peculiarities sufficiently marked to warrant the following proposition: "*The brains of criminals exhibit a deviation from the normal type, and criminals are to be viewed as an anthropological variety of their species, at least amongst the cultured races.*" The two peculiarities on which he lays stress are (1st) the confluence of many of the primary fissures and (2nd) the existence of four horizontal frontal gyri. He proposes to establish a confluent fissure type of brain, and he illustrates its most important characteristic by saying, "that if we imagine the fissures to be water-courses, it might be said that a body floating in any one of them could enter almost all the others." This, of course, means the absence of numerous bridges of nerve matter which normally separate the fissures—defects, marking an inferior development of the brain. Between the normal type with isolated fissures and the type with confluent fissures there will naturally be transitions, but he calls attention to the number and variety of the connections in his series of the brains of 22 criminals as supporting the truth of his proposition. He states that the brains of individuals in the lower grades of society approach nearer to the 2nd type, and it is probable, though, as yet, full data are wanting, that the brains of the inferior races of men also conform more closely to this than to the type with isolated fissures. Let us see now how far he has been able to establish the truth of this view. Of 38 hemispheres from the 22 criminals the following were some of the most interesting points:—

I. The *fissure of Rolando* communicated with:

(*a*) *fis. Syl.* completely in 18, incompletely in 6.

(*b*) with *3rd* or *ascending frontal*, complete in 11, incomplete in 2.

* On the Brains of Criminals, Vienna, 1879. Translated by Dr. Fowler. (Wood & Co., New York, 1881. *Cent. f.d. med. Wissenschaften*, 1876, and *No.* 46, 1880.

(*c*) with the 1*st* or *superior frontal sulcus*, complete in 9, incomplete in 1.

(*d*) with *inter-parietalis*, complete in 7, incomplete in 4.

Of the 19 brains there was not one in which the *fissure of Rolando* had not on one side a connection with some other fissure. Altogether there were 58 connections, 35 on the left and 23 on the right side.

II. The *Sylvian fissure* communicated with :

(*a*) *fis. R.* in 18 completely, in 6 incompletely.

(*b*) with *frontal sulci* in 18, incomplete in 7.

In 7 brains it existed on both sides ; only absent on both sides in 3.

(*c*) with *fis. inter-parietalis* in 22, incomplete in 6.

(*d*) with 1*st temporal* in 18, incompletely in 4.

III. The *fis. inter-parietalis* communicated with :

(*a*) *fis. R.* complete in 7, incomplete 4.

(*b*) *fis. Sylv.* complete 22, incomplete 7.

(*c*) 1*st T.* complete 19, incomplete 6.

In the 38 hemispheres there were 51 complete and 16 shallow connections of the inter-parietalis.

IV. The *scissura hippocampi* communicated with : *parieto-occipital*, complete 17, incomplete 2.

V. The *calloso-marginal fissure* : with *parieto-occipital*, complete 8.

VI. The *parieto-occipital :* with *inter-parietalis* and *horizonal occipital*, complete 21, incomplete 6.

These were the most important connections ; the others I shall not refer to.

The second peculiarity which Prof. Benedikt has noted in the brains of criminals is the existence of 4 horizontal gyri springing from the ascending frontal or anterior central convolution. This he regards as an animal similarity, and a reversion, so to speak, to the typical four primitive gyri of the brains of carnivora. The fourth gyrus is formed by the splitting, by a deep fissure, of either the 1st or 2nd convolution. In his latest communication

on this point,* the results are given of the examination of 87 hemispheres (from 44 criminals), of which only 42 presented the normal type of frontal convolutions, and 27 showed four gyri. In these the additional gyrus resulted in 8 from the splitting of the superior; in 16 from the division of the middle convolution. In 13 there was an imperfect division into four gyri. In two hemispheres there were five frontal convolutions.

Through the courtesy of Dr. Desmarteau, Jail Surgeon, I was present at the autopsy, and secured the brain of the man Hayvern who was executed for the murder of a fellow-convict; and the Department of Justice permitted me to secure the brain of Moreau, who was executed at Rimouski.

I.—Hayvern, aged 28, was a medium-sized man, of no trade; Irish descent; parents living, and respectable; no insanity, inebriety or neurotic disease in the family. He had been a hard drinker, and as a child was stated to have had fits. There is no evidence of the recurrence of these in adult life. He was serving a term in the Penitentiary, having been sentenced for highway robbery in 1879. He had previously been in jail more than twenty times, and may be taken as a good representative of the criminal class. The details of the murder show deliberation, and there was no evidence to show that the act was performed during a paroxysm of epileptic mania.

The skull was somewhat ovoid in shape, dolicho-cephalic; the forehead rather low and retreating. The calvaria was of moderate thickness; no signs of injury, old or recent.

Brain, last organ examined. Pl. I.—Vessels were empty; drained of blood by the opening of the vessels of the neck, both in front and behind. Membranes were normal. Weight of organ, 1326 grammes (46½ ozs.) Cerebellum completely covered by cerebrum. I obtained the left hemisphere for special study, and the details of its structure are as follows:—

Antero-posterior diameter	16.5 cm.
Hemispheric arch	24.8 "
Anterior curve (tip of Fr. lobe to Fis. Rol.)	14 "
Middle curve (from Fis. Rol. to Par.-occip. Fis.)	6.2 "
Posterior curve (from Par.-oc. to tip of Occip. lobe)	4.8 "

* *Centralb. f.d. med. Wissenschft.*, No. 46, 1880.

Sylvian fissure (*Fig.* 1), in addition to the normal *ascending* and *horizonal* rami, presents a radial branch which passes into the *frontal gyri* (*a*), a short radial extension into the *asc. parietal* (*b*), and a shallow communication with *retro-central sulcus* (*c*).

The *fissure of Rolando* (F.R.) or *central sulcus* is separated from the F.S. by a very narrow bridge of brain substance. It has no other connections.

There are four well-marked *frontal gyri* [1, 2, 3 *and* 4]; the extra one (2) appears to be formed by the splitting of the *superior* or 1*st gyrus*, though its base, where it joins the *asc. front. gyrus*, is in the position of the *middle* or 2*nd. fr. gyr.* As can be seen in the plate, there are two radial sulci which pass from a point just behind *asc. ramus* of *fis. Sylv.* and ascend almost to the *long. fis.* They are deep, and the hinder one has a crucial extension in the position of the 2*nd fr. sul.*

The *sulcus inter-parietalis* presents a well-marked radial portion which passes up behind the ascending parietal convolution in its whole length (*asc. pariet.* or *retro-central* sulcus); the sagittal part passes back into the parietal lobe and divides into two branches, one of which (*d*) curves round the *supra-marginal gyrus* and unites with the 1*st temporal fis.*; the other (*e*) ascends to the median border, and is continuous with a sulcus which joins the *parieto-occipital.*

The *asc. par. gyrus* (retro-central) is well developed, as are also the *angularis* and *supra-marginal.*

The *horizonal* (or *sup.*) *occipital* sulcus is well developed; it does not join the *par. occip.*, but sends branches into the *gy. cuneus.* It appears to join the 2*nd temp. sulcus*, but the brain is lacerated at this point, and it is difficult to make out the connection.

The 1*st temporal sulcus* is strongly marked, passes up and joins the *inter-parietal.* The 2*nd temp.* cannot be well made out on account of the laceration.

On the median surface (*Fig.* 2), the *calloso-marginal sulcus* is strongly developed, presents numerous perpendicular branches, and terminates by two, one of which (*f*) ascends to the usual position behind the *retro-central gyrus*, the other (*g*) curves

round and divides the *gyrus fornicatus* from the *pre-cuneus* (or quadrilateral), extending to within a short distance of the calcarine fissure, and uniting with the *fis. cruciata.*

The *gyrus fornicatus*, in the anterior half of its extent, presents a well-marked sulcus running along its centre.

The *parieto-occipital* is deep and well marked; it has a branch (*h*) which curves over the border and unites with the *inter-parietal.* The *calcarine* fissure unites with the *par. occip.*, and the conjoined sulcus communicates with the *scissura hippocampi* by a wide groove (*i*).

The *sulcus collateralis* joins the *calcarine* by a large fissure (*j*), which ends just at the handle of the fork of the *par.-occip.* and *calcarine.* Another sulcus (*k*) passes from it round the under surface of the occipital lobe, dividing the *temporal gyri* from the *occipital.*

The *orbital gyri* are separated from the frontal anteriorly, by a well-marked fissure (fronto-marginal of Wernicke).

The convolutions of the *insula*, normal.

According to Benedikt's views, this hemisphere is a-typical in the following particulars:—

(*a*) The union of the *Sylvian* with the 1*st frontal sulcus.*

(*b*) The junction of the *inter-parietal* with the *parieto-occipital* and with the 1*st temporal.*

(*c*) The extension of the *calcarine* fissure into the *scissura hippocampi.*

(*d*) The extension of the *calloso-marginal* fissure between the *gyrus fornicatus* and the *pre-cuneus.*

(*e*) The union of the *collateral* and *calcarine* fissures.

(*f*) The fission of the 1st frontal convolution into two parts, so that there appear to be four frontal gyri—a condition which Benedikt lays great stress upon as a marked *animal similarity* in the human brain.

II.—Moreau, a small farmer in the county of Rimouski, aged 40, French-Canadian, murdered his wife last summer, and was executed on the 13th of January. He was a short, very powerfully-built man, uneducated, and of a morose disposition; was temperate, and had never before been convicted of any crime.

He had not lived happily with his wife, and quarrels had been frequent; one day, when in the woods together, he cut her head open with an axe. The deed was apparently premeditated, as it came out in evidence that he had offered money to a man to do it for him. After the act and during the trial he maintained his usual stolidity, and did not appear to take a very deep interest in the proceedings. Indeed, it is stated that he was unaware, until some time after the sentence, that he was to be hanged. The autopsy was performed, about an hour after his death, by Dr. Belleau, and the brain was secured by H. V. Ogden, B.A., and brought to me in excellent condition for examination.

Organ large, weighed about 1587 grms. (56 ozs). [*Pl. II.*] The hemispheres, though large, did not completely cover the cerebellum. Membranes were normal; vessels of the pia mater and the subjacent grey matter deeply engorged.

Left hemisphere (*Pl. II., fig.* 3).—*Fis. Sylv.* is separated from ascending *parietal* by a very narrow and grooved gyrus, and joins the *inf. front.* by a shallow sulcus (*a*).

Fis. Rolando sends a deep fissure (*b*) across the upper end of *asc. par. gyr.*, which curves round the margin and unites with *fis. cruciata* of the *pre-cuneus*. There is not a well-marked *asc.* or 3*rd front. sul.* The 1*st fr. sul.* has a short vertical branch, and only extends for 2.5 cm. from *asc. front. gyr.*, when the 1st and 2nd convolutions fuse, but beyond this it is again apparent. 2*nd front. sul.* has a short vertical branch, and joins the fis. Sylv. by a narrow groove. Its anterior extension is well developed. The 3*rd front. gyr.* is large in comparison with the 1st and 2nd. The *asc. front. gyr.* is large.

The *asc. par. sul.* (retro-central), which is usually united with the inter-parietal, and called its radial portion, is isolated, and only joins the fis. Sylv. by a shallow furrow (*c*). The *asc. par. gyr.* is narrow.

The *inter-parietal fis.* runs almost parallel to the *asc. par.* and *fis. Rol.*, being separated from the former by a narrow convolution which joins the *sup. parietal lobule*. Below it joins the 1*st temp. sul.* (*d*); above it does not extend to the margin. Gyri of parietal lobe well developed.

The 1*st temp. sul.* is crossed in two places by bridging gyri uniting the 1*st* and 2*nd convolutions*. Posteriorly this sulcus has two branches—one which joins the *i. par.*, the other the *inf. occip.* The 2*nd temp. sul.* is not well marked.

The *sup. occip. sul.* joins the *par. occip.*; the *inf. occip. sul.* the 1*st temp.*

On median surface, *par. occip. fis.* unites with *sup. occip.*, and by a shallow sulcus with *fis. cruciata* of *pre-cuneus*.

Calcarine fis. normal; *cuneus* small.

Fis. collateralis long, and sends numerous fissures into *gyri lingualis* and *fusiformis*.

Sul. calloso-mary. has many fissures entering the 1*st front. gyr.* *Gyr. fornicatus* is fissured longitudinally. *Orbital gyri* normal; well marked *frontal marginal sul.* No external orbital fissure. *Insula* well developed, and has 9 gyri.

Right hemisphere (*Pl. II., fig.* 4).—*Fis. Sylv.* joins 3*rd* or *asc. front. sul.* (*a*), and the *asc. par.* (*b*) (retro-central) by shallow furrows. *Fis. Rol.* unites with 1*st front.* (*c*) and *asc. par.* (*d*) *sulci* by narrow grooves.

The *asc. front. sul.* arises by a shallow fissure from the *fis. Sylv.*, and then at the base of the 2*nd front. gyr.* joins the 2*nd front. sul.* 1*st*, 2*nd* and 3*rd frontal gyri* are well developed and distinct posteriorly. Anteriorly they are fused and crossed by many secondary sulci. *Asc. frontal gyr.* is very narrow in its centre.

Inter-parietal fis. has a well marked radial portion (the asc. par. or retro-central). The sagittal part passes back and presents three divisions—one (*e*) enters the *sup. par. lobule*, a second (*f*) passes directly back and joins a fissure in the position of *inf. occip.*, which reaches to the tip of occip. lobe, and the third (*g*) part passes vertically down and unites with 1*st temp. sul.* and has a branch which crosses the 2*nd temp. gyr.*

Asc.-par. convolution is large below, narrow above. The *angular*, *supra-marginal* and *sup. par. lobule* are much fissured.

1*st temp. sul.* joins *i.-par.*; the 2nd is not marked. Several oblique sulci cross the 2nd and 3rd temp. gyr. *Sup occip. sul.* joins *par. occip.*

On the median surface, *par. occip. fis.* joins *sup. occip.*; the *calcarine* enters *scissura hippocampi* and joins the *fis. collateralis* by a shallow groove. *Fis. collateralis* large and deep.

The *cuneus* is small; *pre-cuneus* (lob. quad.) is large and its anterior boundary ill-defined.

Calloso-marginal fis. extends to level of base of 1st frontal, and then curves up to the margin of the hemisphere, being interrupted by a broad annectant uniting the *gyr. fornicat.* with 1*st front.* Beyond this there is a short extension which joins a complex series of sulci in the *pre-cuneus.*

Orbital gyri normal. There is a narrow *fronto-marginal sul.* There is a well-marked *external orbital fissure.*

The chief points to be noted are:—

1. The absence of complete covering of cerebellum by cerebrum.

2. On both sides the *pre* and *retro-central fissures* were separated from *fis. of Sylvius* by very narrow and grooved gyri.

3. The left *fis. Rolando* joins *fis. cruciata* of *pre-cuneus*, and on the right side it is imperfectly separated from 1*st front*, and *asc. par. sulci.*

4. The *inter-parietal*, on both sides, joins the 1*st temp. sul.*, and on the right side is much more developed and joins the *occipital.*

5. On the median surface the *calcarine* on the right side enters the *scissura hippocampi.*

There remain two questions for consideration: first, to what extent does Professor Benedikt's confluent fissure type of brain prevail among ordinary members of the community, and how far is it reliable as an indication of defective development?

With a view of ascertaining how far the confluent fissure type of brain exists among the lower classes in this community, I have examined carefully 63 hemispheres from 34 individuals, all of whom were patients in, and died at, the General Hospital. Most of these were preserved by Giacomini's method, and as no special note exists as to the social standing or character of any of the individuals from whom they were obtained, the results are of value only so far as they show to what extent confluence of fissure occurs in that class from which the Hospital wards are recruited.

1. The Fissure of Rolando communicated with—
   a. *Fissure of Sylvius*, in 3 completely, in 7 incompletely.
   b. *Frontal sulci*, complete in 12; incomplete, 9.
   c. *Inter-parietal sulci*, complete in 7; incomplete, 9.
2. The Fissure of Sylvius joined—
   a. The *F. R.* [see above.]
   b. The *frontal* in 20.
   c. The *inter-parietal*, complete in 26; incomplete, 8.
   d. The 1*st temporal*, in 15.
3. The Inter-parietal united with—
   a. The *F. R.* [see above].
   b. The *F. S.* [see above].
   c. The *parieto-occipital* in 18.
   d. The *horizonal* or *sup. occipital* in 14.
   e. The 1*st temporal* in 19.
4. The *Calcarine* entered the *scissura hippocampi* in 25.
5. The *calloso-marginal* joined the *par.-occipital* in 1.
6. The *parieto-occipital* joined—
   a. The *inter-parietal in* 18.
   b. The *horizonal occipital* in 3.

From these limited observations we may conclude—

1. That a considerable proportion of the brains of Hospital cases are of the confluent fissure type.

2. The chief difference to be noted between Prof. Benedikt's series of criminals' brains and those which I have just gone over is the somewhat greater number of unions between typical fissures, more particularly between the *fis. Rol.* and contiguous ones. Thus in his set this fissure connected, completely or incompletely, with the *fis. Syl.* in 24 instances; in my series in only 10. In the other fissures the disproportion is not nearly so great.

3. Considering the number of brains of ordinary Hospital patients which present in some degree the confluent fissure type, it would seem more reasonable not to assign as yet any special significance to it until we have fuller information about the arrangement of the convolutions in the various races, and until a much larger number of the brains of criminals of all countries have been examined.

Professor Benedikt's cases were nearly all Slavonians or Hungarians, and though Betz of Kieff, a leading authority, acknowledged the atypy of his specimens, it would have been more satisfactory to have had a comparison between these specimens and an equal number taken from law-abiding members of the same races. It may be urged that in Hospital patients the brains should conform in considerable numbers to this 2nd or confluent fissure type, as many of them are individuals in the lower ranks of life, and not a few belong to the criminal class. This applies, however, much more forcibly to dissecting-room material, which, as Dr. Benedikt says, "consists of the remains of those who have suffered complete shipwreck in life through low grade of intelligence, imperfect motor development, or through crimes and vice." In the series of brains which I examined, there were no dissecting-room specimens, and it did not include the brain of any notorious criminal so far as I am aware.

As to how far confluence of fissures is indicative of a low type of cerebral organization we also want fuller information. When existing in high degree, there is certainly an absence of many important annectants or bridging areas of brain substance, but when we consider the variable size of convolutions bounding the typical fissures, it is easy to see that defect in one part might be more than compensated for by excess in another part, and even a neighbouring part. In several of the brains which I examined, notably No. 10, the confluent fissure type existed in an organ with a rich convolution system. In the brain of Moreau, the retro-central fissure on the left side was separated from the inter-parietal by a distinct gyrus, which might as well be regarded as an excess, as absence of an annectant and confluence of two fissures might be considered a defect.

With reference to the type of four frontal convolutions which Prof. Benedikt has found in such a large number of his specimens, I will only say that in 10 of the hemispheres examined it was observed in a greater or less degree of development. Nowhere was it better seen than in the brain of Hayvern. To enter upon the anatomical significance of this would be beside the question on this occasion.

Professor Benedikt's conclusions are those of a thoroughgoing somatist, who would bring all human conduct within the range of organic action. "The constitutional criminal," he says, "is a burdened individual, and has the same relation to crime as his next of blood kin, the epileptic, and his cousin, the idiot, have to their encephalopathic conditions." And again, "the essential ground of abnormal action of the brain" (*i.e.*, I take it, bad conduct,) "is abnormal brain structure. His 44 criminals were what they were because of defects in the organization of their hemispheres: they belonged to the *criminal variety* of the *genus homo*. No wonder he says "that this proposition is likely to create a veritable revolution in ethics, psychology, jurisprudence and criminalities." He wisely adds that it should not yet serve as a premise, and should not, for the present, leave the hands of the anatomists, since it must be repeatedly proven before it can finally rank as an undoubted addition to human science.

Crime is commonly regarded as the result of yielding to an evil impulse which could have been controlled; and this element of *possible control* is what, in the eyes of the law, separates the responsible criminal from the irresponsible lunatic. The belief in a criminal *psychosis* is spreading, and is the outcome of sounder views of the relation of mind to brain; and these investigations of Prof. Benedikt, to which I have so frequently referred, may serve as a foundation to a natural history of crime. But if this *is* the case, how are we to regard our criminals? What degree of responsibility can be attached to the actions of a man with a defective cerebral organization? Where is there scope to eschew the evil and to do the good, when men are "villains by necessity, fools by heavenly compulsion, knaves, thieves and treachers by spherical predominance." Any one who believes that with all our mental and moral processes there is an unbroken material succession, must consistently be a *determinist*, and hold, with Spinoza, that "in the mind there is no such thing as absolute or free will, but the mind is determined to will this or that by a cause which is determined by another cause, this by yet another, and so on to infinity." For a long time to come, how-

ever, the majority of individuals—including some who are inconsistent in so doing—will continue to hold the *intuitionist* view, nowhere better expressed than by Shakespeare, when he puts into the mouth of that arch-criminal, Iago, the words: "'Tis in ourselves that we are thus and thus. Our bodies are our gardens to the which our wills are gardeners; so that if we will plant nettles or sow lettuce, set hyssop and weed up thyme, supply it with one gender of herbs or distract it with many, either to have it sterile with idleness or manured with industry, why, the power and corrigible authority of this lies in our will."

"Theft and murder," as Huxley well says, "would be none the less objectionable were it possible to prove that they were the result of the activity of special theft and murder cells in the grey pulp." One thing is certain, that, as society is at present constituted, it cannot afford to have a class of *criminal automata*, and to have every rascal pleading faulty grey matter in extenuation of some crime. The law should continue to be a "terror to evil-doers," and to let this anthropological variety (as Benedikt calls criminals) know positively that punishment will follow the commission of certain acts, should prove an effectual deterrent in many cases, just as with our dogs, the fear of the whip exercises a restraining influence—immediate as well as prospective—on the commission of canine crimes.

Fig. 1. Plate I

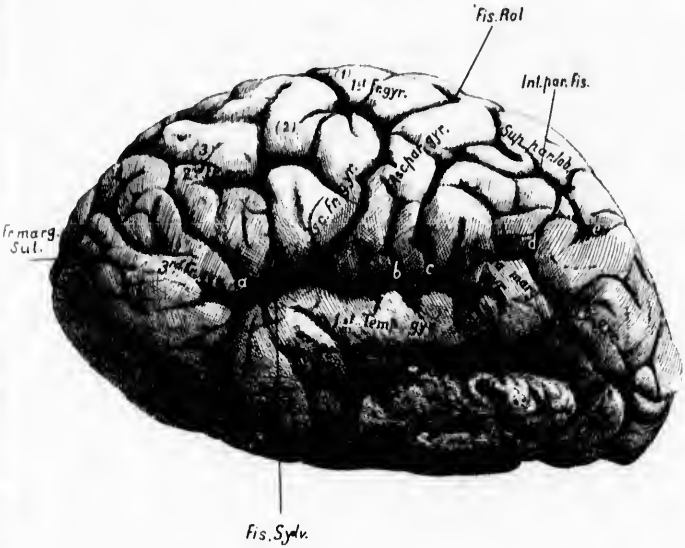
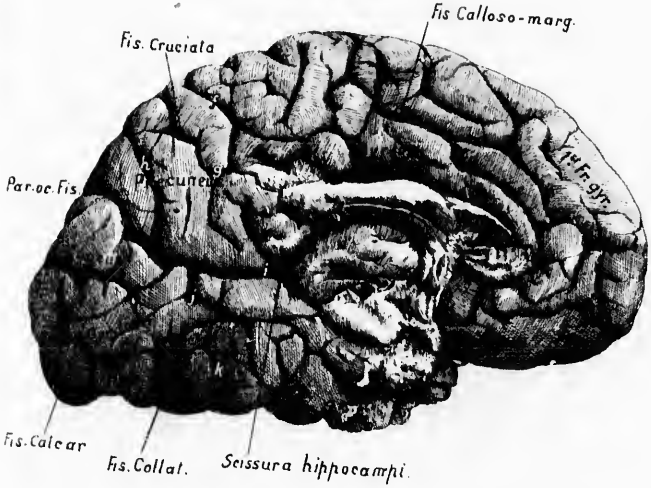


Fig. 2.



Inter

Par. oc. Fis.

Fig 3. Plate 2

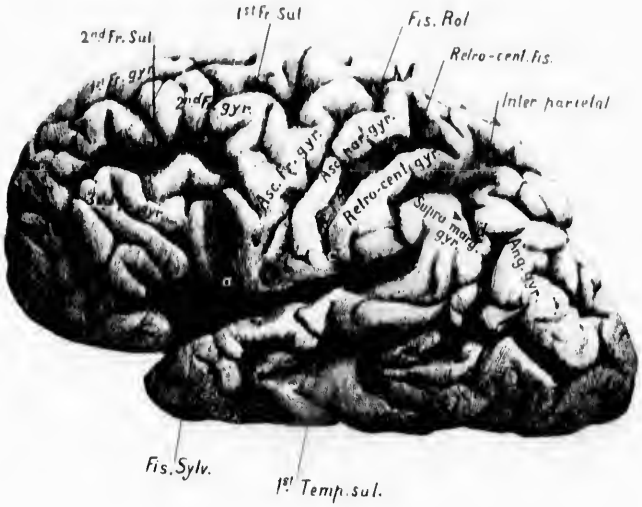
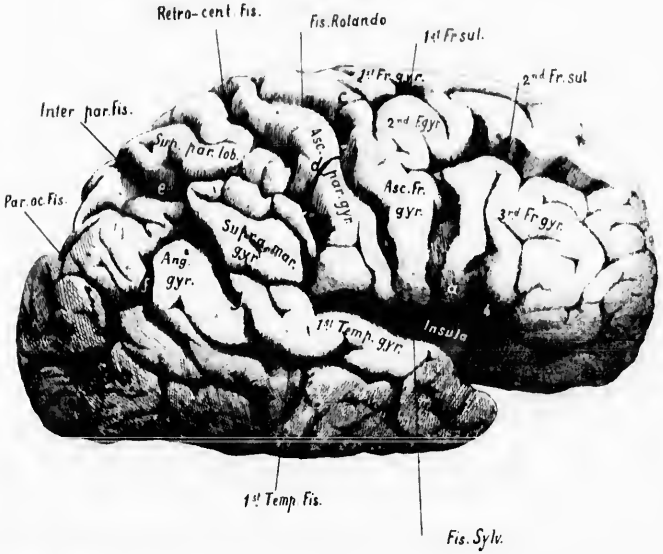


Fig. 4



XLVI

CASE OF OBLITERATION OF THE PORTAL VEIN (PYLEPHLEBITIS ADHESIVA).

By William Osler, M.D., M.R.C.P. Lond., *Professor of the Institutes of Medicine, McGill University, Montreal.*

Thrombosis and suppurative pylephlebitis are the affections most commonly met with in the portal vein. A few instances of calcification and extreme fibroid thickening of the walls are reported. Organic occlusion, by conversion of the vein into a fibrous cord or mass of connective tissue, is a very rare lesion, as in cases of thrombosis life is usually terminated long before organisation of the clot can take place. The following instance of it presents many interesting features, anatomical and clinical:—

J. C., aged 28, admitted into the General Hospital, under my care, June 17th, 1881, in a condition of extreme exhaustion, consequent upon loss of blood by vomiting. My house-physician, Dr Andrew Henderson, obtained from him the following history:—Has always been strong and healthy; somewhat intemperate, but a steady worker. Has never had syphilis. No constitutional disease in his family. Last September, when engaged in some very hard work, was obliged to give up on account of weakness and dull heavy pain in the upper region of the belly. It was never very localised, and was not aggravated by eating. Patient had to be in bed most of the time, and at about the end of a month had an attack of hæmatemesis, vomiting more than two quarts. Did not leave his bed for some weeks; does not remember whether his legs or abdomen were swollen. Did not go to work until about April, when he got employment in a manufactory as fireman. Latterly, he was put to heavy work, piling bags of sugar, and yesterday (16th) he had to give up owing to feelings of great weakness. This morning he vomited a large quantity of blood, partly fluid, but mixed with clots. When admitted in the evening he was in a state of great exhaustion; surface blanched; pulse very small—135; temperature, 100°; respirations, 20. Shortly after getting to bed he

vomited about four ounces of dark altered blood. A peculiar cadaveric odour was noticed in the breath.

June 18th. At the morning visit patient was examined, and the following condition noted:—He is a large, well-made, muscular man; lies on his left side in a drowsy, semi-conscious state, but can be roused. Face and general surface blanched; no distension of abdomen; superficial veins not visible; no œdema of the feet. Examination of *chest*, negative; *abdomen* flattened; skin of marble whiteness; visible epigastric pulsation; on palpation, marked pulsation in umbilical region, forcible, vertical in direction; no tumour to be felt. On auscultation a remarkable double murmur was heard midway between the navel and tip of ensiform cartilage; to be heard also a little to the right of the middle line, but was very feeble to the left. There was not a cardiac murmur. *Liver*—edge could not be felt; area of dulness much diminished; could scarcely be detected in sternal line; was 3 cm. in mammary, and 4 cm. in axillary lines. *Spleen*—not to be felt below costal border; area of dulness increased, 11 cm. in vertical, 13 cm. in transverse, directions. Patient did not complain of pain during the examination. Bowels have not been moved; a large external pile, filled with coagula, was found on the right margin of anus. Urine clear, and normal.

19th. During the night patient vomited a large quantity of bright, liquid blood, soaking the bed and covering the floor in the neighbourhood. He was found in an apparently dying state, but rallied on the administration of stimulants. The examination at the visit did not elicit any new facts; the epigastric murmur was not so distinct.

20th. No further haemorrhage, debility extreme, and a tendency to delirium. Slight œdema of feet. The cadaveric odour was very perceptible.

On the 21st and 22d patient remained in a state of profound exhaustion, and there were no additional abdominal symptoms. On the 23d there were repeated syncopal attacks, during one of which he died.

Autopsy.—Body well nourished; skin blanched; no distension of abdomen; cutaneous veins not visible; slight œdema of feet.

In abdomen the coils of small intestines were of a very dark

slate colour; peritoneum smooth; colon distended; no exudation; liver and spleen did not appear below the costal border. In thorax a few ounces of serous fluid in each pleura.

Heart was flabby and pale; chambers contained small clots; valves were healthy. Aorta normal.

Lungs pale, œdematous at bases.

Spleen greatly enlarged; weighed 675 grms.; was intimately adherent to the diaphragm and stomach. Capsule was very thick, in places wrinkled, and a firm, semi-cartilaginous plate existed at its convex border. On section organ cut with great resistance, creaking under the knife; the trabeculæ thickened, rough, and in spots gritty. Some of the veins were dilated, and contained thrombi. Near the hilus was a wedge-shaped calcified mass, the size of a walnut. The artery was very tortuous, and at the hilus presented a group of small saccular aneurisms, the size of large peas; the coats thickened, partly calcified, and one of them contained an old thrombus, which had softened in the centre.

Liver small, and closely united to the diaphragm and to the abdominal wall on the right side. It measured 25 cm. in breadth and 16 cm. from front to back. The shape was retained, but the left lobe was almost completely atrophied, only a small thin tonguelet remaining. The surface was smooth, but towards the right border and behind, many fibrous bands passed between the capsule and the diaphragm. The capsule on the under surface was opaque but smooth. On section, tissue uniform, pale reddish-brown colour; acini distinct, but no perceptible increase in the inter-lobular tissue. The anterior border and the remnant of the left lobe were firmer, and the connective tissue strands between the lobules could be seen. The hepatic veins were of full size. Portal canals not numerous, small; artery and duct distinct (condition of portal vein will be described under venous system).

Microscopic examination showed the liver cells to be somewhat fatty; the connective tissue on the greater portion of the right lobe was not specially increased, but at the anterior border and in the small portion of the left lobe the secreting substance was a good deal atrophied.

Gall-bladder contained a quantity of yellow bile. Gall duct normal. Hepatic artery almost double the usual size.

Stomach was capacious and contained a quantity of dark liquid mixed with food. Veins beneath the muscular coat could be seen dilated and tortuous. The mucosa was pale, here and there marked with spots of capillary injection. There were two small superficial losses of substance near the cardiac end; the tissue about them was not injected, and their bases were scarcely as deep as the submucosa. About the pylorus the membrane was mammillated, and on section very tough.

Intestines contained dark tarry fæces; mucosa pale throughout. Rectum presented a number of enlarged veins just within the sphincter and the external tumour was found to be a collection of enlarged and thrombosed veins.

Kidneys of normal size, pale, a little firm. On section a large quantity of thin watery fluid oozed from the surface. Ureter and bladder normal.

Venous System.—On dissecting the gastro-hepatic omentum the portal vein was found to be obliterated from a point 2 cm. beyond its origin, and converted into an irregular, fibrous cord, with ill-defined margins, being matted with the surrounding tissues. In this state it entered the hilus of the organ, and penetrated the main divisions of the portal canals; no trace of the natural appearance of a vessel could be seen. On section the tissue was spongy, not indurated, and somewhat reddish in colour. There were no remnants of a thrombus, nor any cretaceous or calcified portions. The main branches within the organ were also occluded; the connective tissue of Glisson's sheath was abundant, and firmer than normal. Both artery and duct in these parts could be slit open readily. There was not any special contraction about the hilus, and the liver substance in immediate neighbourhood of the portal canals looked normal. The remaining portion of the portal vein and its branches were in the following condition:—Just beyond the junction of the splenic and superior mesenteric was a large saccular dilatation, the size of a walnut, with thickened walls, and here and there a calcified plate beneath the intima. It was in contact with the under surface of the right lobe close to the hilus. *Superior mesenteric* was much dilated; the terminal part, just behind the pancreas, presented several small sacculi, the intima of which contained atheromatous plates. The mesenteric

branches were moderately enlarged. *Splenic vein* admitted the index finger freely, and all its branches were dilated. Several of those on the anterior margin of the spleen were full of firm thrombi. The vasa brevia from the fundus of stomach were dilated, and some of the larger branches contained thrombi. The left gastro-epiploic was almost as large as the splenic, and at the curvature presented several large dilatations, one of which admitted the top of the thumb. The gastric vein emptied into the dilatation just beyond the junction of the superior mesenteric and splenic, and was also enlarged. The walls of all of these vessels were thickened, the intima a little roughened, and in spots calcified. The *inferior mesenteric* was moderately enlarged; the hæmorrhoidal branches were distended. *Inferior cava* normal; openings of hepatic veins presented nothing unusual. Among its branches the lumbars appeared large, particularly one passing by the side of the third lumbar vertebra. To the left of the aorta was a large vein nearly equal in size to the inferior cava; it terminated below by two branches, one of which passed over and joined the junction of the external and internal iliacs on the right side; the other joined the common iliac of the left side. The appearance of the parts after dissection suggested a double inferior cava. Unfortunately the liver, together with stomach, pancreas, and spleen had been removed before this condition was detected, so that the upper termination of this vessel could not be made out. Two large branches joined it above, but their connection could not be traced. The *iliacs* were large; many of the branches of the internal divisions were thrombosed. The *diaphragmatic* veins formed a close plexus, particularly in the œsophageal region, which united with the veins of the coronary and lateral ligaments of the liver. The *œsophageal* veins were numerous and large, and formed a rich network about the cardia. The veins in the suspensory or round ligaments were not dilated. In the thorax the lower intercostal veins were very large, particularly one running along the lower margin of 10th rib. The *vena azygos major* almost equalled the inferior cava in width, and admitted the index finger easily; the azygos minor was also of large size.

Remarks—Such a case as the above presents many points of

interest. Sudden and violent hæmatemesis in a young man; no ascites, no enlarged abdominal veins, small liver, large spleen, and a localised murmur in the epigastric region—the diagnosis was not easy, but it lay, I thought, between cirrhosis of the liver, splenic anæmia, and an aneurism. For cirrhosis as a cause of the hæmatemesis were—history of spirit-drinking, diminished volume of liver, increase in size of spleen, and the existence of piles; against were—the age of patient, and the absence of many important signs, as gastric or intestinal catarrh, ascites, and enlarged veins. The well-nourished state of the man, the moderate enlargement of the spleen, and normal aspect of the blood, were opposed to the idea that the primary trouble was splenic. The suddenness of the attack, the brightness of the vomited blood, together with the existence of a localised murmur in the epigastric region—the origin of which remains obscure—suggested the occurrence of a small aneurism, either of the aorta or one of the branches of the cœliac axis; but the hæmorrhage in September, the absence of any pulsating tumour, and the state of the liver and spleen, seemed fatal to this view. Altogether, in spite of the absence of many of the important symptoms usually present, the most satisfactory diagnosis appeared to be portal obstruction from cirrhosis. The evident reduction in the volume of the liver was strongly in favour of this view, and as I had also met with several instances in which severe hæmorrhage had been the initial symptom, I was the more inclined to regard it as an anomalous case of this nature. The history of a hæmorrhage in September, followed by an obscure illness of some months' duration, pointed to a chronic malady.

The history of the case offers no clue to the cause of the obliteration of the vein, but we may suppose it to have taken place in the way in which veins usually become occluded, viz., by the formation of a thrombus which organised, and was ultimately converted into a fibroid cord. Apart from marasmatic conditions, in which portal thrombosis occasionally occurs, coagulation of blood in the portal vein is met with—1st, as an effect of compression, as in cirrhosis, in which the pressure is exercised within the liver, or in tumours in the neighbourhood of the hilus, which compress the main trunk in the gastro-hepatic omentum; 2d, by extension of inflammation from the

bile passages, as in cholangitis from obstruction by gall-stones; and 3d, by the extension of inflammation or transference of emboli from suppurating or ulcerative foci in the territory of the portal vessels, but in these instances the thrombi which form rapidly soften, and suppurative pylephlebitis is the result. I have met with cases of pylethrombosis from the above causes, but, so far as can be ascertained, none of them have prevailed in this case. The only possible source which is suggested by the *post-mortem* is the cretaceous area in the spleen, representing the final stage of a small abscess or infarct, which, when in an active state, might have induced, by direct extension or embolism, the pylethrombosis.

The state of the liver is worthy of note. Though shrunken, particularly in left lobe, the greater part of the organ was smooth and not in the least cirrhotic. In the few instances of chronic occlusion which have been reported, the condition has been variable. In Cruveilhier's case[1] in which the obstruction must have lasted for years, the organ is described as smooth and healthy. In others it has been cirrhotic. Solowieff[2] has produced a fibroid condition of the liver by inducing occlusion of portal branches in the dog, but that this is not an invariable sequence, in man, is shown by this, as well as other cases. Nor is there any good anatomical reason why it should occur. After complete exclusion of portal blood from the organ, the lobular capillary plexus continues filled, as the venules which collect the blood from the capillaries of the hepatic artery empty directly into the portal interlobular vessels, and the blood-supply is in this way maintained. Hence the function of the gland is not materially interfered with, and bile continues to be formed from the blood furnished by the hepatic artery, which may, as in this case, undergo a compensatory enlargement. That the arterial blood can in this way act as substitute for the portal supply is well shown by such a case as the one under consideration, which forms an interesting counterpart to the one of aneurism of the hepatic artery[3] which apparently demonstrated that the converse is not true, but that, as Cohnheim and Litten

[1] *Atlas d'anat. path.* livr. xvi. Pl. 6.
[2] *Virchow's Archiv*, lxii.
[3] *Canada Med. and Surg. Journal*, 1877, Drs. Ross and Osler.

state,[1] the portal blood cannot replace the hepatic if the latter be completely excluded from the organ.

There is no more interesting subject of study than the way in which channels of collateral circulation are established in occlusion of large vessels. In the case of the portal vein, numerous opportunities for this purpose are afforded in cirrhosis of the liver, in which the obliteration of many interlobular branches necessitates the development of circuitous routes, by means of which the blood-current in the portal system is equalised, and the reduced carrying capacity of its vessels counterbalanced. In some instances, so adequate is this compensation that the cirrhosis may reach an extreme grade without producing symptoms. These collateral channels have been fully described by Sappey, and are chiefly:—(1) the anastomoses between the coronary veins of the stomach and the œsophageal plexus, which discharges into the lower intercostal and azygos veins, and also communicates with the diaphragmatic vessels; (2) veins passing in the coronary and suspensory ligaments of the liver and in the adhesions which often form between the liver and diaphragm; (3) in some cases a small vein in the round ligament dilates enormously, and affords free communication between the portal vein and the epigastric vessels. Some regard this as a redistended umbilical vein, but Sappey states that it is one of the small vessels which he describes as the *venæ portæ accessoriæ*. I have recorded an instance[2] of advanced cirrhosis, with great narrowing of the portal branches, in which no symptoms of increased blood-pressure existed in the portal system owing to the presence of this vein, which was as large as the little finger; (4) certain veins, forming what is known as the system of Retzius, which, originating in parts of the intestinal canal, and anastomosing with the radicles of the portal vein, discharge into the inferior cava or its branches; (5) the communications which exist between the superior and inferior haemorrhoidal plexuses. In this case the collateral circulation appeared to have been carried on by the first, fourth, and fifth of these channels. There were extensive communications between the gastric and œsophageal veins, and through the latter with the azygos and liver intercostals. The *vasa brevia* and others about the fundus

[1] *Virchow's Archiv*, lxvii. [2] *Montreal General Hospital Reports*, 1880.

of the stomach were highly developed, and joined the dense network about the cardia and the diaphragm in the immediate vicinity. Many of these branches were plugged with thrombi. Doubtless a large share in the supplementary circulation was taken by the veins of the system of Retzius and the peritoneal branches emptying into the cava. The large vessel to the left of the aorta may have been a greatly distended azygos minor which Henle figures as joining with the left iliacs, but unfortunately its connection could not be made out owing to the removal of the viscera before the nature of the lesion was suspected. The blood in it probably reached the azygos, which was of large size. In the case of obliterated vena cava, recorded in this *Journal*,[1] I met with a similar vein. The haemorrhoidal plexuses were not greatly distended, but the branches of the internal iliacs, particularly on the left side, were very large, and many of them contained thrombi. The epigastric veins were not dilated.

The collateral circulation must have existed for some time perhaps for years, and was fully compensatory. The somewhat sudden onset of the final symptoms may reasonably be attributed to interference with this free circulation by the thrombi in the gastric veins, and in branches of the internal iliacs.

[1] Vol. xiii.

Sep.-Abdr. a. d. Centralblatt f. d. med. Wissenschaften 1882. No. 30.

Ueber den dritten Formbestandteil des Blutes.

Von Prof. Dr. Osler, McGill Universität, Montreal.

Während meiner Arbeit in dem Laboratorium des Universitäts-Colleges in London im Jahre 1873 wurde meine Aufmerksamkeit auf die sogenannten „Körnchenhaufen" im Blute gelenkt, welche damals zuerst von M. Schultze beschrieben worden waren. Die Ergebnisse der Untersuchung wurden damals der „Royal-Society" mitgeteilt und veröffentlicht*). Ich suchte dort zu beweisen, 1) dass diese „Körnchenhaufen" eine Ansammlung von kleinen, nicht übereinstimmenden, mikroskopischen Körperchen sind, die ein Achtel bis zur Hälfte der Gröfse der roten Blutkörperchen besitzen; 2) sagte ich, dass diese „Haufen", als solche, nicht im Blute existiren, sondern dass deren individuelle Elemente frei unter den anderen Blutkörpern circuliren. Zum besseren Verständniss gebe ich hier einen Auszug aus dem dort Gesagten:

„Während der Untersuchung eines Teiles loser Bindefasern von dem Rücken einer jungen Ratte bemerkten wir in einer grofsen Vene, die sich zufällig in denselben fand, dieselben Körnchen, jedoch nicht massenhaft zusammengedrängt, sondern vereinzelt, unter den Blutkörpern. Wiederholte Beobachtungen machten es uns klar, dass in einem Tropfen Blut, von diesen jungen Tieren genommen, wir stets diese Körnchen in Haufen zusammen fanden, während auf der anderen Seite in den Blutgefäfsen (seien es Arterien, Venen oder Capillaren) ganz desselben Tieres wir stets diese Körnchen als vereinzelte Elemente vorfanden, die keinerlei Neigung zeigten, aneinander zukleben. Die „Haufen" bilden sich deshalb erst im Augenblick des Entziehens des Blutes durch Körperchen, die vorher frei in demselben sich bewegt hatten."

Zum Oefteren habe ich meinen Studenten und anderen Fachmännern die Existenz dieser Elemente vordemonstrirt und sie unter dem Namen „Schultze's granulirte Massen" und „Schultze's

*) s. Proceedings 1874, No. 153.

Körperchen" eingeführt. Zweifellos fallen sie mit Zimmermann's Elementarkörperchen und mit Havem's Hämatoblasten zusammen.

Neuerdings hat Bizzozero*) dieser Sache frisches Interesse zugewendet. Während ich jedoch die Richtigkeit der Ueberschrift seines Aufsatzes: „Ein **neuer** Formbestandteil des Blutes" zu beanstanden wage, gestehe ich, dass ich Tatsachen begegnete, welche seine Ansicht bekräftigen und den Einfluss der beregten Körper auf das Gerinnen und die Klumpenformation des Blutes dartun:

1) Das Faserstoffnetz, das sich auf der Glasplatte aus dem Blute ausscheidet, ist in der Regel dichter und stärker da, wo sich Schultze's Elemente am zahlreichsten vorfinden, als z. B. in Schwächefällen, bei Septhämie, Phthisis u. s. w.

2) Der Verlauf der Endokarditis bringt, wie allgemein bekannt, fibrinöse Wucherungen hervor. Ich habe in manchen solchen Auswüchsen — mögen sie warziger oder ulcerativer Natur sein — runde corpusculäre Elemente gefunden, die mit Schultze's „Körnchenhaufen" identisch sind**).

3) Bei einem alten Manne, der an Carcinoma ventriculi litt, war an der Aorta ein aufserordentlicher Befund. Sie war sehr atheromatös und stellenweise verkalkt. Gerade über der Bifurcation fand sich eine grau-weifse Masse, etwas abgeplattet, 3—5 Ctm. im Durchmesser, sich jedoch 1,5 Ctm. über den Rand erhebend, mit welchem sie fest verwaahsen war. Es sah sich wie eine Neubildung an und ich hielt es anfangs für eine secundäre Krebsmasse, welche die Ader durchbrochen habe. Nach genauerer Prüfung zeigte sich jedoch die ganze Masse als zusammengesetzt aus kleinen farblosen, eng aneinander geschlossenen Körperchen, die in jeder Beziehung sich identisch mit den individuellen Elementen von Schultze's „Körnchenhaufen" verhielten. Jede Möglichkeit, sie irrtümlicher Weise für veränderte rote oder weifse Blutkörper zu halten, war ausgeschlossen. Weiter fanden sich 6 oder 8 kleinere Flecken an der Intima auf einer Balggeschwulst aufsitzend. Das Fasernetz in diesen Massen war nicht erkennbar und an keiner derselben befand sich coagulirtes Blut.

4) In zwei Fällen von Aneurysma habe ich dieselben in grofser Anzahl auf Thromben sitzen sehen. Im ersten Falle, bei einem Aneurysma der Aorta thoracica von geringer Ausdehnung, das den Oesophagus durchbohrt hatte, fanden sich merkwürdig verzweigte, fadengleiche Filamente auf der Oberfläche des Thrombus, die sich scharf gegen den dunkelroten Untergrund abhoben. Diese Filamente waren aus den beregten Schultze'schen Körperchen zusammengesetzt, untermischt mit Fibrinniedersehlägen. — Der zweite Fall war ein grofses Aneurysma am Aortabogen. Hier erschienen sie auf der äufsersten Ablagerung des Thrombus, entbehrten jedoch des fadengleichen, netzartigen Ansehens.

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*) s. d. Bl. 1882, No. 2, 10 und 20.

**) Ueber ulcerative Endokarditis. Seguin's Arch. of med. 1881, Febr.

Ueber die Entstehung dieser Corpuscula wissen wir nichts, aber das eine wissen wir, dass weder sie, noch die von ihnen gebildeten Massen, ihren Ursprung in der Zersetzung der weifsen Blutkörper haben, wie gewöhnlich angenommen wird. Auch über ihren Zweck ist uns nichts bekannt, noch auch welchen Einfluss ihr häufiges Vorkommen hat. In einer oben erwähnten Abhandlung über den berührten Gegenstand beschrieb und stellte ich auch noch gewisse Veränderungen dar, welchen diese Körnchenhaufen unterliegen, wenn sie im Blutserum einer Temperatur von 37—38° C. ausgesetzt werden. Das beste und geeignetste Object zum Studium derselben bildet wohl die neugeborne Ratte.

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SUMMER SESSION CLINICS.

BY

WM. OSLER M.D., M.R.C.P., Lond.

McGILL UNIVERSITY.

No. I.

CASES OF INHERITED SYPHILIS.*

GENTLEMEN,—In the out-door department and on the surgical side you will have many opportunities of seeing acquired syphilis in its recent forms. The inherited disease presents many manifestations which come under the physician's care, and at the present time I have three examples in my wards which we may study to-day with advantage. And first a word of caution. Do not use the term syphilis before your patients, particularly as in the case just to be brought in of a mother and her child. Many a poor woman has lived in blissful ignorance of the precise nature of her child's affection until an incautious word has suggested to her the cause, and then, for her, "farewell the tranquil mind." We shall use the old term *lues*.

CASE I.—M. O., æt. 6 weeks. Admitted on 12th inst., with snuffles and skin eruption. Mother has been married two years; family history good; has no signs of disease; nipples were sore, but not specific; had one miscarriage at 7 months; the father of the child, she says, is healthy (?).

The *child was born healthy*, had no snuffles and no skin trouble; in two weeks began to snuffle; at four weeks spots appeared on the body and about the buttocks; on admission had an eruption on the buttocks, groins, genitals, face and nose. The

* Reported by Mr. C. E. Cameron.

eruption consisted of irregular blotches, and about the anus some soft mucous patches, and here and there a pustule. The patches were erythematous, and the scrotum also was swollen and sore. About the mouth the skin was rough, raw and red, but no pustules nor papules could be seen; on the arms and hands papules now exist. On the 14th inst. was given gr. ½ Hydrarg. cum Creta, t.i.d., and a piece of mercury ointment about the size of a pea was rubbed into the skin at night. Since that time the child has improved; the eruption about the face has faded, leaving a reddish coppery stain; the buttocks have also improved in condition; the nostrils are still stuffed, but not so much as when first seen; no distinct mucous patches are to be seen inside the mouth.

Now, gentlemen, I would ask you to make a careful study of the child. Do not suppose that it is only in hospital practice that you will find these cases; lues is no respecter of persons, and there is no station in life in which you may not expect to meet it.

Within the womb the fœtus may be blighted and abortion occur at the fifth, sixth or seventh month. If it affects the child in utero, as a rule it kills there, and the child is born dead; if not affected in utero, the child is born healthy, and in about two weeks it begins to snuffle, and a rash appears upon the buttocks: there may be also a rash about the mouth, and this may become general. About the buttocks there may be soft, raised, injected spots—mucous patches. The above appearances are characteristic.

To *treat* this condition give mercury, the mercury and chalk powder in gr. ½ doses three times a day, and rub in a little of the mercury ointment every night, or the latter may be spread on the child's flannel roller; or you may give corrosive sublimate, gr. ½ in ℥vi. of water, and of this give ℥i every three or four hours. These cases, as a rule, do well.

Infantile lues may lead to characteristic appearances in the child; the eruption causing fissures about the mouth, which, when healed, leave scars which radiate from the angle of the mouth to the cheek. In the infant before you the present

rash is healing, but during the first year there may be occasional skin eruptions, or mucous patches in the mouth. If the child survives the first year the disease usually remains latent, but as puberty is approached again declares itself, as you will see in the next cases to be brought in. Now that the patient has left the room, we may ask the question, Who is responsible for this—the father or the mother? The latter, so far as we can gather, seems healthy; has had no skin eruptions, or throat trouble. The husband is away, and though she says he is healthy, and never had any particular disease which she knows of, I am inclined to think that he is at fault. What about the woman herself? Is she syphilized? Most writers think that a woman who has borne a syphilized child is contaminated in some degree, though showing no positive signs. A strong proof is the fact, that you cannot innoculate her with syphilis. If the child you have just seen were given to a healthy nurse, with its condition of lips, it would give the woman a chancre of the nipple. This is sometimes known as Colles's law.

The next cases illustrate some interesting later manifestations.

CASE II.—Girl, æt. 13, showing severe ulceration of throat.

History.—Mother healthy; no symptoms of lues; father has no evident disease, (?) but is dissipated. This child is the last of seven; several of the others died early, one with blisters; all had stuffed noses; four out of the seven died within the year; one lived to five years and the other to six years. This girl was born healthy, and remained so till two years ago, and then became blind; cured by Dr. Buller; last year got deaf; this also cured; has had sore throat for six months, not much pain, but some difficulty in swallowing.

Present Condition.—Small; well nourished; has not the syphilitic countenance. *Teeth*—Upper central incisors are eroded at the neck, not dwarfed, a little honey-combed, but are not Hutchinson's specific teeth. In the *mouth* nothing is seen on the tongue or cheeks, but in the throat there is extensive disease; the uvula and velum are gone; there is a cicatrix on the posterior wall of the pharynx, linear in direction; the mucous membrane of the right side is much thickened, especially below

the orifice of the Eustachian tube ; as low as can be seen in the pharynx on the posterior walls are cicatrices with reddish fleshy outgrowths; nothing else noticeable. *Eyes* are apparently clear, but on careful inspection both corneæ are seen to be slightly turbid and hazy. She has had interstitial keratitis, a common affection in secondary syphilis, which comes on usually between the twelfth and sixteenth year, is specific, and if properly treated, generally curable. Secondary acquired lues in man rarely destroys the structures of the throat. In the inherited form the throat affection is apt to be more intense and phagadænic, as in this child. *Ear* trouble is not uncommon in inherited lues. In this instance it may have extended from the pharynx ; but middle ear disease may occur without throat complications. In this case the disease in the pharynx is not progressing. She is on potas. iodid., grs. x, t.i.d. To do any good, these cases require early and energetic treatment, as the ulceration is rapid and destructive.

Case III.—Girl, æt. 23, admitted Feb. 10th with Bright's disease ; dropsy of the legs and face. Family history uncertain. This girl presents, as evidences of inherited disease, large tibial nodes, onychia, and a suspicious-looking spot of ulceration on her forehead *Nodes* are, in acquired pox, common on the forehead, clavicles, tibiæ, &c., and are the result of specific periostitis, caused by virus in the blood. They may be absorbed, or go on to the formation of bone. They are also important features in inherited syphilis. Nodes produced in the congenital form differ from those produced in the acquired, inasmuch as they affect more often the bones of the upper and lower extremities, are generally symmetrical, are much larger, and may occur over the whole extent of the bone ; they are rarely painful, and often disappear under treatment.

The tibiæ of this girl are enlarged, thickened, and misshapen: almost a uniform node from ankle to knee. The fibula on the left side is thickened, especially about the lower part. I remember, on several occasions, hearing Mr. Hutchinson call attention to the fact that these large nodes were often mistaken for Rickets. I pass around one of his plates illustrating this form of node.

Teeth—Lower incisors eroded at the root; upper ones well formed, nothing suggestive about them. *Nails* of the thumb, ring and little fingers of right hand are mal-formed, rough, dry, discoloured, scaly, and are typical instances of *Onychia sicca*, or psoriasis of the nails.

You noticed that I examined the teeth of these two cases with special care. I did so because these organs sometimes give valuable or even positive evidence of inherited syphilis. Mr. Jonathan Hutchinson first called attention to this fact, and I have here for your inspection his Plates illustrating the subject. The teeth in case II. would be called by some "specific," but they are not so, and I gladly take this opportunity to impress upon you the characters of the teeth which this profound observer has been led to regard as distinctive. At the Congress last year he complained very justly that men had not sufficiently studied his writings on the subject, and were too apt to regard any malformed teeth as syphilitic. The facts are briefly these: 1, Teeth giving information are the permanent ones. 2, The specific ones are the upper central incisors. 3, Characters are: dwarfed, stunted in length and breadth, and narrower at the cutting edge than at the root. Anterior surface has usually the enamel well-formed and not eroded or honeycombed; the cutting edge presents a single notch, usually shallow, sometimes deep, and in that notch the dentine is exposed.

Other irregular teeth, eroded at the surface, are indications of an early *stomatitis*, an inflammation of the mouth, perhaps from mercury, or associated with convulsions.

Children who have been the subject of syphilis frequently grow up with a very characteristic physiognomy, recognizable at a glance. The following are chief points in a *Syphilitic countenance:* 1, forehead prominent, especially the frontal eminences; 2, saddle-nose, bridge being defective, owing to early coryza and inflammation; 3, often striated lines from corners of mouth, and the skin is colourless and muddy.

No. II.

ACUTE BRIGHT'S DISEASE.

GENTLEMEN,—Since I took charge of the wards you have had opportunities of studying three cases of acute nephritis, and to-day I propose that we shall go over them together, and see what lessons we can learn about this important affection. And first let me remark, that under the common designation *Morbus Brightii*, several separate diseases must be distinguished; a good natural classification is as follows:—

I. Acute Bright's disease—acute parenchymatous nephritis.
II. Chronic Bright's disease.
    (1) Chronic parenchymatous nephritis.
    (2) Interstitial nephritis.
    (3) Amyloid disease.
    (4) Mixed forms.

The cases are briefly as follows:—

CASE I.—*Scarlet fever—Acute renal dropsy—Death.*—W. M., æt. 13. Admitted February 9th, under Dr. Ross, with dropsy and shortness of breath. Was healthy a year ago. Had mild scarlet fever, and some time after it began to have severe headaches, and the feet became swollen in the evenings. In November he quit school, and has been laid up ever since. Dr. Blackader, under whose care he was, states that the chief symptoms have been, up to the date of admission, headaches and dropsy, which sometimes would become general. Urine has been albuminous, and contained blood and casts. When admitted was pale, and had œdema of feet and legs; no fluid in abdomen; slight dulness, with râles at right base. Urine scanty, 6 ozs., smoky; sp. gr., 1020; contains much albumen, finely granular and epithelial casts, with blood cells. T., 99.5; P., 132; R., 142. Ordered milk diet, and Liq. Amm. Acet 5ii, with Inf. Digital. 5ii

every four hours, and a few days after pilocarpine, $\frac{1}{8}$ of a grain, which produced salivation and copious sweating. By the 17th the swelling of the legs had subsided, but eyelids were puffy; urine clear and more abundant, 50 ozs. Up to the end of the month patient varied; on the 22nd urine was again bloody, and the loins were cupped; pilocarpine continued at intervals. Early in March not so well. General œdema came on, with great oppression of breathing. A systolic murmur has been heard at apex for a couple of weeks. Hot air bath caused much restlessness. The urine varied much; was at times very bloody, and again clear. On the 17th the œdema became more intense; urine scanty, 14 to 15 ozs.; much albumen. Was taken home on the 22nd, and died about the 1st of April.

Case II.—Mary C., æt. 8. Admitted March 6th, under Dr. Ross, with severe vomiting, headache and slight swelling of feet and legs. Taken ill on 4th, two days before admission. Child had scarlet fever over a year ago; recovered completely, and has been strong and well since. Had mumphs three weeks ago. On above day (4th), had been out and exposed; complained of boots being tight; legs were found slightly swollen. On the evening of the 5th was restless, and had headache, vomiting, and nose-bleeding.

On admission, puffiness of eyelids, moderate œdema of feet and legs, headache and vomiting. Passed 28 ozs. of urine in 20 hours; dark, smoky, large amount of deposit; sp. gr., 1015; albumen abundant. Microscope gave casts, hyaline and epithelial, and many free blood cells. Heart beat strong; a soft bellows murmur in 4th interspace, close to sternum. Had mustard and linseed poultices to loins. Next day cupped, and ordered Liq. Amm. Acet. and Inf. Digital. āā 5ii every four hours. By 9th, vomiting, nose-bleed and headache had stopped; œdema less; urine more abundant, 35 ozs. of same characters. Ordered hot air bath every evening. By 11th, urine 61 ozs., still dark, but not so bloody. Hot air bath has acted very well. General symptoms improved. On 13th, 65 ozs. of urine, smoky, but not very dark; contains less albumen; very few casts; œdema gone.

Temperature, which has ranged from 100 to 100.5°, is now normal. On 18th, hardly a trace of albumen, about 62 ozs. daily, still a little smoky; granular casts. Hot air baths to be stopped, also the Digital. and Liq. Amm. Acet., and Basham's Mixture (Tinct. Ferri Muri., Acetic Acid and Liq. Amm. Acet.) substituted. On night of 20th, not so well; not so much urine, 40 ozs., and darker; many granular casts. Improved until April 9th, to which date urine ranged from 40 to 65 ozs.; sp. about 1010. On April 11th, urine again a little reddish and albuminous; child appears quite well, but is a little feverish. Went out on 13th. A few days ago she came to report herself as continuing well.

CASE III.*—Jas. B., æt. 23, a well-built labourer. Admitted April 26th, with dropsy. Nothing of note in family or personal history. Has been working on the railroad. One Sunday, about three weeks ago, he went with some comrades to a village seven miles distant and drank heavily. On returning to the shanty that night he was unable to keep up with his companions, and lay down on the snow for some hours, until his friends returned for him. The next day he had a slight chill, with pains in the back and in the left side. These continued for three or four days, and he then noticed that his face was puffy, and the hands and legs began to swell. He does not remember about the urine; thinks he passed as much as usual. Had no vomiting, no headache. On admission, feet and legs œdematous, the left more than the right; face swollen. Nothing special detected in examination of heart and lungs. Tongue coated; appetite impaired. Urine—amount for first 24 hours in which it was collected, 46 ozs.; brownish red color, smoky, acid reaction; sp. gr., 1016; contains a large amount of albumen, and on microscopical examination presents red blood corpuscles and numerous casts, of which three varieties have been detected—(*a*) hyaline, with a few scattered granules; (*b*) epithelial casts, or rather cylinders with round cells, resembling leucocytes; (*c*) blood casts, composed chiefly of red blood corpuscles. Of

* Report by Mr. J. R. Johnson.

these the delicate hyaline casts have been most abundant. For four days we kept him in bed, on a light diet, without any special treatment, and since that date he has had a couple of jalap powders to keep the bowels loose. The œdema of the face is gone, the legs are less swollen, while the amount of urine is about the normal, containing very little blood and less albumen; the urea, however, is diminished. The man has been able to walk upstairs, and has done remarkably well.

You will notice that these three cases present a striking uniformity in the chief symptoms—alterations in the character of the urine, with dropsy; hence the appropriateness of the old term, Acute Renal Dropsy.

Let us now briefly review the affection, as illustrated by our cases. *Ætiology*—It is a disease of early life; the great proportion of the cases are in persons under 20, and as the years increase, the less frequently it is met with. The case of Prof. ————, who, nearly ten years ago, at the age of about 50, had acute nephritis, and in whose continued good health we now rejoice, is an instance of the occurrence of this disease at an unusually late period of life. *Scarlet fever* and *cold* were the causes which prevailed in our cases, and these obtain in the majority of individuals attacked. It is one of the most dreaded sequelæ of scarlet fever, and, as in the boy M—, not infrequently follows an attack which is so trivial as to be almost overlooked. *Diphtheria* is an occasional cause, and the other infectious disease may at times be followed by an acute inflammation of the kidneys. After cold and scarlet fever, you will find, as practitioners, that *pregnancy* comes next in order of frequency in inducing this affection. How it does so we need not stop here to inquire, as the explanations usually offered are not altogether satisfactory.

The *morbid anatomy* has been much discussed. In the early stage we do not often have an opportunity of dissecting the organs, but doubtless we would find them congested and swollen. At the period in which we commonly inspect them—from three weeks to three months after the onset—the organs are much enlarged, weigh 8 to 10 ozs., and have the appearances known as characteristic of the "large smooth kidney," or the mottled kidney.

The capsule is thin, and strips off easily ; on section, the cortex is seen to be increased in thickness and anæmic, or of an opaque yellow-white aspect ; the Malpighian tufts and the arterial twigs are injected, as are also the large collecting veins which convey the blood from the stellate veins of the surface. The pyramids are usually congested, and offer a striking contrast to the pale cortex. The histological changes are chiefly in the cortical parts, and consist in swelling of the epithelium, which becomes more granular, and may degenerate into a molecular *debris*, distending the tubules. Other tubes may contain blood-cells and leucocytes, with casts. In later stages, fatty changes may cause patchy opacities. Intertubular changes, in the form of connective tissue proliferation, have also been described, and probably always take place in cases which last several months. These have been specially described by Klein in the scarlatinal form. Bowman's capsule and the contained glomerulus are also involved. Klebs first called attention to these changes (glomerulo-nephritis), but he believed them to be entirely of the nature of proliferation of the cells between the capillary coils. Probably the epithelial coating, as well as capsular epithelium, is affected. I pass round Langhans plate (Virchow's Archiv., Bd. 76), in which these changes are well figured.

Symptoms.—In the majority of cases the appearance of œdema gives the first indication to patient or doctor. In the man B—, a slight chill, with feverishness and lumbar pain, preceded the œdema. In case I, persistent headaches appear to have accompanied the onset ; and in case II, which followed cold, headache and vomiting were the first symptoms. The latter is not infrequent in the early stage of scarlatinal nephritis. The most marked feature, dropsy, may vary from mere puffiness of the eyelids and œdema of the ankles to extensive general anasarca, with exudation into the serous sacs. The milder grade you see in this man (case III) ; the more intense you witnessed in the boy M.

The alterations in the urine are of the utmost importance. In the early stage it is reduced in quantity, may be only a few ounces, or the secretion may even be suppressed. The *colour* is increased, usually dark red, from admixture with blood ; very

commonly it has a *smoky, lake colour*, very characteristic of the presence of blood, and which resembles a dilute solution of reduced hæmoglobin. The various shades of intensity of this you have had an opportunity of seeing in case III. The blood may disappear and then recur, as it did in cases I and II. The *specific gravity* is increased at first, 1020 to 1030, owing to the relatively small amount of water. When the quantity rises to normal, the specific gravity is, as a rule, lowered. On standing, a copious sediment usually falls, reddish or reddish-brown in colour, and consisting of blood and urates. Chemically, the most striking change is in the presence of *albumen* when you heat the urine in a test tube, or add cold nitric acid. So much may be present that the urine solidifies, and 50 to 60% by bulk is not uncommon. The *urea* is diminished in amount. In case III, the estimates made by Messrs. Renner and Gooding with Dupré's apparatus give: 28th, 46 ozs. 287 grs.; 29th, 70 ozs. 403 grs.; 30th, 65 ozs. 250 grs.; 2nd, 68 ozs. 228 grs.; 3rd, 63 ozs. 257 grs.: 4th, 56 ozs. 247 grs.

The normal amount for the 24 hours is between 400 and 500 grs., and an approach to this or an excess is a happy indication. A material reduction is to be feared, as uræmia is apt to follow.

Tube casts furnish important evidence in this disease, and their recognition is one of the earliest lessons which you should learn in clinical microscopy. Their characters have been well marked in this man (Case III.) When first examined a few well-formed *blood casts* were seen; cylinders or moulds of the tubules made up of blood corpuscles imbedded in an indifferent matrix. *Hyaline* or *faintly granular* have been the most abundant forms, very delicate and translucent, so that the inexperienced among you have had difficulty in seeing them; and thirdly, *epithelial casts*, not very numerous, but commonly consisting of a hyaline cylinder, with a few granular cells imbedded in it. I called the attention of some of you to a form of cast, consisting almost entirely of rounded cells, like colourless blood-corpuscles—leucocytes; this, Dr. George Johnson believes, is a variety met with when a glomerulo-nephritis is present.

The varied course of the disease is well illustrated by the first

two cases, one of which went from bad to worse, while the other rapidly improved. The first six months in the majority of instances concludes the case one way or the other. Not that recovery is impossible after this date, but it is more uncertain, and the possibility is great of permanent damage to the organs and of the establishment of chronic parenchymatous nephritis. The favourable signs are diminution and disappearance of the dropsy, increase in the amount of urine, with reduction in albumen and maintenance of normal urea excretion. In the most rapid cases three or four weeks at least are necessary before the condition of the urine becomes normal. I have known the albumen to disappear, while the tube casts continued. Circumstances which warrant unfavourable prognosis are long duration, persistence of the albumen in large amount, material reduction in urea and the onset of symptoms of uræmia, some of which are sudden and rapidly fatal.

What are the indications for treatment? Mild cases would probably recover, indeed, have done so, left to nature. Case III received no special treatment for four days, and improved during this time. The rest in bed, recumbency and the quiet do much, but there are few cases which do not call for active interference. In the early stages, where the congestion of the organs is marked, the urine reduced in amount and bloody and the lumbar pain present, dry cupping the loins and warm fomentations do much good, acting as derivatives. You know on general principles that the first thing to be done with an acutely inflamed organ or part, is to give it, if possible, functional rest. With the kidneys this is impracticable, but we can relieve and assist them in various ways. A spare diet and rest diminish the amount of solid materials to be excreted. Purgatives and diaphoretics call to aid the bowels and skin, which supplement the action of the kidneys, and, as it were, help them in a friendly way when they are disabled. In the early stages and in mild cases, there is no necessity for severe purgation. Keep them loose by a daily dose of Glauber's Salts (Soda Sulph. ʒss), and perhaps an occasional Jalap purge (Pulv. Jalapæ co. ʒss). In the more chronic cases, where the dropsy is great and uræmia threatening, hydra-

gogue cathartics will be of great service. Of diaphoretics, the one in common use and most efficacious is *jaborandi*, or its active principle, *pilocarpin;* of the former may be given ♏x of the Fl. Ext. every two hours until copious sweating is induced; of the latter a hypodermic injection of ⅛ to ¼ gr. But of all measures at our disposal to produce sweating, the *hot air bath* is, in my experience, the best, the easiest employed, and has the additional advantage of being in many instances a diuretic, so that after a most copious sweating the amount of urine for the 12 or 16 hours subsequent may be actually increased. On our return to the ward we shall give our patient B. such a bath that you may see the ease with which it is applied. Some of you may remember two sessions ago the case of a little girl in the children's ward with acute renal dropsy, and how admirably the air baths acted with her without any medication. The *warm baths* are much used in some hospitals, but they are inconvenient. The *wet pack*, wrapping in a wet sheet and rolling in blankets is unpleasant for the patient, and has no special advantage. What about diuretics? In the early stage, with active congestion and bloody urine; no, but later they may be advantageously employed, and good fresh water may be taken freely and often answers the purpose. It is of importance to keep up the amount of urine for two reasons: first, the larger the quantity the more solid matter will be removed; and, second, the *tubuli uriniferi* are thereby flushed (Dickenson), the *débris* washed out, and *choking* of the renal drains is in this way prevented. If a special diuretic is indicated, the Inf. Digitalis, as used in cases I and II, may be given. The diet should be light and nutritious; not much meat. Milk is much used in these cases, and the diet may be restricted to it as in case I.

Nos. III. and IV.

PNEUMONIA.*

GENTLEMEN.—The commoner diseases which you study in the wards often do not attract the attention which they deserve. Students too frequently look out for the rare, less common, but to them more interesting, forms of disease, to the neglect of those which they are more liable to meet with in private practice, and of those which it is important for them to know thoroughly and accurately. Among affections which it is of paramount importance for you to thoroughly know, pneumonia perhaps heads the list. There is no acute affection of the same importance so often met within this country. So frequent is it, that from 5 to 6 per cent. of fatal cases of disease are attributable to this cause. In this hospital you have opportunities of studying it in all its varieties. The four cases which you have been following in ward 11 shall serve as my text for the next two lectures, and I will first read to you brief notes.

CASE I.†—Louis Phillippe, æt. 58, labourer, admitted April 13th with cough and pain in the side. Chill five days before admission. Temperature 101°F.; pulse 106; respirations 26. Expectoration not bloody. Physical signs of pneumonia over right lower mammary, infra-axillary, scapular, and infra-scapular regions. During the first ten days in Hospital patient made no satisfactory progress; temperature ranged from 99° to 103°; he was heavy and dull, not delirious; pulse weak, 100 to 120. Ordered whiskey 3 x and supporting diet, with Liq. Am. Acet. and Ammon. Carb. On 23rd, defective resonance in infra-clavicular regions on right side; in mammary region, a flat tympanitic note. Behind, absolute dulness, feeble blow-

* Stenographical report by James Crankshaw, Esq., B.C L.
† Reported by H. J. Harrison, B.A.

ing breathing; a few râles on deep inspiration. On the 29th, the note over right mammary was markedly tympanitic. Patient emaciating. No heart murmur; very little expectoration, muco-purulent, not bloody. On the 9th he had a chill, and the temperature went up to 104°. No change in physical signs. Died at mid-day on the 10th.

Autopsy showed uniform solidification of right lung, grey in colour; a few purulent depôts, and several areas of commencing fibroid change.

Case II.*—W. R., æt. 43, admitted April 13th; said to have had pneumonia for ten days. History of a distinct chill, followed by fever, cough and pain in the right side. When admitted was quite delirious. Temperature 104°F.; pulse 92; respirations 36. Physical signs confined to right lung; dulness as low as angle of scapula and extending round in axillary and mammary regions. Feeble-blowing breathing and râles; a loud friction above angle of scapula. Cough slight, no expectoration. He was at once put on brandy, and had ʒss doses of Potas. Bromid. until quieter. We learnt that this man, some months ago, had been attended by Dr. Kennedy for trouble at right apex, from which he appeared to have recovered. Up to the 20th he continued delirious and very noisy at night. Temperature not high, 99° to 102°. Has been on whiskey 12 ozs. and Ammon. Carb. grs. v. every six hours, and the Potas. Bromid., with Chloral, when needful. Expectoration purulent. On 22nd, physical signs not much changed; dulness marked in infra-scapular area. On 28th, very slight fever; cough troublesome; expectoration purulent and more profuse, a little fœtid, occasionally streaked with blood. Note is clearer behind; râles still numerous.

On the 4th the note reads: Still a little delirious at times. Temperature 101°. Lung has cleared somewhat in front; there is a loud creaking-sound friction above the nipple. Heart sounds very distinct on this side; behind, still dull in upper regions. To-day (12th) he is much better; no fever; appetite improving; cough less frequent; expectoration muco-purulent, and the lung is clearing.

* Reported by Mr. C. B. H. Hanvey.

CASE III.*—J. W. C., æt. 20, admitted April 24th with consolidation of the greater part of the left lung. Has been a healthy young man. Sixteen days before admission, was taken with pain in chest and shortness of breath, and was in bed a week. Some doubt as to the nature of this attack. Went out on the 18th, but next day had to go to bed, where he has been ever since, with fever and cough. He had no chill. On examination, very slight movement of left chest; tender on pressure about left nipple, and he feels pain here on drawing a full breath. Tactile fremitus *is less marked* on this side. Percussion gives a flat note from level of 3rd rib in front and over the left back, except supra-scapular region. Blowing breathing over the dull areas, with a few fine râles. Vocal fremitus *increased*. Expectoration tenacious, muco-purulent, a little rusty. Temperature 102°; respirations 64; pulse 108. Ordered poultices to the chest, and Liq. Ammon. Acetat. 3ss every three hours. On the 26th, temperature 101°; respirations 48; pulse 104; feels much better. 29th—Has continued to improve; temperature 98°; pulse 92; respirations 28. Note is clearer in front; no change behind. Tactile fremitus *continues weak* on this side compared with the opposite. Takes food well. Since this date he has done well, and is now (12th) without fever, and the lung is clearing rapidly.

CASE IV.†—M. B., æt. 35, admitted May 8th. Has been a healthy man, and looks of good constitution. Four days ago was at work and well. On the night of the 4th was awakened by a severe darting pain in the right side; felt feverish; had no chill; but in the morning felt very ill, and began to cough and get short of breath. These symptoms have continued. When admitted, temperature 103°; pulse 104; respirations 29. Face flushed. On inspection, chest well formed; expansion greatest on left side. Palpation gives increased tactile fremitus over the right lung. Percussion on right side clear in front as low as nipple; below this, and extending into the infra-axillary and

* Reported by Mr. C. J. B. Hanvey.

† Report by Mr. H. J. Harrisson, B.A.

infra-scapular areas, there is a flat, tympanitic note. Auscultation over these parts gives blowing-breathing, with fine râles on inspiration; vocal fremitus much increased. Ordered Liq. Am. Acetat. and light nourishing diet; no poultices. To-day (12th) temperature is 98°; pulse 76; respirations 22. Sputum very tenacious and rusty, is expectorated with difficulty. He has done well, and in a few days will be convalescent.

Now, the first question to ask with reference to pneumonia is, what is it? A local inflammation? or, a specific, essential fever? Is it simply a local trouble in the lung, and the constitutional disturbance, the fever, caused by that? or, is it a specific fever, like typhoid, of which the local lesion is the special expression; just as the lesion in typhoid fever is the special expression of a constitutional disorder? The opinion is gaining ground in the profession, particularly on this continent and in Germany, that it is in reality a specific essential fever. Among the grounds which are supposed to favour this are its occasional occurrence in epidemic form. Epidemics of pneumonia have been recorded in the last century, and even in previous centuries; and a recent epidemic has been reported in Germany. The lesion cannot be produced experimentally. You cannot get ordinary pneumonia by any methods of experimentation. You can get a catarrhal affection but fibrinous or croupous pneumonia cannot be produced by local irritation, or causing animals to inhale hot air or other such methods. The remarkably uniform course, and the absence of any positive relationship between the extent of lesion and the constitutional symptoms also point in this direction. Cohnheim and some other German writers class it with the miasmatic contagious affections. For good articles bearing on this question let me refer you to Dr. Sanders' papers in Seguin's Archiv. for June and August of last year.

With reference to the *etiology* of the disease, the most important points are as follows: It is an affection which attacks all ages—from infants to persons in advanced life. The majority of cases occur, however, in the middle periods of life, and males are more frequently affected than females. Of 353 cases of

pneumonia within ten years in this hospital, 265 were males and 88 females. Of 60 autopsies of which I have records, only two were in children under 2 years old. The great majority were in adults from the ages of 25 to 45. Though healthy, robust persons are affected, it is specially prone to attack debilitated individuals in a community, and persons already affected with some disease. Season would appear to have a great influence on this affection. The months in which we have the largest number of cases are March, April and May. Next are the autumn months, or rather the early winter months, November and December. During the full winter time, January and February, the cases are not so numerous, though they are more numerous than in the summer months, the time when such cases are fewest in number. These are facts based on the 353 cases of pneumonia admitted into the hospital, as contained in the statistical report of Dr. Bell.* It varies in different years. We have not as many this year as last year; and last year we had not as many as the year before. You will notice from this that it would not appear to be in the coldest months that we get the greatest number of cases of pneumonia, but in those months in which the variations of temperature are marked.

Next, as to the *morbid anatomy* of the affection. The term *lobar* is frequently applied to this form of disease in contradistinction to lobular. In this form of pneumonia the rule is for either a considerable portion of a lobe, an entire lobe, or the whole lung to be involved in the disease. You rarely find a pneumonia less in extent than the area of the palm of the hand. The lower lobes of the lung are more frequently involved than the upper lobes. The right lung is more frequently involved than the left. In the 60 autopsies to which I have referred, 40 occurred in the right lung and 20 in the left. An exception to the rule, which states that it is most frequent in the lower lobes, is the pneumonia of old people and of drunkards. In these it most frequently involves the upper portion of the lung; hence the

* Montreal General Hospital Reports, Vol. I, 1880.

term apex pneumonia. And this variety sometimes presents special clinical features, which are of great importance.

The stages of the disease are as follows. They are usually spoken of as four in number:

(1) The stage of *engorgement.*
(2) The stage of *red hepatisation.*
(3) The stage of *grey hepatisation.*
(4) The stage of *resolution.*

We rarely have opportunities of seeing a lung in the stage of *engorgement;* but we can sometimes gather what the condition is from a death which takes place early in the disease. A very favourable instance for the observation of this occurred a few years ago, owing to an unfortunate accident by which a patient took two drachms of solid morphia instead of two drachms of the Liquor Morphiæ. This patient died in the course of 12 or 14 hours, and at the autopsy we found that there was a commencing pneumonia in the lower lobe of the right lung. This part was heavy, feebly crepitant, contained much blood, and portions excised from the superficial part floated, but in the central portion in four or five isolated areas, about the size of marbles, the lung was firm, and had the usual appearance of red hepatisation, and no doubt represented the commencement of solidification; if he had lived another 24 hours, he would doubtless have had uniform hepatisation of the lung. In the stage of *red hepatization*, the characters of the lung are exceedingly well marked. We have had three autopsies this week on cases of pneumonia; and I have reserved for this lecture two specimens, showing the condition of the lung in the second stage. On inspection, the first thing you notice is that the surface of the pleura over the affected part has lost its glistening appearance; it is turbid and lustreless, or, as you see in the second specimen here, it is covered with a distinct layer of lymph. Now, my experience is that this superficial pleuritis is a constant feature in pneumonia; so soon as the inflammation reaches the pulmonary surface, it of necessity involves the pleura. You may have, as you see in this first lung, only turbidity of the pleural surface. You may have, as you see here, in this second one, a thin sheeting of fibrin;

but you also may have a layer of fibrinous exudation from half an inch to an inch and a quarter in thickness. I have one specimen which shews general hepatization of the lung, and a uniform sheeting of exudation over an inch in thickness, extending from apex to base. Secondly, the lung in red hepatization does not collapse; it is full in volume. Third, to the touch it is firm and nowhere crepitant. There is a solidity about it resembling one of the solid organs, as the liver—hence the appropriateness of the term hepatization. Indeed, with the eyes closed you could not tell by touch a portion of liver from a portion of hepatized lung. It has lost the crepitant feel of healthy lung. On section, the appearance is the following:—The surface is of a uniform reddish hue the color varying very much; in the early stage a bright red, in the later stages a dusky red, as you see here in this specimen. Not much fluid bathes the section. On close inspection, you can see that the surface presents numerous small fine granules, which are very characteristic of this stage of the disease, and which consist of fibrinous plugs filling the air-cells. Usually they are not of the same intense red as the alveolar walls, and can be seen in contrast to the portions about them, though in the early stage these fibrinous plugs may be just as red as the surrounding parts. The lung is friable—breaks very easily. This is in marked contrast to healthy lung. Try to tear a portion of healthy lung; it is done with great difficulty, and you cannot easily put your finger into it; but with a bit of pneumonic lung you can put your finger in with the greatest ease, and it breaks with an irregular fracture. The bronchi, more particularly the smaller ones, often contain fibrinous plugs, the consistence of which varies much, some being simply muco-purulent, others being distinctly fibrinous and firm. The pulmonary vessels are occasionally thrombosed.

In the third stage of the disease the picture is considerably modified, more particularly as regards the colour of the lung, which is changed from a reddish to a greyish yellow or greyish-white. The section is no longer dry, but a considerable quantity of purulent matter bathes the surface, or can be squeezed from it, and this matter looks just like as if it came from a fresh abscess.

In this portion of the lung of the second specimen, you see it passing to the stage of grey hepatisation; and you see here, on the knife, the purulent substance, which can be scraped from it. This grey colour is due to two causes. In the first place, there is much less blood in the lung, owing to compression of the alveolar walls by an increase of the contained cell elements; and secondly, the colouring matter of the blood-corpuscles exuded into the air-cells in the stage of red hepatisation undergoes changes and gradually becomes dissolved. In this portion you see that grey hepatisation is in the early stage. There is not much infiltration of the lung. In the late stage of grey hepatisation you may have the lung so infiltrated with pus that the term *purulent infiltration* has been well applied to it. It looks saturated with or soaked in pus. There is the same friability about the grey hepatisation as about the red, and the changes of the bronchi and pleura remain the same.

Before speaking of the stage of resolution, it will be better to speak of the histology of the process, and the following, briefly, are the chief facts known with reference to it. In the stage of engorgement the blood-vessels are distended, particularly the capillaries of the alveoli; the epithelium of the air-cells is more granular; and some describe a nuclear proliferation, an increase in the cells. In the second stage—red hepatisation—there is an exudation from the blood-vessels into the air-cells consisting of fibrine, red blood corpuscles and colourless blood corpuscles, and mixed with these are the products of proliferation of the epithelium of the air-cells. The fibrine coagulates, and the cells are entangled in its meshes, as you see in this plate taken from Delafield's "Pathological Studies." The number of red-blood corpuscles within the air-cells is very considerable, as you will see in the specimens I will shew you afterwards with the microscope. In the stage of grey hepatisation, the chief change is an enormous increase in the number of leucocytes. Each air-cell appears to be distended with a plug composed of closely-packed colourless elements. The fibrine fibres are much less distinct, and the red-blood cells are no longer to be discovered. In many of the cells fatty degeneration can be seen, particularly in the

larger ones, which results from epithelial proliferation. These changes are well shewn in this plate from Dr. Delafield's work. The tissues of the air-cells undergo little or no change, with the exception of the epithelial lining. With regard to the stage of *resolution*—the terminal stage of pneumonia—that in which the lung is restored to the normal condition, we still lack satisfactory evidence of the precise nature of these changes. The elements within the air-cells undergo fatty degeneration. This we can see in the ordinary gray hepatisation. This is, in reality, the essential change. By this the cells are dissolved, liquified, and the emulsified matter is either absorbed or it is thrown out in the expectoration. It takes some time for a lung to undergo complete resolution, several weeks in all probability, and usually, when a patient leaves the hospital, and is apparently quite well, you will, on careful observation, ascertain some slight changes in the affected region of the lung.

A word with reference to the amount of solid exudation which may occur into the lung in pneumonia. This may sometimes amount to several pounds. One lung—the healthy lung—may weigh a pound or a pound and a quarter, and the other lung may weigh three or four pounds. There may be 2½ to 3 pounds of solid exudation in the lung affected. In the 60 cases of pneumonia referred to, the heaviest lungs that I met with were two, one of which weighed over 2,300 grammes, and the other 2,200.

Unfortunately, the termination by resolution is not the only one which may go on in pneumonia. The following changes may occur, though they are rarely met with: In the first place, in the stage of gray hepatisation there may be the formation of *an abscess*. The purulent infiltration may be so intense, may infiltrate the parenchyma of the lung to such a degree, that in certain localized areas the tissue breaks, with the result of forming small pockets of pus. Now, this is an exceedingly rare termination. In these 60 cases, only three presented small abscesses which were formed in this way. Cases 32 and 35 both presented small purulent foci. In one of them, two of the pockets were as large as walnuts, and in the other they were the

size of marbles. This unfortunate termination in pneumonia is most frequent in old or debilitated people.

Gangrene is a second and still more untoward event. In this set of autopsies there were two cases in which a fatal termination was induced by gangrene. One of these many of you had an opportunity of seeing last year under the care of Dr. Ross. During the winter session a patient was admitted with pneumonia, a very debilitated woman, and death occurred within a week from gangrene. There was a gangrenous mass at the upper part of the lower lobe, and the remainder of the lung was in the condition of red hepatisation This may come on in the stage of red hepatisation, and may be due simply to the intensity of the inflammation, but more commonly, it is thought, to the blocking of the pulmonary arteries.

Whether the exudation of lobar pneumonia in a healthy man ever undergoes *caseation* or transformation into cheesy matter, is still much disputed. Niemeyer and several other German writers think it may. Professor Buhl, of Munich, holds that in any case in which a caseous degeneration is discovered *post-mortem*, though there may be no doubt about the caseous nature of the change, there is much doubt of accuracy of diagnosis. In only one instance in the past six years have I met with a case that appeared to justify a belief in the transformation of the inflammatory products of lobar pneumonia into these cheesy substances. The case is recorded in my first pathological report.

The last and rarest of all the modes of termination of lobar pneumonia is the non-resolution of the exudation, the persistence of the process, and the gradual onset of fibroid change in the lung (chronic or interstitial pneumonia.) Now, in the case of the man Phillippe, who was under our examination here for nearly three weeks, and who died the day before yesterday, this change was beginning. His right lung, as you see here, was uniformly solid, greyish in color, with recent pleuritic exudation, and the surface, on section, bathed with serous fluid. On carefully inspecting the cut section, three features call for attention. In the first place, in certain regions you can still see the air-cells with their fibrinous plugs, of a very

opaque white consolidation undergoing fatty change. These are to be seen over considerable areas. Secondly, there are small pockets of pus, localized areas densely infiltrated with pus, and breaking down into definite abcesses. The largest of these is about the size of a marble. And thirdly, in several areas of the lung there are spots which have a very translucent aspect, are firm, smooth, homogeneous, not granular, and have the look of a recent connective tissue. These are spots of special interest to us, because in these areas a *fibroid* change is going on in the lung; and, as you will see in the specimen under the microscope, the alveolar walls are infiltrated with fibrous elements, and actually the fibrinous plugs themselves filling the air-cells are represented by and transformed into a new growth of connective tissue. This is an exceedingly rare method of termination. It is the first good instance of the kind I have ever met with.

A few words with respect to associated morbid conditions. The condition of the heart in autopsies on pneumonia is very characteristic, so much so that anyone with tolerably large experience can make a shrewd guess at a case of pneumonia from the condition of the chambers of the heart. They are usually found distended with firm clots, so firm that they can be withdrawn from the blood vessels; and, as you saw in the cases this week, the clots could be withdrawn from the pulmonary artery to its finest ramifications. There is no disease in which you meet with fibrinous clots of the same degree of firmness and extending the same length into the veins. The excess of fibrine in the blood in this disease accounts for the exceeding firmness of these clots.

It is very rare to meet with other morbid conditions in pneumonia. We usually find the organs healthy, except the slight changes associated with high fever, if of long standing, the turbidity of the various organs. The state of the spleen is of some interest, particularly as to the point whether pneumonia is a local disease or a general essential fever. Professor Fredreich, of Heidelberg, calls attention in one of his lectures to the fact that the spleen is usually much enlarged in pneumonia.

In very many of the autopsies that I have performed, the spleen has been enlarged; but in fully half of the cases the organ has been of normal size. The kidneys rarely show any important change, though, as I will tell you in the next lecture, the state of the kidneys influence the prospects of an individual affected with pneumonia. In a very considerable number of the cases, chronic atrophic changes are met with in the kidneys. Dr. Bristowe called attention to croupous *colitis*, a sort of dysentry in this affection. He met with it sixteen times out of some 48 cases, a very considerable proportion. In these 60 cases of ours, it has only occurred on five occasions, and there was one instance of croupous or diphtheritic gastritis. Ulcerative endocarditis is a complication of which we had a considerable number of cases. Out of the twelve instances of this disease which we have had in this Hospital in the past few years, seven have occurred in connection with pneumonia.* Meningitis is a complication of which we have also met with a considerable number of cases. In the 60 autopsies there were five cases of meningitis, and four of these were associated with endocarditis.

Symptoms.—The affection is usually ushered in with a distinct rigor. There is no disease which so constantly begins with a single severe chill. Following this—in fact, during it—the patient becomes feverish, and usually complains, too, of pain in the side. The next symptoms in order are cough and shortness of breath; and with these the patient usually comes under your observation. He has had a rigor, is feverish, and has pain in the side, with shortness of breath and a cough. These are the prominent features that you meet with in cases when you examine them first, as you saw in that woman whom we have just left in ward 24. The flushed face, the quick and short respirations, with dilating *alæ nasi*—so striking are these features in many instances, that you can at once recognize a case when you enter the ward.

To analyse these symptoms a little more closely; the shortness of breath is due to several distinct causes. In the first place,

* *Vide* papers in Seguin's Archiv., 1881, and Transactions of the International Medical Congress, London, 1881.

the fever. There is increased need of oxygen, and, consequently, the respiratory movements have to be increased in number. We see the importance of this factor in the dyspnœa, when the fever leaves at the crisis; though there may be no change in the amount of *consolidation*, yet the respirations will sink from 45 or 50 to nearly normal. Another cause of the dyspnœa is the amount of solid exudation in the lung—the breathing-space is very considerably diminished. And thirdly, there is usually enough pain in the side to prevent the patient taking a long breath. These are the three chief reasons for the increased respiratory movements in pneumonia. The fever range is extremely characteristic; it reaches its height suddenly, and is maintained throughout the course of the disease with only slight variations, the evening temperature being, as a rule, higher than the morning, but the variations are not extreme. The temperature may reach from 104° to 106°, but it is more common, as in the cases you have been watching in ward 11, for the temperature not to rise above 103 or 104. The most striking feature about the temperature is the sudden fall at what is called the crisis of the disease, which usually happens upon the fifth, seventh or ninth day. In this the temperature suddenly drops perhaps as much as 7 degrees. You visit your patient in the evening; you find him sitting up, the respiration 50, the pulse 130. You leave him, feeling not a little anxious as to his condition. The next morning you find him lying comfortably in bed; respiration, 24, the pulse 85 or 90, and the temperature normal or even subnormal. The crisis has taken place, and you are at once relieved of anxiety as regards the patient. There is no other disease that we know of in which the transition from extreme danger to comparative security takes place with such rapidity. In neither of the cases we have studying has the termination by crisis taken place in the typical manner. The temperature did not fall with that abruptness seen in the typical cases. There were one or two drops or jumps before the normal temperature was reached. The *cough* in pneumonia is characteristic. It is short, hacking, and, as it were, restrained. The patients do not like to cough, because it hurts them, and

they constantly appear to suppress it, owing to the pain. The expectoration in the early stage is exceedingly viscid, small in amount, and of a rusty colour, being admixed with a certain amount of blood. This viscidity is one of its marked features. So glutinous is it that you can turn the spittoon over and it will not run out. In the latter stages it becomes more fluid: the rusty colour is less marked, and, it may be, more muco-purulent. The expectoration is never very profuse. You rarely find the expectoration of 24 hours amount to half a pint. In none of the above cases has the expectoration been excessive. In debilitated persons the expectoration may be more liquid, and of a prune-juice colour. In old persons there may be very little expectoration. The *pulse* at the outset is full and bounding, ranging from 110 to 130. The heart acts forcibly; the arteries are well filled. As the disease advances, the pulse gets weaker, and requires watching with great care. Increased rapidity, with feebleness or intermission, should at once attract your attention, as the treatment hinges largely on the condition of the circulatory system, as is well expressed by an old maxim, "*sine pulsu nulla therapeia.*" The urine is usually high-coloured; the urea is increased, the chlorides are diminished. Nitrate of silver gives no reaction; albumen is occasionally present. A symptom which requires special comment is delirium. As I have told you on several occasions, delirium in pneumonia may occur under the following circumstances:—In the first place, from the intensity of the fever, just as in any acute febrile affection an individual may be delirious at the outset. Secondly, in debilitated individuals, and particularly when the apices of the lungs are involved. In these cases it may be a low delirium, or it may amount to a heavy stupor, with occasional mutterings. This form is particularly seen in what are called asthenic cases, where the patient is much debilitated, and in pneumonia attacking aged and enfeebled persons. Thirdly, the most important perhaps is the delirium accompanying the pneumonia in individuals who are accustomed to take largely of alcoholic liquors. Yesterday you had an illustration of this. A young man was taken ill on Friday; he had a chill, and has since been

suffering with the usual symptoms of pneumonia. We found him in the ward restrained by the nurse and an attendant. The cheeks were flushed; but what attracted attention at once was the restless eye of the patient, and his anxiety to get out of bed and get away. He was actively delirious, and the delirium was of the character resembling *delirium tremens*. As you saw, he was picking at the bed clothes, and when I went at first to the bed-side he was talking to an imaginary person on the other side of the bed. This feature is of extreme importance for you to bear in mind, because you may overlook the essential character of the disease. You may treat your case as one of *delirium tremens*, when in reality it is pneumonia, complicated with peculiar delirium. I remember an instance of an individual who was confined in a strait jacket, and believed to have *delirium tremens*. There were no special lung symptoms. A few days after we had an autopsy, and it was found that he had extensive apex pneumonia. In the majority of these cases the apex of the lung is affected, as in the young man you saw yesterday. Occasionally the delirium is exceedingly violent. A few weeks ago I performed an autopsy for Dr. Rodger at Point St. Charles on a man who was furiously delirious for three or four days during the disease. He required several strong men to hold him in his bed, and he died simply exhausted from the violence of his efforts.

The stage of resolution may be supposed to come on with the crisis. In this the patient is tolerably comfortable,—does not complain of much except perhaps a little weakness, and you often have difficulty in keeping him in bed, as you remember in the young lad (Case III.)

With reference to the physical signs, I may briefly state the following:—In the first place, on inspection you notice that the affected side does not move as much as the opposite one; the intercostal spaces are not bulged, nor is the side as a rule enlarged, the latter being distinctions between pneumonia and pleurisy. The apex beat is not displaced. Palpation gives an increase in the tactile fremitus; the voice sounds are communicated to the fingers through the solidified lung very much more readily than through the air-containing lung of the opposite side.

Percussion in the early stage, when the engorgement is just passing into red hepatisation, gives, over the affected area, a tympanitic note, which may be of very varied degrees of intensity, from a full tympanitic, such as you heard over the chest of that man Phillippe, to a flat tympanitic note that may require an educated ear to recognize the tympanitic quality. But usually in following a case of pneumonia from its inception to the close, you meet with this tympanitic quality of the note more or less marked. In the full hepatisation, if it reaches the surface of the lung, you then get an absolutely flat or dull note, and you feel an increased sense of resistance on percussion. The flatness is usually not so *wooden* as in cases of extensive pleuritic effusion.

In the first stage, and as the engorgement is passing on to hepatisation, you have what is called the pneumonic crepitus; at the end of inspiration you hear a series of extremely fine dry crepitant râles. They are the finest and the dryest râles you listen to in the chest, and may be compared to the sound made by the crackling of salt when burning, or to the rubbing between the fingers of a bunch of hair. When the lung is fully hepatised, the breathing becomes distinctly bronchial or tubular in character, similar to the sound you hear in the bronchi at the sterno-clavicular joints or adjoining the vertebræ in the interscapular regions. You must remember that this bronchial sound is simply the normal sound which the air makes passing in and out of the bronchi, but which, in the case of a healthy lung, is not transmitted to our ears with the same intensity as in a solidified lung, because in the latter the air-cells are filled up with exudation, and transmit the sound much better. You will not always have this evidence—bronchial or tubular breathing—in cases of pneumonia; in many instances it is weak, and has a feeble, tubular character as resolution proceeds. In the *later* stages you then begin to have râles which are moister and much more abundant, and accompany both inspiration and expiration. These persist for a very considerable period of time. As resolution proceeds, the dulness usually diminishes; and as you were able to follow in that case of the lad (case III), certain areas of

the lung cleared up entirely, and you got a full resonant note. It is not at all uncommon, as in his case, for the base of the lung to remain slightly dull for a long time; that dulness may be due to diminished resonance in the lung, or to a thick layer of pleuritic exudation in that region. The heart sounds present no special changes further than that the second sound at the pulmonary cartilage is increased in intensity.

The *prognosis* in the disease is usually good; but it depends much upon the class of individuals you have to treat. Thus the prognosis in cases admitted into this hospital is not as good as in the cases outside among the better classes. The mortality here is exceptionally high, in some years over 20 per cent. A large number of the cases die within 48 hours of their admission. In the 170 cases of pneumonia treated by Dr. Howard during 20 years, the mortality was between 5 and 6 per cent. In some 40 consecutive cases which I have had in the past three years, most of them in this hospital, there have been but three deaths. Among the circumstances that influence the prognosis are: 1st, Age. As you may suppose elderly individuals do not resist the fever as well as young, healthy persons. 2nd, The habits of the individual. Drunkards and persons debilitated from any cause are exceedingly bad subjects to take pneumonia, and it usually in them early assumes an asthenic type. That is one reason why our mortality is so high. We get sent in here chiefly the lower classes and debilitated individuals; and very many of the cases of pneumonia are in persons in the habit of taking a considerable amount of alcohol. 3rd, Existing disease is an important factor. In persons who receive an injury—as a broken leg—and then take pneumonia, the disease is more liable to run an unfavourable course than an healthy person. *Intercurrent* pneumonia, as it is called, is always more serious than an attack in a healthy person. Of all affections that would seem to have a bad influence in pneumonia, chronic renal trouble comes, I believe, first. In looking over the records of *post-mortems*, some 60 in number, I was surprised to find in how many the kidneys were stated to be extra firm or roughened, or the capsule did not remove readily—facts pointing to chronic

atrophic changes in the organs. Dr. Goodhart of Guy's Hospital has called attention to this fact.

We now come to the important subject of the *treatment* of pneumonia, and the lessons you may learn from this should constitute your "principia" in therapeutics. The *first is* that there is an inherent tendency in many diseases to recovery quite irrespective of any treatment. In a remarkable work by that remarkable man, the late Jacob Bigelow of Boston, entitled "Nature in Disease," he lays down the proposition that most affections are *self-limited*. His words are as follows: "By a self-limited disease I would be understood to express one which receives limits from its own nature and not from foreign influences, and which, after it has obtained a good hold on the system, cannot, in the present state of our knowledge, be eradicated or abridged by art, but to which there is due a certain succession of processes to be completed after a certain time, which time and processes may vary with the constitution and condition of the patient, and may tend to death or recovery, but are not known to be shortened or greatly changed by medical treatment."

Pneumonia is a strictly self-limited disease—in fact, the most strikingly so of any with which we are acquainted. We cannot cut it short, the cases run a definite course.

The *second* lesson is that nature, in the majority of cases, is quite competent to restore the patient to health. The natural therapeutics, as Professor Harvey of Aberdeen calls the *vis medicatrix naturæ*, in contradistinction to applied therapeutics, are capable in 80 per cent of cases of dealing with the disease. As Professor Guebler puts it, "L'organisme se guerit lui même." Cases III and IV received no special treatment beyond a little Liq. Ammon. Acet., and they both made satisfactory recoveries.

Let me advise you, before worshiping at any special therapeutic shrine, to pay your vows to Nature, taking the motto of Edmund in Lear, "Thou, Nature, art my goddess, to thy law my services are bound."

The *third* lesson is that the functions of the physician are to co-operate with Nature, to aid her where she fails, and, above

all, to combat certain tendencies to a fatal issue, which tendencies are due either to an inherent or acquired viciousness of constitution, or the intensity of the inflammation. And here arises the importance of an accurate knowledge of the natural history of any disease in order that we may recognize early fatal tendencies and be on our guard against impending danger.

Now, let us apply these principles to the treatment of pneumonia. In the first place, as I have just stated, the majority of cases do perfectly well when left to themselves. It is a self-limited disease, and though for the sake of the patient, and still more for the sake of friends, you may have to give a "placebo," the treatment is outside of your own hands; it is in the hands of Nature. You may give what you like, and you may flatter yourself that you are curing the disease, but the percentage of mortality has been shown to be just as light on the expectant method.

What are the fatal tendencies in cases of pneumonia? for on the answer of this hinges the whole question of treatment.

In the first place, exhaustion by the fever. Fever, when long continued, or when high, is always dangerous; and to reduce the fever is one of the first indications for treatment. When not above 103° or 103½°, I do not think it calls for any special treatment; but where it is above 104° or 105°, as in the case of that woman you saw a few minutes ago, you should use antipyretic remedies, choosing the ones you think best. If you were in Germany, where physicians and patients are accustomed to the system, you would give the patient a bath; but we have never been able to introduce the cold water treatment here. The antipyretic remedy which I have most faith in is quinine. The fever in that woman you saw before the lecture was 105°; she has been given 25 grains of quinine, and I shall be disappointed if in a few hours the temperature is not down to 101° or 102°. In my experience there is no better remedy for reducing temperature than large single doses of quinine. We have had numerous proofs of it, and where you have a remedy, the adoption of which has been *tried*, grapple it to your therapeutic soul with hooks of steel.

Secondly, failure of the heart. Most cases of pneumonia, when they come to the *post-mortem* table, present distended heart chambers, full of dark clots. The condition of the unaffected part of the lungs varies very much. In some instances the areas are in a state of intense œdema; in other instances, as in one case last week, they are as dry as a bit of leather: no blood, no serum. Now, the heart is embarrassed in pneumonia; first, because there is obstruction in the pulmonary circulation. In a large area of the hepatised lung, the amount of blood entering and passing through is trivial compared with the amount which is passed through in health. The consequence is that the right heart is overworked; it has more work to do; it is distended, and has to increase the force of the systole to overcome the increased tension in the pulmonary system. In the next place, the effect of shutting off a considerable area of the pulmonary system is to increase the blood pressure in the healthy parts. Now, that increase in the blood pressure may be accompanied in certain instances by great dangers. The blood vessels may relieve themselves by exudation of serum, and you may have a collateral œdema of the other portions of the lung. Some regard this as a great bug-bear in pneumonia, but looking over my reports of *post-mortem* cases of pneumonia it struck me as not a little remarkable in how many was the healthy part of the lung neither congested nor œdematous. This state of collateral œdema is doubtless important in some instances, though not as much so as some think it. Another effect of the impeded flow of blood through the lungs is that the left ventricle receives a less supply of blood than normal. Therefore, the coronary arteries are less fully filled, and the nutrition of the heart is not kept up to its standard. Then, again, in addition to these sources of embarrassment of the heart, you have the influence of fever on the heart muscles. When fever lasts for any time, there is muscular weakness. The action of fever produces degeneration and weakness of the muscles; and some observers hold that the cardiac weakness in pneumonia is largely due to the fever. In nine out of ten serious cases of pneumonia, the tendency to death is at the heart.

Now, how is that to be counteracted? In the first place, through stimulants. If I had my choice to treat the next 50 cases of pneumonia which will fall under my care, with all the remedies of the pharmacopœia at my disposal without alcohol, or with alcohol alone, I would say, Let me have the alcohol. I have seen in this disease better effects from this medicine than from any other with which I am acquainted. Juergenson, in his article on pneumonia, fully expresses my opinion as to the efficacy of alcohol in this disease, when he says that, "It is not only the whip to the horse, but the oats as well." When you find your patient's pulse fail, when it begins to flicker; if it runs up and gets weak, begin your stimulants at once. Do not wait; you cannot do any harm by giving a few ounces of whiskey in a day, even early in the disease, more particularly if your patient is of debilitated habit. In the cases III and IV, the patients were pretty healthy individuals, both with moderate attacks of the disease, and they did not need it; but in the cases I and III, alcohol was given freely and early. So, pin your faith, if to nothing else, to alcohol, in pneumonia. Of other cardiac stimulants which may be used in certain instances with great benefit, I would next mention camphor. Three and four grain-doses of camphor in the form of emulsion, or spirits of camphor in 25 to 30 drop doses, have, in some instances, an astonishing effect. Musk, in ½ to 2 grain-doses, may also be given, and I have seen benefit from it.

Shall we bleed in pneumonia? This is an important question. And if we should bleed, when? Now I would say this at the outset, that the man who never bleeds in pneumonia will, if his experience is large, certainly lose, in the course of his experience, several cases that he would have saved if he carried a lancet in his pocket and used it; whereas the man who will carry and systematically use the lancet in pneumonia will lose many patients that he otherwise might have saved. The chief indications for the use of a lancet are when, in a strong, full-blooded individual, the right heart is seriously embarrassed, over-distended, when there is intense dyspnœa, and when there are signs of the beginning of pulmonary œdema. Some of

you may remember, two years ago, the case of a man in ward 11, whose life, I believe, was saved by timely venesection to xxv ℥. The relief vas something remarkable. The only other condition, I believe, in which you can bleed with satisfaction is in the early stage where you have a full, vigorous man, without any vice of constitution. Twenty ounces of blood is neither here nor there in such a man, and it will reduce his pain and fever. The chief fatal tendency, then, to death is from the heart. Of course, individuals may die from exhaustion, particularly if resolution does not take place, as in case IV ; but in the majority of fatal cases of pneumonia they die of cardiac failure. Shall we give arterial sedatives—digitalis, aconite, veratrum viride, and the like? Except at the onset, and in vigorous persons, they are not indicated. Antimony I never use. Local treatment to the chest is often advantageous. We use poultices very much in this hospital, and they are soothing to the pain and grateful to the patient. I never use cold, though I have seen it applied with apparent advantage in German hospitals.

What shall we do if resolution does not take place normally? And how long can a lung remain solid without damage? The rule is for resolution to begin after the crisis, and in a week or ten days the lung is pretty clear ; but there are many instances in which no crisis takes place, the lung remains solid, a slight fever keeps up, and the patient may cause you mental disquietude. You may fear the breaking of the lung and the formation of abscesses, but even if resolution be delayed to the seventh or eighth week, it may ultimately follow and the lung be completely restored. I reported* one case which was delayed to the fifth and another to the eighth week, and then the lung in both cleared up satisfactorily, and the patients made good recoveries.

I will just supplement my remarks on pneumonia of debilitated individuals and drunkards by shewing you this specimen, obtained yesterday from a patient of Dr. Wilkins, a feeble old man. I do not know his habits ; he came in delirious, and after a few days died with extensive pneumonia of the right apex of

* *Canada Lancet*, December, 1880.

the lung. You see here the whole of the upper lobe, with the middle lobe, uniformly solid. It weighs over 2,000 grammes. There is a pleuritic exudation over the surface. On section, you see that it is of a reddish-grey colour. I show you this to impress upon you the lesson you should have learned from the case you saw in the wards yesterday, as it is somewhat similar to it, and on account of the fatal issue of so many of these cases.

No. V.

LEUCOCYTHEMIA.*

GENTLEMEN,—There are certain diseases which affect principally the blood and the organs of the hæmato-poietic system. Of these the principal are :—

1. *Anæmia.*
2. *Chlorosis.*
3. *Leucocythemia ;* and
4. *Lymphadenoma*, or *Hodgkins' Disease.*

These are characcrized by profound alterations in the constitution of the blood, and certain of them are accompanied by definite changes in those organs of the body which we regard as the blood-making ones. The form of anæmia which particularly belongs to this class is that known as *pernicious* or *essential.*

Of the affections characterized by an alteration in the structure and appearance of certain of the blood-forming organs, the most important are *leucocythemia* and *Hodgkins' disease.* In these affections, either the spleen alone, the lymphatic glands alone, or the spleen with the lymphatic glands are affected. In the former we have, in addition to the changes in the spleen

* Stenographical report by James Crankshaw, Esq., B.C.L.

and lymphatic glands, a special alteration in the blood, characterized by a great increase in the colourless elements. Hence the term, Leucocythemia, or Leukæmia. In Hodgkins' disease there is no such increase in the number of colourless corpuscles, though the characters of the changes in the organs may be identical; hence the term Pseudo-Leukæmia is sometimes applied to it. I have here to-day, owing to the kindness of Dr. Lapthorn Smith and of the patient himself, an exceedingly interesting case illustrating a disease met with but rarely in this country, and yet one which it is very important for you to know accurately and well. The history of this case is as follows:

— Vervais, æt. 39, has been a healthy man. Has been a moulder, but for the past eight years kept an hotel. Always lived in Montreal. Never had ague. Mother died at age of 80; father dead of an accident. Got hurt 17 years ago in the left side; strained while lifting. Ill now for 13 months; began with swelling of hands and legs, which continued for five or six months; then the belly began to swell. Had pain in belly, and noticed a swelling in left side. Occasional vomiting in morning. Never passed blood in stools, or vomited it. No palpitation at heart. I saw him about New Year's in consultation with Drs. Hingston and Trenholme, and we found great œdema, with ascites and enlargement of the spleen. Since that time he has been under the care of several physicians. The chief symptoms have continued to be: dropsy, for which he has been tapped three times, weakness, and shortness of breath on exertion. Within the past month the patient has improved, and I see a great change for the better in him.

We will now examine the patient and ascertain the symptoms he presents. The first thing you notice is that he has an enlarged abdomen, with slight dropsy of the feet and legs; this is not nearly as much as it was when I saw him last. His face does not present a specially cachectic appearance. He is looking now much better than a month ago, but has not got quite so good a healthy look as when I saw him first about the New Year. The breathing is, you notice, a little short. The pulse is about 108. On examination we find the following: The abdomen is

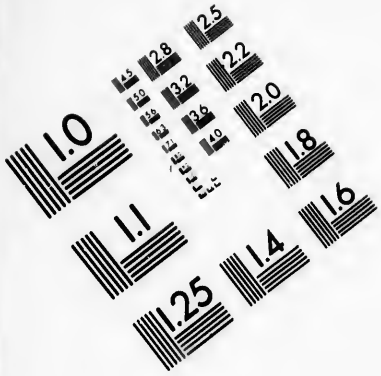
uniformly distended, not more on one side than the other, and measures about 45 inches. A few large veins are seen, but they are by no means prominent. On palpation, the abdominal walls yield; they are not tense; there is no increased sense of resistance until the fingers reach the left side of the abdomen. You then feel a distinct solid mass. It is firm, hard, and reaches below the level of the crest of the ilium. There is a definite edge, and at about the level of the navel and at a distance of three inches to the left you feel a distinct notch at this edge. This resistant mass can be felt well into the left hypochondriac region, and far back into the left lumbar region. On percussion there is a dull note, while over the greater portion of the abdomen, a flat, tympanitic note is obtained. In the umbilical and the hypogastric region there is a distinct wave which can be seen and felt on percussing one side of the abdomen. So that we find here a large collection of fluid in the abdomen, and evidences of a tumour in the left side. The liver cannot be felt below the ribs; its upper limit of dulness is half an inch below the nipple. The chest is well formed. The apex beat is in the fourth interspace, and just within the nipple line. On auscultation, a soft, systolic murmur is heard. The lungs appear normal. The lymph glands are not enlarged.

Now what we have found here, gentlemen, is simply dropsy of the abdomen, with œdema of the legs, and a tumour on the left side of the abdomen. The questions are, first, what is the nature of this enlargement on the left side? What is the cause of the dropsy? and of the tumour here in this region? You would think at once of an enlarged spleen or kidney. When I saw this patient with Dr. Hingston and Dr. Trenholme, the doubt was whether it was renal or splenic. It is so far back in the lumbar region; it is not very moveable; and it was thought that perhaps it might be an enlarged kidney. But, on the other hand, against that are the facts that the border can be felt very distinctly; a notch is evident; and on percussing and palpating towards the left hypochondriac region, it is found that this mass emerges from below the ribs on the left side; the dull line extends nearly to the level of the nipple. From its position, the

distinct feel of the edge of the notch, and the way it emerges from the left hypochondrium, there is no doubt about its being an enlarged spleen.

As to the cause of that enlargement, you have, in the first place, to think of chronic malaria; then, in the second place, of simple splenic enlargement not induced by malaria, but, by causes unknown to us, accompanied by anæmia, and sometimes called splenic anæmia; and, thirdly, whether this is the enlarged spleen of leucocythemia. Now, the only possible way in which you can decide between these conditions is by examination of the blood with the microscope. It is impossible for you to make an accurate diagnosis unless you proceed to this. You can say now, so far as we have got, that it is a case of enlargement of the spleen, with dropsy, but that is all until you examine his blood. If you examine this, and find that there is simply a decrease in the number of red-blood corpuscles, you will call it a case of splenic anæmia, whether dependent on malaria or not; but if you examine it, and find the number of white corpuscles greatly increased, so that the ratio is one white corpuscle to twenty, or less, red-blood corpuscles, you will call it a case of leucocythemia. In this instance the blood has been examined, and we find that the ratio is about one white-blood corpuscle to eight red ones. There is very great leukæmia. The examination of the blood decides the question of the nature of the affection, namely, that it is a case of splenic leukæmia. We find also that, in addition to the disproportion of the white and red blood corpuscles, the latter are greatly diminished in number. There is also marked anæmia.

Of the causation or etiology of the disease we have almost everything to learn. It occurs most frequently in individuals of middle period of life, though it is met with not unfrequently in children. The youngest case I have known is that of an infant eight months old, a case of Dr. Howard's. It affects males more frequently than females. Of circumstances which have been stated to influence it, in some respect, malaria is one which by many is thought to have an important influence. I have lately been going over a large number of leukæmia records,



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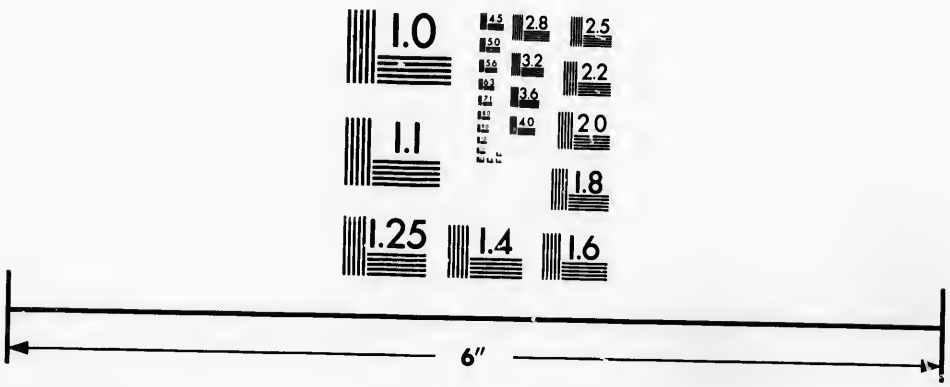

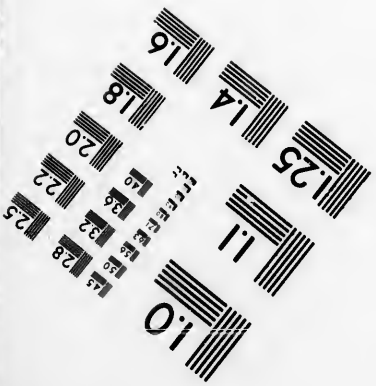

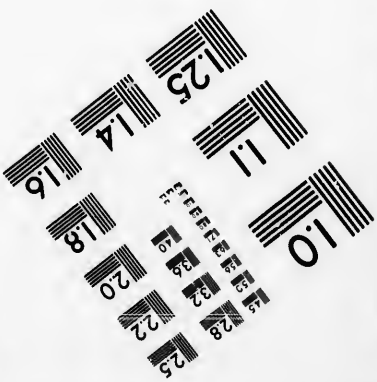

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particularly of American cases, and I have been surprised to find how few were the cases in which any definite connection with malaria could be ascertained. We know very little, indeed, of the circumstances which induce this affection. Of the morbid anatomy, in the splenic form the spleen is chiefly involved, and it forms a large *cake*, as it is called. The size of the tumour may range from a couple of pounds to 16 or 17 pounds. Some of the largest abdominal tumours are of this splenic variety. This one, from a patient who died under the care of the late Dr. John Bell, is the largest specimen we have in our museum; it weighed 7 pounds when it was fresh. Here is a second, not so large, and a third, larger in proportion than the others, as it was taken from an infant eight months old. The organ in this affection is large and hard. It is in a condition of what is called chronic hyperplasia. It cuts with difficulty; the section is uniform and the trabeculæ of the gland are unusually distinct. On examination with the microscope, we find that the change is chiefly in the network of adenoid tissue of the gland, which is greatly increased; and between the little meshes are the spleen corpuscles. In a large number of cases the lymphatic glands are also enlarged, more particularly the lymphatic glands in the neck and in the axillia, less frequently in the groins and in the internal glands. The enlargement in the lymphatic glands is simply hyperplasia. They are enlarged and firm, but otherwise look natural. In addition, in a very considerable number of cases of leukæmia, there are definite growths of lymphoid tissues in organs in which we do not usually see such growths. Thus, for instance, in the liver you may have definite tumours, whitish in appearance, varying in size from a walnut to a hen's egg, composed entirely of new growth of lymphoid tissue. These may also occur in the lungs. The glandular elements in the small intestines are sometimes enlarged. The tissue of the bone-marrow has attracted attention in this disease. It is converted into a reddish, soft, pulpy material very much resembling spleen pulp. It is believed to play a very active part in the production of many of the features of the disease Neuman, Mosler and others speak of a myelogenous form of leukæmia,

induced by changes in the bone-marrow. These are the chief changes in the organs and parts of the body. In *post-mortems* the condition of the blood is often found most remarkable, owing to the increase of the white corpuscles. The blood, when clotted, may present a greyish-red appearance, or in clots where the corpuscles have separated from the liquor sanguinis, before coagulation has taken place, you may have the auricle of the heart filled with a substance looking like pure pus. In the first case reported in Canada (by Dr. John Bell), when we opened the right auricle of the heart, Dr. Bell exclaimed in precisely the same terms as are related to have been used by one of Virchow's assistants in a similar case, "Why, we have an abscess of the heart," so puriform did the clots look that filled the right chambers.

With reference to the symptoms of the disease, the first that attracts attention is usually a sense of fullness and uneasiness in the left hypochondriac region, or in the upper zone of the abdomen. Accompanying this there is usually failing health. The patient becomes languid, the appetite is impaired, and they notice that they are paler than usual. Dropsy of the legs soon succeeds. In the patient you have just seen, dropsy of the legs and of the hands appear to have been his first symptom; and throughout the case it has been the chief trouble. The condition of the blood on examination is, of course, one of the essential symptoms of the affection.

The following are the characters by which you may know leukæmic blood: In the first place, when you prick the finger, you find that, instead of the deep purplish-red drop of the normal blood, the colour is changed to a chocolate brown colour, or even, when the leukæmia is very intense, a greyish-red colour. In this patient the colour is not so marked as one might expect from the number of white-blood corpuscles; but the colour, you must bear in mind, does not depend so much on the increase of the white-blood corpuscles as the decrease of the red-blood corpuscles. In a case where the anæmia is very profound, and the number of red corpuscles much decreased, you find the blood almost of a chocolate colour. On examination

with the microscope, the colourless corpuscles are greatly increased in number. Instead of seeing two or three white-blood corpuscles in the field of a No. 7 Hartnack, you may find as many as 60 or 70. In fact, one usually supposes, on first examination of leukæmic blood, that the white-blood corpuscles greatly exceed the red in number. It is rather a hazardous thing to estimate, without accurate measuremnt, the proportion of white-blood corpuscles to the red. The red-blood corpuscles are always more numerous than they appear, for the reason that they collect together in clumps. You do not see how many there are owing to formation of rouleaux; whereas the white corpuscles remain isolated, and so they look much more numerous. Secondly, the colourless corpuscles frequently present great variations in size. You will notice this in the slide of blood which I have here for examination. Some are much larger than normal; others are smaller. In cases in which the lymphatic glands are greatly involved—lymphatic leukæmia—there is a much larger proportion of small white corpuscles. Thirdly, the red-blood corpuscles usually present a somewhat paler appearance than usual; occasionally there are great discrepancies in size and irregularity in the outline. Fourthly, you may have, added to the blood, an element not seen in health, namely, nucleated red-blood corpuscles which exist normally in the bone-marrow. These occur not unfrequently in leukæmic patients. In the last case I had they were remarkably abundant. In one instance, in the field of a No. 9, I counted ten nucleated blood corpuscles. I never before saw them so abundant. Lastly, Schultze's granule-masses are, in certain cases, very numerous. These characters you will see in the specimen of blood which I have taken from this patient.

Among other symptoms in connection with leukæmia, *hemorrhages* take a prominent place. In some instances hemorrhages occur very freely, and may be the very first symptoms which a patient complains of. In one of Dr. Howard's series of cases (Montreal General Hospital Reports, Vol. I), vomiting of blood was the first serious symptom that the lad had. In another instance, which I believe to have been a case of leukæmia, the

girl died of the most profuse hæmatemesis. She appeared, prior to this attack, to be in fair health. We found at the autopsy a marked increase in the colourless blood corpuscles. The hemorrhage may occur early in the disease, or as a late symptom, and is a grave omen There is usually vomiting; it may be due simply to the pressure of the large spleen on the stomach. In one case of Dr. Howard's, the vomiting was a persistent symptom throughout. Diarrhœa is occasionally met with. Most of these patients are febrile. There is a slight evening elevation of temperature. This patient has not had much fever. I have taken his temperature several times. The dropsy in this man has been marked. This may, in great part, be anæmic, depending upon the condition of his blood. The marked dropsy of the belly is doubtless due to interference with the portal circulation. Perhaps he has enlarged glands in the gastro-hepatic omentum, which would account for the dropsy in this case. But bear in mind that enlargement of the spleen alone, without any pressure on the portal vein, may account for the dropsy in the belly. This patient has a heart murmur, anæmic in character.

The pathology of the affection is still, unhappily, very obscure, largely depending upon the fact that our knowledge of the growth and development of the corpuscles is still wanting in so many particulars. It is only natural to suppose that the condition of the blood and of the blood-making organs should be intimately associated.

The treatment of this disease is highly unsatisfactory. It is a hopelessly incurable affection. The patient usually goes from bad to worse. Two years sees the termination. There are occasional intermissions of the symptoms, periods during which the patient improves a good deal. It is one of these intermissions that the patient you have just seen is in. It may be, of course, due to the remedies; but these intermissions are known to occur without being influenced by the medicines. Excision of the spleen was the remedy proposed many years ago; it was carried out in some 18 or 20 cases without any success. The patients either died on the table or shortly afterwards. The chief remedies which have been used have been directed either

towards reducing the size of the spleen or improving the general condition of the patient's health. Among the remedies used to reduce the size of the spleen have been electricity, which has proved very serviceable in reducing the size of the organ. Quinine, also, and ergot, given internally or injected into the substance of the organ, have been used. Of the medicines used to improve the general condition of the patient and the blood-making powers, iron, arsenic and phosphorus are the ones commonly employed. This patient was on arsenic for some time, and also, I believe, on phosphorus. He is now on iron, and attributes largely his improvement to the large doses of iron he has been obtaining. Tranfusion has been practiced in some cases, in the hope, perhaps, of giving the patient a better blood; but this has proved futile. In a patient—as in this one whom you saw here—with extensive dropsy, you have to relieve the distressing symptoms by tapping. This man has been tapped four or five times.

There is one symptom that I did not refer to, namely, the condition of the retina. This comes in under the symptom of hemorrhage. Many of these cases have a form of retinitis which consists of hemorrhages into the substance of the retina. This man's retinæ are normal. The patient has been sent to one of the wards. We will go in, and some of you will have an opportunity of examining him. These cases rarely occur in the hospital. There has been only one in the past ten years; and I am sure we are much indebted to Dr. Smith for allowing his patient to come up here, and giving us an opportunity of seeing him.

XLIX

CESTODE TUBERCULOSIS.

A SUCCESSFUL EXPERIMENT IN PRODUCING IT IN THE CALF.

By PROFESSOR OSLER, M.D, McGill University, and A. W CLEMENT, of Lawrence, Mass., student in the Montreal Veterinary College.

(Reprint from the AMERICAN VETERINARY REVIEW, April, 1882.)

It is a curious fact, and one that requires further study and explanation, that while the Tænia Saginata is the common tape worm of this country, its larvæ, the measles of beef, are very seldom met with. On the other hand, while T. Solium is by no means so prevalent, yet its larvæ, the measles of pork, are not at all infrequent. Cobbold* refers to this, and states that "not a single instance has been recorded of the occurence of these cystic parasites in the United Kingdom, except in our experimental animals." Of course much more fresh beef and veal is consumed than fresh pork, and the former is, as a rule, less thoroughly cooked, and it may be, as we shall state hereafter, that measly veal is not as readily detected as measly pork. The prevalence of tape worm is directly dependent upon the efficiency with which the meat inspector and the cook perform their duties. No infected carcass should escape the one, and a measly steak or a fillet of veal from the kitchen of the other, could be eaten with impunity.

Experimental proof of the relation between the beef cysticercus and T. Saginata was offered by Leuckhart, who, in 1861, successfully reared the measles by feeding a calf with ripe segments. Mosler, Gurn and Zenker, in Germany, St. Cyr., in France, Perroncito, in Italy, and Cobbold and Simonds in England, have repeated the ex-

*Parasites, 1879.

periment, in most instances with a positive result. So far as could be ascertained, no experiments of the kind have been made in America.

In order to procure specimens of measly veal, and to afford the students of the veterinary college an opportunity of studying a case of cestode tuberculosis, we fed a calf with fifty ripe segments of a tape worm, believed, from the characters of the segments, to be the T. Saginata.

The animal, a female calf, aged three days, weighing seventy-five pounds, was fed, November 22d, at the veterinary college. The temperature after the feeding was 103–4°. The animal was kept under observation for seven weeks, and a daily record kept of the chief symptoms, which briefly summarized, were as follows: During the first week no special change was observed; the animal fed well and seemed lively. With the exception of the observation made just after the feeding, the temperature did not rise above 102–5°. The pulse range was from 112 to 130. The fœces were soft, one day mixed with a quantity of gelatinous material. No segments were observed, but microscopical examination on the third day after feeding determined the presence of numerous ova. In the second week the animal did not appear so well. On December 2d the temperature rose to 104–6°. The pulse kept over 100, of moderate volume. On one day the animal seemed stiff in the limbs and disinclined to move about, but next morning was as lively as before. The fœces kept tolerably consistent; no ova were found on subsequent examinations. During the third week there were no special symptoms to attract attention; the food was taken very well, and superficial observation would have judged the calf to be healthy. The temperature kept up over 103° and on two days above 104°. The pulse decreased in rapidity, sinking below 100, the range being from 86 to 95. In the fourth week the temperature was above 104° on five days, and the pulse was a little quickened. There were no intestinal symptoms; muscles not stiff, and beyond a slight weakness, the animal did not appear very ill. During the fifth and sixth weeks the *status, quo* was maintained; temperature, between 103° and 104°; pulse about 90. During part of the Christmas vacation the daily record was not kept. In the seventh week no special change; food was taken well and the animal was active. It had got thinner, but this may have been owing to an insufficient supply of nourishment. On January 12th, fifty-one days after the feeding, the animal was killed,

as it was thought that the *cysticeri* had sufficiently developed. *Post-Mortem.*—Body somewhat wasted; *panniculus* adiposus thin. The general lymph glands were much swollen. Apart from the presence of the measles, nothing abnormal was found, so that the record may be limited to an account of their distribution. In the *abdomen* they were numerous in the omentum and in the fatty capsules of the kidneys. The liver was almost free; only two were found. Each kidney contained six or eight. In the thorax, none; in pleura, a dozen or more in each lung; in the heart, tolerably numerous, particularly in the right ventricles. They were very evident beneath both peri and endo-cardium. The voluntary muscles were, as usual, the favorite locality, and presented a moderately abundant infection. The diaphragm did not contain very many. The tongue was in places thickly studded, and they could be easily seen beneath the mucous membrane; of the skeletal muscles those of the thorax and back were most affected, and every muscle contained several examples.

As regards their obvious characters, the cysts were ovoid, with semi-translucent appearance, and usually a central opaque spot. They varied in length from three to six mm. The cysts were tightly embraced by the intercellular tissue in which they lay, but a little careful tearing was sufficient to disengage them. Microscopical examination showed the larvæ to be in an advanced stage of development: in the majority the head, with its disks, was well formed; some were immature, and the head imperfectly developed.

The experiment was as successful as could be wished, and we have procured a supply of measly veal.

Among points of interest in connection with the case, the symptoms take the first place, as the clinical history of the affection has not been carefully studied in many instances.

The severity of the symptoms in any case of cestode tuberculosis will depend upon the number of ova ingested and the number of larvæ which penetrate from the intestines to the system at large. The more numerous, the greater the constitutional trouble. If only a moderate number of ova are ingested, the animal may not display any special symptoms. In Leuckhart's original experiment, the calf, three weeks old, received scarcely fifty ripe segments, but death followed on the twenty-fifth day, apparently caused by the eruption of the cysticerci throughout the body. In one of the calves of the Cobbold-Simonds series, over four hundred ripe segments were given during two months,

yet the animal did not appear seriously ill. But when killed, it was estimated that over twelve millions of cysticerci were in the organs and flesh. In the present instance, the constitutional disturbance was slight and the fever moderate, and there was no special affection of the muscular system. The normal temperature of the calf is about 103°, so that there was no fever until the second week, when the temperature ranged to nearly 105°; slight pyrexia kept up through the third, fourth and fifth weeks, and it was the persistence of this which led us to suppose that the animal had become infected. There was no sudden rise of temperature, such as might be supposed to occur at the period of migration of the proscolices. In Zurn's case, *which is the only one we can find witha carefully recorded clinical history, the temperature range was much higher, and the general disturbance very great, death occurring on the twentieth day. In our animal the more severe course might have been expected from the large number of ripe segments administered; but, perhaps the passage of many of the eggs in the fæces may have had something to do with the mildness of the attack.

How does it happen that the T. Saginata is so prevalent, when its "measle" is so scarce? Several causes bring this about. In the first place, the beef "measle" is smaller than that of the pork, and is not so opaque; in consequence, it is more readily overlooked; we are sure that any meat-inspector, unless specially instructed, would have *passed* the flesh of our experimental calf. The larvæ did not at once catch the eye in the red flesh, as in the case of *cysticercus cellulosæ*, but required to be looked for, though five to six mm. in length. Secondly, it is not improbable that many of the animals from which the infected meat is obtained are not extensively diseased, but present only one or two examples, easily overlooked in dressing the carcass. Calves and oxen are much less likely than pigs to get an entire strobile of a tape worm, or even many segments. And, thirdly, a very much greater quantity of beef and veal is consumed in a fresh state than pork, and the former meats are not, as a rule, so thoroughly cooked. It is quite common to see joints on the table, the central parts of which have not been raised to a temperature sufficient to kill the larvæ.

*Die Parasiten des Menschen Kuchenmeister und zum 2te Auflage 1881.

[Reprinted from THE MEDICAL NEWS, July 29, 1882.]

A CLINICAL LECTURE ON EMPYEMA AND ITS ANTISEPTIC TREATMENT.[1]

Delivered at the Montreal General Hospital, June 24th,

BY

WILLIAM OSLER, M.D., M.R.C.P. LOND.,

PROFESSOR OF THE INSTITUTES OF MEDICINE, MCGILL UNIVERSITY.

GENTLEMEN: I wish to speak to you to-day on the subject of empyema and its treatment by the antiseptic method. You saw yesterday a case which was operated upon in this way, and I will first read to you the clinical report.

Mary S., aged twenty-seven, was admitted June 6th. Is unmarried, a servant. Nothing special in the family history. She has been a healthy girl. Four weeks ago she had chills and pain in the left side; no cough or expectoration. She was attended by Dr. McCallum, who diagnosed pleurisy, and on Thursday, June 1st, drew off with the aspirator three pints of turbid, greenish yellow fluid; the patient was relieved by this tapping, but on the 6th the temperature had risen; she was not so well, and she was recommended to come to the hospital. On admission she was noted to be pale, fairly well nourished, cheeks flushed, temperature 103°. On examination of the chest, the left side did not expand as much as the right. The intercostal spaces were not so distinct, the tactile fremitus was absent. Apex beat to the right of the sternum. On percussion there was dulness over

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the whole lung, except in the infra-clavicular region. The two sides were of equal size. She complained of a good deal of pain, and the skin was hyperæsthetic. On auscultation, the breathing was exceedingly weak and distant. The evening temperature on the 7th, 8th, and 9th, reached nearly 102°. On the 12th, she was again aspirated and fifty-one ounces of pus removed; she got considerable relief from this. The respirations were reduced from about forty to twenty-four in the minute, and the temperature remained at about 99° in the morning, reaching 100° in the evening. On the 20th, the temperature went up to 103.5°; on the 21st and 22d, it remained at about 102°. She did not seem so well, and we then determined to make a free opening in the chest and treat the case antiseptically. The operation was performed by Dr. Fenwick in the following way. He made an incision in the eighth intercostal space on the left side, on the outer margin of the infra-scapular region, just at the junction of this with the infra-axillary region. He then opened the pleural cavity and put in a silver canula, which was devised several years ago by Dr. Roddick, after repeated trials, for special use in cases of empyema. The canula, which is slightly curved, has the following dimensions: orifice is oval, three-quarters by one-half an inch; a wide flange surrounds it, two and a half by one and a half inches, and provided with eyelets for tapes. The tube is bevelled at its inner end, and measures about two inches in length, and has twelve small perforations. A shorter tube was found to slip out. In cases in which it has been used, this one has given great satisfaction, as it allows of very free drainage from the pleural cavity, and being solid prevents the pressure of granulations and secures a space of constant size through which the pus can exude. As you saw, the most careful antiseptic precautions were taken. About thirty-two ounces of pure pus were removed. It was dressed antiseptically. The cavity was not injected and the layers of antiseptic gauze, soaked in 1 to 40 carbolic acid, were placed directly over the tube, tow was placed outside this, and the side then bandaged. The rule is to repeat the dressing as soon as the discharges get to the edge. Dr. Duncan, last night, dressed the case again, as the discharges had saturated the tow and gauze; and it was dressed

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CASE I.—The first case I had treated in this way was a delicate looking lad, aged 16, who was admitted June 13, 1880, with empyema of left side; all the physical signs well marked. He had been ill four or five weeks, and the chest had been aspirated once by Dr. Ross; the fever was irregular; pulse weak; respirations much accelerated; profuse sweating. The tube was inserted on the day of admission and about four pints of pus removed. This lad was in a very critical condition, very weak and debilitated, and we had grave fears as to the result; however, he did remarkably well. The chest was dressed whenever the discharges reached the edge of the dressing. For some weeks he remained feeble, the temperature going up occasionally as high as 103°. After about a month he began to improve, the discharge got less, and the side of the chest began to fall in. After a treatment of about two months he was materially better, discharge very slight, and on the 27th of September he was discharged perfectly cured and in very good condition, having increased considerably in weight. We had removed the tube some weeks before he left the hospital. I saw him a couple of months afterwards and exhibited him to the Medico-Chirurgical Society; he had then gained forty or fifty pounds in flesh, and had returned to work. There was a slight contraction of the left side of the chest, but he had made a satisfactory recovery.

CASE II. was under our care during last summer session. This was a French lad, aged 20, who was also sent in by Dr. Ross. He had empyema of the left side. It had lasted for several weeks, and he had been tapped once and a quantity of pus drawn off. When he came to the hospital, he had irregular fever and sweating and considerable constitutional disturbance.

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CASE III. was also under observation last summer—a man named Clarke, aged about forty-three. He was in the hospital for a couple of weeks with pleural effusion on the right side. There was irregular fever, and we suspected that the fluid was probably purulent. On using the hypodermic needle, we found that there was pus, and he was treated in the way I have already described. The pus was drawn off, and antiseptic dressings were applied every day or every second day, according to the amount of the discharge. This man was admitted April 19 and discharged July 4, perfectly well, having been seventy-five days in hospital. The tube had been removed several weeks before he left the hospital, and at the time of his discharge the breath sounds were audible at the angle of the scapula. He had improved in general health, and he went back to his work. I saw him several months afterwards, and he had kept well.

These three cases of empyema stand out very distinctly in my memory, inasmuch as they are among the few instances in which I have seen good recoveries in this disease. It is always regarded as an exceedingly serious thing for a person to have pus in the pleural cavity. The liability to constitutional disturbance, the difficulty of getting the suppurating pleural membranes to granulate and heal, are well known, and render this disease extremely difficult to treat satisfactorily. Under the antiseptic plan I believe many of these difficulties are obviated. In these cases the temperature after operation, particularly in the man Clarke and in the second case, remained normal, and it would seem that

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As you are aware, in this woman we aspirated the chest first; and the rule is in a case of empyema to draw off the fluid with the aspirator at least once. A few cases do well with a single aspiration, and in children this is almost the rule. But in adults, unfortunately, the case usually goes from bad to worse, unless a very free opening is made. In these four cases the intercostal spaces have been of sufficient size to admit the tube. In some instances the space is not large enough, and you may have to resect a portion of a rib, in order to get plenty of room.

And now a few general remarks on the disease. In some cases the fluid appears to be purulent almost from the outset. In the case of this woman, the fluid, when first drawn off, was turbid, of a cream-yellow color, and probably became purulent shortly after its formation. Of course, the ordinary sero-fibrinous fluid of a pleurisy contains numerous leucocytes, and the conversion of such a simple effusion into a purulent one is a matter of multiplication of these. Purulent fluid is simply the serum densely infiltrated with the leucocytes. In debilitated persons the fluid is much more apt to become purulent than in the strong and healthy. There is but one invariable and sure means of ascertaining whether the fluid is pus or not, and one that is easily applied. Take your hypodermic needle, and thrust it into the chest, and draw off some of it. A simple enough method, but one which is not often enough resorted to. There are numerous practitioners throughout the country who never think of using the hypodermic needle except for purposes of medication, whereas it is of almost as much importance in diagnosis. In cases of pleural effusion, or of doubtful dulness, in the posterior part of the chest, you need never hesitate to thrust the hypodermic needle into the regions affected. It is so simple an operation that it does no harm, while the indications you get from it are of the greatest value.

Professor Bacelli, of Rome, described a few years ago a new sign by which to distinguish between simple and purulent effusions. I tried it in the case of the woman, but it was not very satisfactory. It is as follows: The affected side of the chest is auscultated, and

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the patient turns the head to the opposite side and whispers. If the fluid is serous, the voice sounds are conveyed to the ear; if it is a purulent fluid, the whispered sounds are not so conveyed. In some instances this method proves useful, and in some it does not. In one case, particularly, it proved to be correct.

Another point worth noting is that, in cases of simple effusion, the patients usually lie on the affected side; whereas, in cases of purulent effusion—why it is I do not know, but it has been specially noted by Dr. Churton, of Leeds, and I have observed it myself—they usually lie on the opposite side.

What becomes of the effusion if it is not removed? It may be absorbed. Adhesions form between the pleura in certain parts, and you may have multilocular empyema, which may be cured naturally, though it will be a struggle and tax the vitality of the patient. It may perforate into the lung to be discharged through the bronchial tubes, which I think is a very favorable way. The cases we have had in this hospital of perforation into the lung and discharge have done exceedingly well. Dr. Ross has had two such cases which recovered perfectly. Dr. Wilkins has a case at present, I believe, in the wards, in which the pus perforated the lung and was discharged by coughing. It may also perforate the diaphragm, but that is rare. It may perforate externally (empyema necessitatis) and discharge for months or leave a permanent pleural fistula. A point to be borne in mind, in cases of left-sided empyema, when they begin to pass towards the surface, is that they sometimes pulsate, and the pulsation is exceedingly likely to be confounded with that of an aneurism. In the chronic cases the patients have irregular fever, and the prolonged discharge is likely to induce either amyloid disease of the organs, or else the sound lung on the other side becomes affected and they get tuberculous.

The effects of a large pleural effusion, whether purulent or not, upon the lung are very well seen in this specimen, which was taken from a case of empyema, in which the patient died of acute pneumonia of the opposite lung. You see here that the lung is flattened to a cake-like mass, pressed back against the side of the vertebral column.

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Among the advantages of the antiseptic method in empyema appear to be:

(1.) Ample provision is made for free and continuous drainage.

(2.) The avoidance of putrefaction; in none of the cases were the discharges in the slightest degree offensive.

(3.) The ease with which the operation is performed and the small amount of trouble entailed in the subsequent dressings.

(4.) The healing is more rapid, and serious consequences, as amyloid disease and phthisis, are less likely to follow.

Note.—July 11. The patient operated upon on the 4th. Has done remarkably well. Temperature normal, except on one evening; dressings changed now every third day; discharge very slight.

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*Die Parasiten des Menschen Kuchenmeister und zum 2te Auflage 1881.

the patient turns the head to the opposite side and whispers. If the fluid is serous, the voice sounds are conveyed to the ear; if it is a purulent fluid, the whispered sounds are not so conveyed. In some instances this method proves useful, and in some it does not. In one case, particularly, it proved to be correct.

Another point worth noting is that, in cases of simple effusion, the patients usually lie on the affected side; whereas, in cases of purulent effusion—why it is I do not know, but it has been specially noted by Dr. Churton, of Leeds, and I have observed it myself—they usually lie on the opposite side.

What becomes of the effusion if it is not removed? It may be absorbed. Adhesions form between the pleura in certain parts, and you may have multilocular empyema, which may be cured naturally, though it will be a struggle and tax the vitality of the patient. It may perforate into the lung to be discharged through the bronchial tubes, which I think is a very favorable way. The cases we have had in this hospital of perforation into the lung and discharge have done exceedingly well. Dr. Ross has had two such cases which recovered perfectly. Dr. Wilkins has a case at present, I believe, in the wards, in which the pus perforated the lung and was discharged by coughing. It may also perforate the diaphragm, but that is rare. It may perforate externally (empyema necessitatis) and discharge for months or leave a permanent pleural fistula. A point to be borne in mind, in cases of left-sided empyema, when they begin to pass towards the surface, is that they sometimes pulsate, and the pulsation is exceedingly likely to be confounded with that of an aneurism. In the chronic cases the patients have irregular fever, and the prolonged discharge is likely to induce either amyloid disease of the organs, or else the sound lung on the other side becomes affected and they get tuberculous.

The effects of a large pleural effusion, whether purulent or not, upon the lung are very well seen in this specimen, which was taken from a case of empyema, in which the patient died of acute pneumonia of the opposite lung. You see here that the lung is flattened to a cake-like mass, pressed back against the side of the vertebral column.

When seen at the mid-day visit was quieter, but did not answer questions intelligently. Face flushed, venules on cheeks and nose dilated. Pupils slightly contracted, react to light; ophthalmo-

Reprinted from the ARCHIVES OF MEDICINE, Vol. vii, No. 2, April, 1882.

Among the advantages of the antiseptic method in empyema appear to be:

(1.) Ample provision is made for free and continuous drainage.

(2.) The avoidance of putrefaction; in none of the cases were the discharges in the slightest degree offensive.

(3.) The ease with which the operation is performed and the small amount of trouble entailed in the subsequent dressings.

(4.) The healing is more rapid, and serious consequences, as amyloid disease and phthisis, are less likely to follow.

Note.—July 11. The patient operated upon on the 4th. Has done remarkably well. Temperature normal, except on one evening; dressings changed now every third day; discharge very slight.

Left Hospital. Sept 14th quite well.

2/11/82. Patient called to day has some pain in the side but is

6/11/82. Examined this evening. Slight dulness at the base just below the scar. Air enters the whole lung. Murmur is not a little harsher over the dull region. No rales. Tactile fremitus defective. Percussion not as sound this side has always been a little.

*Die Parasiten des Menschen Kuchenmeister und zum 2te Auflage 1881.

URÆMIC DELIRIUM AND COMA AT A VERY EARLY STAGE OF INTERSTITIAL NEPHRITIS.

By WILLIAM OSLER, M.D., M.R.C.P. Lond.,
PROFESSOR OF THE INSTITUTES OF MEDICINE, Mc GILL COLLEGE, MONTREAL.

The chief points of interest in this case are: (1) the onset of the symptoms with delirium; (2) the mental worry which preceded the attack—a prominent factor in some instances; (3) the apparently normal state of the kidneys, which gave evidence of changes only on microscopical examination.

J. W., aged 44, a large, powerfully-built man, railway foreman, was admitted into the general hospital, May 6th, with delirium. For past fifteen years had been temperate; prior to this had taken a good deal of alcohol. Up to present attack had enjoyed good health; his wife states that she had noticed of late that he got up at night to make water, and he passed rather more than usual. For about a week he had been greatly worried, as a strike had occurred among the men in his department. On the morning of the 4th he had a chill, and felt unwell all day. On the 5th, though still ailing, he went to work, but returned in the afternoon complaining of soreness over the whole body, headache, and chilly feeling. In the evening he became delirious and was noisy and excited all night; could not be kept in bed, but walked about incessantly talking and directing his men at their work. On the 6th the delirium persisted, and in the evening he was brought to hospital. On admission the temperature was 100°, pulse 120. He passed a very restless night, and was with difficulty kept in bed. In the morning (7th) he was quieter; temperature 100°. When seen at the mid-day visit was quieter, but did not answer questions intelligently. Face flushed, venules on cheeks and nose dilated. Pupils slightly contracted, react to light; ophthalmo-

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scopic examination of eyes negative. No special symptoms in chest or abdomen. No dropsy, nor œdema of ankles. Heart's impulse not forcible; apex in normal position, but difficult to feel; pulse full in volume, tension plus; radials not stiff. Urine was passed in bed; that drawn off with catheter, high colored, sp. gr. 1039, highly albuminous, with numerous finely granular casts, many of unusual length. Toward the afternoon he slept. In the evening was very torpid; did not know his wife. Temperature normal. On the 8th, after a quiet night, he was very drowsy, roused with difficulty; pulse 120, temperature 99½°. Pupils of medium size, react slowly. Passed 24 oz. of urine; same characters as before noted. Toward the evening he became deeply comatose; the respirations increased. He was bled to 20 oz., with the effect of reducing the rapidity of pulse and respirations. Pupils dilated; temperature rose to 103½°. The coma increased, and death took place at 3 A. M. on the 9th. The treatment consisted in bromides and chloral in the early stage; purgatives, pilocarpin, and vapor baths.

Autopsy.—Brain: Arachnoid turbid at base and over the sulci; much serosity about the membranes, which stripped off very easily. Several slight ecchymoses in gray matter of right hemisphere; one at top of ascending frontal gyrus was the size of a small pea. Ventricles contain a moderate quantity of fluid; walls not softened. On section, substance of the organ not specially moist. The arteries at the base not atheromatous. *Heart* weighed 382 grammes; valves healthy, muscle substance of good color; walls of left ventricle measured from 15–18 mm.; chamber, 8.5 cm. from apex to aortic ring. Aorta presented a few scattered patches of atheroma. Nothing of special note in *lungs*, *spleen*, *stomach*, or *intestines*. *Kidneys:* right, 190 grammes; left, 175. Capsules detach readily and leave smooth surfaces; nowhere granular. Organs cut with moderate firmness; cortices not diminished; medullary rays very distinct; intervening vascular regions with the tufts injected. Arteries at bases of pyramids not unusually prominent. Pyramids look normal. Renal arteries not atheromatous. Altogether, the *macroscopic* appearance of the organs did not appear to substantiate the diagnosis of uræmia which had been made. Beyond a slight increase in firmness the glands certainly did not present appearances which would have attracted further attention had not the symptoms demanded it.

On microscopical examination the only striking change was in the Malpighian tufts, a number of which were found atrophied and

surrounded by an increased growth of fibrous tissue. In some, where the process was far advanced, the tuft was converted into a small homogeneous mass, without nuclei; in others, portions of the tuft appeared normal. There did not appear to be any special proliferation of epithelial elements within the capsule, but there was a very general thickening of the delicate zone of fibrous tissue about even healthy-looking ones. In the neighborhood of several atrophied tufts there was a small-celled or nuclear growth separating the tubules. The small arteries presented decided hypertrophy of the muscle elements, particularly in the circular coat; no hyaline degeneration of the intima. The epithelium was everywhere healthy-looking, distinctly granular, but not swollen; and there were no collections of epithelial *débris* observed in any of the tubules. Except in the vicinity of the atrophied tufts no increase in the intertubular connective tissue was noticed. In the pyramidal portion some of the tubules presented finely granular casts.

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ON CERTAIN

Parasites in the Blood of the Frog

By WILLIAM OSLER, M. D.

(From *Canadian Naturalist*. Vol. X, No. 7.)

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(From Canadian Naturalist. Vol. X, No. 7.)

ON CERTAIN PARASITES IN THE BLOOD OF THE FROG.*

By William Osler, M.D., M.R.C.P., Lond.

Fellow of the Royal Microscopical Society of London. President of the Microscopical Society of Montreal. Professor of the Institutes of Medicine, McGill University.

In my Practical Histology class, during the winter of 1881–82, while the students were working at the blood of the frog (*Rana Mugiens*), I noticed in one of the slides a remarkable body like a flagellate infusorian. I thought that it was one which had got into the blood at the time of withdrawal, from the water on the web of the foot. Meeting with examples in the slides of several other students, my attention was again directed to it, and I made several sketches and wrote down the following description:—"Finely granular protoplasmic body, somewhat triangular in shape, about the size of a colorless corpuscle. The narrow end is prolonged into a cilium, while the other presents a broad band of rapidly undulating protoplasm, which at one angle is prolonged into a long lash-like process. The undulating fringe and the cilia are in constant motion, giving the appearance of rapid waves passing from one corner to the other, the waves of protoplasm gradually increasing in length and tenuity until they have the appearance of projecting cilia.

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* Read before the Montreal Microscopical Society.

No nucleus can be seen. Though in constant action no change of locality takes place." Fig. 1.

On looking up the subject I found that the little organism was the *Trypanosoma sanguinis* which had been described originally by Gruby as an entozoon in the blood of frogs, and by Ray Lankester (not at the time knowing Gruby's observations) as *Undulina*, the type of a new group of Infusoria.

Though a trifling little object it possesses considerable interest as there is still a doubt concerning its real nature and the movement which it displays is unusual, being neither the slow, creeping rhizopodal motion, nor yet truly ciliary. Minute protoplasmic organisms usually display one or other of these types of movement, but in the object under consideration, there is a peculiar wavy undulation along one margin of the creature together with a lashing vibratile action. Studying the margin under a high power a rapidly succeeding series of waves is seen to pass from one side to the other, increasing in length until at one corner the wave is extended into a lengthened cilium resembling the whip-like flagellum of an infusorian. In the specimens which I examined the undulations always passed in one direction and it appeared as if from the tips of any of the waves the protoplasm could be extended into cilia, though usually only those at one end presented them. It is this latter feature, together with the peculiar wavy character of the motion that gives the creature a special interest and makes it quite an exceptional one among organisms of its class. A fine hair-like extension from the narrow end was also in constant motion and appeared to vary considerably in length, as if it were only a delicate process of the protoplasm, and, unlike a true *cilium*, capable of elongation or retraction. I kept one under observation for over an hour, during which time the movements kept up, but got slower towards the close. The undulatory motion at last ceased, but the tail-like

projection and the flagellum at the margin of the broad end continued to move (the appearance is represented at fig. 2.)

Fig. 2.

and were evident after motion had ceased. This would favor the view that these processes were "cilia," and not merely temporary extensions of the protoplasm, though the remarkable manner in which the cilia were extended and retracted shows that they were not similar in all respects to the cilia of Infusoria or of various animal cells. Professor Lankester speaks of it as "a mouthless infusorian, closely allied to Opalinidæ, from which, however, it differs essentially, as well as from *Infusoria ciliata* generally in possessing no cilia." Gruby described it as a parasitic entozoon, while Siebold * states that it is not an independent organism, but simply an undulating membrane swiming freely. Dr. Gaule † has advanced some rather startling views concerning this little body which he believes originates in, or is a transformation of a colorless blood cospuscle. He states that on the warm stage the process of conversion of the white blood corpuscle into the *Trypanosoma* may be readily followed and takes place by the development at one margin of a vibratile cilium and a rapidly undulating membrane. He recognized four or five types of these transformed blood corpuscles and calls them "Kymatocytes." They may return to their original corpuscular condition. I have tried to follow these observations of Gaule but without success and adhere to the opinion that we have to deal here with a minute parasite, the affinities and life history of which have yet to be worked out. They were not abundant in the blood of my frogs and were only met with in two. I have not found them this season in any of the frogs in my tanks.

This session my attention was called by a member of my Histology class to what he thought was a peculiarly elongated white corpuscle in the frog's blood, but which I recognized as another

* Micrographic Dictionary—Undulating Membranes.
† Arch. f. Anat. u. Physiol. (Phy. Abt.) 1880.

parasitic form. The blood examined by the student on that day was taken from two bull frogs (*Rana Magiens*), but only one contained the parasites. The organism presents the following characters:—Body an elongated oval, sausage-shaped, ends conical, one sometimes narrow and prolonged. Length somewhat more than half a red corpuscle. The protoplasm is homogeneous and more translucent than that of colorless corpuscles and shows two or more small central vacuoles (?) with a few granules. Movements slow and creeping, accompanied by an occasional bend or twist of the body, go on at ordinary temperature; a little accelerated but not altered in character on the warm stage. The tail-like end though produced does not terminate in a cilium. Fig. 3.

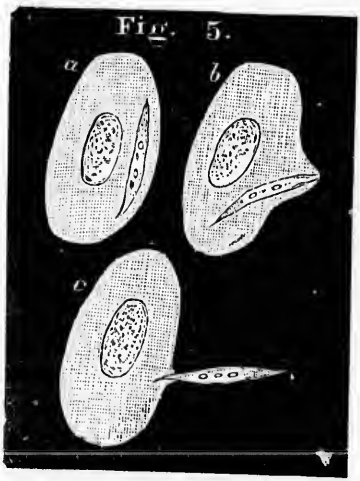
Fig. 3.

This parasite was originally figured by Ray Lankester, when describing the Undulina (Trypanosoma) but he has only recently, in the *Quarterly Journal of Microscopical Science*, for January, 1882, given a full description of it, and established its position. He calls it *Drepanidium ranarum*. Dr. Gaule, of Leipzic, has studied these bodies and has come to conclusions as remarkable as those at which he arrived concerning *Trypanosoma*. He calls them "Wurmchen," *vermicles*, and believes that they are protoplasmic portions of the corpuscles of the blood which assume an elongated form and display movements. He has found them within the cells not only of the blood but of the spleen, kidney and liver and has seen them penetrate and enter blood corpuscles by their active movement.

Dr. Lankester shows very clearly that these organisms are truly parasites belonging to the Gregarinidæ or Sporozoa, those lowly protozoal forms, many of which at some time of their existence are parasitic in the interior of cells. He suggests that it is a young stage and the more developed or Gregariniform condition of the parasite exists in some part of the body of the frog. He points out that these bodies have a striking resemblance to those figured by Lieberkühn, as spores or pseudo-navicula from

the kidney of the frog. Within the cells they can best be seen on the addition of salt solution 3 %. I have found, after trying a number of solutions, that Pilocarpin ½ % brings them out very clearly. In one frog the red corpuscles contained, in addition to the Drepanidia, smaller irregular masses, fig 4.

In blood from a small frog they were very abundant, and could be seen well without any reagent. Fig. 5 *a* represents a corpuscle with one inside which travelled round the cell four or five times, and then migrated from it as shown at Figs. 5 *b* and *c*. This curious phenomenon was witnessed several times, and did not seem to injure the corpuscles very much, some presenting no trace of the point of exit, others a slight depression.



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(From Canadian Naturalist. Vol. X, No. 7.)

ON CANADIAN FRESH-WATER POLYZOA.*

By William Osler, M.D.

The Polyzoa, or Bryozoa as they are sometimes called, form an exceedingly interesting group of animals. From their extensive distribution in geological formations and from the abundance and great beauty of the marine species at the present day, they have attracted an unusual share of attention from naturalists, while the elegance and plant-like appearance of many of the forms make them at the sea shore and in the museum favorites with the public. For a long time the Polyzoa were classified with the hydroid polyps among the Radiata, and even by Owen, in 1855, this method was adopted. Dr. J. V. Thompson, in 1830, was the first to separate them and apply the name Polyzoa to the whole class. At present they are classified as the lowest division of the Mollusca, forming together with the Tunicates and Brachiopods the class Heterobranchiata in the old system, or the division Molluscoida in the new. The Polyzoa are divided into two orders, 1st, the Phylactolæmata, in which the tentacles are arranged in the form of a horse shoe or crescent, and which are provided with a valve guarding the throat. 2nd, the Gymnolœmata, in which the tentacles are arranged in a circle, and the throat is not provided with a valve. In the Phylactolæmata there are three sub-borders, of which the first, Lophopea, contains almost all the fresh-water species. Prof. Allman divides the Lophopea into two great families, the Cristatellidæ and the Plumatellidæ—in the former the animal is locomotive, in the latter fixed. The genera in which Canadian species occur, as far as we know at present, are Cristatella, Plumatella and Pectinatella, and the five species which I have identified *Cr. ophidioidea*, *Pl. diffusa*, *arethusa* and *vitrea*, and *Pect. magnifica*.

As I have nothing new upon this subject to bring forward, I shall proceed to make some general remarks upon the structure and life history of these creatures, and demonstrate the specimens on the table before you. I may as well here explain one or two terms which will be frequently used in the descriptions. The term *cœnœcium* when employed indicates the common system and solid basis of the animal. The external coating is

* Read before the Natural History Society.

called the ectocyst, the internal the endocyst, and the horse shoe shaped disk supporting the tentacles the *lophophore*—strictly the bearer of the plume. The first species to which I will direct your attention is the *Pectinatella magnifica* of Leidy, described by him in the proceedings of the Academy of Science of Philadelphia, for Nov., 1851, and defined as follows;—*Cœnœcium* massive, gelatinoid, hyaline, fixed, investing bodies. Orifices arranged in irregular lobate areolæ upon the free surface. Lophophore crescentic. Ova lentienlar, with an annulus and marginal spines. The specimens on the table show well the hyaline gelatinous nature of the *cœnœcium* and the arrangement of the Polyps upon the surface. This is perhaps the most abundant freshwater Polyzoon in the country, being found in the quiet waters about the mouths of the numerous streams, and in the small lakes. It is not very abundant in Quebec, but it has been found near St. Andrews, and I obtained a beautiful specimen from Lake Memphremagog. I have not seen it in the neighborhood of Montreal. This species prefers quiet, still waters, not too much exposed, nor of large extent and subject to commotion from waves. Thus I have never found it in Lake Ontario itself, but always in little sheltered marshy bays, where it is found encrusting logs, upright sticks, and the stems of rushes. My attention was early directed to this form as it exists in extraordinary profusion in the Desjardin canal, which leads from Burlington Bay to my native town Dundas. The wooden sides of the canal basin in the months of July and August are almost uniformly covered with this magnificent species. The growth begins about 1½ to 2 feet below the surface and extends in depth for the same distance or even further, rarely, however, deeper than six feet. The masses form extensive sheets usually a few inches in thickness, or else beautiful symmetrical projections, 6-12 inches in thickness, which spring either from a bed of the Polyps or are isolated. In the summer of 1867, during a visit of my friend, the Rev. W. A. Johnson, of Weston, I showed him the masses, and we agreed to subject them to examination with the microscope, not having any idea as to their real nature. Judge of our delight when we found the whole surface of the jelly was composed of a collection of tiny animals of surpassing beauty, each of which thrust out to our view in the zoophyte trough a crescent-shaped crown of tentacles. Recognizing it as a Polyp we were greatly exercised as to its position, presenting as it did

in the method of growth, such variation from the ordinary species described in our zoological text books. Happily in the American Naturalist for that year we met with Mr. Alpheus Hyatt's papers on the Fresh-water Polyzoa, then in course of publication, and obtained full information therefrom. On examining the surface of a mass of Pectinatella the polyps are seen to be arranged, as seen in the spirit preparation, in close areolæ, which, being crowded and compressed together, often assume hexagonal outlines. From the periphery of these irregular areas the polyps project, the central part being as a rule unoccupied. When in the water the protrusion of the innumerable tentacles gives a fine velvety appearance to the surface, which entirely disappears on touching the polyps or agitating the water. This species is, however, much less timid than some others, and the polyps over even a small mass do not all withdraw on a slight irritation. The color of the polypidom is a light brown, or when the tentacles are extended, a faint rosy red hue, due to the color about the throat, glimmering through them. Towards the central part of the areolæ, white, brown and dark spots are seen, representing ova at various stages of development. The cœnœcium composed of the dense aggregation of polyps is closely united to the subjacent gelatinous mass, which constitutes here the ectocyst. On removal of the polyps the surface of the jelly presents patterns corresponding to the arrangement of the animals, irregular areas grooved in a radiate manner. The superficial portion of the ectocyst has often a reddish tint, and the deeper parts slightly greenish from the presence of a confervoid growth. Many masses of large size present a jelly perfectly colorless and pure throughout. Upon the development of this jelly, which is to be regarded as a definite excretion or secretion from the animal, the size of the polyp masses depends. When encrusting boards they are usually flat, larger conoidal projections occurring at intervals. Around the stems of rushes the most beautiful masses are found. The small one before you gives a good idea of the graceful symmetry of the growth. I have measurements of such a symmetrical cluster about a reed which was 14 inches in length and 10 in circumference, the weight 9 lbs. In some seasons the luxuriousness of the growth of these creatures is extraordinary. In the still quiet water in the marsh on either side of Desjardin canal, just before it passes through the Burlington heights, I have met with masses which would not go into a pail. The largest I have ever seen lay at

the bottom in about nine feet of water. I could hardly believe it was a mass of polyps, but, to satisfy my curiosity, I stripped and went in for it. With the greatest difficulty I brought it up in my arms, but could not get it out of the water for the weight, which must have been close upon 25 lbs. It resembled in form one of those beautiful masses known as brain coral.

On account of the colorless nature of the ectocyst and the extent to which the polyps protrude, this species is the most favorable to study the general arrangements of the organs, the perfect transparency allowing every detail in the structure to be seen. I have found it best to cut a thin vertical slice from the mass, containing on the surface not more than one or two rows of polyps, and examine in the zoophyte trough with a half-inch glass. It is much easier in this way to obtain a view of the complete animal than in the live box. The shock of the section and removal to the trough causes complete retraction of the polyps, and the surface of the cœnœcium looks smooth, or presents only slight tuberous elevations, corresponding to the situation of the orifices. On watching one of these, the sphincter closing it may be seen to relax, and the ends of the tentacles protrude through the orifice, feeling about from side to side as if to ascertain whether the "coast was clear." Finding no cause for alarm, the relaxation of the sphincter proceeds, the tentacles are pushed out still further, resulting at last in the complete evagination of the polyp. The beautiful crescentic tuft is arranged in the form of a horse shoe, or the letter U inverted, the tentacles spring from each side of the summit of the double outline, the mouth being at base. The number of the tentacles ranges from 50–80; they are sigmoid in outline and increase slightly in length at the extremities of the arms. The inner rows incline towards each other, the outer curve gracefully in the opposite direction. The surface of the tentacles is covered with cilia, which are in constant motion, creating a vortex, at the apex of which the mouth is situated. The tentacles act independently as well as in concert, and thrust and bend in any direction, pushing away objectionable matters which may have got into the throat, or are present in the neighbourhood. Frequently one of the large infusoria coming within the vortex is carried down and attempting to escape is prevented by the interlacement of the tentacles which bending over form a cage. The sensitiveness of these ciliated arms is extreme and through them the creature obtains warning of approaching danger, and instantly withdraws itself.

From beneath the crescentic lophophore the alimentary canal hangs, which presents the following parts for observation: the epistome, a valve-like projection overhanging the mouth, the œsophagus or throat, the stomach, intestine and anus.

The epistome is a tongue-like organ arising at the junction of the inner arms of the lophophore, and serves as a valvular protection for the mouth. It possesses a set of muscles by which it can be readily moved and jerks up and down very frequently. It appears to keep materials in the throat rather than prevent the entrance of anything obnoxious. Like the tentacles it is covered with cilia. All the parts about the region of the epistome have a dark rose-red color, and this gives a peculiar brilliancy to the animals. A somewhat funnel-shaped mouth leads directly into the œsophagus, a short colorless tube, which widens slightly as it descends. A valve-like construction separates it from the stomach, into which, as soon as the œsophagus is full, the food is expelled by the contraction of the muscular walls.

The stomach forms an elongated tubular cavity in which the food is subject to a constant peristaltic action during the process of digestion. The lining membrane is plicated and the cells upon the folds are of a brown color, containing a fluid which Prof. Allman regards as a biliary secretion. The intestine or cœcum is a short broad cavity separated from stomach by a valve and placed parallel to the œsophagus, opening by an anal orifice immediately beneath the lophophore. The undigested residue of the food is gradually pushed through the cœcal valve and distends the intestine and is expelled by the contraction of the cœcal walls and carried away by the action of the cilia of the tentacles. From the lower part of the stomach a cord-like process, the funiculus, extends, and connects it with the bottom of the cœnœcium.

There is no definite circulatory system in the Polyzoa. A colorless fluid bathes the interior of the cœncœcium and the perigastric cavity. By the action of the cilia which line the interior of the cœnœcium currents are created which are rendered evident by the small particles carried round.

Respiration is probably carried on by the cilia covering the tentacles, but our knowledge of this function is extremely slight.

The nervous system of the fresh-water Polyzoa is represented by a definite ganglion which lies in the neighborhood of the

œsophagus, immediately below the epistome. It is easily seen in Pectinatella and presents curious contractions and expansions. By these the position of the mass is altered, sometimes approaching nearer the œsophagus, at others being in the hollow of the epistome. Nerve branches may be seen proceeding from this ganglion chiefly towards the epistome and tentacles.

The muscular system is well developed and the muscles form either sphincters or elongated branches. A definite sphincter surrounds the orifices of the cœnœcium and closes them tightly when the polyps are retracted, relaxing again for their protrusion. The longitudinal bands arise from the base of the cœnœcium, and passing up are distributed in three different localities, on the stomach, the base of the lophophore, and the tentacles, and are called respectively the gastric, lophophoric and brachial retractions. By the action of these muscles the little animal can be instantaneously withdrawn, and the sphincter closing effectually shields them from injury and attack. Other muscles are described by Hyatt and Allman, in connection with the epistome and endocyst.

The Phylactolœmata are reproduced by budding and true ovulation. From the side of the polyps buds arise which develope into mature forms and in this way the colonies are increased. Another method of budding results in the production of free gemmæ or statoblasts, which arise from the funiculus. These present a horny sheath, usually dark brown in colour, and an annulus or margin, which in some species is provided with spines. In Pectinatella, the spines number from 12–20, in Cristatella there is a double row, one shorter, the other longer, 50–60 in all, and the extremities are furnished with from 4–6 hooklets. The statoblasts float on the surface of the water and the armed ones get entangled in the weeds.

The method of production of true ova was first described by Allman. They originate in a bud-like mass at the upper side of the endocyst and are fertilized by spermatozoa, the testicles being an offshoot from the funiculus.

In the genus Plumatella I have determined three Canadian species, *arethusa*, *vitrea*, and *diffusa*. The members of this genus have dendritic, plant-like cœnœcia, which are firmly attached to the surface of submerged twigs, stones and water-plants. The cœnœcium is composed of little hollow branched tubules, divided into cells, from the apex of which the little polyp

protrudes, while at the other end it is in communication with the parent polyzoon. The branches are generally attached along the greater part of their length, though sometimes, as in this specimen of *P. arethusa*, they are free in nearly the whole extent. The color is owing to the ectocyst which when first secreted is thin and jelly like but soon becomes consistent, and at last dark brown. The endocyst lies immediately within this and is continuous throughout the system of branches.

The species of this genus are widely distributed throughout Canada in the quiet ponds and marshes attached to twigs, submerged logs and the under surface of the leaves of the water-lily

The Cristatellidæ, the most highly organized of the Polyzoa, have a locomotive cœnœcium. There are two American species C. Idæ and C. ophidioidea. The one which I have studied here conforms to the latter, as described by Hyatt, in both statoblasts and number of tentacles. It is not nearly so common as the other forms. I have on several occasions met with the statoblasts in gatherings, but have never found the polyp except in the small lakes near the summer residence of Mr. G. W. Stephens, in the County of Maskinonge, Quebec. In Lac Rouge, the rocks at water's edge, at about the depth of from one to two feet presented numerous specimens about an inch and a half to two inches in length and one-third of an inch in breadth. The movement was slow, in those which I observed in a small basin, not more than an inch in the 24 hours. The statoblasts differ from those of Pectinatella in possessing a double row of hooklets with from two to six points.

Note.—I have received from the Rev. Thomas Hincks, the distinguished authority on British Polyzoa, a reprint from the Annals and Magazine of Natural History for March, 1880, entitled "On a supposed Pterobranchiate Polyzoon from Canada." It is based on a communication from his father, the late Professor Hincks, of Toronto University, in which a short account is given of a polyzoon found on a sunken boat in the Humber river, near Toronto. According to the description "the tentacles, instead of being disposed in a horse-shoe figure and forming a continuous series, as in the ordinary fresh-water species, are borne on two distinct erect lobes, which are separated at the base," the arrangement met with in the Pterobranchiate Polyzoon. At the date of Professor Hincks' letter, Dec. 1868, I was a student in his Natural History classes, and during the autumn of '68 had often

taken him specimens of various sorts, and among them a mass of Pectinatella, which I had found in an old submerged barge near the mouth of the Humber. I remember the fact very distinctly, as it was the first specimen of Pectinatella which I had found near Toronto, and Professor Hincks took a great interest in it, as he had not met with any fresh-water Polyzoa in Canada. Could this have been the specimen? It is a curious coincidence, to say the least, and perhaps in a look through the Museum of the University the specimen might be found, and the statoblasts would be sufficient to decide the question. Professor Hincks gives a sketch of the lophophore and it is hard to think that he could have been mistaken as he was an unusually skilful observer. The submerged barge was for many years a favorite collecting ground, and in some seasons Pectinatella was very abundant in the quiet water inside of it.

AN INVESTIGATION

INTO THE

PARASITES

IN THE

PORK SUPPLY OF MONTREAL.

BY

WILLIAM OSLER, M.D., M.R.C.P., LOND.,
Professor of the Institutes of Medicine, McGill University; Lecturer on Helminthology, Montreal Veterinary College.

AND

A. W. CLEMENT (LAWRENCE, MASS.),
Student Montreal Veterinary College.

MONTREAL:
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1883.

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REPRINTED FROM THE "CANADA MEDICAL & SURGICAL JOURNAL."
JANUARY, 1883.

AN INVESTIGATION

INTO THE

PARASITES IN THE PORK SUPPLY OF MONTREAL.*

In the interests of public health, it is a matter of great importance that the food supply of cities should undergo strict supervision, with a view of excluding possible sources of disease. In this country, the department of the civic governments relating thereto cannot be said to be conducted on model principles. Speaking of Montreal, meat inspection consists in the examination of the carcasses of all animals exposed for sale or killed at the abattoir, and its superficial character is clearly shown by the results of this investigation.

It is to be remarked that, in the matter of meat inspection, there are some affections in which an ante-mortem examination will be of most service, and an animal may be condemned as unfit for food, the meat of which, when dressed, might pass even a careful inspector. There are other affections which, interfering but slightly with the general healthfulness of an animal, render its flesh in the highest degree unfit for food, even though it may, on superficial inspection, look healthy enough.

* *Read before the Medico-Chirurgical Society of Montreal and the Board of Health.*

The flesh of swine forms one of the great staple articles of food in the community, and, fresh or salted, constitutes a very considerable proportion of all meat eaten. The hog is omnivorous, a dirty feeder, refusing nothing, and, regarded from this standpoint, we do not wonder that in the sanitary enactments of Moses it was excluded, though cloven-footed, in the list of animals permitted to be eaten. Vile feeder though it be, the hog has the power of converting, in the laboratory of its tissues, even refuse and garbage into a flesh most wholesome as well as toothsome. Who does not remember Lamb's charming "Dissertation on Roast Pig," and though he speaks of the suckling, most of us can agree with him when he says, "Pig—let me speak his praise—is no less provocative of the appetite than he is satisfactory to the criticalness of the censorious palate. The strong man may batten on him, and the weakling refuseth not his mild juices."

The hog is not subject to many diseases which interfere with the market value of the flesh. Pig-typhoid or hog cholera is the only extensive epizootic disease among them in this country, and by interfering with nutrition and producing emaciation renders the flesh unsuitable for food. The injurious effects which follow the eating of the flesh of diseased animals are really not much known. The juices of the stomach are so powerfully antiseptic and corrective, that the meat, after cooking, is usually digested without difficulty. The Highland shepherds are stated to eat, without ill effects, the flesh of animals which have died of anthrax. In the case of pork, it is not so much the fresh or salted meat which has been known to produce sickness as when it is made into sausages and brawn (head cheese). Many cases of serious illness have been excited by eating these articles. This is not surprising to anyone who has watched their manufacture, particularly sausages. In many establishments the odds and ends go for the mince meat, and, too often, bits of old meat which is just beginning to turn. The experience is only too common of tasting in a mouthful of sausage the disagreeable flavor of a morsel which is high, *i.e.*, is in the initial stages of putrefaction. The septic matter, if abundant, or, perhaps, if produced by bacteria of a special variety, may excite severe intestinal symptoms, and even

cause death. In Whitechurch, England, there has recently been a local epidemic produced by eating brawn.

In relation to public health, the diseases of the hog are of small matter in comparison with the parasites which infest its flesh, and which, eaten by man, may produce serious or even fatal affections. It is as a protection against these that an effective meat inspector may do good service in the community, and annually prevent many cases of illness. To obtain evidence of the prevalence of parasites in the pork supply of this city, one thousand animals have been examined, with the results here stated. Of the parasites which infest the hog, only three are of importance in this connection—the *Trichina spiralis*, the *Cysticercus cellulosæ*, and the *Echinococcus*. We shall consider these in order.

TRICHINA SPIRALIS.

"An extremely minute nematoid helminth, the male in its fully developed and sexually matured condition measuring only one-eighteenth of an inch, while the perfectly developed female reaches a length of about one-eighth of an inch; body rounded and filiform, usually slightly bent on itself, rather thicker behind than in front, especially in the males; head narrow, finely pointed, unarmed, with a simple, central, minute oval aperture; posterior extremity of the male furnished with a bilobed caudal appendage, . . . female shorter than the male, bluntly rounded posteriorly, eggs measuring $\frac{1}{12\overline{7}0}$ of an inch from pole to pole; mode of reproduction viviparous." —Cobbold.

Since Zenker, in 1860, discovered that this worm produces a severe malady in man, a degree of interest has been attached to it, not exceeded by any known human entozoon. The record of epidemics of it sends a thrill of horror through a community out of all proportion to the gravity of the disease; and naturally enough, for the very thought of myriads of these little worms boring and eating the flesh is particularly repulsive, recalling the tragic fate of Herod, on whom the worms are stated to have held an ante-mortem feast. The hog is the natural bearer of the trichinæ, which exist in the flesh, coiled up between the muscle fibres, and are so minute that they cannot be seen on ordinary inspection, but require the use of the microscope. In this state they are undeveloped or immature sexually, and may remain for years in the muscles of the animal without undergoing de-

generative changes. Pork containing them and eaten raw, in any form, or partially cooked, produces disease in the following way: the little worms escape in digestion, pass into the small intestines, grow rapidly, become sexually mature, and assume the form of intestinal trichinæ. The females are impregnated, and the ova develop into minute embryos, which are born alive and free. This process occupies two or three days, and is usually accompanied with some intestinal irritation. The number of embryos will vary with the number of worms ingested and which reach maturity. They immediately burrow through the walls of the intestine, reach the connective tissues of the abdomen, and penetrate the muscles in all direction, and when numerous reach even those most distant. In this migration they produce irritation, fever, and constitutional disturbance proportionate to their number, and the severity of the symptoms may be such that death may follow, though the percentage of fatal cases is small, only about 1.5.

Record of Investigation.—One thousand hogs were examined, chiefly at the Dominion Abattoir, during the past six or eight months. There was no selection made, but the carcasses were taken indiscriminately, as they were found at the time of the visit.

Method.—It has been satisfactorily shown by many observers that the pillars of the diaphragm are the most suitable muscles for examination, not alone because portions can be removed without disfigurement or loss, but chiefly from the fact that here, if anywhere in the body, the parasites will be found, as these muscles lie in the direct route from the intestines. The examination was made with No. 2 Obj. (Verick) and No. 1 Ocular, magnifying about 60 diameters. Small clippings of the muscle were made lengthwise, then placed on the slide, and pressed out with the top cover until thin enough for the purpose. In only four out of the one thousand animals were the parasites present in the diaphragm, and we may take this as representing the actual ratio, though possibly they may, in one or two instances, have existed in other muscles and not in the portions examined. As to the number in the infested bits, in one case there were twelve on one

slide; in the others, not so numerous. The worms were not regularly encysted but coiled up between the fibres. When placed on the warm stage, they displayed movements.

All the animals examined were from Western Canada.

Comparison of local with foreign records.—As the following figures show, the record here, 1 in 250, is by no means high. Thus, in Boston, Mr. Billings examined over 6,000 animals, and in the different groups the ratio ranged from 1 in 17 to 1 in 44. All of these animals were from the Western States. In Chicago, one series gave 1 in 49.8. In Prussia, where a very thorough and systematic pork inspection is carried out, in the year 1876 only 1 in 2,000 was found affected, and in 1877 about 1 in 2,800.

Trichinosis in Canada.—Remarkably few cases of trichina infection are known to have occurred in this country. In 1869 nine persons were attacked in Montreal after eating of fried ham, which was ascertained to be trichinous. They presented severe gastro-intestinal symptoms, and the constitutional disturbance in moderate grade. None of them died. The diagnosis was corroborated by the microscopic examination of a portion of muscle harpooned from one of the patients.* In 1868, three members of a family in Hamilton were attacked after eating portions of an infected ham. Two of these, the mother and daughter, died; the father recovered. At post-mortems and in the dissecting-room, it is not uncommon to find the muscles full of calcified cysts containing the worms or their remnants. These little bodies had been recognized for years before Zenker's discovery connected them with an antecedent disease. Probably many isolated cases occur which are mistaken for acute rheumatism or typhoid fever. In between 800 and 900 autopsies made by Dr. Osler, four bodies have been found trichinous, the cysts in each instance calcified, and in one the worms were nearly all dead. In the other cases the parasites were still living, and with muscle from one of them the disease was artificially produced in a rabbit. So that in all only sixteen cases of the disease have been recognized in this country.

* *Canada Medical Journal*, 1870.

Summary.—So far as it is legitimate to draw deductions from the somewhat limited number of observations, we may say that trichinosis is a tolerably common affection in Canadian swine, though not nearly so frequent as in the neighboring States, still, it is much more so than is desirable in the interests of public health. Should microscopic examination of the flesh be included in the inspection? is a question which at once arises. In answering this, several circumstances must be taken into consideration. In the first place, although, per 1,000, a larger number of swine are infested here than in Germany, trichinosis in man is with us a very rare disease, while in Germany epidemics are of yearly occurrence. If we estimate that 100,000 hogs are killed annually for the local markets, that would give at least three or four hundred trichinous animals, whose flesh is consumed by the pork-eating members of the community. Then, about 3½ million pounds of American pork, representing about 15,000 hogs, have been imported into this city during the past year, and as in them the percentage of trichinæ is considerably higher than in Canadian animals, the probable number of infested carcasses consumed does not, at the lowest estimate, fall short of five hundred. Now, were the habits of the people of this city similar to those of the Germans, there can be no doubt that trichinosis, instead of being a rare affection, would be extremely common. Fortunately, raw or only partially cooked pork is not often eaten here, nor are the various kinds of sausages, so dear to the Teuton, much in vogue. *Knackwürste* and *Bratwürste*, forms of sausages which are very common, and which are eaten either raw or only warmed, have been the sources of a large proportion of the known cases of trichinosis in Germany, 970 out of 1,267. People here almost invariably fry sausages, and smoked meats are not common, nor are they eaten without preliminary cooking. In short, the prophylaxis of the pot and oven in this country and in the neighboring States does more for the public than the most stringent inspection, even as carried out in Prussia, where a microscopic examination is compulsory. If thoroughly cooked, the trichinæ are killed, and may be eaten with impunity; and, fortunately, there is a very widespread idea in the community that pork, in

all forms, should be well cooked, and to this good custom may be attributed the immunity from infection which the public has enjoyed. Still, it is by no means pleasant to think of the quantity of trichinous flesh which is placed on our markets, and which probably exceeds the entire amount of pork confiscated for other causes. The difficulties in the way of systematic inspection are now, under the Abattoir By-law, greatly lessened, but to subject the flesh of every hog killed to microscopic examination would require a staff of trained inspectors and an increased expenditure such as our civic authorities would not likely incur. Moreover, considering the rarity of cases of infection, it may be just as well to leave the matter to the cooks of the community, who have so long and so faithfully protected us, with this injunction, "See that all pork is thoroughly roasted, fried, or boiled."

CYSTICERCUS CELLULOSÆ.

This parasite of pork is not so formidable as the trichina, but is more common and a more frequent excitor of disease. It is the larval or immature form of one of the tapeworms of man, and is popularly known as the "measle" or cystic worm, and an infested animal or its flesh is said to be "measley." In this country man is infested with two chief forms of tapeworm, the *Tænia solium* and the *Tænia saginata*—the former derived from measley pork, the latter from measley veal or beef; hence the one is often called the *pork* and the other the *beef* tapeworm. The life history of the *Tænia solium* is as follows:—the adult worm occupies the small intestine of man, and attains a length of from 12 to 15 feet, or even longer. The segments of which the body is made up progressively increase in width from the head, and about the 400th become mature—*i.e.*, the male and female generative system which each possesses becomes active, and eggs are formed. In a fully grown worm it is estimated that there may be about 200 ripe segments full of ova, the number in each one reaching probably as high as fifty thousand. The hinder segments of a tapeworm are constantly shed, or, indeed, may detach themselves, at the rate of 3 or 4 per diem, and pass away in the fæces. The eggs are small, round, $\frac{1}{700}$ of

an inch in diameter, and each one contains in its interior a little body known as the six-hooked embryo. For their further growth it is necessary that they reach the interior of some animal in which they can develop. The hog is the most suitable, and usually furnishes the means for the subsequent growth of the ova, though the eggs may be accidentally ingested by man and develop within him, but this rarely happens. It is not difficult to understand how hogs become infested; they are such dirty feeders that nothing is refused, and even human excrement is greedily eaten. In country places, a single case of tapeworm may serve to infest many hogs, as the ripe segments constantly pass with the fæces, and one or two will suffice to produce the mischief. The eggs in the stomach of the pig are digested, and the little six-hooked embryos, in this way set free, immediately begin to bore through the walls, and, entering the vessels, are carried to all parts of the system, lodging particularly in the liver and muscles; others pass through the coats of the bowels into the peritoneum and omentum, and may reach the muscles in this way. In these various parts the little embryos gradually develop into cysticerci or "measles," and an animal so affected is said to be measled. It takes about three months for this process, and when completed, the cysticerci present the appearance in the flesh of greyish-white rounded bodies from one-tenth to one-sixth of an inch in diameter, situated between the fasciculi of muscles, and can be picked out, leaving little holes or depressions. When abundant, they give a very characteristic aspect to the flesh. which is quite unmistakeable. In the liver they may attain a larger size, and in the loose tissues of the omentum and peritoneum they are often found the size of a walnut. The cysticercus or measle is enclosed in an external sheath, which, when open, gives exit to a cystic or bladder-like body, which requires careful dissection to make out the structure. It presents a head similar in all respects to that of the adult tapeworm from which the egg was derived, presenting four sucking disks and a circlet of hooklets. A narrow neck succeeds the head, and beyond this there is a bladder-like body called the caudal vesicle.

If flesh containing these "measles" is eaten raw or only partially cooked, tapeworm is liable to result. The cyst wall enclosing the cysticerci is digested away, the bladder worm set free, and passes into the intestine, where the head fixes itself firmly by means of the sucking disks and hooklets. The caudal vesicle is digested away, and by a process of budding the segments are gradually formed. In about two months the worm has attained maturity, and segments are discharged containing thousands of eggs, ready for development in the body of the first pig that accidentally ingests the segments.

Local Record.—Of 1037 hogs examined, 76 were infested—*i.e.*, 1 in 13.6. Only the livers were inspected, as it was impossible to examine the flesh thoroughly. The numbers varied from one or two to many dozen, and in most instances they were fully developed. The liver is more likely to be affected than the other parts, but the occurrence in this organ is a proof that the animal has been exposed, and should lead to a thorough examination of the flesh.

In order to obtain evidence of the extent to which "measled" meat produces disease—*i.e.*, tapeworm—in the community, we issued a circular to the city physicians asking the number of cases under treatment. Replies were returned by thirty-four doctors who reported sixty-two cases. At the Smith Worm Company's office, Bleury Street, about two new cases a week are treated; some of these, doubtless, come from the country, but we shall probably be within the mark if we estimate the number in the city as not far short of 200. How many of these are due to eating measley veal or beef, and how many to measley pork, we cannot say, but from the specimens examined it would seem that the beef tapeworm (*T. saginata*) is the more prevalent. Not that the pork measle is uncommon; the record above given shows just the contrary. To explain the greater frequency of *T. saginata*, we must suppose either that the beef measle occurs in greater proportion, or else the pork is more thoroughly cooked than the beef or veal. Then, too, much less pork is eaten fresh, and the salting and pickling processes are usually sufficient to destroy the measles. A point of in-

terest is the temperature necessary to kill them. The observations of Professor Perronicito prove that they are invariably killed by a heat of 50°C. or 122°F. Indeed they were swallowed with impunity by his students after exposure to a temperature of 113°F.

Fortunately, the presence of a tapeworm does not give rise to such a formidable affection as the trichina, but the amount of suffering and annoyance caused is considerable, and not infrequently an individual has to entertain the troublesome host for months or years, so difficult is it in some cases to dislodge the worm.

A thoroughly efficient inspection would diminish greatly the number of persons annually infected. Of course a hog might contain only a few "measles" deep-seated in the muscles, and these could readily be overlooked—indeed would be even on the most careful examination.

ECHINOCOCCUS.

The presence of this parasite in the flesh of pork has not the direct and close relationship to our individual welfare as the trichina or cysticercus, inasmuch as it represents a larval form of a tapeworm which infests the dog and wolf—never man. The adult worm is very small, not more than a quarter of an inch in length, with only four segments, the anterior of which forms the head, while the hinder one is mature and contains the ova, which are passed in the fæces of the dog, and if swallowed by an animal may develop in its organs or tissues into the structures variously known as echinococci, hydatids, or acephalocysts. A single egg of an ordinary tapeworm, when placed in suitable circumstances, develops into a single larva or measle (*cysticercus*), but a remarkable peculiarity in the life history of the *T. echinococcus* is that a single egg develops into a large compound and complicated cyst, which contains many thousands of larvæ—hydatids or hydatid heads, as they are called—each of which, if transferred to the intestine of a dog, might grow into a tapeworm. Man also harbors the echinococci, which may produce very serious or fatal disease. In some countries, as Iceland and Australia, this affection is very prevalent, and many deaths are annually caused by

the growth of the hydatids in the internal organs, in which they may form large tumors. Man gets infected in the same way as the hog by the accidental ingestion of the ova, and the point of special interest, in relation to public health, is that the occurrence of echinococci in the hog—and in other animals—ensures a constant perpetuation of the species among the dogs of a community and a consequent risk to the individuals thereof, which will be great in direct proportion to general insanitary condition and the liability of the eggs to get into the drinking water.

Result of Examination.—In the 1,037 hogs examined, echinococci were found in the livers of 31, or 1 in 33.4. The cysts ranged in size from a marble to a walnut, and presented an external [illegible]s investment, formed from the tissues of the part, within which was the cyst proper, which could be readily turned out. The ectocyst and endocyst were usually well developed, the fluid clear, but in none of those examined microscopically were the hydatid heads fully developed.

Echinococcus disease in man is in this country a very rare affection; not more than eight or ten cases have been known to occur. In the United States it is also uncommon,* and a considerable number of the reported cases have been in foreigners, who probably brought the parasite with them. The immunity from the disease which human beings here happily enjoy may be explained by the existence on the whole of such sanitary regulations as reduce to a minimum the risk of infection. Dogs are not numerous, nor are they so intimately associated with the every-day work of the people, as in countries like Iceland, where, according to Krabbe, the ratio of canine to human population is very large, and an extraordinary number of the inhabitants suffer from the affection. The adult worm is certainly rare in our dogs; we have never met with a specimen in numerous dissections, but its existence is fully shown by the occurrence of the larval form in many animals and occasionally in man.

* On Echinococcus Disease in America, by Wm. Osler, M.D., *American Journal of Medical Sciences*, Oct., 1882.

CONCLUSIONS.

1. The investigation shows that the hogs slaughtered for our markets present parasites in numbers sufficient to necessitate a more thorough inspection than is at present carried out.

2. As regards *Trichina spiralis*, which was found in the proportion of 1 to 250, we are of opinion that, considering the extreme rarity of cases of trichinosis, and the difficulties attendant upon a systematic inspection, a compulsory microscopic examination of the flesh of every hog killed is not at present called for.

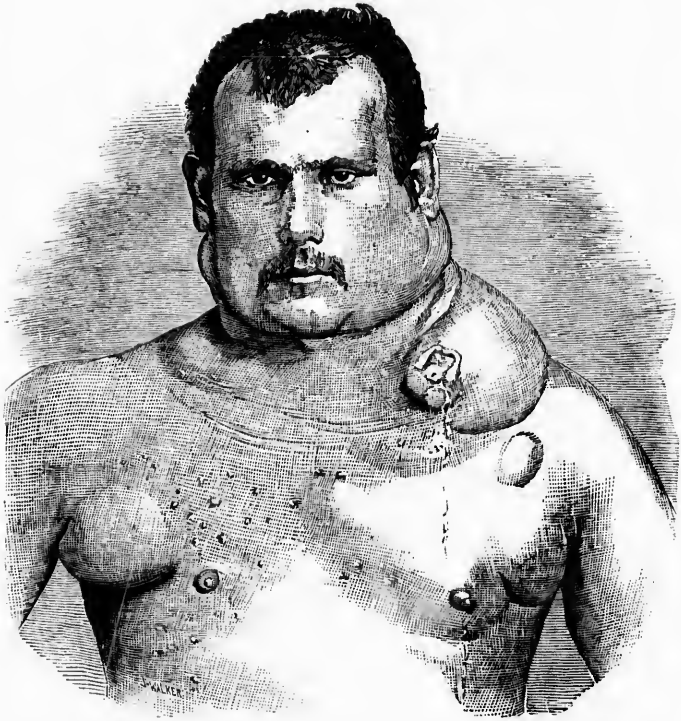
3 In the case of "measles," the liver should be carefully examined, and if present in it, the flesh of the animal should receive the special attention of the inspector; if only in the liver, the entire carcass need not be confiscated.

4. Echinococcus cysts in the liver render that organ unfit for food, but in other parts, unless very numerous and disorganizing, they may be cut out, and the carcass remain marketable.

5. The public should be made aware of the possible dangers of eating, in any form, raw or partially cooked meat. The best safeguard against parasitic affections is not so much inspection of the flesh, unless, indeed, this is minutely carried out, as careful attention to culinary details.

6. To reduce the number of infested hogs, greater attention should be paid to their hygienic surroundings, particularly in the matter of feeding. The danger is not during the period when the animals are penned and fed on grain, &c., but when they are allowed to roam at large and feed indiscriminately.

Our thanks are due to the authorities of the Montreal and of Dominion Abattoirs who kindly permitted the inspection.



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REPRINTED FROM THE "CANADA MEDICAL & SURGICAL JOURNAL."

CLINICAL REMARKS ON A CASE OF HODGKIN'S DISEASE.

(*With a cut.*)

SUMMER SESSION, MEDICAL FACULTY McGILL COLLEGE.

BY WM. OSLER, M.D., F.R.C.P., LOND.

Professor of the Institutes of Medicine in McGill University, and Physician to the Montreal General Hospital.

GENTLEMEN.—The patient before you is the subject of a remarkable disease which was brought to the notice of the profession in 1832, by the late Dr. Hodgkin of Guy's Hospital. Although others had previously described cases, and Dr. Hodgkin had not himself a very clear notion of the relations of the affection, still, his paper forms the starting of our present knowledge, and the majority of English writers have, since 1865, followed Dr. Wilks' suggestion and called the disease after his name. Synonyms of it are General Lymphadenoma or—adenosis, Pseudo-Leukæmia (Cohnheim), and Adénie (Trousseau). The disease is characterized by a progressive enlargement of the lymph glands in certain regions, and anæmia. There may be enlargement of the spleen, and occasionally there are localized growths of lymphoid tissue in different parts of the body. The colorless blood corpuscles are not usually increased. The report of the case is as follows: R— A—, from near Belleville, Ont., was admitted to Montreal General Hospital June 6th, suffering with enlarged glands. Patient is 34 years of age; married; no children. No record of any scrofulous or tuberculous affections in his family. Had jaundice four years ago; ague two years ago; nothing special about these attacks. Otherwise has been quite healthy until present illness set in.

A year and a half ago one of the glands of the neck began

to swell and rapidly increased in size; three months later another one on same side of neck began to enlarge, and still later others became involved. Axillary glands and those of groin became affected six months later than the cervical, but not to the same extent. At times he has had epistaxis and blood-spitting, and he has lately had a troublesome cough.

On inspection, patient is seen to be a fairly well developed man, dark hair and eyes, not anæmic or cachectic looking. The skin is unusually dark, particularly on the back of the hands, is rough and covered with a pruriginous rash. The left arm and forearm are swollen, hand not œdematous. He presents a remarkable appearance from the enormous development of the cervical and axillary groups of lymph glands. From in front, the neck on the left side seems almost obliterated by a large mass which projects over the clavicle and towards the shoulder, and extends from behind the ear to the second interspace on the chest. On one spot there is a slough, and about it the tissues are reddened and inflamed. On the right side the cervical glands are not so much enlarged; the axillary groups form large bunches which project nearly to the nipples. Two isolated glands on the chest above the left nipple are considerable enlarged. The veins are not distended, but there is a good deal of subcutaneous infiltration over the sternum. Posteriorly, the breadth of the neck is very great on the left side from the enlargement of the deep glands. The individual glands in the axillæ and right cervical regions can be felt; but in the large mass in the left side they have more or less fused together, and in spots have involved the skin. To the touch they are soft, elastic and painless. The inguinal glands are moderately enlarged. The abdomen is full; veins not distended. Cardiac area of dulness a little increased; basic systolic murmur; nothing special in right lung; at apex of left, breathing is weak, but it is difficult to examine on account of the swellings in the vicinity. No difference in the respiratory sound at the bases.

Examination of throat and tonsils shows nothing special. No difficulty in swallowing; voice not specially altered, but he thinks he is a little hoarse. No history of any special pain about

bowels. Bowels rather costive. Urine is slightly high-colored, acid, specific gravity, 1025; no albumen. Pulse, 90; temperature, 101°F. Liver and spleen normal. Opthalmoscopic examition of eyes negative. No hemorrhages; discs clear. On withdrawing a drop of blood, it is seen to be of a fairly good color, not watery; on examination the individual cells are seen to be a little pale; colorless corpuscles relatively increased; many smaller than usual; fibrin filaments very distinctly seen. Red cells regular in size. Hæmocytometer shows about 4½ million red cells to the cubic millimetre; a proportion of 1 white to 150 red corpuscles.

The patient will now strip that you may see the extent of the glandular swellings; rarely will you see them more pronounced. From behind the appearance is even more striking. Fortunately for him the large bunches on the left side have grown outwards and have not seriously involved the veins and there is no pressure on the trachea. The only interference with the circulation is by the growths in the left axilla. In this disease much depends on the group of glands involved. This patient tells us that he has had little or no pain and has only the inconvenience of these large tumors which impede the movements of head and arms. Very much less swelling of the internal glands may produce intolerable anguish from pressure on the nerves. I remember well the first case of the kind I saw. A large stout man, whose only symptoms were terrible pains in the back and legs and œdema of the feet. The retroperitoneal and pelvic glands alone were affected and pressure on the nerves produced the severe pains. When in the mediastinum the enlarged glands may compress the trachea or bronchi or the great vessels and bring about a most complicated series of symptoms. The case in No. 11 which interested us so much a few weeks ago—too much, in fact, as he got frightened and left the Hospital—was one of this sort. Extensive pleural effusion on the left side, group of enlarged glands above left clavicle and a large bunch of them in the abdomen. I have no doubt of the nature of the case, but the pleurisy was the most prominent feature, probably dependent on the pressure of mediastinal glands. I pass around

the photographs of a case* in which the mediastinal glands were chiefly involved. Notice the great prominence of the sternum. You notice that the patient before you does not look anæmic, much less cachectic. He has been a robust, healthy fellow, and the calls upon his reserve fund, by the growth of these masses, have been so far well met, and though he has lost flesh, his nutrition is still fairly good. The blood count would seem to tell us this for the percentage of red corpuscles is not far off the normal, but there is a relative increase in the colorless cells and the density and size of the fibrin network which separates out between the rolls of red corpuscles indicate disturbance in hæmatosis.

The pigmentation of the skin is here doubtless due to involvement of the branches of the solar plexus in glandular tumors, though we cannot feel any through the thick abdominal walls. I have read reports of two or three instances of this bronzing in Hodgkin's disease. The patient is quite positive about the deepening of the color and we can scarcely attribute it to the prurigo caused by the papular rash which is on the trunk. Another point in this man's case is the pyrexia. As you see by this chart he has irregular fever, at times reaching as high as 102° F. In the majority of instances the temperature is raised and it may be a continuous pyrexia not as in this patient, remittent.

We know nothing as yet of the causation of the disease. So far as we can ascertain this man comes of healthy stock, and his personal history gives no clue to any morbid influence. Now that he has left the room we can discuss freely some other questions. The lymphatic tumours are due to an enormous increase in the cellular elements of the glands—a progressive hyperplasia. The consistence will depend on the amount of gland stroma; when abundant, the tumours are firm, when scanty, as in these, they are soft. You saw the day before yesterday a beautiful example of lymphoid growth, and as some of you were not at the autopsy, I will demonstrate the specimens again. I have here the right lung, bronchi and trachea, and you see these large tumours about the latter; there is general enlarge-

*Cases of Hodgkin's Disease. Can. Med. & Surg. Jour., Feb., 1881.

ment of the bronchial glands, and here at the root the tissue of the right lung is invaded. Section of one of these glands shows a soft white material which, under the microscope, is seen to consist of ordinary lymphoid cells, with but little stroma. In this case there was a secondary growth on the membranes of the cord, and a small one in the tail of the pancreas. Now what is the difference between these growths and the tumors you have just seen in R— A—? Little enough macroscopically, or microscopically, and yet there is a difference. I told you that the bronchial growths was primary lympo sarcoma; it is distinguished from the lymphoid growths of Hodgkin's disease and leukæmia by a more rapid development, a greater tendency to invade contiguous structures and when it generalizes, *i.e.*, from secondary tumors, they may be in any and every organ and not confined, as in leukæmic and pseudo-leukæmic growths to one or more organs. In this case, the secondary tumors were in the spinal membranes and pancreas. Sarcoma of the lymph glands is apt to early penetrate the capsule of the glands and invade neighboring parts. You see this in the lung here which has been involved. I have a specimen of sarcoma of the tracheal and bronchial glands which crept up and invaded the thyroid.

With lymphatic leukæmia, Hodgkin's disease has many similarities, so much so that the mere absence of one feature, *viz.*, the increase of colorless blood corpuscles, seems scarcely enough to justify their separation. And further there have been cases in which the leucocytosis, as exists, for example, in R— A—, has increased to a positive leukæmia and that within a very short time. The prognosis is as bad as can be. The enlargement is progressive, and though in the instance before us the groups involved have not as yet seriously interfered, either by pressure or otherwise, the gradual impairment of nutrition and the drain upon the system, by the suppuration which is likely to follow in the large mass, will induce asthenia, if pressure effects do not supervene and bring death more rapidly.

With such a prognosis you may judge of the value of treatment in these cases. An important point is, should the glands be excised? If in a localized group, as on one side of the

neck, and there is no constitutional disturbances—yes; but if several localities are affected and there is constitutional affection—no; the results are decidedly against it. In addition to iron, general tonics and good diet, I give arsenic in increasing doses, begining with two or three drops three times a day, and increasing gradually, if the patient bears it, to twenty or thirty drops daily. Under its use I saw the glands on one side of the neck get decidedly smaller, and I have under this treatment at present a lady whose general condition has much improved, and the gland swelling considerably diminished. Phosphorus has been found beneficial by some observers.

PREATAXIC TABES DORSALIS.

A Clinical Lecture delivered during the summer session of the McGill Medical Faculty.

BY

WILLIAM OSLER, M.D., F.R.C.P. LOND.,

PROFESSOR OF THE INSTITUTES OF MEDICINE, MCGILL COLLEGE, MONTREAL.

FROM

THE MEDICAL NEWS,

August 25, 1883.

DORNAN, PRINTER.

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PREATAXIC TABES DORSALIS.

GENTLEMEN: In locomotor ataxia we may, for clinical convenience, recognize three stages, the *preataxic*, in which, without any incoördination, there are certain other well-defined and characteristic symptoms; *the ataxic*, in which the disordered muscular movements predominate; and a final *pseudo-paralytic* stage, in which the patient is a helpless cripple. The man before you is an interesting illustration of the early, or preataxic stage. You see, as he walks around the arena, that the gait is normal, and you certainly would not suppose from his appearance that he was afflicted with this disease. From the fact that locomotor ataxia may exist for years without *ataxia*, the name tabes dorsalis, given by Romberg, is preferable, or posterior spinal sclerosis, which indicates the location and nature of the lesion. When we consider that about fifty per cent. of tabetic patients are not ataxic[1] the name in common use is misleading, and gives undue prominence to a symptom which is often absent.

The clinical record of this patient is as follows: Samuel S., of Sherbrooke, Que., aged 43, Canadian, a cabinetmaker by trade, but for some years (12) past a millwright, came to the hospital to be treated for failure of eyesight. Nothing special in the family history. Has been married nineteen years; two children

[1] Erb, in eighty-four cases, mentions that forty-three were in the initial stage and presented no ataxia.

living, three dead; one, a year old, had a rash on the body, the other two were still-born. Had gonorrhœa; can get no history of chancre. Formerly took spirits freely, but has been temperate for some years. Has used tobacco to excess, also opium. In his occupation as millwright has been much exposed to wet and cold, particularly when working in the flumes, and on several occasions has been for hours in ice-cold water. For nearly four years he has had what he calls rheumatic pains in the legs, at irregular intervals; sometimes six months would elapse, and at others two or three attacks would occur in a couple of weeks. He describes the pains as intense, coming on with great rapidity, localized often in spots not more than an inch or two in extent, which are acutely sensitive when they are present; duration brief, two or three seconds, and then they pass away as quick as they came, to return again in a few minutes. Sometimes they have been so bad that he has not slept; in his own words, "they would just give me breathing spells, and then I had to clinch my teeth to bear the next pain." No tingling or pins and needles. For about a year has noticed that the eyesight was failing; may have been present for a longer time, but he was not conscious of it.

Examination: Patient is a slight, dark man, fairly nourished. Gait is unaffected. Muscles moderately developed. Sensation in legs good; not retarded. Pupils are contracted, round, measure 3.5 mm. They do not react to light (reflex immobility, reflex iridoplegia). Act during accommodation and in associated movements when eyes move upward and inward. Dr. Buller tested the vision, and reports $\frac{6}{100}$ with right eye and $\frac{22}{100}$ with left eye. Considerable limitation of field of vision in upper and outer parts. Optic nerves bluish-white in color; margins well defined all the minute vessels of the disk are gone, [illegible] larger

trunks remain, and they, too, are diminished in size. Color-perception for red and yellow good; he thought the green was dark-brown, almost black. The patellar tendon-reflex is absent. Plantar, cremasteric, and abdominal reflexes are present.

The eye symptoms, lightning pains, and absence of knee-jerk, are the chief features presented by this case, and together they are amply sufficient to establish the diagnosis of tabes dorsalis. Let us consider these symptoms a little more closely, and, first, the ocular phenomena, which are among the earliest and most remarkable nerve disturbances in the disease, and of great diagnostic importance. When I place the patient before the window, shade his eyes with my hand, and then suddenly expose them to the bright light, no change takes place in the diameter of the pupils. Tested with a stronger light, the same peculiarity is noted; the pupils are immobile and do not react to the stimulus. If now, after looking at my fingers at eighteen inches he then directs his vision into the distance, the pupils dilate with the relaxation of accommodation, and contract again when he looks at a near object. While not responding to the stimulus of light, they are active during accommodation. This reflex immobility of the pupil, first described by Dr. Argyl Robertson, and sometimes called after him, is present in a large proportion of cases of tabes. In 84 cases of Prof. Erb it was noted absolutely in 59, and diminished in 12. Of these 71 cases, 43 were in the preataxic stage of the disease. In Gower's address, just to hand, on eye symptoms in spinal disease, the light reflex is stated to have been lost in 48 out of 72 cases. Usually the reflex immobility is associated with myosis, which exists in this man in a moderate degree. The only other affection in which this sign has been specially noted is progressive paresis of the insane. Not only is

the power of reflex contraction of the pupils lost, but reflex dilatation may also be suspended. If you stimulate strongly the skin of a healthy person, a slow reflex dilatation of the pupils takes place, but in the majority of cases of tabes this does not occur. We could not get this reflex on strong galvanic stimulation of the skin of the neck and shoulder of this man. The precise locality of the lesion which causes these early pupil symptoms is unknown, but if you consult the diagram of the pupil centres, which you have in your physiology notes of last winter, you will see that, as Erb says, the local degeneration causing the loss of light reflex must be somewhere in the pathway between the centres of the optic and the third nerves.

The chief complaint of this patient is a steadily advancing loss of sight, which ophthalmoscopic examination shows to be due to atrophy of the optic nerve. Many of you have had an opportunity of examining the disks in the ophthalmoscope room, and studying the characters of the sclerotic atrophy—the blue-gray color, the flatness of the disks, the absence of small vessels, and their sharp distinct outlines. With no other spinal affection is atrophy of the optic nerves so frequently associated. It usually begins early, before the second stage of the disease is reached, and the patient may be quite blind by the time the ataxia develops, or, indeed, before there is a suspicion of tabes. The atrophy is progressive, and ultimately, though it may be after the lapse of months or even years, total blindness results.

Color-perception is often disturbed; most frequently patients lose the power of distinguishing red and green, while that for yellow and blue may be retained. This man says that green appears to him dark-brown or almost black. His perception of red, yellow, or blue is good. There are other eye symptoms, not present in

this instance, which may puzzle you not a little, if unaware of their connection with tabes. I refer to the local palsies of the external eye muscles, and the production of squint, double vision, and ptosis. These, too, are often preataxic symptoms and are quite as common as those which we have considered. Double vision, with or without positive squint, is often a most troublesome feature, and the patient may be for months under the care of an oculist, or, indeed, have an operation performed for strabismus. Some years ago, I knew a gentleman who had intractable ptosis and squint without any other special symptoms. He has since become ataxic. I have at present under observation a gentleman who had external strabismus and double vision for six or seven months, and now has severe pains, bladder trouble, and absence of the patellar reflex. In adult men, the occurrence of ptosis, squint, or double vision, should suggest to you the possibility of early tabes and the necessity of examining for other signs.

Besides the failure of vision, the patient has but one complaint—the terrible pains which have attacked him at times during the past four years. The account which I read to you, is a typical description of the so-called lightning or electric pains of tabes. They are usually mistaken for rheumatic pains, and affect chiefly the lower extremities, sometimes the back and sides, rarely the arms. They vary greatly in intensity and in the frequency of their occurrence; weeks or months may elapse between attacks. The suddenness of their onset, the rapid darting or flashing character, is well expressed in the terms electric, fulgurating, or lightning. They fly about from place to place, and when a bad bout comes the patient may cry out with each pain, and they may recur so rapidly that, as our patient says, there are only breathing spells between

them and just time to clinch the teeth to bear the next stab. The skin over the site of the pain may be intensely sensitive—hyperæsthetic. Occasionally the pains are dull, heavy, and dragging, not sharp and stabbing; this, however, is quite exceptional. Very few, not five per cent., of ataxic patients escape these torments. One other important symptom is presented by this man; when I strike the patellar tendon of the crossed leg with the rim of the stethoscope, there is no response in muscular contraction of the quadriceps extensor, and the leg is not jerked up as in health. The knee-jerk or patellar tendon-reflex is absent, and since Prof. Westphal called attention to this sign, it has come to be regarded as of great diagnostic value in tabes. Exceptionally, the knee-jerk is absent in persons in whom there can be no suspicion of posterior spinal sclerosis; but absence of it in conjunction with lightning pains or any of the ocular phenomena, may be regarded as proof positive of the existence of the disease. Lest you may think that rather a strong statement, let me read you a paragraph from a lecture by Dr. Buzzard, whose work on *Diseases of the Nervous System* I would specially commend to you as embodying the rich clinical experience of an unusually acute observer. He says, "It is of much importance to remember that the two symptoms—on the subjective side, pains of the character described, and, on the objective side, absence of the patellar tendon-reflex (with a fairly normal condition of the quadriceps extensor muscle)—are the most constant, as they are probably the earliest of all. My belief is that if we meet a patient who exhibits them both, we do not need the presence of any other in order to form a diagnosis of tabes dorsalis." The patellar tendon-reflex is absent in about ninety-six per cent. of all cases.

Among other symptoms which may be present in

the first stage are localized regions of anæsthesia, numbness, pins and needles, but more common with pronounced ataxia; attacks of obstinate vomiting occurring without obvious cause, the *crises gastriques* of Charcot, and vesical and rectal troubles. Disturbances in the sexual function are common in tabes; sometimes there is at the onset satyriasis, usually as the disease advances, there is loss of sexual vigor, and finally impotence. In connection with this, I may mention to you an interesting case which I saw today: A gentleman from near Chatham, Ont., has gradually become impotent, and the question has been raised by an eminent American specialist whether the loss of sexual power was not an early tabetic symptom. The man is powerfully built, accustomed to out-door life, had syphilis about fourteen years ago, and has abused his sexual powers to excess. For three months he has been on a strict anti-syphilitic treatment without any benefit, and he is now practically impotent. The testicles are soft and flabby, and there is a large varicocele. There are none of the tabetic symptoms presented by the case we have just considered, though he does complain of dragging pains at times in the legs. In rare instances, impotence is an early, perhaps initial symptom in tabes, but whether it is so or not, in this instance, time alone will tell. Dr. Bray, of Chatham, under whose care he is, will doubtless know in a few years. Possibly the varicocele may have something to do with his trouble.

You doubtless are aware that much discussion has taken place lately regarding the cause of tabes, and many facts have been brought forward by Fournier, Erb, Gowers, and others to show the close connection between it and syphilis. Statistics prove that considerably over fifty per cent. of all tabetics have had

syphilis,[1] but whether this is simply a matter of association, or whether a definite causal relationship exists, is not yet clear. You should be especially careful in obtaining the history of a patient to ascertain if he has had syphilis, as the treatment may be thereby considerably influenced. There are some indeed who regard the occurrence of tabes as in itself a proof of the existence of syphilis, but this is an extreme view and not borne out by facts. In the case you have just seen we can obtain no positive evidence of infection; true, he has been *in the way of it*, having had gonorrhœa, and the death of three children, one with a general rash, is a suspicious circumstance, but he is an intelligent man, anxious to give all details and he seems quite certain that he never had a sore on his penis or any secondary manifestations. It is astonishing how reluctant some men are to acknowledge the pox. Even an intelligent physician will conceal the fact from his best friend and deceive him grossly, as in the following instance. A few years ago, after a medical dinner in London, the conversation turned on this very subject, tabes and syphilis, and one gentleman was very positive about the invariable association of the two. Our host stated that he had under observation a medical man, the subject of tabes, who offered a satisfactory refutation of this view as he had never had syphilis. I ascertained the name of the surgeon referred to, and to my surprise found that it was a man with whom I had been acquainted on the continent, and who at the time was under treatment for secondaries.

Exposure and cold, especially with muscular fatigue, are believed to be potent influences in the etiology

[1] In the Vienna Correspondence of *Canada Medical and Surgical Journal*, Dr. Thomas Stewart states that Dr. Wolfe found only ten syphilitics in one and one cases of tabes.

of tabes, and in this connection it is worthy of note that our patient has been much exposed to cold and wet when working at his trade as millwright, often up to his waist in ice-cold water.

From the fact that he has had lightning pains for over four years you may gather that even the initial stage may be very prolonged. Tabes is perhaps the most chronic of all nervous affections, and in individual cases it is impossible to predict what the course will be. This patient may not become *ataxic* for years; unfortunately for him, the optic atrophy will almost certainly be progressive and lead to total blindness. Occasionally the course of the disease is very rapid. I had arranged to show you another case to-day, a pronounced ataxic, with the characteristic gait, etc., but he sent word that he was too unwell to come. This man has had syphilis, has suffered from cerebral manifestations, and now for nearly two years has presented symptoms of tabes, the incoördination being now so great that he moves about with very great difficulty. When once established, the disease is, as a rule, hopelessly incurable; it is impossible to restore sclerotic nerve tissue to the normal state. The most we can hope to do is to arrest the progress and alleviate some of the more distressing symptoms. Where there is a decidedly syphilitic history, as in the case I just referred to, a thorough course of mercury and iodide of potash should be tried. It has done him no good, but there are instances on record in which such a plan has been of material benefit. Of course, the remedies in vogue in the treatment of the disease are legion. At present great confidence is placed in nitrate of silver, in quarter of a grain doses three times a day, continued for months, intermitting every fifth week to prevent deposition of the salt and staining of the skin. It seems to relieve the pains, and in some cases the incoördina-

tion has disappeared during its employment. We shall put this patient on a prolonged course of the silver, and order galvanism to the spine. Rest is an important element in the treatment, but in many instances, as in this one, impossible to procure. When the electric pains are severe, friction (massage) is beneficial and in very bad spells, hypodermic injections of morphia.

I have no belief in the restitution by therapeutic means of a sclerotic tract in the spinal cord; as well might we hope for restitution of a group of sclerotic (cirrhotic) liver lobules. Curiously enough, even when decided amelioration does take place or a cure is apparently effected, the lesion in the posterior columns may remain unchanged. In one of the recent numbers of the *Archiv für Psych.*, Dr. Schultze reports a remarkable case which illustrates this. A patient of Dr. Erbs' was apparently cured, the ataxia and pains disappeared; absence of patellar reflex and slight vesical trouble alone remained. Twelve years after the appearance of the symptoms of ataxia, and eight after their disappearance, he died of poisoning. At the autopsy the posterior sclerosis was well marked in the lumbar section of the cord, and there was degeneration of the posterior root-zones in the dorsal and cervical regions.

The opinion is gaining ground that locomotor ataxia is not simply posterior spinal sclerosis, but a widespread affection of the sensory nerves; and taking this view the various peripheral nerve changes, the optic atrophy, which is so common, the occasional affection of the auditory, and the degeneration of the cutaneous nerves which has been described—all come in as part of the general affection.

THE THIRD CORPUSCLE OF THE BLOOD.

In addition to the red and white corpuscles, there are in the blood granular bodies of various size, from that of a red corpuscle to masses ten to twenty times as large. These were first described by Max Schultze, and they may be called very appropriately, as I have been in the habit of doing for years, "Schultze's granule masses." In healthy adults they are not abundant as a rule, though exceptionally in persons in apparently good condition they abound. In all cachectic states the granule masses are large and numerous. They form notable features in blood specimens from cases of chronic phthisis, cancer, and wasting diseases generally; also in leukæmia and symptomatic anæmia; but it is not a little remarkable that in pernicious anæmia they are scanty, or even absent. In the lower animals the masses are met with in variable numbers. The blood of the young contains them in larger proportion than in adults. The new-born rat, kitten, rabbit, or guinea-pig may be used with advantage for their study. So common are they in the blood of hospital patients that it is not to be wondered at if mistakes have arisen concerning the signs of their presence in certain diseases. Thus, in *The Lancet* a few years ago, a gentleman described them under the heading of "a new feature in leucæmic blood," regarding them as specific or characteristic elements.

I have been told of a somewhat prominent London physician, connected with one of the special hospitals for chest diseases, who found them so constant

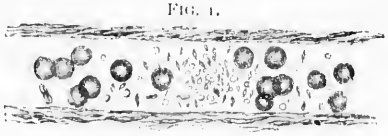
in the blood of phthisical patients that he regarded them as peculiar to the disease, until advised by a colleague of their wide distribution. The most extensive observations upon their presence in disease were made by Dr. Reiss.[1] The common opinion regarding them has been that they represent degenerated white blood-corpuscles, or a granular detritus resulting from their decay. I first showed that they were composed of distinct corpuscles, and that the masses did not preëxist in the blood, but were formed at the moment of withdrawal by the aggregation of the corpuscles. At the edges of large groups, the disk-like corpuscles can be distinctly seen, and in the sulphate of soda solution, such as used for mixing the blood in hæmocytometer work, the corpuscular nature of the masses is quite clear. But what led me to this point was the fact of the impossibility of supposing that masses of the size of some of these could pass through the capillaries. Reiss felt the same difficulty, and suggested that in some cases they might produce embolism. In the blood of the new-born rat they are most abundant, and the subcutaneous tissue was employed to investigate the condition of the masses within the vessels. It was then found that they do not preëxist as aggregations in the blood, but are in the form of isolated corpuscles floating free with the other forms. By far the simplest way of demonstrating the isolated corpuscles in the vessels is to snip a small bit of the subcutaneous tissue from a young rat, and examine in salt solution.

In a small artery or vein, there will be seen with the red and white cells small, pale corpuscles about one-fourth the size of the red ones, often in extraordinary numbers (Fig. 1). A drop of blood from the tail of the same animal will show numerous granule masses, at the edges of which the corpuscles can be

[1] Reichert u. DuBois Reymond's Archiv, 1872.

seen. The corpuscles swell in water, and become pale: dilute acetic acid renders them more distinct;

FIG. 1.



they stain with carmine and methyl-violet. The corpuscles are discoid, pale, structureless (Fig. 2).

FIG. 2.

and often undergo peculiar alterations in shape, elongating or presenting two or three fine hair-like extensions. They measure from $\frac{1}{8000}$ to $\frac{1}{12000}$ of an inch. The largest I have measured was $\frac{1}{5000}$; and the smallest are from $\frac{1}{15000}$ to $\frac{1}{26000}$.

The facts above given are from my paper before the Royal Society in 1874, which was published in the *Proceedings* for June 18th of that year. A considerable part of that communication was taken up with describing the changes in form which the corpuscles undergo when kept for some hours at the temperature of the body, and examined in blood-serum; but the corpuscles were described and figured, and a true explanation given of the structure and formation of Schultze's granule masses. These bodies are undoubtedly the same as those described by Zimmerman[1] as elementary corpuscles which he found when blood was let flow into a solution of a neutral salt; after the subsidence of the colored elements, the supernatant serum contained, in ex-

[1] Virchow's Archiv, Bd. xviii.

traordinary numbers, small, round, colorless corpuscles with weak contours.

In 1877–79, Hayem, of Paris, investigated these bodies very carefully, and by special modes of preparation and examination was enabled to isolate them and prevent their aggregation into masses. He called them hæmatoblasts and believed that they represented embryonic red corpuscles.

From this time on, until last year, little or nothing new concerning these bodies is met with in medical literature, when in a series of papers in the *Centralblatt f. d. medicinischen Wissenschaften*, and more fully the November number of Virchow's *Archiv* (Bd. xc.), Prof. Bizzozero, of Turin, described anew the corpuscles and advanced important views concerning their connection with the process of thrombosis and coagulation. His account of the corpuscles, which he calls "Blutplättchen" (blood-plates), differs in no essential particular from that which I had already given, and his figure of them in a small bloodvessel (Pl. V., Fig. 2, Virchow's *Archiv*, Bd. xc.) is similar to my original one reproduced here in Fig. 1. The observations upon the connection of the corpuscles with thrombus formation are novel and important. When a vessel-wall is injured, or when any foreign body is introduced, the earliest observable phenomenon is the collection of the blood-plates on the wounded spot or on the foreign substance. The white corpuscles appear later and are much less numerous. The blood-plates rapidly change, becoming fused or united together and converted into a granular substance, and this dissolution or disintegration appears intimately associated with fibrin formation. In a portion of a vessel sutured between two ligatures the blood remains fluid so long as the blood-plates retain their normal form and appearance.

The influence which Schmidt and others attribute to the white corpuscle in coagulation, Bizzozero

believes is due to these smaller elements. Certainly no such rapid disintegration of the colorless corpuscles takes place, as is spoken of by some writers. Under favorable conditions they may retain their vitality, as shown by amœboid movements, for twenty-four or thirty-six hours after withdrawal, and many hours after coagulation has occurred. If freshly-drawn blood is whipped with a bundle of threads, the "blood-plates" first adhere to them, and afterwards a few white and red corpuscles. If the threads are then, before fibrin is deposited, washed in salt solution, they will, when placed in a suitable liquid (proplastic of Schmidt), induce coagulation, which, as Bizzozero has shown by other experiments, cannot be attributed to the few red or white corpuscles adhering to the threads. Several facts have come under my observation which corroborate the views of the learned Italian professor. I have been struck with the density and richness of the fibrin network in blood specimens in which Schultze's granule masses were abundant. As is well known, the distinctness with which the fibrin filaments can be seen in blood slides varies very much, and I think the variations will be found to have a close connection with the abundance or paucity of these elements. As one watches the process of coagulation, the filaments first seen are invariably in association with small granules—which represent disintegrated blood plates—or larger Schultze's masses. In cases of extensive atheroma of the aorta, the thrombi which form in the small breaches of the intima may consist entirely of these corpuscles, and in aneurisms they occur on the surface of the fibrinous laminæ. So, also, in the vegetations of endocarditis, these little corpuscles are found associated with the fibrin layers so commonly deposited in these structures.

So far as I can make out, the corpuscles here described are different from the invisible corpuscles

of Professor Norris, of Birmingham. The origin of the corpuscles remains a problem—one of many connected with the blood which await solution at the hands of histologists.

To conclude: 1st. There is in mammalian blood a third corpuscular element, one-eighth to one-half the size of the red corpuscle. It can be clearly seen in the bloodvessels of the living animal or in the vessels of freshly removed bits of tissue. It may be called appropriately the third corpuscle, or "blood-plate," though the latter expression is not a very satisfactory one.

2d. In blood withdrawn from the vessels these corpuscles aggregate together and form the well known granule masses in which the corpuscles rapidly degenerate and lose their outlines. These masses, first described by Max Schultze, should be known by his name.

3d. There is evidence to show that the third corpuscle plays an important *rôle* in coagulation.

ON SOME NATURAL MODES OF CURE IN EMPYEMA.

A Clinical Lecture delivered during the summer session of the McGill Medical Faculty, June 20th, 1883.

BY

WILLIAM OSLER, M.D., F.R.C.P. LOND.,

PROFESSOR OF THE INSTITUTES OF MEDICINE, MCGILL COLLEGE, AND PHYSICIAN TO THE MONTREAL GENERAL HOSPITAL.

FROM

THE NEW YORK MEDICAL RECORD

October 20th, 1883.

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ON SOME NATURAL MODES OF CURE IN EMPYEMA.

GENTLEMEN: Most of you have seen what *Art* can do in the treatment of empyema, and I am thankful to say that, by the plan we now follow of thorough drainage with a large canula and antiseptic dressings, we have had very fortunate results; but to-day I wish to call your attention to two cases which illustrate what *Nature* can do in the way of cure in this formidable affection. Left to itself an empyema may terminate as follows: 1. by perforation of chest-wall, of lung, or of diaphragm; 2, kill by septic or other influences; and 3. it may be absorbed or dry up. Of these three modes perforation is not very common either into the lung or externally, while into the abdomen it is very rare. Septicæmia claims no small proportion of fatal cases. Amyloid degeneration and tuberculosis kill not a few. Inspissation of the purulent contents and gradual absorption is perhaps the rarest of all terminations. A natural cure may take place by perforation of the lung or by the absorption of the pus, and of the three cases of empyema which you have had an opportunity of studying this session, two furnish illustrations of these modes.

Let us first study the case of the Swede who was discharged from Ward 11 a few days ago. The clinical report is as follows:

CASE I.—*Typhoid fever: empyema: expectoration of the pus; recovery.*—Christopher I——, aged twenty-three, a Swede, was admitted to hospital on March 26th with typhoid fever. The attack was moderately severe, but presented no special features. The chest was examined on admission, with negative results. Toward the end of April (28th) as the temperature kept up, and

he had a cough with shortness of breath, the lungs were examined, and absolute dulness found at the right base, extending as high as the spine of the scapula behind, and the fourth rib in front. The breath-sounds were not audible, and both tactile and vocal fremitus were absent. A hypodermic needle was inserted, and about twenty minims of creamy pus withdrawn. Patient had no chills, no sweating: there was usually an evening exacerbation of temperature, two or three degrees, only once reaching 103°. It was decided to wait for a week before operating, and meanwhile to improve his general condition as far as possible. On May 1st, without any aggravation of symptoms, he began spitting up pus, and in the course of twenty-four hours filled the spittoon (capacity 26 ozs.) The cough was very troublesome, not paroxysmal and the pus was brought up in rounded masses surrounded by clear mucus. *En masse* it looked like pure pus, but the isolated sputa resembled closely those of chronic phthisis. No elastic tissue was found; pus cells were the only elements. On May 3d the area of dulness was found to have diminished considerably, and at the angle of the scapula breath-sounds could be heard, distant on tranquil respiration, harsh and distinct on deep inspiration, and these accompanied by *very fine crepitant rales*.

For nearly three weeks the expectoration of pus continued: the amount at first large (15-22 ozs.) was by the 20th reduced to a couple of ounces daily. The dulness gradually diminished, and by the 13th a comparatively clear note was obtained on the portion of the infra-scapular area next the spine. Breath-sounds weak but quite audible; moist sounds on deep inspiration. His general condition improved rapidly, temperature became normal, and he was discharged June 4th. A slight area of dulness remained in the outer part of the intra-scapular region. While under observation a

loud, rough, systolic murmur developed, heard in the third and fourth interspaces to the right of the sternum; not at the apex or at the base. It was transmitted to the right base, and was first noticed during auscultation of this part.

I may safely say, gentlemen, that in no case which has been in the wards this session did we watch with greater interest the progress of the disease, and we can regard the result with equal satisfaction.

That an empyema may perforate the lung and be coughed up has been known for centuries; but a knowledge of the fact that this may occur without the development of pneumothorax, and constitute one of the most favorable modes of termination of the disease, does not appear to be very widely diffused. Hippocrates, indeed knew of it, and in several places speaks of recovery from empyema (after pneumonia) by perforation of the lung and expectoration of the pus.

Traube[1] in an article published in 1872, entitled "On a Natural Mode of Cure in Purulent Pleuritic Exudation," has called special attention to the fact, and mentions, as a curious circumstance, that he alone, of all the physicians who had written on empyema since Hippocrates, had observed it. In this however, he was mistaken, for it had not escaped the notice of the Irish physicians in the palmy days of the Dublin school. Dr. Greene[2] narrated several cases of the kind, and the late Dr. R. L. Macdonnell, the first professor of clinical medicine in this school, and who was at the time clinical assistant to Dr. Graves, in his important paper "Contributions to the Diagnosis of Empyema,"[3] clearly recognized this group of cases.

There appear to be two ways in which an empyema

1 Gesammelte Beiträge, Bd. iii., s. 44, 1878.
2 Dublin Medical Journal, vol. xvii., 1840.
3 Ibid. 1844.

may discharge through the lung; first, by opening into a bronchus and the formation of a fistula; and, second, by a local necrosis of the pulmonary pleura, exposure of the parenchyma, and a soakage of the pus through the spongy lung-tissue into the bronchi. In the first way pneumothorax usually develops and aggravates the danger. When the pus perforates by a large and free opening the patient may be suffocated by the sudden gush of fluid which is passed to the tubes more rapidly than it can be expectorated. Several cases of this kind are on record. The establishment of a bronchial fistula may be followed by temporary relief, but permanent recovery is rare. In the second way the pus is usually discharged without the formation of pneumothorax, and we must regard this as one of the most favorable modesof termination in empyema. Traube[1] was certainly the first to give a satisfactory explanation of the process, as he had an opportunity of studying the condition of the pleura and lung in one of these cases, and found on the lower lobe an oval area two and one-half by one inch with the pleura destroyed, and the lung-tissue fully exposed, but no direct communication with the bronchi. That pneumothorax does not occur he explains on the view that while the powerful coughing efforts compress the chest, and are sufficient to drive the pus through the exposed lung tissue into the bronchi, the affected side is immobile, or nearly so, and the slight expansion during inspiration has not force enough to aspirate air into the pleura.

Greene, in the paper already referred to, clearly distinguishes between the two classes, stating that "in cases of effusion a copious and purulent expectoration is a frequent accompaniment, depending in some insances on a fistulous communication established between the seat of the collection and a bronchial tube, and that when such a communication has taken place it may be recog-

1 Loc. cit.

nized by well-known and characteristic signs. But in other instances the expectoration may be equally copious and purulent, while all the physical signs of communication are absent, and where, consequently, the symptoms in question cannot be referred to such a lesion." In the latter case he thought, as did also Dr. Macdonnell, that the pus was the result of a vicarious secretion from the bronchial membrane, the action of a sort of reciprocity between the serous and mucous surfaces. Dr. Macdonnell draws a very proper distinction between the symptoms in the two groups, which I think holds good in the majority of cases. When a bronchial fistula is established a large quantity of pus is expectorated with violent and sudden paroxysms of coughing, the quantity at times being so great as to cause suffocation; whereas when no distinct fistula is established, but the pus soaks through the spongy lung substance, the expectoration, though amounting to many ounces in twenty-four hours, is spat up gradually and in small quantities at a time. This latter mode appears to be not uncommon, it is decidedly more frequent than the development of a bronchial fistula, and a large proportion of the patients recover, sometimes with great rapidity. We have had several instances in the hospital during the past few years, and when I mentioned the subject at the Medico-Chirurgical Society, three or four instances were narrated by members. Perforation of the bronchus and the establishment of pneumothorax is not always fatal. Attimont in his essay,[2] collected ten cases of recovery after expectoration of the empyema, and some of these were undoubtedly cases of bronchial fistula.

One other point in connection with this case is worth noting. You remember that when the effusion was disappearing, a very fine crepitant râle was heard with in

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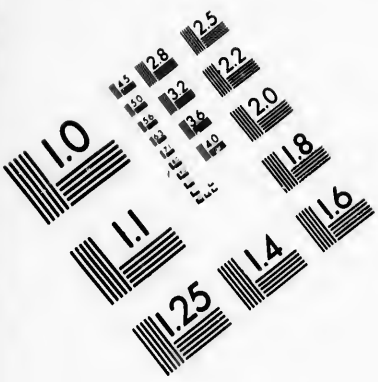
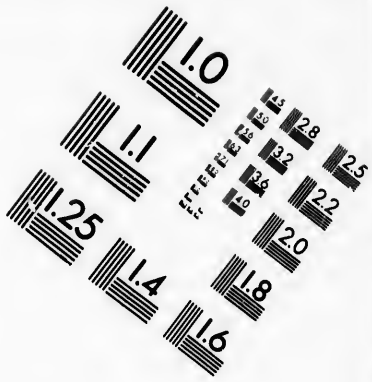
2 Considérations sur les Résultats de la Paracentèse, etc., 1859.





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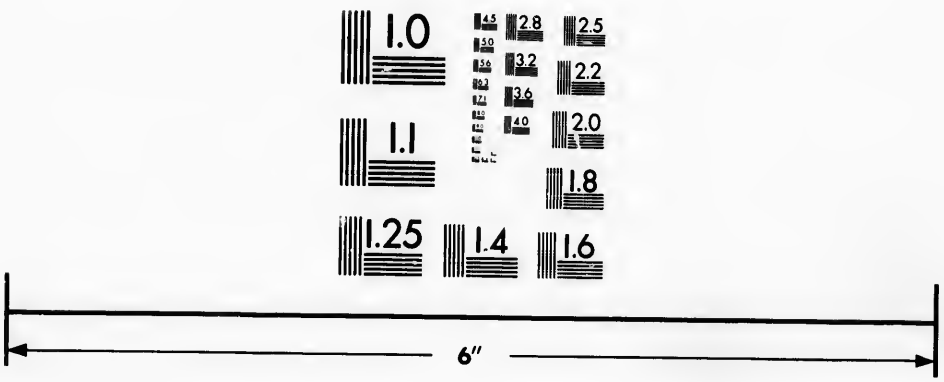

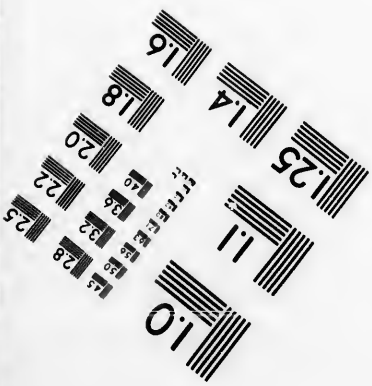

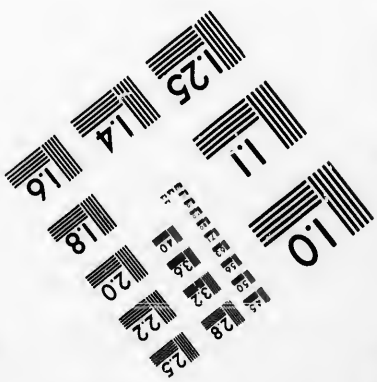

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spiration, at the angle of the scapula. It was as fine as and resembled closely, the pneumonic crepitus. In two other cases of pleurisy I have observed the same phenomenon as the effusion was absorbed, and was not a little puzzled. Dr. Macdonnell, already referred to, also noted this, and described it in another paper, "On Occurrence of Crepitus in Lung after the Absorption of Pleuritic Effusion."[3] Is it, however, in the lung? I mentioned to you at the bedside that it might be *pleuritic*, due to the contact and friction of the two surfaces after the absorption of the fluid, and if so it is in corroboration of the views of Dr. J. R. Leaming of New York, who holds that the pneumonic crepitus is not a pulmonary but an interpleural sound, due to the friction of the sticky surfaces.

The patient before you, who has been in hospital a few days, illustrates a very different process, but one which is leading to a satisfactory termination.

Case II.—*Empyema of seven months' standing; absorption of the fluid with retraction of the chest; local perforations of the pleura with subcutaneous abscesses.*—A. B——, aged twenty-three, from the Eastern Townships, of good stock, and always strong and healthy. Gives the following history: Quite well until November last, when, while lifting a heavy stone, he felt a stabbing pain in the right side, which continued at intervals for two weeks, during which time, however, he was able to get about and do work. He then took to bed, got weak and feverish, particularly at night. Had chills, and often sweated a great deal. Slept on the left side as a rule; when on the right the pain was increased. Had a cough through the winter; not much expectoration. Lost flesh rapidly. Has not been confined to bed all the time but got up and went about when he felt able. Latterly,

3 Ibid., 1844.

he has been improving, cough has disappeared, has no fever or sweats, and thinks he is gaining flesh.

The history points to some chronic chest trouble. When stripped for examination he presents an exceedingly interesting object for clinical study. General inspection shows a tall, bony man, pale and emaciated, and the attention is at once attracted to the lobsided appearance of the body, due to a marked depression of the right shoulder and a decided flattening and shrinkage of the right half of the chest. As he breathes quietly you observe that while the left side expands the right is absolutely immovable, and this is still more marked when he takes a full breath; the left chest expands to an unusual degree, the infra-clavicular and mammary regions swelling out in a striking manner, while the right side remains fixed. From behind the same flattening and want of movement are noticeable. Closer inspection shows very narrow intercostal spaces on the right side, and in the infra-axillary region there are two flat swellings in the seventh and eighth spaces, and in the latter, also, a fresh cicatrix. The apex-beat can be seen in the fifth space close to the edge of the sternum. There is a croton-oil rash on the front of the chest. Palpitation reveals more distinctly the narrowing of the intercostal spaces; the ribs do not appear hypertrophied. The small flat tumors in the seventh and eighth spaces fluctuate, and do not appear to communicate with each other. He states that one has already disappeared, and a fourth was opened and discharged about a spoonful of pus. He has noticed them for a couple of months. Tactile fremitus is marked in the upper part of the right side; below there is no special intensification. The edge of the liver can be felt at the costal border. Mensuration shows the right half of the chest to be nearly an inch smaller than the left, not as much as you might suppose on inspection, but the eye is in this

matter very apt to be deceived. Percussion gives in front, on the right side, a flat somewhat tympanitic note as low as the nipple, flat below this and absolute dulness behind. The left lung is everywhere resonant. On auscultation, the breath-sounds are absent in the dull regions below, feeble in the supra-scapular and infra-clavicular regions, and on deep inspiration a few rales can be heard. Vocal resonance is much intensified on right side, particularly in places. The examination of the abdomen reveals nothing special; the liver is not enlarged. General condition during the three days he has been in hospital has been good. Eats and sleeps well; has no fever; pulse about 80. A needle was thrust into the eighth interspace behind, but no fluid was obtained. There is laudable pus in the small flat tumors. He does not wish them opened, and returns home to-day. With good food, fresh air, and tonics, he will continue to improve. If the small abscesses remain, his attending physician will open them, but they may disappear, as one has already done. He will recover, with a damaged lung and a sh[illegible] side; but with compensatory enlargement of the [illegible] and a gradual improvement and distention of the upper part of the right lung the respiratory area will be amply sufficient for the purposes of an ordinary life.

As to the diagnosis in this case—could you mistake it for anything else? The only other affection which produces a somewhat similiar condition is fibroid phthisis or cirrhosis of the lung, in which there may be the depressed shoulder, flattened and contracted chest, with immobility, dulness, and weak breathing, but the history would be one of long-standing lung trouble, and there would be cough, expectoration, and special auscultatory signs. With the local abscesses perforating the intercostal spaces, the diagnosis in this case is, at present, easy enough; but some years hence, when these have

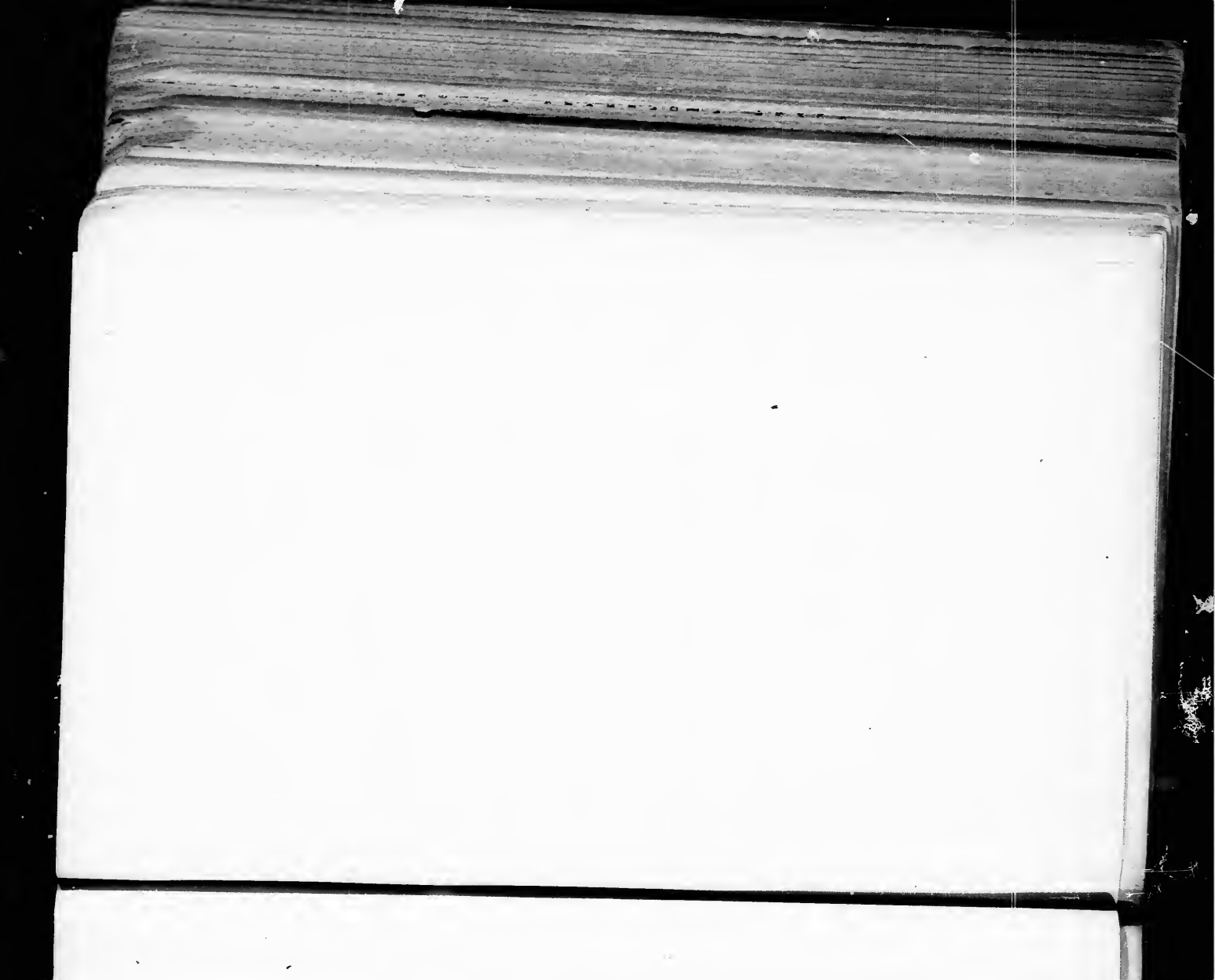
disappeared and nothing is left but the retraction, dulness, and feeble breathing, it might not be so easy without a full history. The condition of this man's chest illustrates in another way what nature can do in effecting a cure when an empyema is not interfered with. The effusion has evidently been pretty copious, and as the weeks and months elapsed became more concentrated and has gradually been absorbed, until now there is probably not more than a few ounces left. With the disappearance of the fluid another change has gone on; the flaky membranous exudation covering both layers of the pleura has become organized and converted into a dense fibrous tissue which may have a thickness of from half to one inch. In the process of absorption pockets of pus may have been left between the thickened pleural membranes, and sometimes this pus becomes caseous or even cretaceous. The angle between the costal and diaphragmatic layers of the pleura may be filled with a wedge of solid fibro-cartilaginous tissue which defies all attempts to separate it from lung or diaphragm. The firmness of these old pleuritic membranes is extraordinary, and in the removal of the lung, in such a case, the only way is to strip off the costal layer and take the attached portion of diaphragm The dulness in front and behind in this patient's right side is due chiefly to these thickened membranes, and corresponding to the seventh and eighth interspaces there are small pockets of pus, perhaps isolated, as they often are, and communicating by sinuses with the small external tumors. The lower lobe of the lung is condensed and airless, the upper and middle lobes, though thickly coated with false membranes, probably contain a good deal of normal and functionally active tissue. What produces the great deformity? When a sero-fibrinous fluid is absorbed, or after its withdrawal by aspiration, the lung expands, and although, as you have had several op-

portunities of observing, for months after there may be basic dullness and defective expansion, there is no retraction. In chronic pleurisy however, the serous layers are unusually thickened, the false membranes organize, and there is produced a large amount of new connective tissue, which gradually shrinks, prevents the expansion of the lung, and little by little drags in the side, narrows the intercostal spaces, pulls down the shoulder, may curve the spine, and displace contiguous organs, drawing the heart over and the liver up, until there is presented such a typical condition of *rétrécissement thoracique* as exists in this case. Although the shrinkage and condensation of the organized membranes play the most important part in the process, some share must be attributed to other agencies, such as posture—the patient favoring the affected side—atmospheric pressure, and muscular contraction. Will this side ever expand again? Not to its full extent or near it. In time the upper regions of the lung will dilate more fully and there will probably be some movement in the anterior part, now absolutely quiet, but the deformity will remain and the lower part of the right side will never expand. It is true that occasionally a remarkable amount of expansion may take place after a *pleuritis deformans*. Sir Thomas Watson refers to two examples of complete re-expansion of the side, contracted after chronic pleurisy, but such cases are extremely rare.

Perforation of the costal pleura and the formation of a subcutaneous abscess constitute the condition known as *empyema necessitatis*, which is not often seen. In this instance the external collections are small, and probably connected with encapsuled deposits within the pleura. One has already disappeared, and a second, which was opened, healed rapidly, and the two which remain are not connected with each other, and probably not with any large amount inside. There are two or three points

of interest about *empyema of necessity* to which I will refer as you are not likely to see another instance of it for some time. When it breaks, or is opened, the fistula which forms may remain for years and be difficult to heal. There is a case on record of one Dr. Wendelstadt a Bavarian, who had such a fistula for over thirteen years and enjoyed fairly good health. Necrosis and caries of the ribs are apt to occur and retard recovery, as the sinuses which result run in various directions and are very difficult to heal. A case of the kind occurred a year or so ago in the practice of Dr. Rodger, of this city, and at the autopsy we found the skin and pleura of the antero lateral region on the left side riddled with sinuses communicating with carious ribs and small pockets of pus within the thick layers of false membrane. Occasionally in *empyema necessitatis* the external tumor pulsates synchronously with the heart, and might be mistaken for aneurism. This is the result of a communicated cardiac pulsation, and was first described by Dr. Macdonnell, in the paper already referred to, and not by Dr. Walshe, to whom the credit is usually given.[1]

1 The mistake has arisen from the fact that Dr. Walshe has described two remarkable cases of intra-pleural pulsating empyema.



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REPORT

ON THE

BRAINS OF RICHARDS AND O'ROURKE.

BY

WM. OSLER, M.D., M.R.C.P., LOND.
Professor of the Institutes of Medicine in McGill University, and Physician to the Montreal General Hospital.

READ BEFORE THE MEDICO-CHIRURGICAL SOCIETY OF MONTREAL.

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(Read before the Medico-Chirurgical Society of Montreal.)

Although Benedikt's conclusions have been shown to be unwarranted, and we shall probably never be able, in a given collection of cerebra to pick out those which have belonged to criminals, still, a certain interest and value is attached to the examination of the brains of individuals who have rendered themselves notorious by the commission of great crimes.

I.—Richards, aged 52, a large, powerfully-built man, murdered a comrade in the Eastern Townships last summer. He was tried at Sweetsburg and condemned to be executed, but the evening before the appointed day he cut his throat with a small pen-knife. He appears to have been a thorough-going criminal, "smacking of every sin that has a name." Dr. H. LeRoy Fuller of Sweetsburg kindly sent the brain for examination, and furnished the following brief report of Richards :—"According to his own statement, he has been a thief, a robber and a liar since ten years of age. A portion of his life was spent in the army, from which he had deserted, and bore the brand on the

left side; was taken back and afterwards discharged as unfit from a moral point of view. About fourteen years of his life were spent in prison, and in addition to hard drinking, he was, according to his own account, much given to women. He may have had syphilis, though there were no external signs of it, nor had he any manifestation during the eight months that he was under my observation. While here he has been healthy, with the exception of an attack of diarrhœa and occasional frontal headaches. He had a scar at or near a point corresponding externally with the small spot of softening found on the frontal lobe. This, he said, was caused by the thrust of a bayonet."

Brain.— Organ weighed 47 ozs.; was well formed; hemispheres cover the cerebellum. Membranes and substance very anæmic. Membranes were normal: arachnoid a little opaque over the sulci. Vessels empty.

Fissures.—In right hemisphere, neither the fissure of Sylvius nor the fissure of Rolando joined contiguous ones, though a shallow groove connected the precentral with the latter. Both the retro- and pre-central were well marked; the latter was longer than the fissure of Rolando, and passed deep into the operculum. A short sulcus passing from the precentral fissure, split the hinder end of the superior frontal gyrus for 3 cm. The sup. frontal fissure was separted by a narrow bridge from the precentral fissure, and, anteriorly, sent three or four secondary sulci into the superior and middle gyri. The inferior frontal fissure was well marked, and had many secondary sulci. The interparietal fissure arose from the middle of the retro-central, and sent numerous secondary sulci into superior parietal lobule and angular convolution, joined the horizontal occipital, passed around the angular and united with the first temporal sulcus. Wernicke's fissure was marked. The temporal fissures were normal. On the median surface, the fissure of the corpus callosum passed deep into and had many secondary sulci in the precuneus; parieto-occipital and calcarine fissures were normal. On the left hemisphere, the fissures of Rolando and Sylvius did not join contiguous ones. The superior and inferior frontal ran out from the precentral, and were exceedingly well defined. The retro-central

was separated by a very narrow bridge from the fissure of Sylvius, and had three deep branches in the superior parietal lobule, and a deep and wide fissure in the hinder part of parietal lobe, which joined the horizontal occipital. The fissure of the corpus callosum was interrupted about the middle of its course by a convolution uniting the gyrus fornicatus and the first frontal. The parieto-occipital and calcarine fissures were very deep, and ran to the sassura. Calcarine was normal. Wernicke's fissure was not marked.

Convolutions.—On the right hemisphere, the frontal gyri were well developed, the ascending was wide and large. The superior was split in its hinder part. The middle and inferior presented nothing special. The orbital gyri were normal. The ascending parietal was narrow. The other parietal and the occipital gyri presented nothing noteworthy. The gyrus fornicatus was narrow. There were five gyri in the insula. On the left hemisphere the ascending frontal was large; the superior, middle and inferior well defined, the first not divided; the middle ran out from the ascending, interrupting the pre-frontal fissure. In the parietal lobe, the ascending was isolated and well defined. The supra-marginal was large; the angular was much fissured. The first and second temporal gyri were divided by fissures, and there was a junction of the two by a narrow bridge. The gyrus fornicatus was split; precuneus well marked. There were five gyri in the insula. On the anterior angle of the third left frontal gyrus, just where it joins the orbital gyri, there was a superficial patch of softening, 1 by 1 cm., apparently hemorrhagic, involving the grey matter.

Summary.—The asymmetry between the convolutions and fissures of the hemispheres was very slight. The organ was not of the marked confluent fissure type. The secondary and cross sulci were not excessively developed. The majority of the convolutions were arranged in a normal and typical manner.

II.—O'Rourke, on the 20th of January, 1882, in the county of Nelson, Ont., killed a farmer and his daughter, with whom he had quarrelled. He was an uneducated man, and had led an irregular life, going about as a day laborer. He had

served two years in the Penitentiary for perjury. Dr. Freeman of Milton writes to me: "He had illusions, believed that he saw ghosts, particularly that of his mother and that of a late Dr. Ford. He was so timid that he required either a light in his room or somebody to sleep with him. The reading of murder trials to him was his greatest treat. He left the house of the Mahers in the morning with the most friendly feelings, went to an hotel and got three pints of whiskey; returning to the house about nine o'clock in the evening, he had some words with Maher and his daughter, and murdered them both with an axe, and attempted to kill the son on his return. He told the neighbors that young Maher had killed his father and sister, but when arrested in the morning he confessed. He was indifferent before and after the trial, and said a person had only once to die. He never expressed any remorse." Insanity was pleaded in his defence.

Brain.—Received in good condition from Mr. Freeman, medical student. Hemispheres symmetrical; they scarcely cover the cerebellum.

Frontal lobes.—Right side—The ascending branch of the Sylvian fissure passed up and formed a precentral fissure extending to within an inch of the longitudinal fissure, completely separating the 2nd and 3rd frontal gyri from the ascending frontal convolution. A short precentral fissure passed parallel to the upper half of the fissure of Rolando, and was then separated from the portion just described by the base of the second frontal gyrus. The first frontal fissure was well marked. A secondary fissure united it in the middle of its course with the lower prefrontal fissure, and divided the 2nd frontal gyrus into two portions. The second frontal fissure was well marked anteriorly. The first frontal gyrus was typical; the second was split in its posterior part, and, anteriorly, the lower division unites with the first frontal gyrus. The third convolution was small. The orbital surface was small, and showed only four radiate fissures. On the *left side*, a deep precentral fissure extended across the hemisphere without interruptions. The first frontal fissure was well marked in the middle region, but did not extend into the præcentral. The second frontal fissure had many

secondary branches. The ascending frontal gyrus was large. The first was typical; the second was much fissured, and, anteriorly, was partially divided into two. The third was normal. Orbital fissures and gyri presented nothing notable.

Parietal lobes.—Right side—Fissure of Sylvius was partially confluent by a shallow groove with the first temporal, and by a deeper one with the retro central. The ascending branch passed far up into the frontal lobe. The fissure of Rolando was not confluent. From a deeply placed, small convolution in the middle of the parietal lobe, five fissures radiated; three passed down, of which the anterior formed a short retro-central fissure, which joined the Sylvian; the middle joined the first temporal; the posterior had two branches, one could not be traced owing to injury of the brain by the saw, and the other passed up and joined a fissure in the situation of the posterior part of a normal interparietal fissure. This lobe was much and irregularly fissured, and the supra-marginal, angular and superior parietal convolutions were greatly intersected. The retro-central gyrus was well developed. *Left side.*—Sylvian fissure was not confluent; fissure of Rolando normal. The retro-central was marked, and the inter-parietal passed out from it at right angles and back into the occipital lobe, but did not join any of its fissures. It had several secondary branches, which passed into the angular gyrus. The retro-central convolution was not so well marked on this side. A small triangular convolution separated it from the supra-marginal.

Temporo-sphenoidal lobes—In the removal both had suffered, particularly the right. So far as could be traced, the first temporal fissure joined the inter-parietal and also the Sylvian by a narrow groove. The third temporal fissure was marked, and joined the calcarine. The first convolution was large. On the left side, neither the first nor the second fissures were marked anteriorly, but vertical sulci divided the convolutions. The hinder part of the lobe was broken. The third was well marked, and joined the inferior occipital and Wernicke's fissures.

Occipital lobes.—The saw had passed through the lateral part of the lobes. On the right side there was a small Wernicke's

fissure, which united with the horizontal occipital and (so far as could be made out) with the second temporal. On the left side Wernicke's fissure was very marked; it joined the third temporal.

Median surface.—Left hemisphere—Calloso-marginal fissure normal. Parieto-occipital deep, and extended an inch on the convex surface. The calcarine also passed over the margin. The continuation of these two passed to the scissura hippocampi. The collateral joined the calcarine by a deep fissure. The convolutions were normal. The precuneus was deeply fissured. On the right hemisphere, the calloso-marginal fissure passed far back, and was separated from the parieto-occipital by a narrow convolution. In its anterior half it was double; one branch fissured the gyrus fornicatus in the front part. An ascending portion formed the anterior boundary of the præcuneus. Parieto-occipital was deep and marked, and curved over the margin. The calcarine was not so well defined. The united fissure ran to the scissura hippocampi, and also joined the collateral by a deep sulcus. The gyrus fornicatus was split into two portions. The precuneus and the cuneus were much fissured. The cerebellum, pons and medulla presented nothing of note.

Summary.—The two hemispheres presented a marked asymmetry in the convolutions and sulci. There was no special degree of confluence of the fissures, with the exception of those of the right parietal lobe. In both frontal lobes there was a partial splitting of the 2nd frontal convolutions, and an approach to the type of four frontal convolutions. The secondary sulci and furrows were unusually abundant.

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REMARKS ON CLINICAL CASES.

By WILLIAM OSLER, M.D.,
Professor of Clinical Medicine, University of Pennsylvania.

Gentlemen,—The case of *Typhoid Fever* which you saw at the last clinic died on Monday. The prominent features of the case were: Illness of over three weeks' duration before coming to hospital—fever, headache, and diarrhœa; in bed on and off during this period, but up and about for days at a time. Came to Dispensary on the 8th, and was admitted. The temperature was 103°F.; pulse 90, dicrotic. He was bright mentally, and did not present the appearance of a man who had been ill three weeks with fever. When you saw him on Thursday last he had all the appearance of a man with typhoid; the symptoms were not grave; temperature not high; pulse not over 100. There were two unfavorable features in the case,—the fact of his having been neglected for three weeks and allowed to be about while the fever was on him, and the nervous twitchings of the muscles. An unfavorable prognosis was given. The subsequent course was briefly as follows: On Friday evening the temperature rose to 105°F., and throughout Saturday and Sunday there was a constant tendency to elevation, kept down but feebly by quinine in 15 and 20 gr. doses, and cold sponging every hour or two. On Saturday the lowest temperature was 101-2°, and the highest 105°. On Sunday it rose to 106.2°. He retained

consciousness in a remarkable and unusual manner. He took stimulants and nourishment every alternate hour. The diarrhœa was never troublesome, but the stomach became a little irritable on Saturday and Sunday, so that the quinine had to be given at times by the bowel. It is exceptional for cases such as these to get well, and when a man walks into your office complaining of fever, headache, and malaise, says he has been ill a couple of weeks and has been fighting against it, and you find his temperature 104° or 105°, you may expect a case of severity. As I mentioned at the last lecture, there is no worse feature than such a history. The nervous or rather muscular twitchings are also of evil omen, indicating implication of the nerve centres. They may even amount to convulsive jerkings of the head, trunk and extremities, and I remember one case in which the muscular spasms were so prominent that the disease was thought to be spinal meningitis.

Heart Disease: Action of Digitalis.—This old man, aged 75, you also saw at the last clinic, and he is brought in to-day to demonstrate to you the beneficial effects of digitalis and rest. He has mitral disease, which probably followed an attack of rheumatism in 1854. On Thursday last, three days after his admission, he was, as you remember, very short of breath, the feet and abdomen were dropsical, the pulse was small and exceedingly irregular, and the amount of urine was reduced. He has had 10 ♏ of the tincture of digitalis every four hours, day and night, and has been kept quiet in bed. The changes are: 1st, The pulse is slower, fuller and only occasionally intermits. Those of you who saw him in the ward-class the day after his admission will recall the extreme feebleness and the irregularity of the pulse. 2nd, The breathing is quite relieved; he can lie down comfortably, and walking is not an exertion. 3rd, The dropsy has disappeared entirely from the legs, and has almost all gone from the abdomen, which, as you see, is relaxed, and only gives indication of a small amount remaining. 4th, The urine has increased from 3 and 3½ pints to 6 and 7 pints in the 24 hours. He has been taking the digitalis ten days, ʒi in the day—not a very large amount, but it has served our purpose.

Caisson Disease.—The man, J. Farrell, aged 30, who came to Hospital yesterday (17th) with a heavy cold in his chest, is also—or rather has been—the subject of an interesting disease to which the workers in the compressed air of the caissons are liable. Two months ago he went to work at Perryville, on the Susquehanna, where they are building a bridge, and in sinking the piers the workmen are in caissons, as they are called, in which the pressure may amount to two or three atmospheres. Until Sunday last (13th) he had never suffered any inconvenience, beyond occasional "bends," as he calls them, to which I shall refer later. At 4 a.m. on Sunday he came up from work feeling all right, but before he could get to his boarding-house the left leg became numb, cold and dead, as he puts it, from the hip down, so that he could not walk, and had to be carried home. It did not appear to be painful, but he says the sensation in it was gone. It remained in this state all day, but towards evening he could move it a little, and on Monday morning the power was quite restored. He did not attempt to go to work again; was too much scared! There were some pains about the legs and arms for a day or so, and a feeling of dizziness, particularly if he looked up or looked from a height. He has now quite recovered, except that on walking, if he looks up, he staggers, and there is a tendency to sway when the eyes are shut. The patellar tendon reflex on both sides is a little exaggerated; no ankle clonus; skin reflexes normal. No other special features. He says that the workmen are much subject to what they call "bends," which, so far as I can make out from his imperfect account, are attacks of pain in the arms or legs, often about the joints, but whether accompanied by spasm or cramp of the muscle does not appear very clear from his statements. These attacks never come on while in the caisson, but *always* a few hours or less after they have come up. So also with the more severe attacks; they invariably come on after leaving the caisson, never in it. He states that two men have died of the affection, and that one man is now in hospital paralyzed in both legs. In the building of the Brooklyn bridge, many cases of this curious disease occurred, and Dr. Andrew

H. Smith of New York made a special study of it, and was, I believe, the first to give the name by which it is now generally known. According to his description, it is characterized by pain in one or more of the extremities, sometimes with pain in the stomach and vomiting. There is paralysis, local or general, but most often in the lower limbs. Headache, vertigo, and coma may occur. Cases may prove fatal with these symptoms, and, *post-mortem*, congestion of the brain and cord has been found. In sinking the piers for the bridge at St. Louis, there were many cases, and there were twelve deaths among the 352 men employed. The disease has been known to French observers for many years, and has also been met with in miners working in compressed air, and in sponge divers in the Mediterranean. There appears to be no difficulty, in the majority of the workmen, in standing a pressure of two or three atmospheres, and, as a rule, no inconvenience is felt further than the temporary pain in the ears, due to the pressure on the drums, which disappears gradually. Naturally, there is a tendency for the blood to be driven into the deeper parts, the superficial vessels are compressed, there is less blood in the skin and more in the viscera. The brain and cord, enclosed in solid, incompressible cases, will also have an additional amount of blood. But this does not appear to produce any inconvenience, and men can work for hours under a compression of three or even four atmospheres. The danger is in the transition from a high to a low pressure, and, as this patient has told us, the men are never affected in the caisson, but always on coming up. The occurrence of sudden death, or a rapid paralysis, suggest hæmorrhage as the cause, but it has been shown by Hoppe-Seyler that there may be a sudden development of nitrogen gas in the blood on removal from high to a low pressure atmosphere, and he attributes the symptoms and the fatal result to the evolution of this gas, the bubbles of which plug the capillaries in the lungs and produce dilatation and stoppage of the heart. Bert states that in an animal under very high pressure, the blood, when withdrawn at low pressure of the atmosphere, will foam from the rapid evolution of nitrogen. The paralysis is probably also due

to this cause, and in one case Leyden has found, 15 days after the onset of the paraplegia, lacerations in the cord, which he attributed to the action of the gas bubbles, distending and tearing the capillaries. Schultze, in another case—death 2½ months after the onset,—could only find disseminated areas of sclerosis. This really seems to give a satisfactory explanation of the cases, and in this man we may suppose that he has had local development of gas in the lumbar region, limited in extent, probably not destructive, but only expanding the capillaries and inducing a monoplegia, which disappeared with the absorption of the gas. Paul Bert found that if the animals which had been exposed to the pressure of several atmospheres were to be kept alive, the transition to the normal atmospheric pressure must be slow and gradual, so as to permit of the gradual diffusion of the superfluous gas absorbed by the blood under the high pressure. So also it is recommended that, on the first onset of symptoms in men working in caissons, they should be submitted again to the pressure, which should be gradually reduced to the normal standard.

Emphysema—Bronchitis.—This man, J. S., aged 35, came to hospital complaining of great shortness of breath and cough. When stripped, he carries, as you see, the diagnosis in the form of the chest and the peculiar mode of breathing. Inspection shows a short, well-nourished man, with a full, barrel-shaped thorax, into which the head seems set by a very short neck. Watch the peculiar mode of breathing. The inspiratory act is labored, accompanied with more elevation than expansion of the chest-walls, but the abdomen rises considerably. Expiration seems still more labored, and is fully twice as long as inspiration. It looks as if the air were forced by muscular exertion out of the chest; and so it is. With each act there is very audible wheezing, most marked with expiration. The finger tips are a little livid, but there is no cyanosis of the face. On placing the hands upon the chest, ronchial fremitus can everywhere be felt, but most intense at the right apex, in front. Percussion gives a hyper-resonant [illegible] over the various regions, except the left base and lower axillary regions, where there is

defective resonance. On auscultation, there are innumerable whistling and sonorous râles over the whole chest; nothing else can be heard with both inspiration and expiration. The high-pitched ones are most prevalent. There are two places where there are special features. At the right apex the sounds are extremely hollow, and there may be here either a cavity or, what is more likely, dilatation of the bronchial tubes; at the left base, with the piping rhonchi, there are many liquid râles, and there is possibly here some infiltration—œdema of the lung. The cough is most distressing, frequent, and the sputum is got rid of with difficulty. It is tenacious, thick, and purulent. The area of heart's dulness is covered by lung, and the liver is depressed. The points in the history are briefly as follows:—He is a jeweller by trade, and has used the blow-pipe a great deal for 15 or 16 years. He tells us that sometimes he would require to keep up the flame for 15 or 20 minutes, only intermitting enough to catch the breath. The family history is good, and he was always pretty healthy until three years ago, when he was laid up with a severe bronchitic attack for three months, and ever since he has been specially liable to catch cold, and has had four or five spells of shortness of breath and severe cough; none have been so bad as the present one, which came on a week ago, with fever, cough and dyspnœa. Two conditions are here present: Emphysema, a permanent and irreparable affection of the lungs; and Bronchitis, a transitory and curable condition, upon which his chief symptoms now depend. Two weeks ago this man could get about satisfactorily, and, if he took it quietly, could go up stairs without difficulty, whereas now he puffs and blows on the slightest exertion. The emphysema has no doubt been caused by the habitual use of the blow-pipe in his occupation, and every such attack as the present one leaves the lung in a worse condition than before. Just now the bronchitis is the main trouble, and the swollen state of the mucous membrane retards the access of air to the alveoli, while the loss of elasticity in the lungs renders expectoration very difficult, and the cough is in consequence hard and distressing. On his admission, he was ordered a relaxing expectorant (chloride of

ammonium grs. x, with ipecacuanha wine 20 ♏) every three hours, and already, after two days, he is much relieved. Jacket poultices, frequently changed, are very useful when there is much soreness in the chest. The existence of local trouble at the right apex may delay convalescence, but the bronchitic symptoms should disappear in a few weeks.

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ARTICLE II.

A CONTRIBUTION TO JACKSONIAN EPILEPSY AND THE SITUATION OF THE LEG CENTRE.[1]

By WILLIAM OSLER, M.D., F.R.C.P. LOND., Professor of Clinical Medicine in the University of Pennsylvania.

THE case here recorded illustrates the following points: Epileptiform seizures from a very limited lesion; the situation of the leg centre, and certain features in the clinical history of the disease.

The present doctrine of cerebral localization may be said to have had its origin in the study of the effects of very limited cortical lesions, and the labors of Fritsch, Hitzig, Ferrier, and others have removed the subject from the region of speculation to the solid ground of experimental science. Still, as far as man is concerned, while admitting the great and corroborative value of observations upon dogs and monkeys, the careful study of pathological cases offers the only means whereby positive knowledge can be attained. Year by year in the past decade evidence of this nature has been accumulating, and more important results may be expected as the records become more exact and scientific. Fully twenty years ago Dr. Hughlings-Jackson, studying cases of unilateral convulsions or spasmodic seizures limited to one member, found that they were often associated with localized spots of disease on the surface of the brain, and he suggested, in explanation of such cases, that the lesion was of the nature of an irritant to the cells of the gray-cortex, which discharged themselves, so to speak, in an irregular and explosive manner, causing a convulsion or spasmodic action of the muscles over which they normally presided. As the seizures began either in the arm, leg, or face, it was reasonable to conclude that the portion of the cortex affected was different in each instance,—*i. e.*, there were actually centres—motor in character—which when irritated in this way caused the convulsive attacks.

When experiments on animals demonstrated that the gray matter was irritable, and that stimulation of limited areas was followed by contraction of definite groups of muscles, Dr. Jackson's suggestion of motor centres was seen in its true light. Ferrier's observations on monkeys enabled him to indicate approximately the homologous motor centres in the human brain, and an extraordinary impetus was thereby given to the study of cerebral cases bearing upon localization. The result of the ten or twelve years' work enables us to speak with some degree of positiveness of the functions of certain regions of the brain. Thus the motor area has been ascertained to be in the mid-region embracing the convolutions on either side of the fissure of Rolando. Irritative lesions of these parts issue in convulsions more or less limited, destructive lesions cause paralysis, local or generalized

[1] Read before the Medico-Chirurgical Society of Montreal.

according to the extent of the disease. The other areas of the cortex cerebri are silent, *quoad* motor effects when stimulated, and when destroyed do not necessarily induce paralysis. With regard to further specializing of centres in the motor region, as far as man is concerned, the analysis of cases would appear to place the leg centre in the upper part of the central convolutions, particularly the part extending to the median surface—the paracentral lobule; the arm and hand centre in the mid-region of the central gyri, and the centres for the face and tongue at the lower end—a disposition in each instance coinciding more or less closely with the conclusions arrived at by Ferrier from his observations on monkeys.

Dividing cerebral symptoms into those accompanied with loss of function—negative, and those characterized by excess of function—positive, the cases of cortical epilepsy may be taken as examples of the latter group. In Dr. Jackson's phraseology, the proximate cause of the paroxysm is an abnormally highly unstable condition of the cells of the gray matter, resulting in a sudden discharge. "Healthy movement implies a liberation of energy or nervous discharge initially by cerebral cells, at any rate if the movement be a voluntary one. A convulsion, that is to say, a sudden, excessive, rapid, and temporary development of movements—many movements 'run up' into spasm implies of necessity a corresponding, sudden, etc., discharge." In a local spasm only a few cells are in this highly unstable condition; in severe seizures the sudden and excessive discharge of the highly unstable cells overcomes, it is supposed, the resistance of healthy cells in physiological connection with those highly unstable.

These preliminary remarks will enable the history of the case to be more satisfactorily followed, and I may state too, the main points of difference between these epileptiform seizures and true epilepsy; the slow onset, local in character, beginning in, or in mild attacks confined to, one limb or a single group of muscles; the gradual extension until the side is involved, or in severe attacks the entire body; loss of consciousness late, not early and sudden as in true epilepsy, and lastly, the muscular contractions are clonic, rarely or never tonic.

On November 8, 1883, I received from Dr. ——— the brain of his daughter for examination, and with it the following history:—

E. L. M., aged 15 years 9 mo. When sixteen months old fell on her head from a table and appeared to be very much hurt, as she cried violently for a long time after. She appeared to be quite well for about five months, when the left hand was noticed to close firmly, and it seemed to pain her a little from the firmness of the contraction. This continued to increase in severity and frequency for three months, when the left leg became similarly affected, and in two months more she was confined to bed, and the paroxysms had become general all over the body, the mouth being generally fixed open during a spasm.

These spasms lasted in this violent form for about two months, she having as many as eight or ten in an hour. There never was at any

time any loss of consciousness. This makes about seven months altogether. Then suddenly the whole trouble ceased, and she was perfectly well and ran about as healthy a specimen of a child as could be seen.

She remained quite free from spasms for one year, when they returned in the same way, and ran much the same course for six or seven months, and then she recovered perfectly again for about the same length of time, and this went on till she was about eight years of age, or about six years after the first illness, when the left leg began to show signs of weakness and gradually the foot turned in, but she still ran about.

To give an idea of the kind of spasms she had about that time, I will describe one:—

Suppose her at the dinner table, she would suddenly say, "Oh, I am going to have a spasm." (She knew this by the contraction of the left hand.) She would then jump up and go to the sofa, get a cushion, lay it down on the floor, then lie down with her head on the pillow, and jerk away in a spasm for half a minute or a minute laughing or talking all through it, and never losing consciousness. She would then get up, replace the cushion, and come back to the table and finish her dinner.

After each interval, of many months, the seizures were more severe; and shortly after she attained her eleventh year, there was a return of the illness, which never ceased for nearly four years, and during six weeks of that time she lay unconscious, and had from fifty to eighty spasms during each twenty-four hours; but as soon as they became less frequent, she became perfectly conscious, and was able to sit up in bed or an invalid chair and read or do a little fancy work, although the left hand was very feeble, and the joints of the fingers would bend nearly as far backwards as they would forwards; this condition of the joints being the result of the position assumed by the fingers during the seizures.

Last Christmas, when she was nearly fifteen years of age, the spasms suddenly ceased, and she was for ten months without them, and during that time she became fat and rosy.

During all these years she was a remarkably intelligent child, and even very much above the average, for without any education of any consequence she was far beyond those of her age. Her memory was something remarkable.

There were no signs of disease on the body, excepting that the skin of the legs became very rough after the seizures commenced and disappeared after they ceased.

During the last two years the toes of first the right and then the left foot assumed a brownish-yellow appearance, which no amount of washing would remove, and latterly the skin became thickened, and small sections of this dirty brown epithelium pealed off and soon re-formed.

There was very little, if any, wasting of the limbs of the left side, but the foot was flexed inwards at a right angle to the leg, at last, and firmly flexed in that position.

Just a week before death, the spasms returned with great violence and increasing frequency, till they became almost continuous, and for two days there was complete unconsciousness or coma. Three hours before death the spasms ceased, and she died very quietly, as I suppose from congestion of the brain, as the conjunctiva were very much injected and the temperature very high. The post-mortem (so I was told) revealed a very much congested condition of the vessels of the brain.

Just a week before she died she told the nurse to be sure to tell me to

have a post-mortem, as she knew her case was a peculiar one, and that it might be of benefit to some one else, and to the medical profession in particular.

In reply to questions, the doctor supplied the following additional information: "The spasms always began in the left hand and *never* in the leg. For about two months at the beginning of the illness the hand just closed firmly for a few seconds, and there was no twitching, but after the expiration of the two months it always twitched from the onset of the spasm. Frequently she could be seen standing with the hand closed and jerking before the leg became affected, and she had to lie down. The spasms were never confined to the left leg. When the leg did become involved the twitching began in the toes and ran up the limb. At the first the arm alone was affected. When the spasms became unilateral, the face would twitch and the eyes roll to the convulsed side. The left arm though feeble was not *stiff*, and in the same useless state as the leg.

The clinical history may be summarized as follows: Jacksonian epilepsy lasting over fourteen years; the convulsions beginning in the left hand, at first monobrachial, then extending to the leg, afterwards becoming unilateral, and finally general, at first without loss of consciousness. For the first nine years of the illness, remarkable intermissions lasting for six or seven months, once an entire year. Six years after the onset the left leg got weak and stiff. For four years, the tenth, eleventh, twelfth, and thirteenth of the illness, the seizures frequent, during this period, six weeks' unconsciousness in which the spasms were very frequent, fifty to eighty in the day. Ten months prior to final attacks freedom from convulsions. Intellectual faculties unimpaired.

Brain examined on Nov. 9th; organ large and well formed; dura natural; hemispheres symmetrical; no special cloudiness of arachnoid; Pacchionian granulations small; large and small vessels of pia mater enlarged, and gave a very congested appearance to the surface; no adhesions of the membrane; no spots of opacity or thickening; the pia mater stripped off exposed natural looking convolutions of a deep pink-gray color; motor convolutions looked symmetrical, no puckering or depression; vessels at base healthy; right crus badly torn. The cord was cut just at junction with medulla, in the lateral aspect of which there is also a laceration; the organ was sliced after the Pitres method. *Pre-frontal* and *pediculo-frontal* sections normal. A section passing 3 centimetres in front of the fissure of Rolando shows nothing abnormal. In making the *frontal* section the knife met with increased resistance on the right side, and the section which passed through the ascending frontal convolution, exactly 2 cm. in front of the fissure of Rolando, exposed a firm fibrous mass occupying the upper part of this convolution in the superior fasciculus of white fibres. It measured 14 mm. in width by 15 mm. in vertical length, was 8 mm. from the surface towards the longitudinal fissure, 10 mm. from the top of the convolution at the margin of the long fissure, and 15 mm. from the external surface. It ran up to the gray matter, but did not appear to involve it except towards the median surface.

In a section 7 or 8 mm. behind the *frontal* the mass was still visible as a small round puckered area, situated just at the edge of the gray matter at the bottom of a sulcus passing into the asc. frontal from the fissure of Rolando, about 15 mm. from the longitudinal fissure. It extended to within 4 or 5 mm. of the fissure of Rolando. Thus the entire mass was within the upper end of the asc. frontal gyrus, having an antero-posterior extent of about 17 mm., and a vertical diameter of 15 or 16 mm., almost entirely within the white substance, but bordering on the gray matter at several places.

Unfortunately the torn state of the crus and medulla made it impossible to trace any descending sclerosis in these parts. Histologically the growth presented the characters of a firm glioma, consisting of 1st, and chiefly, a dense felt-work of fibres, in places coarse and devoid of cell elements; 2d, cells of various sizes, branched and fusiform, the processes of which could be directly traced in connection with the fibres. Towards the peripheral part of the growth the cells were more abundant; 3d, bloodvessels pretty numerous and large considering the amount of fibrous tissue in the mass. The growth shaded into the contiguous tissue in a very characteristic way, and towards the gray matter there was no sharply defined border, although in the microscopic sections it was easy to see where the normal tissue began, and there was a zone in which there were scattered a number of deeply stained small cells like leucocytes. In most of the sections the ganglion cells of the contiguous gray matter looked normal and their nuclei took the logwood dye as usual. On the side of the convolution towards the fissure of Rolando the growth directly involved the gray cortex. A study of the sections did not appear to bear out Klebs's view that the ganglion cells participate in the growth.

The case is unusual in the limitation of the lesion to one convolution and to its fasciculus of white matter, scarcely involving the gray substance which is commonly affected in cortical epilepsy. The accurate localization and the remarkable absence of tissue changes in the immediate vicinity give the case the nature of an exact physiological experiment. It is the rule almost for lesions causing epilepiform convulsions to involve the cortex, such as meningeal thickening and growths, exostoses, gliomas, and other tumors of the surface. They need not, however, directly affect the motor zone, but may be in the vicinity, near enough to excite irritation of the centres. Charcot lays down the following rule for guidance in this matter: When in the intervals of the attacks the patient has not any form of permanent paralysis, the disease causing the convulsions is in the non-motor zone, but when, on the contrary, the patient is paralyzed in the intervals, either monoplegic or paraplegic, we may conclude that there is a destructive lesion of the motor area, more or less limited. For example, a lesion at the base of the second frontal convolution might irritate the contiguous motor cells of the arm centre in the ascending frontal and produce epileptiform seizures without any permanent paralysis; or, if

in the central part of the motor convolutions, might produce irritative effects in the leg and face centres above and below it, while at the same time there was paralysis of the arm from destruction of its centre. In fact from cortical lesions in this region we may have the epileptiform seizures without the paralysis, or there may be paralysis with the seizures, or in some cases limited paralysis without convulsions. In the present instance there was, with a limited lesion of the motor area, permanent paralysis with contracture of one extremity and epileptiform convulsions.

In this class of seizures the spasms may begin in the hand, the face, or the foot, and, according to Jackson, this is the order of frequency, and, as a rule, the attacks begin always in the same place. They may be confined to the one region—monospasm, or may gradually extend until one half of the body is involved—hemispasm. Facial and brachial monospasm are more common than crural. The attacks may be limited at first to a group of muscles in an extremity, or to the entire limb. Thus, in the case of the patient with this disease, which I showed at the society some months ago, there was brachial monospasm, and in the one under consideration, the doctor states that the child might be seen standing while the arm was convulsed.

The order of spreading is important; it is usually up a limb, but it may be in the opposite direction, and in the event of the monospasm extending it is more common for the face to be involved with the arm, or *vice versa*, and the leg with the arm, than the leg with the face. Here from what can be gathered the order of march of the spasm was up the arm, then the leg became affected, and afterwards the face. This is unusual; it is more common for the leg to be affected last. Complete details, however, of the precise sequence of the spasms are wanting. Evidently at first there was brachial monospasm, then extension to the leg, and later hemispasm with rolling of the eyes and affection of the face muscles. Within six months from the origin of the trouble the seizures had become general, but the doctor says there was up to this time no loss of consciousness, such as subsequently took place.

The extension of the convulsions to the other side is explained in one of two ways; either through the direct pyramidal fasciculi with which each side of the brain is connected in a greater or less degree with the same side of the body, or more probably, on Broadbent's theory, that it is owing to "active conditions of the decussating fibres putting in action the associated nuclei of both sides of the cord, and then the bilaterally acting muscles of both sides of the body." The discharge of the nerve cells of the cortex cerebri excites the motor nuclei of the cord, and the violent impulses pass from the spiral ganglia to the muscles. Now it is easy to conceive that when the discharges are excessive and violent, the ganglia of the other side of the cord may be excited through the commissural fibres which unite the nerve cells of the anterior horns.

The long duration, fourteen years, of a glioma, is not without parallel. Dr. Jackson has recorded two cases, in one of which the fits lasted ten, and in the other twelve years. Cerebral gliomata are benign growths, which grow slowly and never produce metastases.

The other feature of interest in this case is the light it throws on the situation of the leg centre. Ferrier placed this in monkeys at the gyri at the upper end of the fissure of Rolando, and the result of pathological investigations in man point to the same situation. Cases of uncomplicated crural monospasm, or monoplegia are not common, but in the observations analyzed and collected by Ferrier and by Charcot and Pitres, the lesion was in each instance in the upper part of the central gyri, or in their extension on the median surface. When this part is simply irritated, there may be spasms beginning in, or limited to, the foot and leg; when the seat of a destructive lesion there is crural monoplegia. In their latest work,[1] MM. Charcot and Pitres bring forward additional evidence in support of this view. In the case here recorded, the fibrous mass was situated entirely within the anterior part of the paracental lobule, limited in extent, confined chiefly to the medullary fibres of the superior frontal fasciculus, and only touched the gray matter in places. A point to be referred to is the absence of the paralysis of the leg for the first six years—for if the convulsions and monoplegia were caused by the same legion, how explain the late onset of the latter? From the fibroid state of the tumor, it might reasonably be inferred that it was originally larger, and had shrunk, but the absence of puckering on the surface, and the way in which the margins merged with the contiguous parts, make it probable that the growth was always small—so small, in fact, that at one period of its development it may have caused sufficient irritation to induce the convulsions, and yet at the same time not involved the special fasciculi of white fibres to the extent of producing weakness of the leg or monoplegia.

In the clinical history, the duration, fourteen years, is the most remarkable feature; it is rare for cases of cortical epilepsy to run such a prolonged course. The irregularity of the seizures, the long intervals and attacks of coma, which characterize so large a proportion of these cases, are phenomena not less difficult of explanation here where a lesion is present, than in cases of ordinary epilepsy in which coarse alterations are not usually met with.

[1] Revue de Médecine, Octobre, 1883.

ARTICLE III.

INTERMEDIATE HOSPITALS FOR THE TREATMENT OF ACUTE MENTAL DISEASES. By JOHN VAN BIBBER, M.D., of Baltimore.

THE nervous system has of late years claimed the attention and study of the best medical minds of all countries, and it is now an evidence of a still further progress in this direction, that mental diseases are no longer allowed to remain in the hands of asylum-superintendents, but are beginning to demand the care and investigation that they undoubtedly deserve from a larger and more active class of specialists. It is by the medium of this development that I have been led at various periods, during the past five years, to investigate the plan of treatment and the management of insane asylums, both in this country and in Europe. And everywhere, both at home and abroad, I have been impressed with the lonely and isolated position which mental diseases hold in the estimation of the general profession, and I may add, in the opinion of those who devote their lives to the care and treatment of insanity.

Indeed, it must seem strange to any one who will devote much thought to the subject, that acute mental trouble should be segregated like small-pox, or some dreadful contagion, far removed from most humanizing influences, and immured in more or less dreary, but always crowded asylums, where each patient, whether irritable, excited, or convalescent, is forced into the companionship with lunatics, and where both patients and physicians suffer the evil effects of a moral and social quarantine.

Now, although a man either of sound or unsound mind can endure the enervating and dispiriting effects of life under the blighting influence of a shadow, which makes humanity look hideous, and makes effort seem almost useless, yet it is a question whether the physician or patients are at their best in such an atmosphere, whether the one can progress and prosper in his science, or the other derive the best advantages from a delicate and careful treatment.

It is, in fact, a curious tradition, which is blindly accepted by most people, that insanity differs entirely from any other form of disease, that it must be removed from sight, and, if possible, from remembrance, and treated only by medical men who live within the walls of an asylum, and devote their lives to the care of this class of patients. No less is it a matter of general belief that the institutions in which this malady is treated are not hospitals but asylums, that their use and purpose, though known, is in some way mysterious, and their existence stands outside and apart from the ordinary ministrations of men.

This uncanny reputation is clearly the result of prejudice, and to some extent the result of the present system of treating and caring for a most unfortunate class of sufferers. It is the remnant of that feeling which,

to a general practitioner, since the condition of the eyes may oftentimes be the only objective symptom which will enable him to arrive at a rational and scientific diagnosis. In fact, such considerations as we have briefly and, consequently, but imperfectly given in the foregoing pages, bring us back to the time-honoured maxim, "Qui bene distinguit, bene medibitur."

156 MADISON AVENUE, New York City.

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ARTICLE XIII.

ON ECHINOCOCCUS DISEASE IN AMERICA. By WILLIAM OSLER, M.D., M.R.C.P. Lond.; Professor of the Institutes of Medicine, McGill University; Lecturer on Helminthology, Montreal Veterinary College; Physician to the Montreal General Hospital.

THE accidental ingestion of the eggs of the tiny *Tænia echinococcus* of the dog produces the most serious and fatal parasitic disease of man. The affection prevails extensively in certain countries, as Iceland and Australia, where the habits of the people or the relations of the canine host to man insure easy means of communication. In Europe the disease is not uncommon, and at any one of the larger clinics several examples are sure to occur during the session. So far as I know, the facts of its occurrence in America have not been investigated, and the object of this paper is to give an account of an inquiry into its prevalence. I was led to make this in connection with an annual course of lectures on the parasites of man and the domestic animals which I give to medical and veterinary students. I could not ascertain, from any writings at my command, whether the disease was common on this continent or not. In this section of the country it is rarely met with, and in the inspection of over 800 bodies only three instances have been found.

The following cases, 61 in number, have been collected from the museums, journals, transactions, and from private sources. The first three cases came under my own observation.

CASE 1. Single cyst in liver. The specimen was found in a subject provided for the class in operative surgery during the summer session of McGill Medical Faculty, in 1877. The man had been a tramp, and died in the hospital of pneumonia. No information could be obtained from him as to his nationality or past history. The cyst was the size of a large orange, and occupied the posterior part of the right lobe, in close contact with the diaphragm. These were daughter and granddaughter cyst, and the scolices were well developed. *Montreal General Hospital Reports*, vol. i. 1880, p. 314.

CASE 2. Cysts in liver, spleen, stomach, omentum, mesentery, and pelvis. An Italian, aged about 35, a resident of the city for four years. Died in the Hôtel Dieu on May 1st, 1880, after an illness of about six months. The chief

symptoms were enlargement of liver and spleen, with nodular tumours in abdomen, irregular fever, sweats, and emaciation. Autopsy revealed the following: Liver enlarged and closely matted to the stomach and omentum. Spleen projected beyond the costal border and reached nearly to the crest of the ilium. Attached to the root of the mesentery by a narrow pedicle was a large pear-shaped cyst the size of the fist. Omentum contained several small ones and the parietal peritoneum five or six, one much flattened and with four subdivisions. A large cyst, the size of a cocoa-nut, filled the entire pelvis and pushed up the bladder to a level with the navel and compressed it against the anterior abdominal wall. The liver was greatly enlarged but retained its shape; the under surface and anterior edge were closely united to the stomach and colon. The left lobe was as large as the right and contained two cysts, one in the anterior and the other in the posterior part; both contained pus and shreds of echinococcus membrane. The anterior cyst had perforated the stomach in two places and the duodenum in one; the orifices having smooth firm edges. There was a large cyst at the fundus of the stomach, completely within the wall and covered by a very thin mucosa. The spleen presented three small vesicles at the hilus, and contained a single cyst the size of a cocoa-nut everywhere inclosed by spleen tissue. (Unpublished.)

CASE 3. Obsolete cyst in liver. Englishwoman, aged about 40; dead of pneumonia. Hooklets in the cretaceous débris. (Unpublished.)

CASE 4. Cyst in liver. No history. Specimen, with those from Cases 1, 2, and 3 in the Museum of the McGill Medical School. (Unpublished.)

CASE 5. Cyst in liver. An Icelandic emigrant woman, patient of Dr. Buchan, of Toronto. Cured by a single aspiration. Scolices in the fluid. (Unpublished.)

CASE 6. Cysts in liver and pelvis. Dissecting room subject; female; Toronto School of Medicine. Two cysts in the liver, one of which had ruptured into the intestine. A third was attached to the walls of the pelvis. (Unpublished. Dr. I. H. Cameron.)

CASE 7. Cyst of liver. Young Englishwoman, patient of Dr. Cameron, of Toronto, who also furnished the notes of 5 and 6. (Unpublished.)

CASE 8. Obsolete cyst of liver. Englishman; inmate of Kingston Insane Asylum for 17 years. *Canadian Journal of Med. Sciences*, Aug. 1882.

CASE 9. Suppurating cyst of liver, bursting into lung; cyst in spleen. Englishman, aged 29, resident of Canada for five years. Dr. Black, of Uxbridge, Ont. (Unpublished.)

CASE 10. Echinococci in brain. No. 566 Army Medical Museum, Washington.

CASE 11. Cyst in anterior edge of liver. From a mulatto. No. 651 Army Medical Museum, Washington.

CASE 12. Cysts in lung, spleen, and bladder. Pole, aged 40. Remarkable history. *New York Medical Record*, Sept. 25, 1880. Nos. 1342–43–44 Army Medical Museum.

CASE 13. Several cysts from liver. Jar labelled P. C. 46, vol. i. Museum of University of Pennsylvania, G. B. Wood Cabinet.

CASE 14. Hydatid cyst of spleen. Same collection.

CASE 15. Liver with a cyst, probably hydatid. Same collection.

CASE 16. Cyst in abdominal wall. From an English sailor lad. Wistar-Horner collection, University of Pennsylvania. I did not see this specimen, but Prof. Leidy told me it was in the collection. He stated also that Nos. 13, 14, and 15 may not be American cases, as he was under the impression that the specimens had been imported from Paris by Dr. Wood.

CASE 17. Cyst in liver. Museum of the Pennsylvania Hospital, No. 1382^{50}.

CASE 18. Multiple cysts in liver. From a French lad. Same collection, No. 1382^{55}.

Case 19. Cyst of liver. From an Italian, aged 55. Same collection.

Case 20. Cyst in liver. New York Hospital Museum, No. 932.

Case 21. Multiple echinococci; one in abdominal wall, one on surface of liver, a third loose in peritoneal cavity, and a fourth in pelvis. No history. Same collection, Nos. 933–34–35–36–37.

Case 22. Single cyst in liver. Bellevue Hospital Museum, No. 865.

Case 23. Cysts in liver. Same collection, No. 866.

Case 24. Cyst of liver—suppurating. Same collection, No. 867.

Case 25. Large cyst of liver. Museum of University of New York (Prof. Loomis).

Case 26. Cyst in liver. Warren Anatomical Museum, Harvard, No. 2381.

Case 27. Echinococci discharged from intestine. Same collection, No. 3773.

Case 28. Cavity at apex of left lung containing echinococci. Same collection, No. 2156.

Case 29. Cyst in liver, from a sailor dead of phthisis. Same collection, No. 3871.

Case 30. Cyst in liver. Dr. Jacobi. *Transactions of New York Pathological Society*, vol. iii.

Case 31. Cysts in peritoneum, in gastro-splenic epiploön, attached to spleen and liver, and one in the pelvis. Woman, æt. 29. Dr. Metcalfe. *Ibid.*

Case 32. Echinococcus of the common bile-duct. Old man, with enlarged liver and deeply jaundiced. Common duct blocked with a polypoid tumour the size of the thumb, which contained three echinococci. Dr. McCready. *Ibid.*

Case 33. Cyst of liver. Man, æt. 38. Dr. Loomis. Perhaps the specimen in museum of University of New York. *Ibid.*

Case 34. Cyst in region of liver. An Englishman, age not given. Passed four quarts of material containing echinococcus shreds; also vomiting some of them. Death from exhaustion. Dr. Keys. *Ibid.*

Case 35. Cyst of right lobe of liver. Woman, aged 29. Opened by caustic and incision. Death. Dr. Jacobi. *Ibid.*

Case 36. Two cysts in liver, right lobe. German, sailor. Dr. Cory. *Ibid.*

Case 37. Cyst of anterior border of right lobe. Dr. Finnel. *Ibid.*

Case 38. Cysts in liver. Opened by incision—recovery. Dr. Van Buren. *Ibid.*

Case 39. Cyst in liver. Opened by caustic and incision—recovery. Dr. Alonzo Clark. *Ibid.*

Case 40. Echinococci vomited. A woman, vomited at different times about a quart of echinococci, supposed to come from liver or omentum—recovery. Dr. Alonzo Clark. *Ibid.*

Case 41. Cyst in liver; held two quarts of turbid fluid; hooks found in the sediment. Dr. McCready. *Ibid.*

Case 42. Echinococci expectorated from the lungs. An Englishman, who had come from Honolulu. Dr. Bernays (Sen.), St. Louis, Mo. (Unpublished.)

Case 43. Cyst of liver, which burst into the bowel. German woman. Dr. Bernays (Sen.), St. Louis, Mo. (Unpublished.)

Case 44. Multilocular cyst of liver. A Bavarian, aged 39. Dr. Dean. *St. Louis Med. and Surg. Journal*, August, 1877.

Case 45. Multilocular cyst of liver, from a negro woman. Dr. Dean. *Ibid.*

Case 46. Cyst of liver. Man, aged 32. Dr. Tyson. *Trans. of Path. Society of Philadelphia*, vol. iv.

CASE 47. Echinococci of liver and pelvis. Frenchman, aged 32. Dr. Hutchinson. *Ibid.*

CASE 48. Tumour in right hypochondrium (liver) for several years. Expectoration of echinococci—recovery. Woman, aged 35. Dr. Minot. *Boston Med. and Surg. Journal*, vol. 61.

CASE 49. Echinococci passed per rectum. Woman, aged 29. Dr. Sherard (Mobile). *Med. and Surg. Reporter*, 1871.

CASE 50. Echinococci passed per rectum. Boy, aged 10. Abdominal tumour for some time. Symptoms of obstruction of the bowels. Recovery after the passage of a large number of echinococci. Dr. Simmons. *Pacific Med. and Surg. Journal*, 1861.

CASE 51. Cyst in gastro-hepatic omentum. Woman, in Bellevue Hospital. Symptoms—pain, jaundice, and peritonitis. Echinococcus cyst lay along the common duct and compressed it. Distension behind the site of pressure, and rupture of the duct. Dr. Polk. *Med. and Surg. Reporter*, vol. 42, 1880.

CASE 52. Echinococcus of brain. No history. Specimen in Cincinnati. Authority of Dr. Hyndman, Medical College of Ohio.

CASE 53. Cyst in liver. No history. Dr. Hyndman, of Cincinnati.

CASE 54.[1] Cyst in fascia of neck. Dr. Sands. *American Med. Times*, 1861.

CASE 55.[1] Echinococcus of lung. F. G. Smith. *North American Med.-Chir. Review*, 1858.

CASE 56.[1] Cyst in liver. J. E. Webber. *New York Med. Times*, 1853.

CASE 57. Cyst in tibia. F. W. Webster. *New England Journal of Med. and Surg.*, 1819.

CASE 58. Cysts in liver. E. Alexander. *Boston Med. and Surg. Journal*, 1838.

CASE 59. Cysts in liver; rupture into peritoneum. Man, aged 35. Dr. Gross. *Pathological Anatomy*, 2d edition, 1845, p. 662.

CASE 60. Cyst of liver.[2] Charity Hospital, New Orleans. Authority, Dr. H. V. Ogden.

CASE 61. Cyst in lung, cured by incision. Italian, aged 37. Dr. Fenger. *Am. Journal Med. Sciences*, Oct. 1881.

The distribution of the cysts throughout the organs of the body in this series of cases was as follows: Liver 44, spleen 1, peritoneum, omentum, and mesentery 7, pelvis 4, lung 5, brain 2, abdominal wall 2, stomach 1, bladder 1, subcutaneous 1, bones 1, in common bile-duct 1, discharged from intestines 5, vomited 2, expectorated 2.

This list, imperfect in many particulars, represents the available American cases of the disease. Doubtless there are many unrecorded instances; indeed, twelve or more of those here given have not been before published. It is evident that *echinococcus hominis* is a very rare affection in this country. Unfortunately we cannot say positively how many of these cases were truly American, *i. e.*, originated here, and how many were imported, but in sixteen it is stated that the patients were Europeans. In the majority the nationality was not given, but in all probability at least one-

[1] These three cases are quoted by Cobbold (Parasites, 1879), but Dr. Brigham, of the Boston Medical Library, could not confirm the references.

[2] I mislaid the notes kindly sent by Dr. Ogden, but, so far as I can remember, it occurred in a woman, a foreigner.

third of the cases were imported, leaving only about forty native cases. This immunity may be due either to scarcity of the adult worm or to the absence of conditions favourable to the infection of man. The *tænia echinococcus* is certainly a rare parasite. In some scores of dogs which I have examined during the past fifteen years I have never met with a specimen nor do I know of its detection by any American observer. Even in England, where the disease is tolerably common (some of the metropolitan museums have from twenty-five to thirty specimens of echinococci), Cobbold states that the only examples of this species that he knows of have been reared experimentally. That it is present in dogs in this country to a greater extent than we might suppose from the above facts is shown by the occurrence of echinococci in the lower animals. In casual visits to butcher stalls and to the shambles I have obtained six or eight large echinococci, and I have the liver of a cat with two large cysts. One of my students, Mr. A. W. Clements, of Lawrence, Mass., examined 270 hogs at the Montreal abattoir and found 10 animals affected.

I do not know of any systematic examination of a large number of animals, but Dr. Dean writes that a considerable proportion of the hogs slaughtered in St. Louis are infested, and Dr. Gross, in his "Pathological Anatomy," 1845, states that one-tenth of the hogs in Cincinnati were at that time affected, and speaks of "whole droves, consisting of three or four hundred animals, all of which were diseased in this way."

The conditions for the development of echinococcus disease in man are certainly present in the country, so far as the existence of the adult worm is concerned, and the immunity which the people enjoy may reasonably be attributed to the existence of sanitary arrangements which reduce to a minimum the risk of infection. Unlike the *tænia* and *trichina*, the echinococcus is not introduced with ordinary food but is probably always obtained by the drinking of water, accidentally contaminated with the fæces of dog or wolf. A single ovum is sufficient to produce the most serious damage, as it possesses such capabilities of growth that a huge cyst may develop, containing daughter and granddaughter capsules, each of which has many thousands of scolices or so-called hydatid-heads. One would think that in the cattle and sheep ranches of the Western and Southwestern States the conditions were very similar to those in Australia where the affection is so prevalent. I am informed, however, that the use of dogs for herding purposes is much less common in this country, but there are probably other factors at work, as some Australian authorities state that the disease prevails in their cities quite as much as in the country.

I have to express my thanks to many persons who have kindly aided me in collecting the facts regarding the distribution of this affection; particularly to the curators of the museums in Washington, Philadelphia, New York, and Boston, to Dr. Billings for access to the MS. of the Sub-

ject Catalogue of Library of Surgeon-General's Office, to Dr. N. S. Davis and Dr. Hatfield of Chicago, Dr. Inglis of Detroit, Drs. Alt and Dean of St. Louis, Dr. Hyndman of Cincinnati, Dr. Atkinson of Baltimore, Drs. Metcalfe and Sullivan of Kingston, Ont., Dr. I. H. Cameron of Toronto, and Dr. Henry Gibbons, Jr., of San Francisco.

ARTICLE XIV.

A CASE OF ELEPHANTIASIS. By THOS. T. S. HARRISON, M.D., Selkirk, Ontario, Canada.

THE following case, which, with some hesitation, I have called "elephantiasis," is in some respects so unique, that I think it should be reported and preserved in some journal, the property of the great body of the profession.

John A., now nearly twenty-one years of age, of German parentage, first came under my notice some eighteen years ago. Father immigrated to this country when a mere child; mother, I think, was born here; they lived all their lives in a healthy rural district, farmers by occupation, perfectly healthy, and parents of a large family. The mother showed him to me, saying that one of his legs was too long. She said that at birth he was a large, well-formed, healthy child; that when about two years old he had the right foot slightly hurt, so as to make him limp; that as she knew, or thought she knew, the cause of his lameness, she made no special examination of the limbs until some four or five months after the injury, when she found the opposite leg, the left, to be considerably the longer. I was at this time away from home, and she had consulted a medical friend.

I found the boy was about three years of age, with the left leg an inch and a half or two inches longer than its fellow. The limbs were symmetrical as to the thighs; below the knee the right leg was normal in shape but looked small; the left was much longer, and had a peculiar loose, flabby appearance. There was no sign of a calf. The skin seemed to hang loosely, as if too large for the leg, which, larger than its fellow at the head of the tibia, increased in size to the malleoli, where the superabundant skin and cellular tissue hung over and covered a small and shapely ankle.

I was puzzled by the case, but finally concluded that there was an arrest of growth in the right leg, which had been injured so as to cause lameness ten or twelve months before, but as to the peculiar appearance of the left leg I could give no opinion. The mother told me that the medical men who had seen the case before me, gave her the same opinion that I had.

I saw the child occasionally on my visits to the neighbourhood, or when attending other members of the family; for, excepting the leg trouble, John was always healthy, and I gradually came to the conclusion that the right leg was normal, but that in the left there was not only increased growth of skin and areolar tissue, but that the tibia and fibula were enormously increasing in length.

THE

GULSTONIAN LECTURES,

ON

MALIGNANT ENDOCARDITIS.

DELIVERED AT THE

Royal College of Physicians of London, March, 1885.

BY

WILLIAM OSLER, M.D.,

Professor of Clinical Medicine at the University of Pennsylvania, Philadelphia.

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LECTURE I.

MR. PRESIDENT AND GENTLEMEN,—It is of use, from time to time, to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what direction we may look for fruitful investigations in the future. With your permission, sir, I propose to do this in the case of that most interesting disease generally known as ulcerative endocarditis, a disease the phenomena of which were first clearly explained by the late Dr. Kirkes, from whose investigations in 1851-52 we date our accurate knowledge of the affection. Some of those who listen to me to-day can doubtless recall, and recall with pleasure, the Gulstonian Lectures of 1851, in which Dr. Ormerod dealt so fully and so ably with valvular affections of the heart; but a reference to them will show how much the past twenty-five years have done to widen our view of cardiac disease, more particularly in regard to the effects of emboli, and the association of valvular inflammation with grave constitutional disorder, and the probable connection of the disease with the presence of micro-organisms. By the labours of Drs. Ogle, Wilks, Simpson, Moxon, Bristowe, and others in this country, of Charcot, Vulpian, and Lancereaux in France, and of Virchow and a host of observers in Germany, a large amount of material has been accumulated; and we may assume that the etiological, clinical, and anatomical characters of the disease have been fairly well ascertained, and that we have got about as far towards a full knowledge of the affection as the ordinary means at our disposal will permit. The inquiry now enters upon another stage, and it remains for experimental investigation to determine, if possible, the relation of the endocarditis to those diseases with which it is most frequently associated. This being the case, the present time has seemed to me a favourable opportunity to summarise our knowledge to date; and, for this purpose, I have reviewed the records of over two hundred cases, which, from the description of the symptoms and lesions, were evidently of the type of malignant endocarditis; and these, with the considerable experience I have had at the General Hospital at Montreal, may perhaps enable me to give a somewhat more comprehensive account, in some respects, than has yet been attempted.

In discussing the subject of endocarditis, we are met at the outset by difficulties of nomenclature and classification. The designation acute may be used to indicate those forms which are accompanied by proliferation of, and exudation upon, the endocardial surface, with or

without loss of substance, as opposed to chronic, in which there are sclerotic changes without vegetations. Subdivisions of the acute form have been arranged on an anatomical basis, as the terms plastic, papillary, verrucose, fungous, ulcerative, indicate. On the other hand, from an etiological point of view, the forms of endocarditis are as numerous as the diseases in which it occurs, and we constantly hear the expressions puerperal, rheumatic, scarlatinal, etc. Some speak of primary and secondary forms; while, from a clinical standpoint, they are arranged in two classes, simple and grave. Anatomically, there appear to be no very essential differences in the various forms of acute endocarditis. Between the small capillary excrescence and the huge fungating vegetation with destructive changes, all gradations can be traced, and the last may be the direct outcome of the first; the two extremes, indeed, may be present in the same valve. They represent different degrees of intensity of one and the same process. A classification of cases, based on the ordinary macroscopic characters of the inflammatory products, into watery or verrucose and ulcerative, will, in many instances, group together cases widely different in their clinical aspects; and, contrariwise, a clinical subdivision into cases of simple and cases of malignant endocarditis by no means of necessity implies that the lesions in the former case are all of the plastic or warty variety, and in the latter of the ulcerative or destructive. The term ulcerative has come into very general use to describe the grave form, and it expresses well an anatomical feature present in a large proportion of cases; but in others it is very inapplicable, as there may be no actual loss of substance, and no more destruction than occurs in the verrucose form; and, on the other hand, there may be great destruction and ulceration from causes of an entirely different nature. The numerous other terms employed—septic, infectious, diphtheritic, mycosis endocardii, arterial pyæmia—while each expressing some special feature, and so far suitable, have never come into very general use. On the whole, it seems to me that the names simple and malignant, which we use often to separate the milder and severe forms of many diseases, might appropriately be employed in describing the cases of acute endocarditis; the simple being those with few or slight symptoms, and which run a favourable course; the malignant, the cases with severe constitutional disturbance and extensive valve-lesions, whether ulcerative or vegetative, the term being more clinical than anatomical.

Malignant endocarditis occurs under the following conditions: 1, as a primary disease of the lining membrane of the heart or its valves, either attacking persons in previous good health, or more often attacking the debilitated and dissipated, or those with old valve-lesions; 2, as a secondary affection in connection with many diseases, particularly rheumatic fever, pneumonia, scarlet fever, diphtheria, ague, etc.; 3, as an associated condition in septic processes, traumatic or puerperal. We shall discuss first the anatomical characters, then the clinical features, and lastly the etiological and pathological relations.

The lesions of malignant endocarditis are by no means uniform, and may be vegetative, ulcerative, or suppurative; and these various forms may occur alone or in combination. The belief that there is always ulceration has led to some confusion; and we must recognise that there are cases with the clinical history of the malignant form in which, *post mortem*, the valvular condition has been that of a severe vegetative or verrucose endocarditis. Such a case was a lad aged 11, a patient of Dr. Molson's, from whom I obtained the specimen which I pass round. He had chorea in July 1880, the second attack. Rapid improvement and recovery under Fowler's solution, five minims every four hours hypodermically, took place. There was a slight murmurish condition of the first sound. When seen again on March 3rd, 1881, the chorea had returned, having begun ten days before. The patient improved

until the 10th, when he began to be feverish; had exacerbations each evening; temperature rising to 104° Fahr. He became unconscious. There was slight paresis of the left side, and death took place on the 16th. The temperature on the 15th was nearly 106°. There were irregular, soft, greyish-white vegetations on the mitral valve, infarcts in the spleen and kidneys, and a small spot of red softening in the right corpus striatum. These photographs from a case of Dr. Musser's illustrate a more advanced condition of the same kind; the vegetations were larger, more abundant, and some were a little irregular and soft on the surface, but, unless a mass were removed, no actual loss of substance was seen. Even in the smallest vegetation there is some destruction of endocardial tissue, if only of the endothelium and superficial layer; while the larger outgrowths are more deeply set in the valve, or may involve the entire thickness. More commonly with or without vegetations, there is ulceration, the frequency of the occurrence of which has given the name most often attached to this form of endocarditis. The loss of substance may be superficial, involving only the endocardium, or it may be deep and destructive, leading to perforation of a valve, of the septum, or of the heart itself. On the valves, extensive outgrowths usually accompany the process, and may conceal the ulcer or project as fungating masses from its edge, as is well illustrated by this coloured drawing. In many instances, the process appears simply ulcerative, without any vegetations to speak of. In the slightest form, only a superficial abrasion exists, perhaps scarcely recognisable; in others, a process of erosion may go on by which half a valve may be destroyed, or there may be (as shown in this drawing) a deep excavation extending beyond the valves, and destroying the muscle-substance of the heart, leading to perforation of the septum or of the wall of the ventricle. These are well known features, however, upon which I need not dwell. In two instances, I have seen superficial necrotic changes without ulceration or vegetations, circumscribed patches, of the size of a sixpence, opaque yellow-white in colour, resembling the necrotic pleura, over a pyæmic infarct of the lung, or a portion of dead peritoneum at the base of a deep typhoid ulcer. Doubtless, these would in time have formed ulcers. I find this condition noted by one or two observers. Lastly, the process may be suppurative, in which case the deeper tissues of the valve appear first involved, and the endocardium only implicated by contiguity. The occurrence of small abscesses at the base of extensive vegetations is not uncommon, but there are also instances in which the suppuration seems the initial step. The combination of ulcerative and fungating outgrowths is, perhaps, the most common condition. The vegetations vary a good deal in appearance and consistence. Soft greyish-white masses, with roughened friable surfaces, to which thin blood-clot adheres, are numerous; or there may be large cauliflower-excrescences, with deep jagged fissures; or, again, long, pendulous, stalactitic masses. In the latter form, we often see, as Dr. Moxon pointed out, the effects of friction, and such a long vegetation from an aortic cusp may produce, by contact, a whole series of smaller outgrowths along the ventricular wall. The pressure of the valves against each other, and the action of the blood, tends to loosen and break the vegetations, and one can sometimes see where masses have been torn off, either entire or by a gradual process of disintegration. Considering the force with which the valves come together, it is curious that the soft vegetations, occupying, as they generally do, the lines of closure, can resist the constant compression to which they are subjected. Some vegetations present a remarkable greenish-grey or greenish-yellow colour. Changes in a conservative direction may go on when the disease is much prolonged. Fibroid induration may take place in the deeper parts, while the superficial portions remain unchanged and necrotic, perhaps also becoming a little harder

and shrinking. Such a process can be seen in this specimen of endocarditis from an ox, in which there were most extensive vegetative and destructive changes. Not unfrequently the vegetations are gritty, from the deposit of lime-salts, which may take place in very acute cases, and is not necessarily an indication of age. It is interesting to note how often inorganic material is deposited in the neighbourhood of micro-organisms, as here on the endocardial outgrowths, in the tonsillar crypts, and about the tufts of actino-myces. Two conditions must be distinguished from the lesions of malignant (mycotic) endocarditis: the atheromatous degeneration in sclerotic valves, which leads to ulceration and extensive destruction of segments, a process which has nothing in common, except in its effects upon the valves, with the acute ulcerative changes above described, but is similar to the atheromatous processes in the aorta. It must not be forgotten, however, that an acute mycotic process may be engrafted, and indeed, often is, upon old sclerotic valves, the seat of atheromatous changes. The firm white globular thrombi of the auricular appendices, and of the interstices of the columnæ carneæ of the ventricles, have sometimes an appearance closely resembling endocardial outgrowths, and when softened in the centre and ruptured, the resemblance may be very close indeed. It is possible that the granular *débris* of an atheromatous abscess or a softened thrombus may possess irritating properties when discharged into the blood.

Histological Characters.—The study of a small fresh endocardial vegetation shows it to be made up of cells derived from the subendothelial layer, round and fusiform, which, by their proliferation, have produced a small nodular projection on the surface of the endocardium. Varying with the rapidity of the growth, the mass will present the characters of a soft granulation-tissue or a tolerably firm fibrous outgrowth. Usually, the round cells predominate; but there may be many elongated spindle-formed cells, with three or four processes. What part the endothelium plays in this growth, has not been determined. Tiny outgrowths may be seen, in which the process appears to be entirely subendothelial; but usually, before the mass attains any size, the smooth surface is lost, and there is deposited upon it a cap of fibrine in the form of a granular, sometimes stratified, material, of variable thickness. Though this resembles an ordinary coagulable exudation, it is probably deposited directly from the blood, and is of the nature of a thrombus. Upon and in this layer may be found, sometimes in large numbers, those remarkable little bodies which have long been known, when collected together, as Schultze's granule-masses, and which have of late become prominent as the blood-plates of Bizzozero and the hæmatoblasts of Hayem. Occasionally, they are very abundant; and I have seen soft warty vegetations composed (superficially) in great part of them. As their connection with endocardial and endarterial outgrowths has not, so far as I know, been referred to, I may be permitted to call attention to these two drawings, which further illustrate this point. The first represents the aorta from an old man dead of carcinoma, in which, just above the bifurcation, three irregular masses are shown, one nearly an inch in length, which projected fully a quarter of an inch from the intima of the vessel. They were attached to atheromatous ulcers, were soft greyish-white in colour, and were composed exclusively of the elements of Schultze's granule-masses, with fibrine-fibrils, and here and there a few white corpuscles. The second drawing illustrates a small aneurysm of the aorta, which has perforated the œsophagus. On the wall of the sac, the artist has represented a number of irregular whitish lines, which were narrow elevated ridges, also made up microscopically of these small discoid elements, the connection of which with fibrine-formation has been strongly insisted upon by Bizzozero. Scattered in and beneath the fibrinous exudation

are numerous small granular bodies, which have the appearance and reaction of micrococci.

The larger vegetations, more characteristic of malignant endocarditis, consist of a granular material composed of altered and dead tissue-elements, fibrinous exudation, and colonies of micrococci; the deeper parts present the appearance of a granulation-tissue, while at the attachment in the valve there is always more or less infiltration and increase of the cell-elements. The granular substance is structureless, and resembles diphtheritic exudation, the resemblance at times being so close that one can readily understand the application of the term "diphtheritic" to the inflammation. It may be distinctly laminated, and, with a high power, fine filaments can be seen, though usually the granules conceal all appearance of structure. Strands of translucent material may occur throughout the mass, as if portions had undergone a sort of hyaline transformation. In some instances, this is very marked. Pale spheres filled with granules also occur, and may be very abundant. They have been described as colonies of micrococci; but some regard them as altered endothelial elements. I have seen them too numerous to be explained on this view. At the attachment of the vegetation, there is a zone of tissue deeply infiltrated with leucocytes, and deeper still the tissue-elements of the valve present an increase of nuclei and cells. The destruction of tissue appears to result in two ways: first, a gradual extension inwards of the necrotic process, doubtless induced by the micrococci; secondly, the softening and separation of valve-tissue caused by the rapid development of leucocytes at the base of the vegetation.

The micrococci are constant elements in the vegetations. All granules of an uniform size met with in the sections are not micro-organisms, nor, indeed, are all which stain by some methods recommended for the detection of these bodies. By far the most satisfactory method is that of Gramm (*Fortschritte der Medicin*, Band i, Berlin), in which the section, after staining in gentian-violet, is transferred for a few minutes to a dilute solution of iodine and iodide of potassium, and then to the alcohol, when it is found that the colour has been extracted from all tissue-elements and nuclei, leaving only the micro-organisms stained. They vary a good deal in number and arrangement, and may be scattered singly in the granular substance or arranged in groups. They are usually very numerous at the deeper part of the vegetations, just where the structureless material joins the granulation-tissue, and they may penetrate deeply into the substance of the valve. Sometimes the smaller vegetations seem made up exclusively of them. Several of my specimens appear to confirm the view of Klebs (*Archiv für Experiment. Pathologie*, Band vi), that the micrococci lodge first on the endocardium, and penetrate into the substance, often as distinct columns. In their immediate vicinity, there is a zone of necrosis, and beyond this an accumulation of leucocytes and signs of reactive inflammation. The micro-organisms found in connection with the malignant endocarditis are not all of the same kind. Klebs distinguishes two forms, one met with in septic, and the other in rheumatic, cases. In some instances, the micrococci are all arranged in zoogloea-like masses; in others, particularly the septic cases, they are in chaplets. Some present distinct capsules. Small elongated bacilli have also been found; I have seen them in one instance, short stout rods, often joined in pairs. Delafield and Prudden (*Text-book of Pathological Histology*, New York, 1885) have recently noted the presence of bacilli in the vegetations of a very acute case of malignant endocarditis. Cornil, in a recent lecture (*L'Abeille Médicale*, No. 51, 1884), stated that the bacillus tuberculosis had been found in the vegetations on the valves in cases of phthisis, and expressed the opinion that before long we should have accurate knowledge of a variety of micro-organisms in endocarditis depending upon the nature of the pri-

mary disease. By culture-experiments alone can we hope to have the question settled.

The following figures give an approximate estimate of frequency with which different parts of the heart are affected. The aortic and mitral valves were affected together in 41 cases, the aortic valves alone in 53, the mitral alone in 77, the tricuspid in 19, the pulmonary valves in 15, and the heart-wall in 33. The right heart is rarely affected alone; this occurred in only 9 instances, in 5 of which the tricuspid, and in 4 the pulmonary, valves were involved. The valves are most often attacked along the lines of closure, as in the simple endocarditis; the auricular faces of the mitral flaps and the ventricular surfaces of the aortic cusps suffering most severely. Mural endocarditis is most often seen at the upper part of the septum of the left ventricle, just below the aortic ring, in which situation some of the most extensive and deep cardiac ulcers occur, leading to perforation of the septum. Next in order is the endocardium of the left auricle on the postero-external wall, as noted by Lepine (*Bull. de la Soc. de Biologie*, 1869).

The local effects of the ulcerative changes are important. Perforation of a valve-segment is extremely common; sometimes there is a clean-cut, punched-out hole, with scarcely any irregularity of the edges; more frequently, however, there are great fungous vegetations which completely close and conceal the perforation. Erosion of the chordæ tendinæ is frequently met with, and an entire group passing to the papilla may be destroyed, the ends curled and encrusted with vegetations. Ulceration of the heart-muscle, leading to perforation of the septum or of the wall of a chamber is a much less frequent occurrence. I have collected notes of eleven instances; three of the septum close to the aortic ring. Ulcers at the aortic ring perforated the left auricle in three instances, the right auricle in one, and the right ventricle in one. In a remarkable case of Dr. Stephen Mackenzie (Pathological Society's *Transactions*, vol. xxxiii), the left ventricle was perforated by an ulcer at the apex. In a case of Dr. Curnow (*Lancet*, 1883, vol. i), the ulceration extended between the coats of the aorta, and then perforated into the lumen of the vessel, and in one of the Montreal cases there was perforation of an aneurysm of the aorta by ulceration, an instance of extensive ulcerative endaortitis with the production of multiple aneurysms. Another common result of ulceration is the production of valvular aneurysm. The anterior flap of the mitral valve is most frequently affected, and then the aortic cusps. In the records of the cases which I have reviewed, I was surprised not to find this condition noted oftener, only in about 12 per cent. of the cases; but, in very many cases, the record of the anatomical condition was meagre. I shall not refer further to this interesting point, as Dr. Legg has dealt with it very fully in a recent lecture at this College (Bradshawe Lecture, August, 1882). I may observe, however, that the atheromatous ulceration is also a frequent cause of aneurysm of the valves.

It was Sir James Paget (*Medico-Chirurgical Transactions*, vol. xxvii), I think, who first referred to the frequency with which sclerotic and malformed valves are attacked by acute disease. Chronic valvulitis is met with in a large number of cases of malignant endocarditis. The records which I have examined give only a percentage of about twenty-five; but the condition of the valves, except as regards ulceration, was often omitted, and thus represents a very much smaller percentage than actually occurs. In more than three-fourths of the Montreal cases, sclerotic changes were present; and Dr. Goodhart found (Pathological Society's *Transactions*, vol. xxxiii), in a series of sixty-nine cases, that sixty-one presented old thickening of the valves. In very many of the cases, the condition of fusion of two of the aortic cusps was present. This abnormality is almost invariably accompanied by sclerotic changes, and to the existence of these is probably due the frequency with which they are attacked by ulceration. In seventeen

instances of fusion of two of the aortic cusps of which I have notes, there were ulcerative changes in eight, in two or three of an atheromatous nature.

In a few instances, the aorta is involved with the heart. The most frequent site is the sinuses of Valsalva, the vegetations growing through the segments spread on to the aortic wall; or it is affected by friction. It is rare for the vegetations to extend into the arch. I have met with one remarkable instance of ulcerative endocarditis in which there was also ulcerative endarteritis, involving the arch and producing multiple aneurysms. The specimen which I here demonstrate was taken from a man aged about 30, who had been the subject of syphilis, and was known to have had aortic incompetency for some time. He was admitted to the General Hospital, Montreal, on June 4th, 1880, with diarrhœa, chills, headache, cough, and fever. Temperature 104°. There were signs of pneumonia at the left base. He became delirious, a low typhoid condition supervened, with chills at intervals, and death took place on July 1st. The aortic valves were curled and hard, and presented extensive recent vegetations; the arch of the aorta presented four aneurysms, three small, not larger than cherries, and one of the size of a billiard-ball. The small ones were not noticeable as aneurysms from the internal surface, but presented the appearance of fresh fungous vegetations, on separating which little slits could be seen leading to saccular dilatations of the middle and outer coats. The large aneurysm was thin-walled, with no laminated fibrine, and presented at the edges of the orifice and over the whole lining membrane of the sac many greyish-green vegetations, some of which had perforated the sac and caused a rupture into the pericardium. It may be presumed that, in this instance, the ulcerations led directly to the production of the aneurysms, certainly in the case of the smaller ones; and the larger sac presented a condition of mycotic endarteritis unique in my experience of aortic aneurysms.

Of associated pathological changes, we have, in the first place, those connected with some primary disease, to which the endocarditis is, in the majority of cases, secondary. Thus, in the endocarditis of septic processes, there is the local lesion, a suppurating wound, a phlegmonous inflammation, or puerperal processes of a septic nature. In a very considerable proportion of cases, there is evidence of recent pneumonia; in others, rheumatic affections of joints; and in a few, diphtheritic processes. In the group of primary cases, the lesions are entirely those of endocarditis, local and general. In the second place, there are the extensive pathological changes due to embolism; and these constitute interesting features in the disease, and may produce a very great variety of lesions in every portion of the body. I do not propose to deal very fully with these, but to call attention only to some special points. The cases may be divided into those without any embolic processes, cases in which the infarcts are simple, not suppurative, those in which there are innumerable suppurative infarcts and cases in which some of the infarcts are simple and some suppurative. It is remarkable how variable these embolic features are. They may be entirely absent in well marked malignant cases. They are not necessarily associated with suppuration; indeed, in a very considerable number of cases, they present the characters of ordinary hæmorrhagic infarcts, but in the traumatic and puerperal cases the infarcts are invariably septic. They may be few in number, only one or two perhaps in the spleen or kidney, or they may be in thousands throughout the various organs of the body. When suppurative, micrococci, in my experience, are always present; but the micrococci may exist in the vessels without inducing this change. In severe forms of the disease, hæmorrhages are very frequent upon the skin, and on the serous and mucous surfaces. The cutaneous ones will be referred to again in connection with the symptomatology. They appear, in many

instances, to be due to the effect of the poison, just as in other infectious diseases; in others, they are undoubtedly embolic, and a minute necrotic or suppurative centre can sometimes be seen. In the membranes of the brain, I have twice met with extensive superficial extravasation. Litten (*Charité Annalen*, Band iii, Berlin) has called attention to the frequency of retinal hæmorrhages, particularly in the endocarditis of puerperal sepsis. In some instances, there are innumerable miliary abscesses, more particularly in the heart and kidneys. They are often associated with hæmorrhage, and the smaller ones look like little extravasations, but the presence of micrococci and suppuration can be easily determined in stained sections. The spleen is most often the seat of infarction, and next in order the kidneys. The lungs are usually affected when the endocarditis is on the right side, and there may be suppuration or even extensive gangrene, but even with destructive lesions of the pulmonary valves there may be no suppurative infarcts in the lungs, as in a case of Dr. Church (Pathological Society's *Transactions*, vol. xxvi). Or again, as in a case of Dr. Moxon's (*Ibid.*, vol. xix), there may be with aortic valvulitis suppurative infarcts in the lungs, and simple ones in the other organs. The gastro-intestinal canal may present very remarkable changes, due to the presence of numerous infarctions, from the size of a pin's head to that of a split pea. They are slightly elevated, greyish-yellow in colour, often surrounded by a zone of deep congestion or extravasation, and on section may show a suppurative centre. Micrococci are present, as in other miliary abscesses, and in several instances I was able to find small embolic plugs in the arteries of the submucosa. The abscesses may discharge and leave a small ulcerated surface. In the stomach there may be similar minute infarcts, and occasionally larger ones. Carrington (*Lancet*, 1884, vol. i), has described a remarkable case in which there was a gastric ulcer, apparently due to embolic process, in a case of severe endocarditis; and Magill (BRITISH MEDICAL JOURNAL, 1884, vol. ii), a case in which the stomach was intensely inflamed, the mucous membrane at the greater curvature being black, almost gangrenous. The liver may present minute abscesses, and in a number of cases in which there has been jaundice degeneration of the cells has been observed (Schnitzler, *Wiener Med. Presse*, 1865). The serous surfaces are often inflamed, pleurisy and pericarditis being not uncommon complications. The pericardium is most frequently affected in rheumatic cases, in which endocarditis and pericarditis may occur simultaneously. Pleurisy is met with chiefly in connection with the traumatic and puerperal cases, and also with pneumonia, which, as I shall show, plays an important part in the history of this form of endocarditis. The cerebral lesions are of the substance and of the membranes. Embolic softening, simple or suppurative, is extremely common, and in very many cases head-symptoms supervene, and there is paralysis of one side or the other. There may be a single embolus, producing extensive suppuration or red softening, or there may be multiple infarcts in various regions. The meningeal complication of endocarditis has not received much attention. Considering the frequency with which it has occurred in the Montreal cases, five instances out of twenty-three, I was quite prepared to find such a large number as twenty-five cases; that is, somewhat over 12 per cent. In the majority of these cases, it occurred in connection with pneumonia. It is almost always cortical, but may extend to the base and involve the nerves, leading in one case, which I saw with Dr. Ross at the Montreal Hospital, to strabismus, and also to ulceration of the cornea from involvement of the fifth nerve. In rare instances the spinal meninges are involved, and the clinical picture may be that of an acute cerebro-spinal meningitis (Hunolle, *Bull. de Soc. d'Anatomie*, 1874; and Heineman, *Med. Record*, New York, 1881, vol. ii). Acute suppurative parotitis was noted in three cases.

LECTURE II.

Symptoms.—In considering the symptoms of endocarditis, it is important to bear in mind the manifold conditions under which the disease may develop. A limited number of cases may be grouped together as forming a primary substantive disease; but in the great majority the affection is either an associated pathological state, or is of the nature of a secondary malady arising in the course of some other disease.

In the primary cases, individuals in perfect health may be attacked, or, more frequently, the disease affects those with chronic valvular endocarditis, with perfect or failing compensation. Where the affection occurs after an injury, or in the puerperal state, the cardiac condition must be regarded as part of the general sepsis, and is of the same nature as the pyæmic foci and the inflammation of serous membranes. The existence of the endocarditis in these cases has no special influence, and the phenomena may be just as marked without it.

When the endocarditis supervenes in the course of some particular disease, as rheumatism or pneumonia, it is usually a secondary process, though indeed it may be regarded as directly produced by the causes which have excited the original diseases.

The different modes of onset, and the extraordinary diversity of symptoms which may arise, render it very difficult to present a satisfactory clinical picture. The general symptoms are those of a febrile affection of variable intensity, which may be ushered in, like any acute fever, with rigors, pain in the back, vomiting, headache, etc. Arising in the course of some other disease, there may be simply an intensification of the fever, or a change in its features. The pyrexia is constant, but variable in type and intensity, and more likely than any other symptom to lead to misinterpretation. Prostration of strength, delirium, sweating, and other signs of severe constitutional disturbance, are usually present.

Cardiac symptoms may be marked from the outset; pain, palpitation, sense of distress, and murmur; in many instances, there has been old valvular disease, but in a considerable number of cases the heart-symptoms remain in the background, hidden by the general condition, and giving no indication; or they may be so slight, that they are not even detected on special examination.

The embolic processes give a special prominence to local symptoms, which may divert attention from the general malady. Thus delirium, coma, or paralysis may arise from implication of the brain or its membranes; pain in the side and local peritonitis from involvement of the spleen; bloody urine and pain in the back from affection of the kidneys; loss of vision from retinal hæmorrhages; and suppuration in various organs, or gangrene, from the distribution of emboli.

So diverse are the features of malignant endocarditis, that a consideration of the symptoms is greatly facilitated by arranging the cases in groups, according as they display special characters. Dr. Kirkes, in 1852, called the attention of the profession to the occurrence of a typhoid-like condition in acute endocarditis, and he subsequently pointed out the fact that inflammation of the valves might

lead to pyæmia. The investigations of Charcot and Vulpian (*Gazette Médicale de Paris*, 1862), of Virchow (*Gesammelte Abhandlungen*), of Jaccoud (*Nouveau Dictionnaire de Médecine*, etc., art. Endocarditis), and others, gradually led to the recognition of these two great types of the disease. Of late, still further separation has been made of the cases with features closely resembling ague or intermittent, and also of cases in which the cardiac symptoms are most prominent; and I shall call attention to certain cases in which the symptoms are those of an acute affection of the cerebro-spinal system.

And first let me direct your attention for a few moments to those cases in which the endocarditis is merely a part of a septic or pyæmic state, the result of an external wound, a puerperal process, or an acute necrosis. Somewhat over 18 per cent. of the cases I have analysed were of this nature, the majority of them occurring in connection with puerperal fever, 11 per cent.; the others in association with various wounds and injuries, or acute necrosis of bone. The puerperal cases appear most frequent after abortion, and the first symptoms usually develop within a week or ten days of delivery, beginning with rigors and fever, and running a course not essentially different from ordinary puerperal septicæmia or pyæmia without endocardial complication. Sometimes the onset of the symptoms may be much delayed, and the patient up and about her duties when the attack comes on. Usually, there is local inflammation of the uterus or ligaments; membranous-diphtheritic-endometritis, and phlebitis, are common. Occasionally, there may be no special affection of the generative organs, as in a very severe case reported by Dr. Moxon (Pathological Society's *Transactions*, xv), in which there was extensive endocarditis of the right heart, and sloughing patches in the lungs. The woman had been delivered within the month, and the uterus appeared in a state normal for the period. The endocardial lesions are not necessarily ulcerative, but may be vegetative, and occasionally suppurative. It is very evident, from the records, that valves with sclerotic changes are most often affected. The visceral lesions are always suppurative, but do not appear to be more numerous than in cases of puerperal sepsis without endocarditis. The heart-symptoms may be completely masked by the general condition, and the attention may be directed to them only by the occurrence of embolism. In this connection, it may be remarked that malignant endocarditis may attack pregnant women, and run a rapid course leading to abortion. In two cases of this kind, Litten (*Charité Annalen*, Band iii, Berlin) found no differences in the clinical features or anatomical condition, as regards valves and metastases. In other instances, there may be the rigors, sweats, and irregular fever, leading to abortion, without the occurrence of any suppurative foci, as in a case reported by Guyot (*Bulletin de Soc. d'Anatomie*, 1879). Dr. Trueman, of Maccan, New Brunswick, has also sent me notes of a case which developed during pregnancy.

The cases of ulcerative endocarditis in traumatic and operative septicæmia are of a similar nature, but do not appear to occur so frequently as in the puerperal condition. Many of the cases occur after very slight injuries, as paring a hangnail, or a corn, a sloughing pile, or the passage of a sound through a stricture. There are usually suppurative infarcts in the lungs; and, even with extensive ulcerative changes in the left heart, the pyæmic foci may be all in connection with venous system and right heart. This was well illustrated in the case of a man, aged 25, who was admitted to the Montreal General Hospital, May 31st, with a wound of the radial artery. Phlebitis followed, and cellulitis of the arm, rigors, septic pneumonia, thrombosis of the femoral vein, and symptoms of pyæmia. At the necropsy, there were numerous foci in the lungs, and a suppurating thrombus in the femoral vein. The mitral valve presented, on the ventricular face of the

anterior segment, a patch, of the size of a sixpence, swollen and greyish white in colour, and opposite to it, on the auricular face, was an ulcer big enough to contain a small pea. There was another also on the wall of the left auricle. There were no infarcts in the arterial system. In these cases of puerperal and traumatic septicæmia, the right heart is more frequently affected than in any other group of cases. Thus, of the thirty-seven cases of this kind, there were thirteen in which the tricuspid or pulmonary valves were involved.

In the acute necrosis of bone or acute osteo-myelitis, a secondary endocarditis may develop; and in some instances the clinical features may strongly resemble malignant endocarditis, as was well illustrated in the case of a lad, aged 10, who died after an illness of less than a week's duration, characterised by high fever, rigors, sweats, etc. No local trouble was complained of, and at the *post mortem* examination there was ulcerative endocarditis of the right side, and a purulent focus in the septum; and it was only after most careful search that the primary trouble was found in a small spot of acute necrosis of the tibia.

These forms do not strictly come within the province of the physician, but they must be taken into account in any description of malignant endocarditis. The source of the poison is very evident in the external wound; the metritis, etc., and the lesions, are chiefly in the territory of the venous system and right heart.

In the pyæmic group of cases, the clinical features are of a decided pyæmic type, and here the source of infection is at the heart, and the metastatic lesions are chiefly in the territory of the arterial system, rendering very applicable the name of arterial pyæmia given by Dr. Wilks to this class of cases. We may recognise two types of the pyæmic form: first, the cases in which the symptoms resemble closely those of ordinary pyæmia, with rigors at intervals, sweats, and other signs of septic infection; and, secondly, an important group, in which intermittent pyrexia is a striking feature, occurring in regular paroxysms like ague, with cold, hot, and sweating stages. These forms may develop as primary independent affections, or come on in the course of rheumatic fever, pneumonia, etc. In our Montreal cases, they have not been so marked as the typhoid type. The following case, with illustrative chart, is a fair example of pyæmic symptoms due to endocarditis developing in the course of pneumonia.

M. W., aged 43, a well built man, was admitted under Dr. Ross, February 26th, 1880. He served his time in the army; he had had syphilis, and had quite recently had syphilitic ulcers; had also been a hard drinker. In October 1879, he was in hospital with pneumonia, and had severe cerebral symptoms. On February 23rd, he had a severe rigor, followed by fever, cough, and pain in the side. On admission, February 26th, there were signs of consolidation at the left base. On the 28th, he was delirious. On March 1st, the crisis seemed to take place; temperature fell to 98°, remained low for three days, and he seemed to be doing very well. At 1 P.M. on the 4th, he had a severe chill, with vomiting, and followed by sweating. On the 5th, he was delirious; he had another severe chill at 2 P.M., in which the temperature rose to nearly 104°. He had five stools; there were no indications pointing to the heart. On the 6th, the morning temperature was normal; the patient was very prostrate, sweated a great deal, and there was low wandering delirium. From the 6th to the 9th, the temperature rose a degree each evening, reaching 105.3°, its highest point. Pulse over 120, and feeble. From this time until the 14th, he gradually sank, remaining unconscious. The lung-symptoms did not extend, but rather improved. The *post mortem* examination revealed extensive ulcerative vegetations on the aortic valves, purulent meningitis, and resolving pneumonia of the base of the left lung.

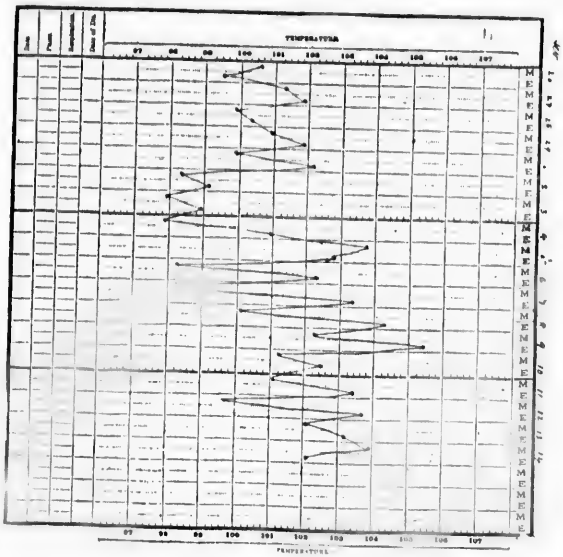
The attack may be ushered in with a single rigor, or more often a

series of chills; and from the outset they may constitute a marked feature, and, with the sweating, prostration, and diarrhœa, give a septic character to the case. A light jaundice may develop, and still further intensify the resemblance. Sometimes the case may run on for a couple of weeks with marked typhoid symptoms, and then pyæmic features develop—rigors, sweats, etc.

But by far the most remarkable cases of the pyæmic group are those which present a marked intermittent type of pyrexia, simulating a quotidian or tertian ague. They may occur without any signs or indications of heart-disease, or the symptoms may develop in individuals the subjects of chronic valvulitis. The cases are not nearly so frequent as those of the typhoid type; but they have been specially studied by Drs. Wilks, Bristowe, and Coupland in this country, Lancereaux in France, Leyden and others in Germany. The paroxysms may have the absolutely typical features of intermittent; the chills, hot stage, and sweating succeeding each other with regularity; and in the intervals there may be an entire absence of the fever. The quotidian type is the most common; the tertian has occasionally been described; and in rare instances two paroxysms have recurred within the twenty-four hours. The cases may be much prolonged, even for three or four months. One of the first references I find to cases of this kind is in a foot-note to one of Dr. Ormerod's Gulstonian Lectures (*Medical Gazette*, 1851), in which a case of Dr. Bond of Cambridge is narrated—an instance of chronic valvular disease, with intermittent fever and diarrhœa, two paroxysms occurring in the day. The case lasted four months. In a remarkable case (Dr. Ray) described by Dr. Wilks (British Medical Journal, 1868), during a six or seven weeks' illness, rigors recurred with such regularity that a tertian ague was suspected for a time, although the patient was known to be the subject of heart-disease. In some instances, the existence of ague previously has rendered the condition much more puzzling. In several of Lancereaux's cases (*Gazette de Médecine*, 1862; *Archives Générales*, 1873), the patients had had intermittent fever a short time before; so also with one of Leyden's cases (*Zeitschrift für Klin. Med.*, Bd. iv, Berlin). But the most extraordinary case of the kind is recorded by Dr. Bristowe (British Medical Journal, 1881). A patient had ague in October, chills once or twice a day; she was ill for six weeks; and, after an interval of two or three weeks, they recurred in the second week of December, and continued until December 23rd. She was well for a few days, and then the attacks recurred after sleeping in a cold bed, and persisted until her admission to hospital on February 12th. For the four weeks previous to entrance, the attacks came every twelve hours regularly. A murmur was noticed; but the history of ague was so clear, and the attacks so characteristic, that a suspicion of malignant endocarditis was at first not entertained. It was only after the failure of quinine and a variation in the character of the paroxysms, that a diagnosis was reached. In Dr. Coupland's cases (*Med. Times and Gazette*, 1882, vol. i), the intermittent pyrexia was also well marked. In none of our Montreal cases was the aguish type very pronounced, though in one or two cases there were regularly recurring paroxysms of chills, fever, and sweating; but the conditions under which the attacks developed rendered the clinical features more like ordinary pyæmia. The majority of these cases appear to arise independently of other affections, and occur among what I have referred to as the primary class of cases; though, as already mentioned, some develop in chronic valvular disease, and others appear associated in some way with ague.

The typhoid type is by far the most common, and the majority of the cases present features which come under this heading. The disease may set in with a single rigor or a series of chills, most frequently the former; often a period of *malaise* or ill health has preceded the attack,

and in very many instances the symptoms develop in the course of some fever. The characters of this form are irregular temperature, early prostration, and involvement of the nervous system, delirium, somnolence, and coma, dry tongue, relaxed bowels, sweats, petechial and other rashes, and occasionally parotitis. Perhaps the majority of cases are mistaken for typhoid, as the heart-symptoms may never be prominent, or even when sought for not found.

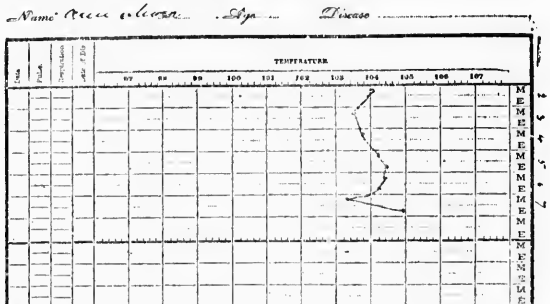


The Case of M. W.

The following cases illustrate the chief features of this form.

Ann O., aged 46, large well nourished woman, was admitted under Dr. Wilkins, June 5th, 1881. She had been a healthy woman. Dr. Blackader saw her on the 2nd, when she complained of severe pains in the back, loins, and hips, which were relieved by poultices. Pulse rapid, tongue furred, no diarrhœa. She was supposed to be suffering from typhoid fever. No reliable history, family or personal, could be obtained, but she had been out of sorts for four or five days previous to the onset of the attack. On admission, temperature 104°; pulse 110; perspiration 32; no eruption; lungs normal; no heart-murmur; no albumen in urine. On the 6th, she passed a restless night. Temperature, 104°; pulse 120, dicrotic; abdomen distended; two stools. She passed 18 ozs. of urine, slightly bloody, which might have been from the menses, which began to-day. On 7th, morning-temperature 103.2°; pulse weak, 120; respiration 54, shallow; loud sonorous *râles* over chest; bowels and bladder emptied involuntarily; stools frequent, high coloured; patient could not be roused. The legs and general surface seemed tender, which caused her to cry out when moved. Urine drawn off by catheter contained much blood, 50 per cent. by volume of albumen, and many granular casts. Pupils unequal; head drawn to the

right. Some rigidity of muscles of arms, most marked on the left; increasing coma, and death at 3.30 P.M. of the 7th, the sixth day of her serious illness. At necropsy, no hypertrophy of heart; mitral valves a trifle thick, with small superficial losses of substance on both curtains. Aortic valves normal; infarcts in spleen. Numerous small hæmorrhagic emboli in kidneys and throughout the intestines. Six or eight suppurating infarcts in brain, chiefly near longitudinal fissure and on median surfaces. The case is a good example of the primary malignant endocarditis occurring in a healthy individual, and running a rapid course, with symptoms of a typhoid character. The diarrhœa was not profuse, though the intestinal lesions were well marked.



The Case of Ann O.

In the following instance, occurring in connection with pneumonia, the profuse diarrhœa and severe nervous prostration were very suggestive of typhoid fever.

J. H., aged 40, drayman, a large well built man, was admitted, May 13th, with pneumonia. He had been a pretty healthy man, though he had had two previous attacks of inflammation of the lungs. He had been in the habit of taking stimulants. His present illness began on the 11th with the usual signs of pneumonia, for which he consulted Dr. Blackader. On admission, he was delirious; temperature 105°, respirations 60, pulse 110, consolidation of lower two-thirds of right lung, with the usual physical signs of hepatisation. On the 6th day, the delirium was less marked and the temperature had fallen to 101.5°. On the 9th day, the fever was 103°, and the condition of lung remained about the same. On the 12th day, I saw him with Dr. Molson. The dulness appeared to be diminishing at the right base; I could detect no murmur at either apex or base of heart. The condition of the

patient resembled closely other cases of pneumonia in which ulcerative endocarditis had developed, and I suggested the possibility in this instance. The tongue was furred; no abdominal distension; no spots; diarrhœa had come on in the past few days; stools thin, yellowish in colour. The patient was dull and heavy, not actively delirious. On the 18th day, temperature rose to 104.5°, and for the next four days kept about that height. On 20th day, diarrhœa, which had been checked, began again. On 23rd day (June 1st), temperature 104.5°, pulse 96, respiration 30. Dulness diminished at right base, still evident in scapular region at lower part; moist *râles* over back of lung; rhonchi, sibilant and sonorous, heard in front. A single large dose (30 grains) of quinine, at 4 P.M. did not affect the temperature, which at 10 A.M. was 105.5°. On 26th day, much the same; temperature had kept about 104°; two or three loose stools each day; low delirium, restless at night. For the next three days, the fever was not quite so high, the diarrhœa ceased, and he became somewhat rational. Still deficient resonance in right lung behind. Respirations kept about 30, and pulse under 100. On the night of June 8th, patient very restless, required constant watching; temperature 105°; pulse more rapid, 130. On the 10th, patient more drowsy; pulse feeble, 140; large moist *râles* heard over both lungs. In the evening he had a rigor; temperature rose to 105°, and death took place on the morning of the 11th, just a month from the onset of the disease. Petechiæ had appeared on the skin during the last few days of his life.

Necropsy, five hours after death. The body was not emaciated; there were petechiæ on the skin in various regions. In the abdomen, patches of dark extravasation were noticed upon the coils of intestines, both large and small. In the thorax, the right lung was intimately adherent. *Heart*, subpericardial ecchymoses. Numerous petechial spots beneath lining membrane of the cavities; some of them are as large as split peas, and on section present a greyish centre, as if they were small infarcts. The mitral segments were natural-looking on the ventricular surface, but on separating the edges, large masses of vegetations were seen blocking the orifice. They were attached to the auricular faces, about 2 to 3 millimètres from the edge; that in the anterior segment was about 2 centimètres in extent, and projected 12 millimètres. It was roughened on the surface. The growth on the posterior segment was smaller, irregularly divided into two bulbous portions, the surfaces of which were smooth. The aortic orifice was blocked with a clot; the right anterior valve presented an enormous mass of vegetation, which occupied the entire curtain, except the edge, and infiltrated the whole thickness, appearing in the sinus as small nodular masses. Two perforations existed between the outgrowths, each about the size of a crow-quill. The posterior segment presented a flattened vegetation, which encrusted the centre of the valve, and extended up to the corpus Arantii. All of these masses had the same appearance; colour greyish-yellow, except where coated with adherent blood-clot; the ones on the anterior mitral segment and on the posterior aortic were roughened, and the granular substance exposed; three others presented smooth surfaces, as if covered by a thin membrane. They were soft, on section granular uniform throughout, and of the consistence of pith. The coronary arteries were free. *Lungs*. The right was closely bound to the chest-wall by old fibrous adhesions. The posterior part of the organ was heavy, but crepitant, except at the upper part of the lower lobe, which, with about 5 centimètres in breadth, of the lower part of the upper, and part of the middle lobes, were firm, airless, and granular on section. Colour liver-red, interspersed with small opaque areas, the plugs in the air-cells undergoing fatty change. The left lung healthy. The *spleen* weighed 185 grammes; pulp soft. No infarctions. The *kidneys* were of average size; numerous small infarcts, chiefly in cortex; small hæmorrhagic areas with

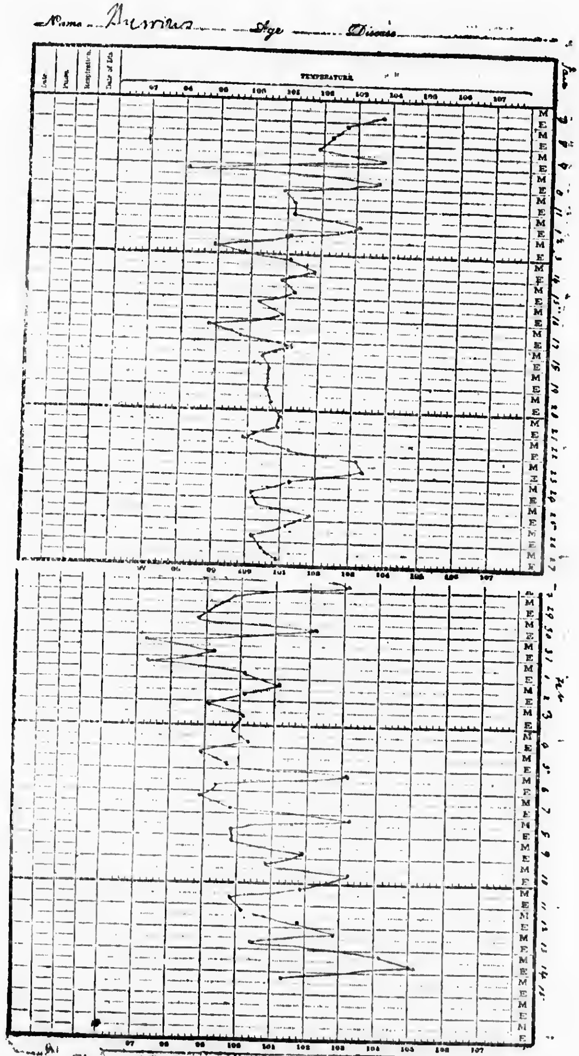
grey centres. *Intestines.* The deeply ecchymotic patches seen externally corresponded with small infarets situated in the submucous tissue, and surrounded by a zone of deeply hæmorrhagic tissue, above which the grey pale glandular layer could be distinctly seen. The infarct itself was about the size of a split pea, a little elevated, on section deep red or greyish red, not in any instance purulent, and surrounded by a zone of extravasation from 1 to 3 centimètres in diameter. They were most abundant in the ileum, about 20 in number. Peyer's glands were not swollen. The *liver* was pale, swollen and soft. *Brain.* Vessels of pia mater full, parts at base normal. Thick purulent lymph beneath arachnoid, covering central part of fissures of Sylvius on both sides, over both frontal lobes at anterior part, over the left intraparietal fissure and on upper part of cerebellum, close to great transverse fissure. A good deal of serosity beneath the membranes. No infarets in substance of brain.

In some instances, the clinical features are mixed; typhoid and pyæmic characters may alternate, as in the following case.

J. B., aged 38, admitted January 7th, 1880, had been a healthy man. Ten years ago, he had a severe attack of pneumonia. On the night of January 4th, he felt uneasy, and did not rest well; got feverish, and in the morning had pain in the side and cough. No rigor. Symptoms continued, and he came to hospital on 7th. On admission, temperature was 103°, pulse 128, and respirations 40. Signs of pneumonia in right lung, lower three-fourths. Characteristic expectoration. During the first week in hospital, nervous symptoms appeared; he became delirious, and passed urine and feces in bed; tongue dry; and on the 9th and 10th there was troublesome vomiting. The temperature was irregular, ranging from 100° to 104°; the evening record usually high, but twice it was lower than the morning. Pulse 120 to 148; respirations 32 to 50. During the second week, the intensity of the symptoms abated; the temperature kept lower, not once reaching 101°. The nervous prostration continued, with tremor of whole body, and the discharges were passed involuntarily. Tongue very dry. A very disgusting fœtor emanated from the body. He lay like a patient in the third week of severe typhoid fever; took food and stimulants well. On the 19th, a painful swelling appeared in the left parotid region, and he began to have chills, and sweated a great deal each day. No objective indications of heart-trouble. The lung cleared very much in the third week, but the prostration continued. During the fourth week, the swelling of the parotid increased, and on February 1st an abscess was opened in this region. On 30th, there were severe chills, with blueness of face and the finger-tips. Much sweating, of a profuse drenching character. He became brighter after the abscess was opened, and the nervous symptoms were less marked. Temperature ranged from 98° to 100°, rising with the chills. In the fifth week, he remained in this state, with but little change, occasional chills and profuse sweats, the picture being more like severe pyæmia. In the sixth week, the prostration increased, and he lay in a heavy unconscious state. No chills, but most profuse sweats. On February 13th and 14th, the temperature rose very high, reaching 105°, and death took place on the 15th, after an illness of forty-two days.

The necropsy revealed extensive mitral endocarditis, as the only special lesion. The base of the right lung was a little firmer than the left, but not granular on section. Only one infarct was found, which was in the upper part of the spleen. The intestines were healthy; there was no meningitis. The parotid abscess had almost healed.

Cardiac Group.—Under this heading may be arranged, as suggested by Dr. Bramwell (*Diseases of the Heart*), those cases in which patients, the subjects of chronic valve-disease, are attacked with febrile symptoms and evidences of a recent endocarditis engrafted upon the old process. I have already remarked on the great frequency with which ulcerative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changes are found in connection with sclerotic endocarditis. Many of such cases present features of the pyæmic, typhoid, or cerebral types, and may be of the most acute character; but, in others, the process appears much less intense, and the cause more chronic. In a considerable series of cases, the history is somewhat as follows. The patient has, perhaps, aortic valve-disease, and is under treatment for failing compensation, when he begins to have slight irregular fever, an evening exacerbation of two or three degrees, some increase in cardiac pain, and a sense of restlessness and distress. Embolic phenomena may develop; a sudden hemiplegia; pain in the region of the spleen, and signs of enlargement of the organ; or there is pain in the back, with bloody urine. In other instances, peripheral embolism may take place, with gangrene of the foot or hand. There may be hebetude or a low delirium. Instances such as these are extremely common; and while, in some, the process may be very intense, in others it is essentially chronic, and may last for weeks and months, so that the term malignant seems not at all applicable to them; still, in a large series of cases, all gradations can be seen between the most severe and the milder forms. Dr. Green (*Lancet*, 1884, vol. i) referred to a case which lasted six months, and to another in which, during eighteen months, there were attacks of irregular fever. I have known the febrile symptoms subside for weeks, to recur again with increased severity; and there are cases which render it probable that the process may subside entirely. The ulcerative destruction, in these cases, may be most extensive; and I have seen the aortic ring with scarcely a trace of valve-substance left. The process in the chronic cases is also mycotic, and it is to be carefully distinguished from the atheromatous changes. In very many instances, there is no history of rheumatic fever or of other constitutional disorder; but the endocarditis appears to attack the sclerotic valves as a primary process, and a very considerable number of the most typical cases are of this kind. A good example was the following case, in which the disease attacked peformed and hardened valves, and the clinical symptoms were prolonged for nearly three months.

H. M., aged 38, was admitted September 8th, under Dr. Ross. He had a good family and personal history; he had always enjoyed excellent health. A month ago he had chilly feelings, fever, and sweating, with vomiting. He kept about until ten days before admission, when he took to bed, with pains at the heart, and fever. On admission, there was marked aortic incompetency; temperature 100° Fahr.; he seemed dull and heavy. On 15th, there was iliac tenderness, and some diarrhœa. For the next two weeks, he remained in same state, temperature rising at times to 103° Fahr. During the first week of October, the prostration increased, and there was slight delirium at night; temperature not higher than 102° Fahr. On the 14th, there was an eruption of petechiæ. From this time, the temperature kept lower—100° to 101° Fahr.—the delirium and prostration increased, and death took place on the 23rd. Two of the aortic cusps had fused, and there were old sclerotic changes; there were recent soft greyish vegetations; the spleen presented six or eight infarcts, one suppurative.

These are the cases of ulcerative endocarditis which present fewest difficulties in diagnosis. The existence of the chronic heart-disease excites attention; and even if compensation has previously been perfect, the ulcerative process may be the very cause of disturbing the balance and producing marked symptoms. In my experience, the existence of fever is invariable when the ulcerative processes are due to micrococci, whereas most extensive destructive changes may occur in atheromatous disease without any elevation of temperature. It may be possible that the granular detritus discharged from atheromatous foci on the valves, or on the aorta, may have irritating properties; yet, in two instances, I have met with most extensive atheromatous ulcers on

valves and aorta, from which large quantities of material must have been discharged, and the patients were not febrile. Dr. Sansom (*Lancet*, 1884, vol. i), however, has referred to a case of ulcerative endocarditis in which there was no elevation of temperature throughout.

Cerebral Group.—A considerable number of cases of malignant endocarditis come under observation, perhaps, in hospital-practice, for the first time, with symptoms of cerebral, or even cerebro-spinal, trouble. In three of the Montreal cases, the patients were brought to hospital unconscious, and presented the appearance of profound cerebral affection. One of the first cases I saw was of this kind. The patient, a woman, aged 29, was admitted on October 22nd in an unconscious state, and no history could be obtained. On the 24th, she became partially conscious, and complained of great pain in the head and back of the neck. Symptoms of slight apex-pneumonia were detected. Temperature up to 104°. On the 25th, she passed urine and fæces involuntarily. There was strabismus of the right eye, and commencing ulceration of the left cornea. Death took place on the 26th. The symptoms were those of an acute meningitis. The *post mortem* examination revealed apex-pneumonia, a patch of endocarditis on the mitral valve, and suppurative meningitis, involving chiefly the cortex. Another case, almost the counterpart, was admitted last year, under Dr. Molson, in an unconscious state, and died eighteen hours after admission, when the necropsy revealed apex-pneumonia, extensive endocarditis, and suppurative meningitis. There may be early unconsciousness or delirium without any meningeal implication, as in a case of primary endocarditis admitted June 5th, 1881. The patient may be wildly delirious or unconscious at the first visit of the medical man, as in a case narrated by Eberth (Virchow's *Archiv*, Band lvii). Very many of these cases die within two or three days of admission, and the question of diagnosis has usually to be suspended; indeed, in looking over the records of eleven instances in which these cerebral symptoms were early, they appear to run a more rapid course than other cases.

In two remarkable cases, there was cerebro-spinal meningitis. Hunolle (*Bulletin de Soc. d'Anatomie*, 1873) records a case of a lad who was admitted with symptoms at first like those of typhoid fever, and then of a marked cerebro-spinal character. There was also a pulmonary affection and endocarditis. The patient lived five days. At the necropsy, there were suppurative meningitis of the brain and cord, pneumonia of one lung, and extensive ulcerative endocarditis, with old sclerotic changes.

A still more remarkable case is reported by Heineman (*New York Medical Record*, 1881, ii). A boy, aged 14, was admitted November 19th. For two days previously he had suffered with pains in back and legs, chills, fever, loss of appetite, vomiting, and constipation; he was rational on admission; tongue coated; temperature 105.2°; condition of heart and lungs negative.

November 20th. Temperature, morning, 103.4°; evening, 105.6°. Fæces and urine passed involuntarily.

November 21st. A purpuric eruption was noticed on the chest, then on the face, and afterwards on the legs and arms. Temperature 104.8°; pulse very feeble; delirium; hyperæsthesia along the spine; no opisthotonos; pericarditis suspected. At 11 P.M. of this day, a second crop of purpuric spots came out; temperature 106°; convulsive movements.

November 22nd, 3 A.M., second convulsive seizure, and death. At the necropsy, there was purulent exudation on the brain, and the meninges of the spinal cord were congested, opaque, and inflamed. There was congestion of lower lobe of the lungs. There were recent vegetations on the mitral valve; and near the apex on the anterior wall of the left ventricle, a small cavity, indicative of probable

abscess and destruction of tissue. Purulent serum was found in the pericardium; the kidneys presented embolic abscesses.

Certain clinical features may be specially referred to in a few words. The fever, as will have been gathered from the previous statements, is of a very variable character. Irregularity is the prominent feature; periods of low may alternate with periods of high temperature, or a remittent may become an intermittent. A remittent type is most frequently met with, but the remissions do not occur with any regularity. Occasionally there may be a continuous high fever, the thermometer not registering below 103° for a week at a time. The pyæmic and aguish types have been sufficiently noted.

The occurrence of a rash has been described by many observers, and, in some instances, has led to errors of diagnosis. The most common form is the hæmorrhagic, in the form of small petechiæ, distributed over the trunk, particularly the abdomen, less often in the face and extremities. They may be most abundant over the whole body, and at times are large and present small white centres. When severe nervous symptoms are also present, the resemblance of the cases to cerebro-spinal meningitis, or typhus, may be very close. In one instance, the case was thought to be hæmorrhagic variola (Duget and Hayem, *Comptes rendus de la Soc. de Biologie*, 1865). An erythematous rash has also been observed.

In a case of Dr. Cayley's (*Lancet*, 1884, 1), there was a mottled red rash on the skin. Colson (*Bull. de Soc. d'Anatomie*, 1876) describes a case in which the rash was erythematous, and in spots distinctly papular.

The mental symptoms may be of a very varied character. By far the most frequent conditions are low delirium, and a dull, semi-conscious, apathetic state. There may be at the outset active delirium, or even maniacal outbursts. In a case of Dr. Habershon's (*Guy's Hospital Reports*, vol. xvii), there was a condition described as mental eccentricity. When there is extensive meningitis, there is usually a condition of deep coma.

Sweating is a very frequent symptom, and is worthy of special notice, from the peculiarly drenching character, which is, as Dr. Henry Thompson remarks (*Lancet*, 1880), second only to ague, and usually far beyond the average mark of phthisis or pyæmia.

The diarrhœa is not necessarily dependent on any recognisable lesion, and may not be very marked, even when the infarcts on the mucosa are most abundant. As noted in several of the cases, it may be profuse, and still further add to the resemblance which some of the cases bear to typhoid fever.

Jaundice may be present, but appears to be a rare symptom. Cases, some of which were mistaken for acute yellow atrophy, are reported by Schnitzler (*Wiener Med. Presse*, 1865), Gubler (*Gazette Médicale*, 1862), Luys (*Ibid.*, 1864), and Mattice and Chalvet (*Ibid.*, 1862).

The heart-symptoms may early attract attention, from the complaints of pain and palpitation; but, as a rule, they are latent, and unless looked for are likely to be overlooked. In those cases with chronic valve-disease, there is usually no difficulty, but where the affection sets in with marked constitutional symptoms, the local trouble is very apt not to attract attention. Even on examination, there may be no murmur present, with extensive vegetations, or it may be variable. There are many instances on record, by careful observers, in which the examination of the heart was negative.

The course of the disease presents many variations, well illustrated by the records I have given; very acute cases may run their course within the week, as in the patient Ann O., already referred to, while in others the duration may be even two or three months. Except in certain cases in which the patients are the subjects of chronic valvulitis, the course is rarely prolonged beyond four or five weeks. Some of the pyæmic group, particularly those with intermittent

pyrexia, appear very prolonged, even two or three months. The most rapidly fatal case is described by Eberth (Virchow's *Archiv*, Band lvii), in which a man, who had enjoyed previous good health, was attacked on the evening of the 25th, with rigors, followed by high fever and rapid unconsciousness. The temperature that night, when seen by a physician, was 41° C., and the case seemed like one of typhus with meningitis. On the 27th, he was removed to the hospital, where he died at 5 P.M. The temperature was 42.4° C. There were extensive ulcers in the aortic valves, and suppurative infarcts in the brain. The duration in this case was scarcely two days. In a considerable number of instances, the disease terminates within a week or ten days.

LECTURE III.

Diagnosis.—Few diseases present greater difficulties in the way of diagnosis, difficulties which in many cases are practically insurmountable. It is no disparagement to the many skilled physicians who have put their cases upon record to say that, in fully one-half of them, the diagnosis was made *post mortem*. In spite, too, of able memoirs in the journals, the disease has not been much known, and it is only of late years that the text-books have contained chapters upon it. The protean character of the malady, the latency of the cardiac symptoms, and the close simulation of other disorders, combine to render the detection peculiarly difficult.

In the group of cardiac cases in which the disease attacks a patient the subject of chronic valvulitis, the matter is usually easy enough. The existence of fever of an irregular type, and the occurrence of embolism, generally suffice to make the case clear. It must be remembered that simple warty endocarditis not unfrequently attacks sclerotic valves, and may be accompanied by slight fever. Of course, in chronic heart-disease, irregular pyrexia may arise from other causes —local suppuration, cellulitis, etc.—which must be excluded.

In rheumatic fever, a disease in which the heart is more systematically examined than in any other, if with the occurrence of a murmur the symptoms become aggravated, and assume a typhoid or pyæmic type, the recognition of the complication should be easy. The onset of severe head-symptoms in rheumatism—delirium, with high fever and coma—requires to be carefully distinguished. Fortunately, the simple endocarditis common in this disease rarely, as I shall have occasion to show, passes into the grave form.

In pneumonia, a prolongation of the course, with the supervention of typhoid or septic symptoms, should lead to a very careful examination of the heart.

The greatest difficulty is met with in those acute cases resembling the malignant forms of the fevers; here the affection may simulate typhoid, typhus, cerebro-spinal meningitis, or even hæmorrhagic smallpox. Even with the detection of a heart-murmur, the judgment may have to be suspended, and many cases die with the general symptoms of profound blood-poisoning, before the development of any special features upon which a diagnosis could be based.

From typhoid fever, with which the cases are most often confounded, the mode of onset, the pyrexia, and the abdominal symptoms offer the chief points for discrimination. The onset of severe endocarditis is more abrupt, not so often preceded by a period of failing health and progressive weakness. In a large number of cases, cardiac pain or oppression and shortness of breath are mentioned as early symptoms. The fever rarely presents, in the early days of the disease, the regularity of typhoid, and from the outset may be very high. A sudden fall to the normal, or even below, may occur: indeed, irregular pyrexia is one of the most important diagnostic signs. The combination of diarrhœa, abdominal distension, and a rose-coloured eruption, points strongly to typhoid fever. The rash, when present, is

usually petechial, a rare circumstance in typhoid fever. The development under observation of pronounced murmurs, particularly of aortic and regurgitant, is most suggestive of malignant endocarditis, and the occurrence of emboli would be a positive confirmation. Rigors rarely occur in typhoid fever, while they are common in endocarditis. It is well, however, to bear in mind that, in many of the most severe cases, death may occur, as in any of the infective disorders, without the development of the special symptoms necessary for a diagnosis.

Many of the cases present the clinical features of pyæmia, a condition which may actually exist, dependent upon the ulcerative lesions on the valves; and here the diagnosis lies between an ordinary septic infection from a wound, or auto-infection from a primary endocardial inflammation.

It is interesting to note the similarity of those cases of acute endocarditis in which death occurs in a few days, without the development of any other than the valvular lesion, with those instances of rapidly fatal acute periostitis and necrosis, and also with those cases of malignant septic infection from a slight external lesion.

It seems strange that difficulties should arise in the diagnosis between malaria and malignant endocarditis, but the records of cases plainly show that for weeks or months a condition of intermittent pyrexia may occur, simulating every type of ague. The paroxysms in regularity, in order of sequence, and in the accompanying general conditions, may fulfil every condition of a quotidian or tertian intermittent; and the development of cardiac symptoms, with breathing of the pyrexial type, may alone determine the nature of the case.

Etiology and Pathology.—With a view of obtaining data upon which to base statements regarding the etiological relations of malignant endocarditis, I have gone over the records of 209 cases. As before stated, 37 of these occurred in connection with pyæmia, traumatic or puerperal. Doubtless this number could have been very greatly increased had I examined files of special gynæcological and surgical journals, but my investigation did not lie so much in these directions. In 45 cases, there was no record of any previous disease which could be taken into account as possibly connected with the endocarditis. In 127 cases, there was a history of past or existing disease with which the cardiac trouble could, with a greater or less degree of probability, be associated.

One or two general considerations may first be mentioned. The period of middle life gives the greatest number of cases. Young children are rarely the victims; there were only three or four instances under 10 years of age, and not many more over 50. The cases occurring in connection with rheumatism presented an average younger age than the others; there were 36 instances under 30 years of age, out of 51 cases in which this point was mentioned.

Of 160 cases (exclusive of traumatic and puerperal), 99 were in males, and 61 in females.

Persons debilitated by exposure or other causes, or addicted to drink, seem particularly liable to be attacked; and in such subjects, during the course of an acute disorder, this complication is much more likely to arise.

As has been already referred to, the existence of sclerotic valvulitis is a very important factor in the etiology of severe endocarditis, a very considerable proportion of the cases occurring in individuals whose valves are thickened and crumpled from chronic inflammation.

The existence of a primary protopathic endocarditis must, I think, be allowed. In 45 cases, no history could be obtained of rheumatism or other affections with which endocarditis is known to be associated. Many of these cases were of the most malignant type; in 10, death took place within a week. A specific statement of the absence of rheumatism was generally given. The onset was usually like that of

a specific fever, headache, vomiting, rigors, pyrexia, and often early delirium and unconsciousness. The very acute cases resemble severe typhoid or typhus, but, when more prolonged, a pyæmic condition may develop. In a number of these cases the disease has attacked persons with chronic valve-disease, some while under treatment, others in whom the compensation was complete and the old lesions only detected at the necropsy. In 5 instances, the ulcerative process attacked aortic valves, 2 of which were fused, and had undergone the fibroid changes always associated with this malformation.

In 127 of the cases, the endocarditis was associated with other diseases, some of the most important of which we shall now proceed to consider.

Rheumatism.—Since Bouillaud called special attention to the frequency of cardiac complications in this disease, its importance in the etiology of endocarditis has been universally recognised. And, as regards the simple form of endocarditis, the general statements are quite true, but, fortunately, the graver and fatal form is much less common, much less, I think, than is usually supposed. In 53 cases, there was a history of rheumatism, past or present. I included every case in which there had been the record of an attack, recent or remote. In only 24 did the symptoms of severe endocarditis arise during the progress of the acute or sub-acute disease. In 29 cases, there was simply a history of rheumatism, often years before, and no mention of the occurrence of joint-troubles at the time of the development of the endocarditis. Dr. Ogle called attention to the fact that ulcerative endocarditis occurred very often in persons in whom no rheumatic history could be traced. Of 21 cases which he reported, some of which were probably atheromatous, in only 3 was rheumatism mentioned. In only 3 also of the Montreal cases was there any positive history of rheumatism, either before or during the attacks. The following case, under the care of Dr. Ross, is a good example of the mode of onset.

B. M., aged 22, a healthy girl until three weeks before her admission to hospital, on January 4th. At that time she was attacked with rheumatism of the wrists and ankles, not very severe, and she did not receive any treatment. A week from the beginning of the attack, she began to have chills, two or three a day, and she became feverish. During the next week she became worse, had occasional chills, not delirious; was brought to hospital on the 4th, in a very low state. On the 5th there was delirium and incoherence. Pulse 130; temperature 100°. Double murmur up and down sternum; joint-troubles not evident. On the 6th, 7th, and 8th, she remained in the same state, no chills; temperature ranged from 100° to 102°. On the 9th, she was more restless. On the 11th a grey membrane was noticed on the fauces. On the 12th, the membrane in the throat had extended, and covered the soft palate. Temperature 103°. On the 13th she died suddenly. The necropsy revealed a large deep ulcer at the aortic ring, nearly destroying one segment, and penetrating deeply between the auriele and the left ventriele. There were small infarcts in the brain, extensive recent diphtheria of fauces.

In a larger number than in any other group, sclerotic valves were found, with the existence of which the past rheumatism could, in many instances, be connected. A primary rheumatic endocarditis was recognised by Latham, also by Graves and Stokes, and it is quite possible that some of the cases which I have grouped as protopathic represented instances of the kind in which, if life had been prolonged, joint-troubles might have supervened.

Cases of acute rheumatism sometimes occur in which there may be multiple miliary abscesses (Fleischhauer, Virchow's *Archiv*, Band lxxii), and a pyæmic condition similar to the case just narrated, but without the presence of endocarditis. Micrococci have been found in these abscesses, and the cases resemble those

rare instances of idiopathic pyæmia. It is worthy of observation that a skin-eruption was most frequently noted in connection with the rheumatic cases, generally an erythema. In a case of Dr. Kirkes (British Medical Journal, 1863, vol. ii), it was observed on both face and hands. The occasional presence of a scarlet rash in rheumatism (Peter, *Union Médicale*, 1870), and in puerperal fever (Hicks, *Obstetrical Society's Transactions*, vol. xii), has long been recognised.

In chorea, with which simple endocarditis is so often associated, the malignant form very rarely supervenes.

Pneumonia, as Bouillaud pointed out, is not unfrequently complicated with endocarditis, but the important part which it plays in the etiology of the malignant disease has not been generally recognised. In the cases I have reviewed, it stands at the head of the list of diseases in which secondary endocarditis of a severe nature develops, 54 instances having been noted, rather more than 25 per cent. of the total number of cases. For this I was quite prepared by our Montreal experience, for, in 11 of the 23 cases, the attack was associated with pneumonia. Of the occurrence of acute endocarditis in this disease, the statements are somewhat diverse. Bouillaud thought that, in a third or fourth of the cases in which there was left-sided pneumonia, there was inflammation of the serous membranes of the heart. Grisolle, in his classical work on pneumonia, states, on the contrary, that it is a rare complication, and this would certainly appear to be the conclusion of the Committee for Collective Investigation; for, in the report upon 1,000 cases, endocarditis is only once mentioned. My experience at the Montreal General Hospital is very different. I have notes of 103 necropsies on cases of lobar pneumonia, and the occurrence of acute endocarditis is noted in 16 cases, over 15 per cent. Of these cases, 11 were of the malignant form. An analysis of these shows that, in 6, the left lung was involved; in 5, the right; in 4, the upper lobe was affected; in 7, the lower. In 9 of the cases was there pericarditis; in 5 of the 11 cases, there was suppurative cortical meningitis. In the 54 cases which I have reviewed, in 36 the lung affected was mentioned, and in 26 the affection was on the right side, and only 10 on the left; figures which are opposed to the statement of Bouillaud, that it is in left-sided pneumonia that endocardial complication most frequently supervenes. In 15 cases, acute meningitis is mentioned, and, in one instance, the meninges of the spinal cord were also affected. The aortic valves seem more often involved than the mitral. In 17 instances, there were old sclerotic changes in the valves.

The clinical features of several cases in which the endocarditis came on during pneumonia have already been given. In many of them, as in the girl, M. D., aged 29, referred to in the second lecture, the patients are brought to hospital unconscious, and die within a few days, with symptoms of a grave cerebral disorder. In others, there is a history of ordinary pneumonia, and the case may pursue the usual course, and defervescence take place, when, in a day or so, fever of an irregular type recurs, and typhoid or pyæmic symptoms appear. The majority of the cases are of this kind. Again, some instances occur in connection with injuries, and the patient succumbs to a lobar pneumonia and endocarditis unconnected with any sepsis. Two of the Montreal cases were of this kind. In three or four cases, there were rheumatic symptoms preceding or accompanying the pneumonia, as in a case of Dr. Mussers, the remarkable temperature-chart of which is here shown.

Elderly persons were more often attacked than in the other groups. There were 10 individuals over 50 years of age. In the Montreal cases, 3 of the patients had had pneumonia before; in 1 it was the third attack, and in every one of them there was a history of either drinking habits or previous bad health. In some cases, the pneumonia had

partially or entirely resolved at the time of death, in others there was red, or, more frequently, grey hepatisation.

The relation of the meningitis to the pneumonia and the endocarditis is particularly interesting. The occasional occurrence of this complication in pneumonia has been referred to by many writers, particularly Grisolle, Huguenin (Ziemssen's *Encyclopædia*, Band xii), and Greenfield (*St. Thomas's Hospital Reports*, 1878). In the 103 cases, I met with it in 8 instances, in 5 of which there was also endocarditis. The frequency of the association of these two conditions in pneumonia is illustrated by the figures already given: of 25 instances of meningitis in malignant endocarditis, 15 cases occurred in pneumonia. In all the specimens I have examined, there were micrococci in the exudation, and in three cases many of the capillaries and small arteries were filled with them; and it seems natural, where the endocardium is involved, to attribute the process to embolism from the valves. But the occurrence of an identical cortical meningitis without any valvulitis shows that it may be due to other causes than the endocarditis. As Huguenin suggests, it may be dependent upon the presence in the blood of infective material derived from the infiltrated lung-tissue.

In connection with these secondary or consecutive inflammations in pneumonia, it is interesting to call to mind the not unfrequent occurrence of pericarditis, and of croupous inflammation of the gastro-intestinal canal. Dr. Bristowe some years ago noted the frequent complication of croupous colitis; and, in 103 necropsies, I have met with this complication in 5 instances; and in one there was extensive croupous or membranous gastritis.

Diphtheria is rarely complicated with endocarditis, and I have only been able to find two or three instances in which severe symptoms were present; yet, in some works, endocarditis is stated to be not an uncommon sequence. Labadie-Lagrave (*Bull. de la Soc. d'Anatomie*, 1877) regards it as such; but it is probable that what he described as vegetations are only Albini's little nodules, the remnants of fœtal structures. In 108 necropsies in diphtheria, Telamon (*Progrès Médical*, 1879) did not meet with a single case of endocarditis; and my experience has been the same in 30 *post mortem* examinations, many of which were in adults.

In *dysentery*, a few cases have occurred. Litten (*Charité Annalen*, Band iii) has recorded an instance in which there was extensive ulceration of the aortic valves, and one of the Montreal cases occurred in connection with acute colitis.

In the *eruptive fevers* grave endocarditis occasionally develops—in typhoid, in scarlet fever, and in variola; but, in the cases I have analysed, these diseases appear of very trivial etiological significance.

In *ague*, as Lancereaux (*Gazette Médicale de Paris*, 1862; and *Archives Générales*, 1873) first pointed out, simple or severe endocarditis may develop. In some of these cases, as in the remarkable one reported by Dr. Bristowe, to which I referred in the second lecture, the paroxysms of true intermittent fever, and those of the ulcerative endocarditis, seem to run the one into the other.[1] In most of the cases, there has been only a history of severe ague, and the endocarditis has followed repeated attacks. Dr. Greenhow (*Pathological Society's Transactions*, vol. xxx) has reported a very instructive case of the kind.

Dr. Goodhart (*Pathological Society's Transactions*, vol. xxxiii) makes the interesting suggestion that ulcerative endocarditis is more frequently met with at periods in which scarlet fever, erysipelas, pyæmia, and diphtheria prevail. The Guy's Hospital records certainly seem to show that the cases appear in groups pretty close together, and at a time when the

[1] Dr. Bristowe informs me that, in the case referred to, he is inclined to regard the intermittent pyrexia as dependent from the outset upon the endocarditis, and not associated with malaria.

diseases mentioned are epidemic. In Montreal, we have had occasionally a "run" of cases together; but I have not noticed the connection referred to by Dr. Goodhart.

Pathology.—I approach a discussion of the pathology of malignant endocarditis with some trepidation, partly due to a sense of incompetency, and partly from a feeling that the time is scarcely ripe for a satisfactory presentation of the subject; and yet there are signs which make one hopeful; and it would not be rash to predict that the knowledge twenty-five years hence will be as much in advance of to-day as our information on the subject is of the time when Dr. Kirkes made his memorable investigations. A serious difficulty exists in the circumstance that we have not to deal with a single form of disease—an entity—but rather with a special manifestation in many affections; affections, too, the pathology of which is, in most instances, by no means clear. No one can doubt that the more severe cases of endocarditis present in a typical manner all the features of those diseases which we call infective, and believe to be caused by the absorption of some poison, the development of which in the blood and tissues profoundly disturbs, and finally annihilates, function.

Briefly stated, the theory of acute endocarditis which at present prevails, and the only one to which I shall refer, is, that it is in all its forms, an essentially mycotic process; the local and constitutional effects being produced by the growth on the valves, and the transference to distant parts of microbes, which vary in character with the disease in which it develops. This very attractive theory can be adjusted to meet every requirement of the case, though as yet lacking certain of those substantial data necessary for full acceptance, but which, having been furnished of late years in other diseases, we may reasonably hope will in time also be forthcoming for this.

Let us see, first, what has been done, and how far the facts at our disposal seem favourable to this view. The constant presence of micro-organisms seems undoubted; only, in the simple acute form, we need more careful observations with our improved methods. Some good observers have not been able to find them (Orth, *Lehrbuch der Speciellen Pathologischen Anatomie*, Lief. i, 1883); others declare them to be invariable constituents of the verrucose outgrowths (Klebs, *Archiv für Exper. Pathologie*, Band iv; Köster, Virchow's *Archiv*, Band lxxii). The careful application of such a satisfactory mode of staining as recommended by Gramm should readily determine this question. A study of the endocarditis of puerperal and traumatic pyæmia will be most likely to yield important information, as here the conditions are simpler, and the relation of the micro-organisms can more readily be determined. The cardiac complication in these cases is only part of a general process, excited by a local lesion, and is entirely secondary and subsidiary. Micrococci arranged in chaplets are constant constituents of the vegetations, and, in the case of puerperal fever, they have a close resemblance to those found in the peritoneal exudation. The well known observations of Koch, Ogston, and others have shown the relation of microbes to pyæmia; and the recent culture-experiments of Rosenbach ("Micro-organisms bei den Wund-Infectionen," *Krankheiten des Menschen*, Wiesbaden, 1884) go far towards demonstration for man what Koch had previously done in the case of the pyæmia of the mouse. In these cases, a study of the modes of growth of the micrococci of the endocarditis, and of the effects of inoculations, and a comparison of these with similar observations in the organisms of the original lesion, or of the metastatic foci, should yield results of great value in the interpretation of the phenomena of secondary endocarditis.

In rheumatic fever, we are still too far from any accurate knowledge of its intimate pathology to dwell on the possible connection of any

organism peculiar to it, and the endocarditis common in its course. Klebs (*Archiv für Experiment. Pathologie*, Band ix) distinguishes the microbes occurring in rheumatic cases from those of the septic forms.

In pneumonia, micrococci undoubtedly abound in the exudation of the air-cells, and their mode of growth in gelatine is peculiar, but the numerous experiments on artificial production are not yet conclusive. The evidence is accumulating which places pneumonia among the infective disorders; and it certainly is a seductive view to take of its pathology to regard the local pulmonary lesion as excited by the growth of micrococci in the air-cells, and the various consecutive inflammations, the endo- and peri-carditis, the pleurisy, the meningitis, the membranous gastritis or colitis, as due to the penetration of the organisms to deeper parts, and their local development under conditions dependent on the state of the tissues. The processes are all of the character described as croupous, and have as common features the presence of micrococci in a coagulable exudation. We have still, however, to settle the identity of the organisms of the air-cells with those of the consecutive inflammations; but we may reasonably hope ere long to have some positive data from investigations in this disease, which, more than any other, offers favourable opportunities for the solution of these problems.

In diphtheria, as we have seen, mycotic endocarditis rarely occurs; and, in the few instances observed in association with scarlatina, variola, erysipelas, and other affections, we lack positive information with regard to the characters of the micro-organisms.

In the way of experimental investigation of the properties of the micrococci, not much has been done of a satisfactory nature. Heiberg (Virchow's *Archiv*, Band lvi) placed bits of vegetations from a puerperal case beneath the skin and in the peritoneal cavity of a rabbit without effect. Eberth (*Ibid.*, Band lvii), Birch-Hirschfeld (*Archiv der Heilkunde*, Band xvii), have produced panophthalmos in the rabbit by inoculating the cornea; and I was able to produce well marked mycotic keratitis in the same animals with fresh material from the valves of two cases. H. Young, of Manchester, inoculated rabbits with pus from an abscess in ulcerative endocarditis, and was able to detect micrococci in the blood.

No conclusive culture-experiments have yet been made. Grancher (*Journal de Médecine de Paris*, December 20th, 1884) has cultivated a microbe from the blood, taken during life with all necessary precautions, but apparently not in series, and no inoculations of animals were made. Cornil (*L'Abeille Médicale*, December 22nd, 1884) has made cultures on gelatine, but apparently no special results have been reached.

How do the micrococci reach the valves? In cases of puerperal and traumatic septicæmia, the external lesion is undoubtedly the source of infection which is conveyed through the venous system; and, in these cases, it will be remembered that the right heart is most often affected. In other instances, where the skin is unbroken, we must suppose them to gain access by the lungs or intestines, most probably the former; and, in these instances, the left heart is the chief seat of the mycosis. Whether they reach the valve with the general blood-current, as Klebs supposes, or through the coronary arteries, as Köster holds, cannot be considered settled; but, from the position of the early vegetations in a non-vascular region of the valves, and from the fact already referred to, that colonies of micrococci can be seen directly upon the endocardium, it seems probable that Klebs's view is the correct one. He suggests, in explanation of the fact that the lines of closure of the valves are the usual seat of the process, that the micrococci, circulating with the blood, are here closely pressed into the endothelium by the firm apposition of the flaps. Whether or not in any given case endocarditis will arise, depends greatly on the

condition of the valve-tissue. In a case of pneumonia or other disease—such as pyæmia—in which we may suppose microbes circulating in the blood, the endothelium of normal valves may be able to resist their invasion, or, even if they do lodge and penetrate, the conditions may not be favourable for their growth; but, where an individual is debilitated, and the tissue-tone lowered, or if, as often seems the case, the valves be diseased, then the micrococci find a suitable nidus, and excite, by their growth, an endocarditis which may be of a malignant type. As Dr. Goodhart suggests (*loc. cit.*), patients with chronic sclerotic valves are walking mushroom-beds, in common times without spawn, but in periods of epidemics taking in germs by various channels, which fertilise in some cases into ulcerative endocarditis; in others, to suppurative processes. Certainly, on paper, so to speak, the view which I have thus imperfectly and hurriedly discussed seems plausible enough, and meets the requirements of the case fairly well; but let us, in conclusion, follow an important rule too much neglected, and get a definite outline for our ignorance. In the first place, we do not yet know, with sufficient accuracy, the frequency of the occurrence of microbes in simple endocarditis. Are they constantly present, or only in forms associated with special diseases? Secondly, we want full information of the various forms of micro-organisms occurring in secondary endocarditis, and of their relation to the microbes assumed to be the cause of the primary disease. And, thirdly, we are only at the threshold of inquiries relating to the culture of these organisms, to the macroscopic characters of their growth, and to the possible experimental production of endocarditis.

I cannot conclude without thanking my late colleagues at the Montreal General Hospital, by whose kindness I have had command, not only of the pathological, but also much of the clinical, material upon which these lectures were based; and lastly, sir, you will allow me to express my sincere regrets that my efforts have not been more worthy of such an intensely interesting subject, and of the distinguished audience which I have had the honour of addressing.

NOTES

ON THE

MORBID ANATOMY OF PNEUMONIA.

BY

WILLIAM OSLER, M.D.,

Fellow of the Royal College of Physicians, London; Professor of Clinical Medicine at the University of Pennsylvania; formerly Professor in McGill University, and Pathologist to the General Hospital, Montreal.

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NOTES ON THE MORBID ANATOMY OF PNEUMONIA.*

By WILLIAM OSLER, M.D.,
Fellow of the Royal College of Physicians, London; Professor of Clinical Medicine at the University of Pennsylvania; formely Professor in McGill University, and Pathologist to the General Hospital, Montreal.

My post-mortem records include 105 cases of lobar pneumonia, all of which, with one or two exceptions, occurred at the Montreal General Hospital. For the purposes of this article, I shall exclude five cases, in which either the data are incomplete, or about which I have some doubt. As is the case at most large hospitals, the death-rate from pneumonia at the Montreal General is high, due to the facts first that, as a rule, only the severer cases are brought in, and second that a considerable proportion of the cases occur among enfeebled and dissipated paupers, who rapidly succumb to such an acute affection as pneumonia. In the statistical report of Dr. James Bell,† the mortality for a period of ten years was somewhat over 25 per cent., one-third of the deaths occurring within forty-eight hours of admission. As a contrast, it may be stated that the mortality of the pneumonia cases in the practice of Prof. R. P. Howard of Montreal, during a period of twenty years, was only 4.8.

The statistical details are as follows:—

Sex.—Of the 100 cases, 70 were in males and 30 in females.

Age.—In 94 instances the age was given; up to the tenth year, 5 cases; between 10th and 20th, 6; from 20th to 30th, 12; between 30th and 40th, 18; between 40th and 50th, 21; between 50th and 60th, 12; and over 60, 20 cases.

Lung affected.—In 51 cases, the right; in 32 cases, the left; in 17, both. As to the position of the inflamed region in the lung the figures are: in the right, whole organ solidified (except,

* Read before the Pathological Society of Philadelphia, April 23rd, 1885.

[This, with other articles on morbid anatomy which will follow from time to time, will constitute my third and last Pathological Report from the Montreal General Hospital.]

† Montreal General Hospital Reports. Vol. I. Dawson Bros. 1880.

perhaps, narrow margin at apex and anterior border) in 17; lower lobe alone, in 18; upper alone, in 7; middle and lower, in 3; middle and upper, in 2; upper and lower, in 3. In the left lung, entire organ in 10; lower lobe in 16; upper lobe in 6. In the cases of double pneumonia, it was most often the lower lobes which were affected together, but in three instances the lower lobe of one lung and the upper of the other were affected; in three cases both upper lobes; and in *Case XLIX* the most extensive inflammation of both lungs occurred—the left was in a state of uniform red-hepatization, with the exception of the anterior border, and the right in the stage of grey-hepatization, except still smaller portions of the corresponding regions. Altogether, in 39 instances a lower lobe was involved, in 19 an entire lung, and in 16 the upper lobe.

Weight of lungs.—To estimate the amount of solid exudation, the lungs were generally weighed. The heaviest was in *Case XLVIII*, a man aged 10, whose left lung, uniformly solid, weighed 2303 grammes, and the right, very congested and œdematous, 900 grammes. (The normal lung weight is between 600 and 700 grammes.) In eight cases the affected lung weighed about 2000 grammes, representing rather more than three pounds of solid exudate.

State of lung tissue affected.—In about one-half the cases, the inflamed area was in a state of red hepatization. In 30 per cent. there were regions of grey hepatization with the red, and in 22 cases there was grey hepatization either dry or passing into the condition of purulent infiltration.

State of uninvolved portions.—Usually the crepitant parts of the affected lung were greatly congested or intensely œdematous. The latter was invariably the case when the whole organ, except the apex and anterior border, was involved, which then presented a condition of almost gelatinous œdema. The unaffected lung was generally congested and œdematous, particularly at the posterior part. It was not uncommon to find the anterior portions quite dry and bloodless, while the dependent regions were full of blood and serum. No doubt this is largely due to post-mortem subsidence. We do not always find extensive congestion or œdema in the uninflamed parts. Thus in *Case XXXII*, in which

the lower lobe of right lung was hepatized, the upper and middle lobes were noted as "very dry and bloodless," whereas the left lung was œdematous, except at anterior borders. So, also, in *Case LVIII*, a woman, aged 50, with red hepatization of left lower lobe, the upper lobe was crepitant throughout, dry on section, no redness, and no blood. The right lung was also crepitant (except a fibroid apex), dry, no œdema, and very little blood.

Air passages.—The bronchi generally contained a frothy, serous fluid—not often the tenacious mucus characteristic of pneumonic expectoration. The mucous membrane was usually reddened, rarely swollen. In the affected regions the smaller bronchi very often contained fibrinous plugs, and in twelve instances these were noted as very abundant and extending into the larger tubes of the inflamed region, forming perfect casts of the bronchi.

The *bronchial glands* were invariably swollen, succulent, occasionally very soft and pulpy. In no instance was there suppuration.

The pleuræ.—When the inflammation reaches the surface of the lung the pleura is inevitably involved, with the result, commonly, of a thin sheeting of exudate, perhaps of such delicacy that it only produces turbidity of the membrane. In only two instances the pneumonia was deep-seated, and did not reach the pleura; in every other instance this membrane was involved in a greater or less degree. In some cases the fibrinous exudate was extraordinarily thick and extensive, as in *Case V*, in which the right lung was uniformly solid, weighing 3 lbs. 6 ozs., and every portion of the pleura was covered by a creamy fibrinous layer an inch in thickness.* In several cases there was copious exudation, amounting to three or four pints. In six cases there was extensive double pleurisy, with pneumonia on one side only. *Case XV* illustrated how readily the inflammation could cross the anterior mediastinum and spread from the pleura of left upper lobe to that of the right.

Among the more uncommon terminations of pneumonia, there were cases of abscess, gangrene, and fibroid induration.

* Specimen in the museum of McGill College.

Abscess.—When a lung in a state of purulent infiltration is examined, we wonder that softening and breaking down of the lung tissue is not a more frequent result of this process. In four instances there were definite small abscesses. In *Case XXXIV*, a woman, aged 56, with grey hepatization of the right upper lobe, there was a small abscess cavity, with shreddy walls, the size of a walnut, in the anterior portion of the lobe. The tissue about it was in a state of purulent infiltration. In *Case XXXVI*, male, aged 60, with grey hepatization of upper half of left lung, there were in the central part of the upper lobe several spots of softening, the size of marbles, irregular, with ragged, uneven walls and purulent contents. *Case LXXVII*, female, aged 64, with almost uniform consolidation of left lung, the upper lobe was in a state of intense purulent infiltration, and there were in the middle portion several large abscess cavities communicating with each other, with ragged walls and purulent contents.

Gangrene.—In three instances this termination was met with. *Case LIV*, a woman, aged 35, a hard drinker, was admitted with pneumonia of the left lung, which had existed for some days, during which she had been neglected and much exposed to the cold. The lower lobe presented at its apex and extreme base signs of consolidation, but in the rest of its extent was represented by a large gangrenous cavity, occupied by shreddy and necrotic lung tissue and blood clots, the whole forming a stinking mass.* The walls were not defined, except at the lower part, where a separation between the sloughing and firmer lung tissue could be plainly seen. In *Case LX*, male, aged 63, with pneumonia of the left lung, there was a spot of gangrene at the apex surrounded by dark consolidated tissue. *Case LXXIV*, male, aged 50, a hard drinker for 20 years, admitted supposed to be suffering with delirium tremens; had had convulsions before admission. Rigidity of muscles of arms, coma and death 36 hours after admission. At apex of right lung a gangrenous mass the size of a hen's egg, surrounded by greenish-black consolidated tissue. Suppurative meningitis of cortex.

* Specimen in museum of McGill Medical Faculty.

Fibroid induration.—The production of a chronic—so-called interstitial—pneumonia from the ordinary croupous form is, perhaps, the most rare termination of the disease. The following case is of special interest, from the fact that the man was under observation almost from the outset, and the induration was in patches and in an early stage:—Louis Phillippe, aged 58, a laborer, was admitted with cough and pain in the side. Had a chill five days before admission. Temperature 101°F.; pulse 106; respiration 26. Expectoration not bloody. Physical signs of pneumonia over right lower mammary, infra-axillary, scapular and infra-scapular regions. During the first ten days in hospital patient made no satisfactory progress; temperature ranged from 99° to 103°; he was heavy and dull, not delirious; pulse weak, 100 to 120. Defective resonance in infra-clavicular regions on right side; in mammary region, a flat tympanitic note; behind, absolute dulness, feeble-blowing breathing; a few râles on deep inspiration. The note over right mammary was markedly tympanitic. Patient emaciating. No heart murmur; very little expectoration, muco-purulent, not bloody. On the 26th day he had a chill, and the temperature went up to 104°. No change in physical signs. Died at noon of the 27th day after admission. The right lung was uniformly solid, greyish in color, with recent pleuritic exudation, and the surface, on section, bathed with serous fluid. On carefully inspecting the cut section, three features called for attention. In the first place, in certain regions the air-cells could be seen with their fibrinous plugs, of a very opaque white character, undergoing fatty change. This state existed in very considerable areas. Secondly, there were small localized areas densely infiltrated with pus, and breaking down into definite abscesses. The largest of these was about the size of a marble. And thirdly, in several areas of the lung there were spots which had a very translucent aspect, were firm, smooth, homogeneous, not granular, and had the look of a recent connective tissue. In these areas a fibroid change was going on in the lung; the alveolar walls were thickened, and the fibrinous plugs filling the air-cells were undergoing transformation into a new growth of connective tissue.

State of the other Organs—Heart.—Distension of the chambers, particularly the right, with very firm, tenacious coagula, is a very constant feature in pneumonia autopsies The right auricle is usually very full, and a solid mould, capped usually with a buffy layer, can generally be removed with the extensions into the cava and many of its branches. I have seen a complete cast of the branches of the superior cava, even to the smaller vessels, and a mould of the inferior cava including the hepatic and the iliac branches. From the pulmonary artery there can be withdrawn, by careful manipulation, a dendritic clot representing the vessels of quite small calibre. In no disease, I think, are we likely to meet with such solid coagula—so firm and fibrinous; and on several occasions, when I did not know the nature of the case, the preliminary incisions for the right chambers have enabled me to make a shrewd guess as to the existence of pneumonia. In many instances the engorged state of the right side and condition of general venous stasis, suggested the possibility that a copious venesection might have relieved the overloaded chambers—and I have in several cases acted with benefit upon this suggestion. In extensive red hepatization the circulation in the inflamed area must be very much impeded, and the work of the right ventricle greatly increased. If we may reason from the experiments of Welch,* the collateral œdema, which we have so much dreaded under these circumstances, has no existence; for he seems to show very clearly that to produce pulmonary œdema the blood pressure must be raised to a point very much beyond that which can be induced by the cutting off of certain territories of capillaries, however extensive, in a pneumonia. Yet there are difficulties in the way of explaining the œdema of the sound portions of the lung on the view which Prof. Welch holds, viz., that the left ventricle is first weakened or paralyzed and the continued action of the right gradually produces the engorgement and œdema. It seems natural to think that the engorged right ventricle would more quickly fail than the left, which is rarely

* Virchow's Archiv. lxxii.

found so full, and certainly has not to bear the strain and tension of the right chamber.

The left chambers usually contained coagula, but were rarely distended, never to the degree often met with in the right.

The tricuspid orifice was frequently found dilated, measuring from five to six inches in circumference.

Turbidity and moderate fatty change were sometimes noted in connection with the heart muscle. The endocarditis will be considered with the complications.

Spleen.—Friedreich and others have called attention to the very general enlargement of this organ in pneumonia. The normal weight may be taken at about 170 grammes. In only 35 cases was the weight over 200 grammes—the heaviest, in *Case LXXV*, was 670 grammes. In 12 cases the weight was under the average; in *Case LV* it was only 72 grammes. Usually the pulp was very soft; but in four cases the note is, "pulp firm, and cuts well." In many cases the weight was not recorded, but the note entered was either "normal" or "slightly enlarged."

Kidneys.—In exactly 25 per cent. these organs showed signs of interstitial changes, being hard and fibroid, with adherent capsules and often small cysts. In eight cases there was marked parenchymatous swelling; in *Case XXIII*, chronic parenchymatous nephritis; in *Case XXV*, amyloid degeneration, and in *Case XXXII* extensive fatty changes in the tubules.

Other Diseases and Injuries.—One case occurred in connection with diabetes and one with erysipelas. Three cases followed injuries, one a burn, and one came on in the course of a carbuncle. In all, the pneumonia was fibrous and lobar. These cases of "contusions-pneumonia," as Litten terms this form,* are very interesting, and may come on after slight or severe injuries, or after operations.

COMPLICATIONS.

Pericarditis occurred in five cases. In two there was extensive double pleurisy with the pneumonia. In one there was

*Zeitschrift fur Klin. Medecin., Bd. V.

endocarditis as well. Except in *Case XCIII*, a portion of lung contiguous to the pericardium was involved in each case.

Endocarditis.—I have on several occasions called attention to our exceptional experience in this respect, though, indeed, a review of the literature shows that the occurrence of this complication in pneumonia is by no means infrequent, In 16 cases there was endocarditis, either of the simple or malignant types, most often of the latter. In five instances these were simple warty vegetations, and there were no special cardiac symptoms. In 11 cases the lesions were more extensive, usually of the ulcerative form, and the character of the disease was much altered, or even masked by this complication. Our cases bear out Bouillaud's suggestion that endocarditis most frequently complicates left-sided pneumonia, but in a review of 36 cases of endocarditis occurring in this disease, and in which the lung affected was mentioned, I find that in 20 it was in the right side and only 10 in the left, so that it seems doubtful if contiguity has anything to do with it.

Meningitis.—In eight cases there was meningeal inflammation, in seven pia-arachnitis, and in one dura-arachnitis. In five of these cases there was also ulcerative endocarditis. Brief details of the cases may be given :—*Case II*, male, aged 38 ; red hepatization of upper lobe of right lung, extensive exudation at base of brain, in longitudinal sinus and along the Sylvian fissure.

Case LXVII, woman, aged 64. Grey hepatization of left lung, with small abscess cavity ; the under surface of the dura-mater of left hemisphere covered by a sheeting of recent lymph, which could be detached in flakes. No lymph beneath the arachnoid or at the base.

Case LXXXIV, male, aged 50. Grey hepatization of right upper lobe and a spot of gangrene. Intense congestion of cortical meninges and exudation of lymph in patches over the frontal and occipital lobes ; none at the base.

The following cases were associated with endocarditis :

Case XXVIII, female, aged 29. Upper half of right lung hepatized. Mitral ulcerative endocarditis. Meningitis of the cortex. A thick flake in the neighborhood of the left fifth nerve, and another about the optic chiasm.

Case L, male, aged 40. Lower lobe of right lung. Extensive endocarditis of mitral and aortic valves. Thick creamy lymph over sides and upper surfaces of the hemisphere. None at the base.

Case LXXIX, male, aged 43. Lower half of left lung affected. Endocarditis, mitral and aortic. Meningitis of the left hemisphere, with exudation of lymph over the frontal and parietal convolutions. None at the base or on the right side.

Case LXXXVII, male. Double pneumonia; right apex. Ulcerative endocarditis of mitral. Cortical meningitis. No lymph at the base.

Case XCIX, female, aged 19. Red hepatization of central part of right lung. Endocarditis of anterior segment of mitral valve. Meningitis of cortex—both hemispheres.

The complication of meningitis is one of the most serious that can occur in pneumonia, and it would appear, in a considerable proportion of the cases, to be associated with ulcerative endocarditis. We may suppose the inflammation of the heart and the meninges to be induced by a common cause, or, what would appear likely in many cases, the meningitis is embolic in origin, for it also occurs in malignant endocarditis, unassociated with pneumonia. In 20 cases of meningitis in this disease, only 15 occurred with pneumonia. The infective material may possibly be derived directly from the infiltrated lung tissue, and carried off by the pulmonary veins. We know that occasionally large emboli may be derived from this source, as in a case of pneumonia occurring at the General Hospital in 1879, in which, during the progress of the disease, and not associated with endocarditis, there was embolism of one femoral artery and gangrene of the leg, necessitating amputation above the knee.

The inflammation in these cases is almost always cortical, and the chief symptoms are initial delirium, then stupor and coma, sometimes rigidity of the muscles.*

* The literature of meningitis in pneumonia is scanty. From Vulpian's clinic a good thesis was written by Surugue (1875). In the St. Thomas' Hospital Reports, 1878, some cases are given by Greenfield, and there are valuable references in that storehouse of clinical material, Traube's Gesammelte Abhandlungen.

Croupous Colitis.—In *Cases III, XXVIII, XLII, LXXXV* and *XCIX* this unusual complication was met with. In *Case III* the cœcum was covered with a thin layer of adherent lymph, and scattered throughout the colon and sigmoid flexure there were numerous elevated patches of lymph, about the size and shape of rupia-crusts, which on section were found firmly attached to the mucosa. In this instance, the process was very extensive and the patches much thicker than in any subsequent case. More often there is a thin, flaky exudation, involving only the surface of the mucous membrane. In none of the cases was there ulceration.

Croupous Gastritis.—In *Case IV*, the stomach and duodenum were found "greatly distended with gas. The mucosa was pale, except about the fundus, where, just to the left of the cardia, there was an extensive area of croupous inflammation, represented by a thick, adherent greyish-white exudate, covering an area 12 by 8 cm. Beneath the mucosa the membrane was deeply injected."

This paper is meant to be merely a statement of facts, a record of observations, upon a common and well-known disease; but as opinion is still divided as to the general or local nature of pneumonia, it is interesting to note how strongly the evidence from morbid anatomy tends towards the former view. The frequency of the occurrence of various consecutive inflammations finds a parallel only in some of the specific fevers.

While this paper has but a trifling value as a pathological contribution, to the writer, as doubtless to the students who performed the autopsies under his direction, the careful study and observation of the cases upon which it has been based has been of the greatest service. In the investigation of disease a knowledge of the morbid phenomena observed during life and of the organic alterations found after death are inseparable. The teaching of the post-mortem room must supplement and illustrate the lessons of the ward, and, as Bichat says, it is neither from the one nor the other, but from both, that "la veritable pathologie" can be gained.

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NOTES ON THE MORBID ANATOMY OF TYPHOID FEVER.*

By WILLIAM OSLER, M.D.,
Fellow of the Royal College of Physicians, London; Professor of Clinical Medicine at the University of Pennsylvania; formerly Professor in McGill University, and Pathologist to the General Hospital, Montreal.

Historical note.—The careful study of the morbid anatomy of continued fevers led to the recognition of typhoid or enteric fever as a specific disease. The younger men among us can scarcely realize that the generation has not yet passed away by whose labors the profession finally reached a clear and positive knowledge of the differences between typhus and typhoid fevers. The dates 1813 and 1850 include the modern discussion of the subject. Long before 1813, however, many observers had noted the clinical differences between the diseases, so well laid down by Huxham in his essay on Fevers (2nd ed. 1750); and Baillie had figured and others had described the intestinal lesions of fever, but in that year Pierre Bretonneau of Tours distinguished "dothinenterite" as a separate disease, and Petit and Serres described entero-mesenteric fever. Trousseau and Velpeau were students of Bretonneau, and in 1820, when they went to Paris, were instrumental in making known his views to Andral and others. In 1829, Louis' great work appeared, in which the clinical and anatomical features of the disease were presented in a manner not previously attempted. The constancy of enteric lesions was demonstrated, and the name *typhoid* given to the disease. At this period, in Paris, typhoid fever alone prevailed, and it was universally believed to be identical with

* Part of third Pathological Report from the Montreal General Hospital.

the continued fever of Great Britain, where, in reality, both typhus and typhoid existed together, and the intestinal lesions were regarded as accidental occurrences in the course of ordinary typhus. Meanwhile Louis' students, returning to their homes in different countries, had opportunities of studying the prevalent fevers in the thorough and systematic manner of their master. Among these were certain young American physicians, to one of whom, Gerhard of Philadelphia,* is due the great honor of having been the first to clearly establish the difference between the two diseases. His papers, published in 1837 (*Amer. Jour. Med. Sciences*), are undoubtedly the first in any language to give a full and satisfactory account of the clinical, pathological and anatomical distinctions such as we now recognize. No student should fail to read these articles—among the most classical in American medical literature. Louis' influence was early felt in Boston, to which, in 1833, James Jackson, Jr., had returned, and in the same year demonstrated in his father's wards at the Massachusetts General Hospital the identity of the common typhus of the country with the typhoid of Louis. He had already in 1830 noticed the intestinal lesions in New England typhus. Though cut off at the very outset of his career, we may reasonably attribute to the inspiration of the younger Jackson the two elaborate memoirs on typhoid fever which, in 1838 and 1839, were issued from the Massachusetts General Hospital by James Jackson, Sr., and Enoch Hale. These, with Gerhard's articles, contributed to make typhoid—as distinct from typhus—widely known to the profession in America long before the distinctions were recognized in England. The recognition in Paris of a fever distinct from typhoid, and without intestinal lesions, was due largely to the influence of the able papers of G. C. Shattuck of Boston and Alfred Stillé of Philadelphia, which were read before the Société Med. d'Observation in 1838. At Louis' request Shattuck went to the London Fever Hospital to study the English disease, and quickly saw that there were two distinct affections, and brought back a report which must have been very convincing

* Pennock was associated with Gerhard in his studies upon Typhus.

to the members of the Society. Stillé had the advantage of going to Paris knowing thoroughly the clinical features of typhus, for he had been Gerhard's house-physician at the Philadelphia Hospital, and had studied the disease under him in the epidemic of 1836. At La Pitié with Louis he saw quite a different affection, while in London, Edinburgh, Dublin and Naples he recognised his old Philadelphia foe. The results of his observations were given in an exhaustive paper, which presented in tabular form the contrasts and distinctions, clinical and anatomical, between typhus and typhoid fevers.

British physicians were curiously slow in recognizing the affections as distinct, and persisted in regarding the enteric lesions as only occasional concomitants of typhus. There were, however, notable exceptions. My preceptor, Bovell, always maintained that Bright, whose pupil he was, knew and taught the differences. True, we are indebted to the distinguished Guy's physician for the most admirable description and delineations of the morbid anatomy of the intestinal lesions in his Reports of Medical Cases, Vol. I., 1827, and in the first article of the first volume of Guy's Hospital Reports he pleaded, from the facts of morbid anatomy, for a more rational method in the treatment of fever, and denounced the administration of irritating purgatives as tending to keep up the intestinal disorder; but I cannot find that he had a clear and distinct idea of two forms of fever—one with, the other without enteric lesions. Bright, however, strongly impressed upon his pupils and the profession the evil consequences of the purgative plan of treatment in fever—a plan by which, as Stokes asserted, British practitioners had killed thousands.* In Great Britain, the non-identity of typhus and typhoid was first clearly established at Glasgow, where, from 1836-38, Dr. A. P. Stewart

* The treatment of Fever forms an interesting and instructive chapter in the history of therapeutics, and illustrates the necessity of correct pathological views in the management of a disease. Nathan Smith, who in 1824 described the typhous fever of New England, was one of the first to advocate the rational or expectant treatment of the disease. With trifling exceptions, his method corresponds to "the most approved treatment of enteric fever of the present day" (1884), as given by Mahomed in the "Year Book of Treatment."

studied the continued fever. The results of his observations were published in 1840, and his memoir has been reprinted (1884) by the New Sydenham Society. In the decade which followed many important works were issued and the more correct views gradually gained acceptance, but it was not until the publication of Jenner's observations, 1849-50-51, that the question was finally settled in England. The Irish physicians, to whom we owe so much on the pathology and treatment of fever, were among the last to abandon the old views, and even as late as 1861 the identity of the diseases was maintained among them.

The extraordinary difficulty of establishing on an incontrovertible basis any great truth in medicine, is nowhere better illustrated than in the history of the subject which I have outlined in this imperfect and sketchy manner. Too often a truth has to grow to acknowledgment with the generation which announced it. After the intellectual climacteric—*la crise de quarante ans*—we assimilate new truths slowly,* and some by training become incapable of their reception. This was the case with many an ardent student of Fever, whose education had unfitted him to see a truth which the untrammelled mind readily grasped. Dwelling now in the clearer light and with fuller knowledge and looking back over the half century of doubt, dispute and discussion upon the question we have just considered, what lesson may we learn? Surely to see in it a picture of our own times—a picture the counterpart of which we can find any day in our current journals. The mists of doubt hang over many problems, disputes rage with the old intensity, discussion waxes hot, but by the light of history we can read with faith and trust the larger hope—in no faint manner—that a similar happy solution awaits many of the questions in pathology which to-day vex the mind of the profession.

Of the workers who were actively engaged in defining the distinctions between typhus and typhoid fevers three only, so far as I know, remain with us—Shattuck of Boston, Stillé of Philadelphia and Jenner of London. They, with their fellow-

* True to-day as in the time of Harvey.

laborers who have passed before, have a claim on the gratitude of the profession which time can not efface but will rather deepen.

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From 60 to 80 cases of typhoid fever are admitted yearly to the wards of the General Hospital; of late the number has, on several occasions, exceeded 100 annually. For the ten years ending May 1st, 1879, 660 cases were admitted, and the death rate was a little over 10 per cent. I have notes of 53 autopsies, which are arranged in tabular form at the end of the article.

Thirty-six of the cases were in males and 17 in females. As Dr. James Bell's statistical report shows,* very many more men are admitted to the hospital with fever, and the death-rate among them is slightly lower than in the women. Of 45 cases in which the age was given, 26 occurred in persons under 25 years of age.

In 16 cases there were no special complications.
" 11 " there was perforation with peritonitis.
" 9 " there had been hæmorrhage from the bowels.
" 6 " there were diphtheritic affections of mucous membranes.
" 2 " there was thrombosis of veins.
" 3 " pyæmia.
" 9 " affections of the respiratory organs.

Anatomical Lesions.—We shall speak first of the condition of the *alimentary canal*, in which the specific morbid changes chiefly occur.

No ulcers were met with in *pharynx* (or *larynx*). These parts were not examined in more than half the cases. In Germany ulcers in these regions seem to be much more common; the only cases I have ever seen were in the Berlin and Vienna post-mortem rooms. Murchison refers to them as rare in England. Necrosis of the laryngeal cartilages may occur. I have four or five large pieces of the alæ of the thyroid which were coughed up by a convalescent from typhoid,

* Montreal General Hospital Reports, Vol. I., 1880.

and I have recently had a patient with acute periehronditis which fortunately terminated in resolution.

There were no special alterations noted in *œsophagus* or *stomach*. The lesions of the *intestines* were all distinctive. The affection of Peyer's glands may be considered under the four stages recognized by all writers:

1st Stage. *Swelling and Hyperplasia.*—No matter at which period of the disease a patient dies, some of the patches will be found in this condition. It is rare, however, for death to take place before necrosis or sloughing has occurred. In *Case XVII.*, a girl, aged 24, died about the end of the first week with severe nervous symptoms. The patches of Peyer were much swollen, pitted and cribriform, but no sloughing had taken place. *Case XXXII.*, a man aged 63; there was great hyperplasia of the glands, particularly of the isolated follicles, but neither necrosis nor ulceration. The usual condition met with is sloughing or ulceration of the lower patches and swelling of the upper ones. In the early involvement one can frequently see with the unaided eye, or, better, with the assistance of a lens, the enlarged hemispherical follicles in a patch. The increase in size is due to a hyperplasia of the lymph elements, a process which also extends to the adenoid reticulation of the patches and the contiguous mucosa. The swollen condition of the lower part of the ileum is largely due to the great increase, intertubular and sub-mucus, of the lymph elements. The affected patches usually appear with great distinctness, projecting from the mucosa for a distance of a line or two, and present a greyish-white appearance. They can be seen from the peritoneal surface, and the portions of the bowel in which they occur can be felt to be thicker and firmer than contiguous parts. The solitary follicles are not always affected; usually they are more or less swollen, and in rare cases they have been alone involved. They range in size from a pin's head to a large pea, and may be very deeply imbedded in the sub-mucosa. In the cæcum, appendix and colon the solitary glands may be greatly swollen. In *Case XXXII.* the solitary follicles of the ileum were very prominent, many of them almost pedunculated, which gave a very remarkable appearance to the bowel. There is generally

hyperæmia of the mucous membrane, particularly about the patches, the situation of which may be plainly marked from the serous surface by deep congestion or ecchymosis. The swollen follicles undergo one of two changes—resolution or necrosis. In a majority of the patches the former process goes on. Even in the most severe cases, when six or seven feet of the bowel are involved, necrosis and ulceration do not often attack the uppermost ones; while in mild, abortive cases the swelling probably subsides without proceeding in any patches so far as sloughing and ulceration. On the other hand, a fatal result may occur while the glands are still in this stage, due to the intensity of the fever or the action of the poison on the nervous system. In connection with resolution, a curious condition of the patches is produced whereby the surface assumes a reticulated or cribriform appearance. These *plaques à surface réticulée*, which were first accurately described by Chomel, are very common, and may be produced in two ways. Either the swollen follicles of a patch undergo resolution and shrink more rapidly than the surrounding framework, or, what is more usual, I think, the follicles alone, owing to the intense hyperplasia, become necrotic and disintegrate, leaving little pits to mark their places. Small, superficial hæmorrhages may result from the rupture of vessels in this process. I have several times seen small ulcers which seemed to have originated from the fusion of several of these little pits.

Some have thought that the pigmentation which is found about the glands in the patches of Peyer indicated past swelling or disease of these parts, but it is so common that in persons over 25 or 30 years of age we may consider it almost normal. It is represented in Peyer's original figure.* It is important to remember that this condition of hyperplasia of the lymph elements is not peculiar to typhoid fever. In children it is exceedingly common, particularly when death has occurred from intestinal affections. I have seen it, too, in measles, diphtheria and scarlatina. E. Hale† gives a good account of it as met with in

* De glandulis intestinorum 1637.

† Typhoid Fever, Boston, 1839.

children, and Bruns* discusses the various conditions under which it has been found. While there is nothing specific and distinctive about the swelling of Peyer's patches in typhoid, yet in adults we rarely meet with affection of these glands, associated with fever, in any other condition. Cases of typhoid occur in which death takes place rapidly before any distinctive symptoms are manifested, and inspection of the small bowel alone reveals the true nature of the disease. Such a case I saw not long since with Dr. Sinkler. A lady came to town, a distance of several hundred miles, to see a specialist about her eyes, arriving on Thursday morning feeling apparently well. On Friday and Saturday she was seriously ill, high fever, temperature reached 105°, diarrhœa and semi-coma. Death took place on Sunday, less than sixty hours from the first visit of the attending physician. The nature of the case was demonstrated by Dr. Longstreth, who made the autopsy, and found swelling with commencing ulceration of Peyer's patches. No doubt before she left her home she must have had slight fever, and we had been dealing with a case of ambulatory typhoid, with sudden accession of fever and head symptoms.

2ND STAGE. *Necrosis and Sloughing.*—When the hyperplasia of the lymph cells reaches a certain grade resolution can no longer take place, the vessels become choked, a state of anæmic necrosis is induced, and a slough forms, which must be separated and thrown off. The process may be quite superficial, affecting only the mucous tissue of the patch or even only a part of it, but usually it extends to and involves the submucosa. In *Case XXVI*, there were many thin sloughs adhering to the patches, in which the follicles and pitted appearance could be distinctly seen. It is always more intense towards the valve, and in severe cases the greater part of the mucous membrane of the last foot of the ileum may be represented by a dirty brownish-black eschar. The solitary glands may also be capped with small sloughs. They have a yellow-brown color from the bile pigments. The depth to which the necrosis extends depends

* Vol. X Transactions of Pathological Society of Philadelphia.

on the intensity of the lymphoid infiltration; it may be deep in the muscular coat, or even reach the serosa.

3RD STAGE. *Ulceration.*—The separation of the sloughs is gradually effected from the edges inwards, and is associated with great and unavoidable dangers, of which the opening of blood-vessels and perforation of the coats of the bowel are the most serious. The size of the ulcer is directly proportionate to the depth and extent of the necrosis. When superficial, the entire thickness of mucosa may not be affected, and small, shallow losses of substance may frequently be seen in swollen patches. It is more common for the slough in separating to expose the submucosa and muscularis, particularly the latter, which forms the floor of a large majority of all typhoid ulcers. It is not common for an entire patch to slough out, and the perfectly ovoid ulcer opposite the mesenteric attachment is rare. Irregularly oval or rounded forms are the rule. A large patch may present three or four ulcers, divided by septa of mucous membrane. Very often the terminal six or eight inches of the ileum is one large ulcer, with islets of mucosa left here and there. The smaller circular ulcers have often a punched-out appearance, and may be funnel-shaped, the central deeper part of the slough having reached through the transverse fibres or even to the serosa. The edges are usually swollen, soft, sometimes congested, but in cases in which death has taken place late in the disease, they are thin and pale, and not always undermined. At this period the ulcers near the valve may have very irregular sinuous borders. Sometimes on a patch we may see an ulcer which has encroached upon the neighboring mucous membrane as if the ulceration had extended after the separation of the slough. The base of a typhoid ulcer is smooth and clean, usually formed of the circular layer of muscle fibres, occasionally of the peritoneum alone.

4TH STAGE. *Healing.*—When death occurs late in the disease from exhaustion or perforation, we may have an opportunity of studying the process of repair in the ulcers. Thus, in *Case XXIX*, death in the seventh week from septicæmia, all the ulcers in ileum were cicatrizing and one or two had completely

closed. The process begins with the development of thin granulation tissue, which covers the base and gives to it a soft, shining appearance. From the edges, the mucosa gradually extends over this on all sides with a new growth of epitheleum. The site of a healed ulcer is a little depressed, and is marked by pigmentation. Occasionally one sees an appearance as if an ulcer had healed in one part and was extending in another, but this is unusual. In some instances of relapse, with ulcers healing in places there are fresh ulcers higher up in the bowel and patches in a state of hyperplasia. Theoretically, we may assume the healing to begin so soon as the sloughs have separated; indeed, when resolution is impossible, the removal of the necrosed parts is itself the first step in the process of repair, but practically we do not often in fatal cases meet with evidences of cicatrization. The majority of deaths occur before this stage is reached.

Large Bowel.—The cæcum and colon are frequently affected, but not to a severe degree. In nearly a third of the cases there were ulcers in the cæcum, and the solitary glands in this part and in the ascending colon were greatly swollen. In *Case XXIII.* the glands in the ileum were very small, while in the larger bowel they were very prominent. In one instance there was an ulcer in the appendix. In 1877 I dissected a case at the hospital, in which the patient died three or four months after an attack of typhoid fever. The appendix was perforated and surrounded by a localized abscess, and there was inflammation and suppuration of the mesenteric and portal veins with empyema.

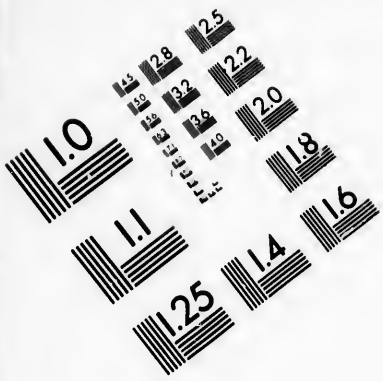
Many cases of perforation of cæcum and of appendix in typhoid fever are on record.

Perforation.—In eleven instances death was caused by perforation and peritonitis. Of the ten cases in which it was noted, the orifice was found in seven within 8 inches of the valve. In only one was it distant 18 inches. In *Case XL.* there were two perforations—one at a distance of 7 inches, the other 2½ inches from the valve. In five cases the perforation was in

ulcers from which the sloughs had separated, but in three of these it appeared, from the condition of the other patches, that the perforation was directly due to the extension of the necrosis through all the coats. In only two the perforation at the bottom of clean, thin-walled ulcers. In *Case I* the fatal result could be directly traced to an indiscretion in diet nearly two weeks after the temperature had been normal. In six instances the sloughs were still partially adherent about the site of perforation. A majority of the cases were in small, deep ulcers. Peritonitis was present in every case; in two it was localized in the lower abdominal and pelvic regions. In several instances the base of ulcers was formed, wholly or in part, of thin, greyish peritoneal tissue, evidently necrotic, and great care had to be exercised to prevent tearing in removal of the bowel. I have once or twice seen the serous coating covered with thin flakes of lymph in the vicinity of such patches.

Hæmorrhage occurred in nine cases, and contributed directly or indirectly to the fatal result. In two, perforation also occurred. In five there was blood more or less altered in the cæcum and colon; in one case in the ileum itself. In most of the cases the bleeding seemed to result directly from the separation of the sloughs, but in no instance was the bleeding vessel found, not even in *Case XXXVIII.*, in which only one patch had sloughed, and the clot was still adherent. The soft, swollen edges of the patches may have been the seat of bleeding in one or two instances.

Mesenteric glands —Except in two or three cases in which death took place late in the disease, the group corresponding to the ileum was invariably involved—swollen, sometimes congested, more often in a state of intense hyperplasia. I have seen softening and suppuration in several cases; the softening is apparently due to an anæmic necrosis similar to that which affects the lymph elements of the bowel. The glands may be very deeply congested, and I have found in such specimens many cells containing red-blood corpuscles. As has long been known, there are, in addition to the ordinary lymph cells, many larger cells with two or three nuclei.



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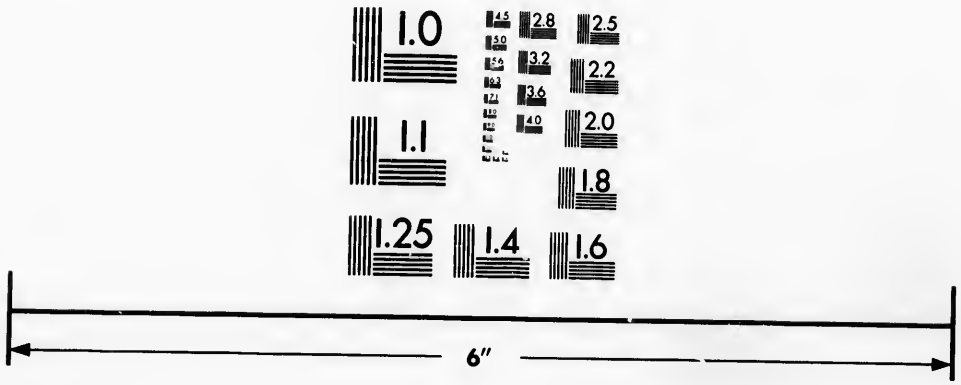

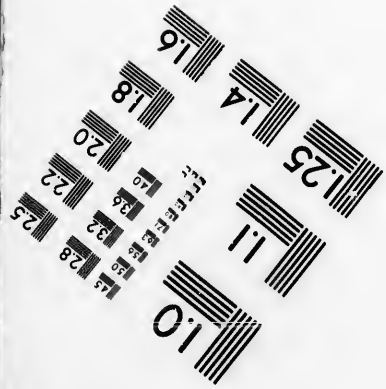

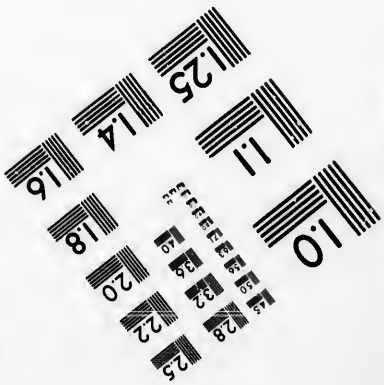

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Spleen.—Moderate enlargement of this organ constantly takes place in typhoid. It is rare—in my experience—to be able to palpate the anterior edge under the left costal cartilages. Of 35 instances in which the weight was accurately noted, in only one case did the organ weigh over 20 ozs.; in three about 19 ozs. In four cases the weight was below the average.

Complications—*Pulmonary.*—The hypostatic congestion is almost always met with when death occurs slowly. In 6 instances there was actual pneumonia, in 2 simple pleurisy, and in 1 empyema.

Pyæmia.—In *Case XXVIII* there were suppurating infarcts in the lungs, and in *Case XXXIII* infarcts in spleen and kidneys. In neither case could any disease other than the intestinal be discovered.

Thrombosis.—In *Case IX*, the right circumflex iliac veins were distended and filled with firm thrombi. The superficial veins on the right side of the abdomen were enlarged and prominent. In *Case XXIX*, in the 6th week, a thrombus formed in the left femoral and iliac veins, and in the former proceeded to suppuration, with intense phlebitis and involvement of the inguinal glands.

Diphtheritic affections.—Secondary membranous inflammation of the mucous surfaces is rare in typhoid fever. Louis mentions three cases in which diphtheria arose as a complication, and Murchison states that he has had several examples.

Six of the cases I have dissected presented more or less extensive inflammation of a croupous or diphtheritic character.

Case I (No. 12), female, aged 23. No special clinical features. Mucous membrane of pelvis of left kidney covered with a firm, greyish-white membrane, which could be stripped off in the form of a mould of the parts; deep congestion of subjacent tissues.

Case II, woman aged 35, admitted Nov. 25th. Had been ill for about two weeks. The case was tolerably severe, and lasted over eight weeks. Temperature-range during the first fortnight in Hospital was 103° to 104.5°. On December 31st it became

normal. There was a good deal of nervous depression throughout. She had retention of urine, and was catheterized on several occasions, the first time on Dec. 4th. On the 14th there was a bloody discharge from the vagina; on the 23rd, bloody urine, and from this time shreddy matter was passed from the bladder. There was great pain on the passage of the catheter. Urine not diminished in amount. Death on Jan. 3rd. Temperature normal for four days before the end. At the autopsy, healing ulcers were found in ileum. Spleen 95 grammes. The condition of the genito-urinary organs was as follows: *Kidneys* not enlarged, substance pale. On section, the pelvis and calyces were covered with a thick greyish-yellow exudation, in the left organ involving the entire membrane, in the right only the upper third. The surface of the exudation was rough, and on section it was seen to extend deeply, in some places 3 m. in thickness. It could not be lifted off the mucosa, but infiltrated it. The papillæ in two of the calyces were also covered. The ureters were not affected. *Bladder* contained a quantity of greyish, shreddy material and a membranous cast of the upper part of the organ, which had separated. It was about 2 m. in thickness, and was beginning to disintegrate. The parts about the neck were covered with a thick greyish exudation, which was with difficulty detached. In the central zone, there were many isolated patches projecting 2–4 m. The wall was of a dirty greenish colour, and was, in the greater part of its extent, denuded of mucous membrane. The orifice of the urethra was free, but the tissue about it was hæmorrhagic. *Vagina*—Mucosa in the lateral walls covered with a greyish membrane, which, in the right side extended, to the os, covering part of its margin. Towards the vulva the membrane surrounded the entire canal. It could be stripped off in flakes. The uterus was normal; no exudation in its cavity.

Case III (No. 36), male (young), admitted Feb. 22nd, with well-marked typhoid fever. All symptoms mild, except the diarrhœa, which was difficult to control. Pain and tympanites were troublesome. He was doing well, temperature had not once reached 103°, when on March 4th he complained of soreness in the caruncles beneath the tongue, and there was swelling

beneath the chin at a corresponding point. The sore part was touched with nitrate of silver. On the morning of the 5th the swelling under the jaw had become more diffuse. Up to this time no increase in temperature, which was 101°, and the general symptoms did not indicate any serious change. In the evening the neck had become greatly swollen, and there was exudation on the pharynx. Temperature 102½°. Voice husky. Swallowing impossible. Pulse weak. He passed a bad night, and on the 6th died asphyxiated at 2 p.m rather unexpectedly, as at 1 p.m. the laryngeal symptoms were not very marked. Temperature at 11.30, 105°. The autopsy showed many ulcers and sloughs in lower part of ileum. There was great infiltration of all the tissues of lateral and anterior regions of the neck. Two small losses of substance on either side of frænum linguæ; œdema of pillars of fauces and uvula. Posterior part of soft palate was covered with a greyish membrane, which extended into the nares for a short distance. Posterior wall of pharynx covered with a similar membrane. Membrane on upper surface of epiglottis. Œdema and swelling of laryngeal folds; no exudation.

Case IV (No. 50), male, aged 39. Ordinary course, until perforation. No special symptoms. Pelvis of right kidney inflamed and covered with a thin sheeting of firm exudation.

Case V (No. 51), female, aged 43. Course of moderate intensity, and then severe laryngeal and bronchial symptoms. Many large ulcers in ileum. Excensive diphtheritic laryngitis, and a uniform membrane extended down the trachea and into the tubes of medium size.

Case VI (No. 52), female, aged 18. Death from the fever and exhaustion. Many intestinal ulcers. The vagina presented several patches of firm membranous exudation, beneath which the tissue was deeply congested.

Cases II, III and V may be regarded as instances of true diphtheria occurring in typhoid fever; the other cases as examples of local membranous inflammation, such as we meet with from time to time in the specific fevers.

Cases of Typhoid Fever examined post-mortem at the Montreal General Hospital, May 1876 to May 1884.

No.	Sex.	Age.	Cause of Fatal Result	Ulceration of Small Intestine.	Ulceration of Large Intestine.	Spleen.	Other Morbid Changes.

Cases of Typhoid Fever examined post-mortem at the Montreal General Hospital, May 1876 to May 1884.

No.	Sex.	Age.	Cause of Fatal Result	Ulceration of Small Intestine.	Ulceration of Large Intestine.	Spleen.	Other Morbid Changes.
1	M	18	Perforation..	8 round ulcers in process of healing..	0	19 ozs.	Peritonitis localized in lower part part of abdomen.
2	M	17	F*	Much swelling; few ulcers....	0	11 ozs. ...	——
3	M	23	Pneumonia..	14 patches ulcerated.....	0	10 ozs.	Great swelling of kidneys.
4	M	40	Perforation .	7 deep ulcers in ileum.....	0	7 ozs.	Lymph only on coils in the pelvis.
5	M	25	F	4 small ulcers, sloughs detached	0	15 ozs.....	Peculiar brown color of upper Peyer's patches.
6	M	40	F	Glands swollen, no sloughs, one small ulcer.....	0	15 ozs.	Solitary glands much enlarged.
7	M	29	Perforation .	Sloughs adherent and detaching	0	395 grms.....	Hæmorrhage beneath left pleura and into lung substance.
8	F	18	F	Great swelling of glands, lower ones ulcerated.....	0	.....	Old peritonitis; tubercles in lungs.
9	M	27	F	Patches very large, ulceration beginning in lower ones...	0	Much enlarged.	Enlargement of veins on right side of abdomen. Thrombi in circumflex iliac veins.
10	F	20	Pneumonia..	All patches much swollen; six ulcers in lower ones....	0	215 grms.....	——
11	M	25	F	Ulcers healing in places; some patches much swollen.....	A few ulcers.....	315 grms.....	Cutaneous and sub-serous ecchymoses.

* F stands for fever and exhaustion.

Cases of Typhoid Fever examined post mortem at the Montreal General Hospital May 1876 to May 1884.

No.	Sex.	Age.	Cause of Fatal Result	Ulceration of Small Intestine.	Ulceration of Large Intestine.	Spleen.	Other Morbid Changes.
12	F	23	F	Only in lower 18 inches; two ulcers, many sloughs.....	One in cæcum ...	320 grms.....	Diphtheritic pyelitis in left kidney.
13	M	....	F	Lower 3 feet; ulcers deep, in places to the peritoneum ..	0	360 grms.....	——
14	M	30	Perforation .	Many sloughs and ulcers.....	0	Enlarged.....	——
15	M	22	Hæmorrhage.	3 feet; great infiltration and swelling, sloughs detaching, adherent clot on one ulcer.	0	360 grms.....	Much blood in colon.
16	M	30	F	5 feet; patches swollen, 3 ulcers in lower 8 inches.....	0	560 grs.	Great swelling of mesenteric glands.
17	F	24	F	All lymph elements swollen; patches cribriform	0	200 grms.....	Mesenteric glands scarcely swollen.
18	M	17	Perforation .	1 foot only; patches 1½ feet from valve normal; sloughs separating, one on the valve ...	0	153 grms.....	Heart muscle very pale.
19	F	24	Perforation ..	Only last foot and a half; sloughs detaching	0	270 grms.....	Deep congestion of lungs.
20	M	16	Hæmorrhage.	Extensive ulceration near valve, upper glands swollen.... .	Ulcers in cæcum..	450 grms.....	Much blood in colon.
21	F	17	Pneumonia ..	18 inches, sloughs detached ...	20 ulcers in cæcum.....	195 grms	——
22	F	25	Hæmorrhage.	2 feet; ulcers deep, sloughs separated; vessel not found.	0	220 grms.....	Great enlargement of mesenteric

				sloughs detaching	O	270 grms.....	Deep congestion of lungs.
20	M	16	Hæmorrhage.	Extensive ulceration near valve, upper glands swollen.... .	Ulcers in cæcum..	450 grms.....	Much blood in colon.

21	F	17	Pneumonia ..	18 inches, sloughs detached ...	20 ulcers in cæcum.....	195 grms	——
22	F	25	Hæmorrhage.	2 feet; ulcers deep, sloughs separated: vessel not found.	O	220 grms.....	Great enlargement of mesenteric glands.
23	M	30	F	2 feet; sloughs detaching.....	One ulcer, 20 x 20 millimetres..	380 grms.....	Extravasation of blood about abdominal aorta.
24	F	25	F	3 feet, great enlargement of patches, sloughs forming...	O	400 grms.....	Solitary glands remarkably prominent.
25	F	35	Diphtheria ..	Ulcers healing.....	O	95 grms.....	Diphtheritic vaginitis, cystitis and pyelitis.
26	F	20	Pneumonia ..	Several feet; many sloughs; only one detached; ulcer extends to serosa	O	260 grms.....	Heart large and dilated.
27	M	33	F	2½ feet; many ulcers, some extend to peritoneum, a few healing.....	O	227 grms.....	Deep congestion of lungs.
28	M	....	Pyæmia.....	8 ulcers in ileum; one with slough in appendix	15 small ulcers in cæcum, many in colon	610 grms.....	Pyæmic infarcts in lungs.
29	M	26	Septicæmia..	3 feet, many ulcers, some have cicatrized	Many small ulcers in cæcum and colon.....	180 grms.....	Suppurating thrombus in left femoral vein.
30	F	34	Perforation .	Sloughs adherent, ulceration beginning	O	Very large	Peritonitis very extensive.
31	M	13	Empyema ...	Patches swollen and congested, no ulceration	O	Large.....	Pleurisy. Hæmoptysis seven days before death; no lung disease.

Cases of Typhoid Fever examined post-mortem at the Montreal General Hospital, May 1876 to May 1884.

No.	Sex.		Cause of Fatal Result	Ulceration of Small Intestine.	Ulceration of Large Intestine.	Spleen.	Other Morbid Changes.
32	M	63	F	Patches enlarged, cribriform, peritoneum hyperæmic, extraordinary enlargement of solitary glands	O	Not enlarged ..	Mesenteric glands enlarged.
33	M	....	Pyæmia	2 feet; many ulcers	Many ulcers in cæcum	Large suppurating infarct	Pyæmic blocks in kidneys; abscess in abdominal wall.
34	M	25	F	2 feet, two large patches; great swelling, no ulceration	Solitary glands much swollen	533 grms.....	Tuberculous cavities in lungs.
35	F	21	Perforation .	3 feet, many ulcers.....	O	Very large	Heart pale.
36	M	....	Diphtheria ..	3 feet; sloughs and ulcers, some extend to peritoneum, one at orifice of Meckel's diverticulum ilei	Follicles much swollen	633 grms.....	Diphtheria of fauces.
37	M	36	Hæmorrhage	2 feet, deep ulcers, sloughs detached.....	Few in cæcum...	320 grms.....	Hypostatic pneumonia.
38	M	28	Hæmorrhage	2½ feet, patches swollen; one slough separating.....	Glands enlarged	350 grms.....	Ileum and colon filled with blood; hæmorrhagic œdema of arachnoid.
39	M	....	F	18 inches, little swelling; one small ulcer.....	O	Slightly enlarged...	Congestion of lungs.
40	F	24	Perforation .	2 feet; nine sloughs adherent; two perforations	O	240 grms.....	Hæmorrhage also; peritonitis chiefly in pelvis.
41	F	17	F	4 feet, sloughs on lower patches, one patch 5 inches in length	O		

39	M	....	F	18 inches, little swelling; one small ulcer.....	O	Slightly enlarged...	Congestion of lungs.	
40	F	24	Perforation .	2 feet; nine sloughs adherent; two perforations	O	240 grms.....	Hæmorrhage also; peritonitis chiefly in pelvis.	
41	F	17	F	4 feet, sloughs on lower patches, one patch 5 inches in length.	O	11 ozs	Great enlargement of mesenteric glands.	
42	M	....	F	18 inches, few ulcers.....	Ulcers in cæcum.	5 ozs.....	——	
43	F	19	Hæmorrhage	3 feet, sloughs adherent; one deep ulcer with adherent clot	O	Enlarged	——	
44	M	29	F	4 feet; sloughs adherent.....	O	20 ozs.....	Temperature over 109°.	
45	M	19	Perforation .	1 foot; patches above this normal. Small deep ulcers near valve	O	153 grms.....	Hæmorrhage as well. Death on 50th day.	
46	M	27	F	2 feet; sloughs separating	6 or 8 sloughs...	380 grms	Petechiæ in skin. Extravasation along aorta.	
47	M	16	Hæmorrhage	3 feet: great enlargement of patches and solitary glands, sloughs deep and separating.	O	Enlarged.....	——	
48	M	36	Pneumonia .	Ulcers close to valve; above, sloughs adherent	O	Slightly enlarged ..	——	
49	M	....	F	3 feet; many sloughs; ragged ulcers near valve.....	Small ulcers in cæcum.....		——	
50	M	39	Perforation .	12 inches; deep ulcers.....	Follicles swollen.	300 grms.....	Pyelitis of left kidney.	

Cases of Typhoid Fever examined post-mortem at the Montreal General Hospital, May 1876 to May 1884.

No.	Sex.	Age.	Cause of Fatal Result	Ulceration of Small Intestine.	Ulceration of Large Intestine.	Spleen.	Other Morbid Changes.
51	F	43	Diphtheria ..	4 feet; many large ulcers	0	355 grms.....	Pleuritic effusion in left side. Extensive diphtheritic laryngitis, with extension of membrane into bronchi.
52	F	18	F	5 feet; patches swollen; ulcers near valve	0	.....	——
53	M	....	F	15 patches, covered with sloughs; one large ulcer ..	0	Very large	——

CONTENTS.

EXTRACTS FROM PATHOLOGICAL SOCIETY OF PHILADELPHIA, VOLUMES XII. AND XIII.

Sarcoma of the left frontal lobe.

Unknown man, admitted December 8th. He was unconscious and thought to be drunk, and was placed in the ward for inebriates. He had slight fever, but no local disease could be detected. Death took place on the third day.

Brain: Slight turbidity of vessels at base. Under surface of frontal lobes looked smooth and full, particularly noticeable near chiasm. Immediately above the left olfactory bulb the pia was swollen and congested. The brain substance beneath it for an area equal in size to a quarter dollar, was ecchymosed. Vessels of circle of Willis normal. On separating the longitudinal sinus the membranes were infiltrated and œdematous; no extravasation. The arteries, large and small, at the base were unusually distended with blood. On the surface of the brain the veins were very full. The small vessels over the convolutions were very prominent. The left frontal lobe was swollen. In the frontal section by Pitres' method, there was exposed a tumor the size of a walnut, occupying the anterior extremity of the frontal lobe, extending close to the apex; at its lower part it was cystic and contained a yellowish fluid. The second section, cut at a distance of two and a half inches from the fissure of Rolando, exposed an infiltrated yellow tissue; the white matter in the neighborhood was much swollen and œdematous. The third section, immediately through the base of the frontal convolutions, exposed a normal white matter. This section cut through the anterior extremity of the corpus striatum. Section through ascending frontal convolution showed no change. Section of the optic nerve near the eye showed the sheaths swollen; no neuritis. Examination showed the tumor to be a gliosarcoma, with cells of larger size than usual *January* 27, 1887.

Embolism of left anterior cerebral artery; softening of left frontal lobe.

Thomas K. was admitted to hospital with fractured thigh and other injuries, the result of an accident. Death took place about ten days after admission with symptoms of coma.

Brain: The left frontal lobe tore on removal, and a soft puriform fluid exuded. This lobe looked flatter and was softer than the other. At the base vessels looked natural, a few thin plates of atheroma. On tracing anterior cerebrals, the left vessel, three-quarters of an inch beyond anterior communicating artery, was swollen, became tortuous, and was closely united to the inner face of the first frontal convolution. At this point the vessel walls were thin, looked infiltrated, and of a grayish color. At the region of softening on the walls of the artery the two anterior cerebrals were adherent together. The vessel was plugged for the length of three-quarters of an inch, firm except at the spot above referred to, where the walls were quite soft. The first frontal convolution, as far as its base, was softened. On section, there was a distinct puriform softening at the apex of the left lobe. In the white matter this extended back to the anterior horn, gradually becoming less. Superficially it involved the anterior part of the third, the gray matter of the anterior portions of the first and second convolutions not much involved. Small foci of softening in the inner section of the left lenticular nucleus just above anterior perforated space. No further change noticed in brain.

There were no thrombi in the femoral veins. Heart normal. There was suppuration at the seat of the fracture. *June* 9, 1887.

Hemorrhagic pancreatitis, with swelling of the semilunar ganglia and Pacinian corpuscles.

The specimens were removed from the body of a man, æt. 58 years, whose lungs were emphysematous to a remarkable degree, and whose body presented slight œdema, accompanying the heart trouble due to emphysema. The Pacinian corpuscles, about forty in number, were found in the connective tissue behind the duodenum and pancreas, showing as bluish-white, translucent, rounded, ovoid, or reniform bodies, with a central white axis. They varied in size from the largest, 6 mm. long by 4 mm. thick, to some not larger than normal. They were all plainly attached to nerve filaments, most of them scattered and single, a few in groups of three or more. The increase in size was due to an œdematous condition of the concentric sheaths. This form of enlargement of the Pacinian corpuscles seems to have almost completely escaped observation, for it is not referred to in any of the text-books on morbid anatomy; but Dr. E. Przewoski, in Virchow's *Archiv*, Bd. lxiii., describes five cases in which these bodies were affected in this way. In two the subjects were œdematous, and it is probable that, if looked for, they would not infrequently be met with. The semilunar ganglia,

though to the naked eye large and succulent, presented under the microscope no decided lesion, only an increased number of small round cells, with a cloudiness and indistinctness of the ganglion cells.

The pancreas presented an interesting lesion. Everywhere the connective tissue was filled with extravasated blood. Especially was this the case toward the tail, where there were even actual clots. In the body of the gland the acini themselves were not involved, but appeared as grayish-white areas, surrounded by a dark-red hemorrhagic exudation. The loose tissue in the neighborhood was infiltrated with serum. Klebs gives a good account of hemorrhage into the pancreas, and has collected several cases in which death took place in a very short time, and this was the only lesion found. The subject has been more recently discussed by F. W. Draper, of Boston, who describes five cases (*Transactions of the Association of American Physicians*, vol. i.). The patient in this case complained for several days of intense pain in the epigastrium, which was also very sensitive to pressure. He winced at the slightest touch, and it was thought possible, as he had lost flesh, and had a haggard appearance, that he might have a cancer of the stomach. There was nothing found to account for the pain, except the swollen state of the semilunar ganglia, and the condition of the pancreas above described. The mode of death was peculiar. He had taken his breakfast as usual, after a tolerably comfortable night, and at 9 o'clock was found by the ward attendant lying on his side, as if in a deep sleep, but breathing in a strange manner. When seen by the resident, Dr. F. A. Packard, he could be roused, but the pulse was almost imperceptible at the wrist, and there was typical Cheyne-Stokes respiration, with unusually long periods of apnœa. In this state he continued till 11.30, when death took place. The chambers of the heart, particularly those of the right side, were found to be dilated. The brain was normal. It has been suggested in these cases that the rapid death may be due to reflex inhibition of the heart, induced by the sudden shock to the solar plexus, which may be supposed to occur when hemorrhage takes place into the pancreas and adjacent tissues. It is analogous to Goltz's "Klopf-Versuch," in which a tap on the peritoneum of a frog inhibits the action of the heart.

January 28, 1886.

Three cases of abscess of liver.

Case I. *Chronic dysentery; small abscesses of left lobe, two of them communicating with duodenum.*—C. B., æt. 41 years, baker, was admitted to the Philadelphia Hospital August 9, 1886. He had typhoid

fever when fifteen years of age. Two years ago the present trouble began with pain in abdomen, vomiting, and diarrhœa. At times he would be better, but not for long. There was blood in the stools at first, and he had much burning pain in the rectum during defecation. At time of admission he had four or five soft stools daily, not containing blood. He had slight fever at first, but subsequently the temperature was normal. He had lost flesh, and had a sallow, cachectic appearance. He had chills and fever shortly after the trouble began, but none during his stay in the hospital. On September 18th, the following note was made: Abdomen flat, veins not distended; epigastrium prominent, and on palpation a firm, smooth mass is felt, occupying the entire region from the navel to the sternum. An indistinct edge can be felt a little to the right of, and also below, the navel. To the right the mass does not reach the nipple line, and here the fingers can be placed beneath the costal border. The mass is extremely tender; it moves with inspiration. In the sternal and right parasternal lines the liver dulness is directly continuous with that of the mass in the epigastrium. In the nipple and mid-axillary lines there are four and five inches of liver dulness. On October 11th, the note was: Mass above the navel rather more prominent, still very tender; it cannot be separated from the left lobe of liver; right lobe certainly not enlarged. The vomiting was variable and latterly was not so troublesome. He continued to have two or three soft motions daily. The emaciation and weakness became most profound, and he died on November 10th. Post-mortem notes as follows:

Body extremely emaciated; abdomen depressed. On incising the abdominal wall, an abscess was opened, which is between the peritoneum and right lobe of liver, and extends for an inch from ensiform cartilage to navel; this communicates directly with an abscess cavity in the right lobe of the liver. There is no peritonitis. Omentum is adherent at the right lobe. The right lobe of the liver does not extend beyond the costal border. The left lobe extends three inches below the ensiform cartilage.

Stomach: A little distended; contains a quantity of semi-digested food. The pylorus is free, mucous membrane soft and congested. In the œsophagus just above the cardiac orifice, there is an oval tumor, about the size of a bean, which is submucous, freely movable, and on section is firm, grayish-white in color; looks like a sarcoma. The duodenum is normal. Orifice of the bile-duct pervious; a clear bile flows out. The duodenum, one inch below pylorus, is closely adherent to the hilus of the liver, and on squeezing this organ pus flows from two orifices through which a lead pencil could be passed. The tissues in gastro-

hepatic omentum thickened. The hepatic artery not increased in size. The portal vein is pervious; both branches free. No thrombi.

Spleen: Is enlarged, is amyloid in reaction.

Liver: Not enlarged. Tissues about suspensory ligament thickened. The anterior portion of left lobe is adherent to the abdominal wall, and abscess cavity has perforated from the liver substance and is directly in contact with the abdominal muscles. It was this mass that was evident externally. This abscess is the size of an orange and contains a creamy pus; it is lined by a thick membrane; it communicates directly with the duodenum; it is confined to the lower and anterior part of the lobe. The right lobe of the liver is firm and is amyloid in reaction.

The *colon* is thickened, the mucosa roughened, irregular, and in many places ulcerated—evidently an old dysenteric condition.

The prominence of the gastric symptoms, the distinct tumor, and the progressive emaciation, led to a diagnosis of cancer of the stomach in this case. On two occasions a careful examination was made with a view of deciding whether the mass was associated with the liver, but it was not found practicable. Sufficient stress was not placed upon the intestinal symptoms, which had, however, passed the acute stage. The extreme sensitiveness of the mass is a point worthy of note, as it was much more than the ordinary pain and tenderness of malignant disease.

Case II. *Acute dysentery; three recent abscesses in liver.* — Hugh McB., æt. 50 years. Admitted November 16, 1886. Had been ill about ten days with diarrhœa and great pain in the abdomen. He had kept about and tried to work until a few days before admission. Had always been healthy, but had been a very heavy drinker. When seen on the 17th, appeared to be in collapse, face covered with sweat, tongue furred and dry; respiration 50; pulse 130, very small. Abdomen greatly distended, tense, and drum-like, and extremely tender. On percussion, tympany everywhere; liver pushed up; area of dulness diminished. There had been vomiting, which was now checked. The diarrhœa still continued; the stools small; much mucus and some blood. The temperature was 102° on the evening of admission, sank to 98° on the morning of the 17th, and rose to 100° on the evening just before his death.

Body that of a middle-aged, well-nourished man. Abdomen distended. Right inguinal hernia. Coils of intestines greatly distended, and here and there flakes of lymph over surface. Large intestine enormously distended, the transverse portion equal in size to thickest part of arm. In spots the peritoneal surface was covered with lymph, and the wall of gut had, in places, a grayish sphacelated look. The small intestine removed; no adhesions; it was dilated, swollen.

Large intestine: Cæcum was thickened and inflamed. The membrane was in enormous folds transversely placed, blackish in color outside, and sphacelated in places to a depth of from three to five lines. This condition extended up the ascending colon and was very marked, also, in transverse and descending portions. Some of these necrotic areas were isolated and ranged from a quarter to half an inch in size, and presented a cap of dark gangrenous tissue surrounded by a zone of grayish-white tissue from a quarter to half an inch in diameter. The necrosis in some of these spots extended through to the peritoneal coat.

On the right side a knuckle of the lower portion of the sigmoid flexure was nipped in the inguinal ring, projecting about an inch beyond the level of Poupart's ligament. The hernial sac, when opened, was about the size of a small orange, contained lymph and serous fluid, and at its upper part the knuckle of intestine was thickly covered with lymph. The orifice of the ring was large; the portion of gut was adherent only to the inner and lower aspect.

On slitting open the sigmoid flexure and rectum, a knuckle of bowel was adherent to ring as above described. From within, the mucous membrane was dark and gangrenous; the gut for a distance of three or four inches above and below this part was greatly thickened; mucous membrane sphacelated.

Stomach and duodenum presented no special changes. The small intestine was swollen and presented no lesion of the mucous membrane.

Liver looked normal. In the right lobe were two spots, the size of large marbles, of a grayish-brown color, well defined from liver substance, yet without a limiting capsule. These spots represented the commencement of a hepatic abscess. On further incision of organ there were three recent abscesses, the size of oranges, softening at centre and presenting fragile necrotic liver tissue at periphery.

Case III. *Chronic phthisis; multiple small abscesses in liver.*—M. B., admitted to Philadelphia Hospital, June 6, 1885. The clinical history of the case is of interest from the early and persistent symptoms of dropsy associated with disease of the kidneys. The autopsy showed extensive disease in both lungs and large amyloid kidneys. The liver was a little enlarged and on section presented very many small abscesses, none larger than a marble, containing a creamy, in places, bile-stained pus. They could not be traced in connection with the portal vein, the branches of which were free. There were a few ulcers in the lower part of the ileum. The mesenteric veins were not involved; no inflammation about appendix or pelvis. *December* 9, 1886.

Two cases of cancer of the stomach.

CASE I. *Large open cancer of anterior wall and lesser curvature.*—P. H., æt. 52 years; laborer. Admitted to the University Hospital in April, 1886. Family and personal history excellent. For three months had pain in abdomen with frequent eructations. Appetite poor; gradual loss of flesh and strength. When admitted was fairly well nourished and muscular; face pale. Inspection showed a depressed abdomen, with marked fulness in umbilical region, which was altered somewhat in shape, with a peristaltic movement. Palpation revealed a firm, hard tumor in epigastric region extending to the navel; uniform, not nodular. The centre of the mass was about an inch and a half above the navel, and it had a percussion limit three inches in diameter. There was moderate dilatation of the stomach. The liver, spleen, and the thoracic organs were normal. He remained in the hospital nearly four months. At first the vomiting was very troublesome, but toward the end it became much less frequent. The vomited matter contained an extraordinary number of the sarcina ventriculi During the last month of his life diarrhœa was severe. He emaciated rapidly and died early in August.

The stomach was large and the specimen showed a large ulcerating cancer of the anterior wall and lesser curve, extending to the pylorus. There were several soft sloughs, and it was only at the edges of the mass that the infiltrated thickened wall had a cancerous appearance. There were no secondary masses in the organs.

CASE II. *Annular cancer of pylorus.*—A. B., æt. about 56 years, patient of Dr. Bolling, was seen in May, 1886. He had been ill for nearly a year with dyspeptic symptoms and failing health, and there had been considerable difference of opinion as to the nature of his illness. At the first visit the most striking feature was the profound anæmia, with very moderate wasting. There was pain after eating and occasionally vomiting, but with careful dieting the latter symptoms were readily controlled.

Examination revealed a small, hard, tender nodule, about two inches below the ensiform cartilage. The stomach did not appear to be dilated. The general and local symptoms were thought sufficient to indicate organic disease of the stomach. I saw him on three occasions and on the last the small mass in the epigastric region was still more distinct, and the condition had improved somewhat. I did not hear anything more of the case for four months, when Dr. Bolling asked me to be present at the autopsy. The stomach symptoms had become more pronounced and the emaciation extreme. The disease was found limited

to the stomach, in the pyloric region. The sections here shown illustrate its characters. The pylorus was involved with the duodenum for an inch, and the stomach for at least two inches, forming a uniform annular mass. The little finger could be passed into the pylorus, but, as the sections show, the lumen was much narrowed by the projection of irregular masses, which gave a sinuous outline to the cross sections.

December 9, 1886.

Hernia of cæcum and appendix; perforation of latter; old perityphlitic abscess; recent larger one; general peritonitis.

C. J., æt. 50 years; cook. Admitted to University Hospital, March 4, 1887.

On Sunday night, February 27th, after having taken a walk, was suddenly seized with intense pain in the hypogastric region. Immediately took to his bed, vomited two or three times, and on the following day noticed that his abdomen began to swell. On Wednesday night had forty stools. Dr. Wharton gave him a hypodermic of morphine, which relieved the pain for that night. On Friday was admitted to hospital. Abdomen greatly distended and tympanitic. Breathing rapid and difficult. Pulse 112. Complained of great pain, chiefly in hypogastric region. Temperature 100°. Was given enemas of turpentine with sweet oil; whiskey every two hours; poultice over abdomen.

March 5. Dr Wharton gave history of the existence of right inguinal hernia. Temp. to-day, 99°. Feels much relieved, but still complains of pain and difficulty in breathing. Vomited this morning twice; dark-green in color, but no fecal odor. Bowels have not been opened.

6th. Complains this morning of intense pain. Is vomiting constantly. Was given a half grain of morphine in two hours, which relieved him for a short time. Hoffmann's anodyne and rectal tube gave no result in relieving tympanites. Punctured three times without relief. Died that night at 11 P. M.

Autopsy.—Well-built man; abdomen distended. In nipple line not more than two finger's-breadth of liver dulness. Three punctures of abdominal wall, one in right lumbar region and two in epigastric. On opening peritoneum gas escaped; moderate amount of fluid, chiefly in flakes, sero-purulent. Coils of small intestine greatly distended, one crossing at the level of navel as large as arm above wrist; toward pelvis not so large. The general surface of intestines was injected. Peritoneum

coated in places with recent lymph. Colon moderately distended. Cæcum and ascending colon contained consistent fæces, those in former very dry. Cæcum was adherent to the iliac fascia and passed into ring, and was adherent in it for the distance of two inches. Ileum looked normal, and finger passed freely through ileo-cæcal valve.

The *liver* was separated from parietes by an air space. Over promontory of sacrum the coils of intestine were closely adherent, and between and behind them there was an abscess cavity, circumscribed, and walls partly formed by folds of mesentery. Abscess extended into Douglas's pouch. Bladder contracted, walls thickened. Sigmoid flexure and rectum opened; no perforation; walls of abscess were formed by several inches of sigmoid flexure; ureters not involved. In searching for appendix the proximal orifice was found at the extreme end of the hernia of cæcum, in the inguinal canal; it then curved upon itself, passed back into abdomen immediately behind terminal portion of the ileum; passing to the left it was adherent directly to abscess cavity. The lumen was free; terminal three-quarters of an inch thick, sloughing, and opened directly into a smaller circumscribed sac with pigmented and indurated walls, the size of a large walnut, which communicated directly with larger one. The boundaries of the larger cavity were formed by mesentery and ileum in front, sigmoid flexure and retro-peritoneal tissues behind. It was along the sigmoid flexure that the abscess passed into Douglas's pouch.

Spleen large and soft.

Kidneys somewhat swollen.

Heart valves normal.

Lungs normal.

Remarks.—We have here an illustration of a very common event in perityphlitis, viz., the occurrence of general peritonitis by extension of inflammation from a localized focus of suppuration, the result of perforation of the appendix. The smaller circumscribed abscess behind the terminal part of ileum, into which the appendix opened, had doubtless existed for some time, and may not, when forming, have excited serious symptoms. The frequency with which we find evidence of past appendicitis, indicated by adhesions, fibroid and pigmentary changes, and obliteration of the distal part of the tube, points to recovery as the termination of a considerable proportion of the cases of perforation.

The hernia of the cæcum and appendix is an interesting point, and the curious course taken by the latter made the dissection very difficult, and it took both time and care to make out the precise relationship of the parts.

The fact that he had an old hernia, which Dr. Wharton had at one time reduced, suggested the possibility of the trouble originating about it. Laparotomy was advised, and Dr. Ashhurst came out one evening for the purpose, but the patient refused his consent.

February 24, 1887.

Pyo-pneumo-thorax subphrenicus.

W. S., æt. 24 years, was admitted to the surgical wards of the University Hospital on November 13, 1885, having fallen under the wheels of an engine. The left arm was crushed and he had a deep scalp wound. The arm was amputated at the upper third. For a week he had hæmaturia and he complained of a pain in his left side. Subsequently erysipelas developed in both arm and face. About three weeks after admission, signs of inflammation appeared in the left infra-scapular region, indicated by a rise of temperature, dulness and feeble, blowing breathing, and he was transferred to the medical ward. The stump at this time had almost healed. Examination of the chest revealed circumscribed dulness at the left base, extending nearly as high as the angle of the scapula, and, laterally, to the midaxillary line. Tactile fremitus was diminished; on auscultation, feeble, blowing breathing, and on deep inspiration râles. Slight cough, very little expectoration. A septic pleurisy was suspected. The condition remained practically unchanged for several weeks, during which there was irregular septic fever. He complained at times of pain in the ilium and left side, particularly when he drew a deep breath. He soon began to spit up fetid pus, and in twenty-four hours brought up several ounces. It was concluded that a localized empyema had perforated the lung. On examination, tympanitic resonance, amphoric breathing, and metallic râles were found low down in the postero-lateral region, beneath the ninth, tenth, and eleventh ribs, indicating pneumo-thorax.

The autopsy showed the existence of a large abscess behind the left kidney and descending colon, extending from the diaphragm to the crest of the ilium. The chief part of the abscess lay above the kidney, beneath the ribs, and in this region there was a distinct cavity, partially occupied by dirty-brown pus, similar to that which the patient had expectorated during the last two days of his life. Part of the diaphragm was in a sloughy condition, and two orifices, through each of which the point of the index finger could be passed, communicated directly with an abscess cavity in the lower lobe of the left lung. The pleural membrane

of this part were greatly thickened, and there was a small localized empyema between the layers. There were areas of recent broncho-pneumonia throughout the other lobes. The left kidney was small, and presented at its upper part a distinct cicatrix, to which the capsule and adjacent tissues were strongly adherent.

The sequence of events in this case was, probably, as follows: Wound of kidney with bruising of tissue in lumbar region; subphrenic abscess; localized empyema, probably from contiguity with subphrenic abscess; perforation of diaphragm and lung, with discharge of pus; development of a subphrenic air-containing cavity which gave, in the lower and lateral aspects of the left side, the signs of pneumothorax.

Most of the cases of subphrenic pneumothorax have been in connection with perforation of the stomach, duodenum, or colon, but Sänger, in *Archiv der Heilkunde* for 1878, describes two cases, not unlike this one, following injury. The literature, together with the record of a case occurring with perityphlitis, is given by Dr. Gardner, in vol. ix. of the Canada *Medical and Surgical Journal*.

January 28, 1886.

A case of retroperitoneal spindle-celled sarcoma with extensive thrombotic and hemorrhagic changes.

In addition to features of general clinical interest, the following case is worthy of record from the rarity with which spindle-celled sarcomata form large abdominal tumors, and still more so from the remarkable hemorrhagic destruction which the greater portion of the growth had undergone.

Michael D., æt. 60 years, machinist, resident of this country for thirty years, was admitted to the University Hospital, September 25, 1884, with a tumor of abdomen. Had been a moderate drinker, had used tobacco to excess. Had been healthy, "never sick a day" until present illness. Family history good; had nine healthy children. About six months ago he noticed that the abdomen was getting large, but felt no inconvenience, and it was not until two months ago that he began to feel uncomfortable after eating, and began to lose flesh and strength. Had lost about eighteen pounds in weight. His appetite had, at times, been ravenous, and the thirst excessive. Bowels obstinately constipated, no movement without purgatives. No pain of any kind in abdomen, only an unpleasant fulness after eating.

Present condition: Moderate emaciation; weight 117 pounds. Complexion muddy. Temporal arteries prominent and tortuous. Tongue

clean; appetite good, but he cannot take large meals on account of sensation of fulness. Says he is in good health, only weak. Passes about seven pints of pale urine of a specific gravity of about 1004, with a trace of albumen; no casts, no sugar. Examination of thoracic organs negative. Abdomen presents a symmetrical prominence in the neighborhood of the umbilicus, rather wide and flat. Superficial veins not distended. On palpation a solid tumor is felt, occupying the hypogastric and umbilical regions, and extending laterally into the flanks. It is irregularly nodular on the surface, slightly movable, and the rounded outlines above and laterally can be distinctly felt. Below, the outline is not clear and cannot be defined. Grasped firmly, it can be moved as a solid uniform mass, occupying a median position. No one part is softer than another, and there is no sense of fluctuation. Percussion gives a dull note over the tumor, tympanitic above in the epigastric region and in the lateral part of the umbilical. From spleen and liver the mass can be easily separated both by percussion and palpation. There is no pain in handling. Measurement round umbilicus thirty and three-quarters inches. Glands in groin not enlarged, feet not swollen.

He stayed in hospital until November 11th, the condition remaining unchanged, except that he gained three or four pounds in weight, and his general health had improved. The condition of the urine was of interest: for several weeks he continued to pass more than seven pints daily of pale urine of a low specific gravity, with a trace of albumen, but in the last three weeks in hospital the amount fell to about three and a half pints. On October 18th he was made the subject of a clinic, when the diagnosis of Lobstein's retroperitoneal sarcoma was made. The polyuria was attributed to irritation of the renal nerves caused by the pressure of the tumor.

On the 10th of November he went home. Subsequently he was admitted to St. Mary's Hospital, under Dr. O'Hara, and the upper part of the mass, which had become soft, was aspirated by Dr. Mears, and a couple of quarts of bloody fluid removed. He was taken to his home, where he died in April, and I have to thank Dr. Miller, under whose care he was, for an invitation to be present at the autopsy, and for permission to utilize the specimens.

Autopsy, with Drs. Mears and Miller. Considerable emaciation; abdomen distended, discolored in upper part. A solid tumor could be felt occupying a large part of the cavity, firm below and soft above. On exposing the peritoneum a large mass occupied the lower three-fourths of the cavity, pushing up the intestines. The membrane was smooth, in places covered with small grayish-white nodules, and in the flanks there

were a few adhesions. At the top of the tumor a coil of jejunum was adherent, and of a dark pigmented appearance. Many large veins coursed over the surface of the tumor, which was covered by the glistening peritoneal membrane. In the upper flaccid portion was an orifice, through which blood oozed, and in the peritoneal cavity there were about two pints of fluid of a similar character. The intestines were carefully removed; there was only the one adhesion, already mentioned. The mass, which was covered by peritoneum, occupied a median position, lying upon the spine, and extending to the brim of the pelvis. The hand could be placed behind it and passed down the vertebral column, and into the concavity of the sacrum, and in these regions the tumor had no adhesions. Below and to the left it was loosely united to the lower part of the sigmoid flexure, but the chief attachment was to the brim of the pelvis on either side of the fundus of the bladder, and particularly to the right side. The bladder itself was not disturbed in position; the top of it could be seen lying between the symphysis and the tumor. The adhesions, which could be readily separated, were closest to the transversalis fascia on the right side near the pubic bone. The weight was estimated at about eight pounds.

The tumor consisted of two parts, an upper cystic, flaccid portion, and a lower solid one. When opened, the cyst contained rather more than a pint and a half of bloody fluid, with flakes of yellowish-brown material, which also lined the wall, giving an appearance not unlike a large aneurismal sac. The walls were thin, and consisted of a peritoneal investment, within which was a firmer, condensed fibrous tissue. The blood removed at the tapping had evidently come from this sac. A transverse section across the solid part showed a central, firm, dry, yellowish-brown tissue, which cut with resistance, and which was everywhere surrounded by extravasated blood, occupying a position just within the capsule, and in some places extending into the substance. In this section there was nothing suggestive of a neoplasm, the tissue resembled the dry, leathery contents of an old aneurism, except that there was no lamination. Section of the lower part of the mass near the pelvis revealed several soft, grayish-red portions, cerebriform or encephaloid in appearance, and evidently of a sarcomatous nature. They formed, however, a very insignificant part of the entire mass.

There was no special enlargement of the retroperitoneal or mesenteric lymph glands. The stomach and intestines presented nothing abnormal. The pancreas and spleen were unaffected. The liver contained one secondary mass in the left lobe, the size of an orange, and several smaller ones. The kidneys were fibroid, and the ureters and pelves dilated, par-

ticularly the right; due, doubtless, to pressure. The heart showed moderate hypertrophy of the left ventricle. Aorta smooth. Lungs much carbonized, and somewhat emphysematous. Brain not examined.

Histological examination: Teased portions showed that both primary and secondary growths were composed of large spindle cells, closely packed together. The remnants of the original growth situated at the lower part of the tumor were quite distinctive, and had not undergone degeneration. There were also, in some places, portions of sarcomatous tissue just within the capsule, separated from the central dry thrombus by freshly extravasated blood. Sections of hardened portions showed a typical spindle-celled growth. The thrombus presented a finely granular basis-substance, between strands of translucent, hyaline material. All traces of cell structure were gone.

Remarks.—The points of interest about this case may be briefly considered under the following heads.

The character of the growth: Spindle-celled sarcomata rarely form large abdominal tumors. In the examination of a considerable number of new growths of all sorts, removed from the peritoneal cavity, I have not met with a similar one.

The situation of origin was unusual. I fully anticipated that we should find it springing from the lumbar retroperitoneum, the common point of origin for large abdominal sarcomata. Here the growth seems to have begun in the subserous connective tissue in front of the symphysis, not from the peritoneum, for it was quite loosely attached. It is interesting to note that spindle-celled sarcoma not infrequently originates in the connective tissue of Scarpa's space, a tissue directly continuous with that from which the tumor in question grew.

The looseness of the attachment and the readiness with which the tumor could be lifted out of the abdominal cavity, made us regret that we had not yielded to the patient's urgent solicitation to have the abdomen opened.

The character of the regressive changes: So soon as a tumor obtains any [illegible] we expect to find in it areas of degeneration, fatty, caseous, or calcareous, or, if a rapidly growing neoplasm, hemorrhages. Sarcomata are particularly prone to hemorrhage; indeed, when growing actively, it is rare not to find foci of extravasation in them. The effused blood not unfrequently becomes encysted, and the dark contents appear to result from the liquefaction of the coagulum. In a large tumor several such cysts may exist. Small scattered hemorrhages are more common, and the blood gradually undergoes changes without materially altering the appearance of the growth.

The condition in the case here reported is very unusual, as the greater part of the tumor had become converted into a dry, hard thrombus, while a considerable portion was occupied by a blood cyst, so that the mass resembled a huge hæmatoma rather than a neoplasm. Such general hemorrhagic destruction of a large tumor is not often met with, and I have not been able to find the record of a case with just such extensive thrombotic changes as here described. The mode of production can be readily understood from the appearances presented by the mass. No doubt softening and destruction by hemorrhage first occurred, as existed, indeed, at the upper part of the tumor, which formed a large blood cyst, the walls lined with thrombi, and in the fluid contents of which were flakes of firm fibrin. This cyst had been much larger, as nearly two quarts of bloody fluid were removed from it by aspiration. Had life been prolonged, the blood thus extravasated would, doubtless, have become inspissated by the absorption of the more fluid parts, and the remainder have been converted into just such a dense, dry mass as existed at the lower part of the tumor. It seems reasonable to infer that the firm, hard thrombus which constituted more than one-half of the entire tumor, was formed in this way. Possibly the hemorrhages beneath the capsule, which were very general, aided the process, though nowhere could a distinct lamination be detected.

The polyuria: Pressure of new growths in the abdomen upon the solar plexus or upon the renal nerves, may cause a very great increase in the flow of urine. The irritation in this case was transitory, as the amount fell to normal before he left the hospital. We do not yet know the precise conditions under which this occurs. Instances of it are rare, and we need careful observations on the state of the nerves. Dickinson, in his work on *Diabetes*, mentions a case in which degeneration of the solar plexus was found. Owing to the unfavorable circumstances under which the post-mortem examination was performed, no dissection of the nerves could be made in this case.

Dr. J. E. Mears thought the growth could have been removed, though the removal would have been attended with some hemorrhage.

Dr. Tyson would like to ask Dr. Osler what, in his opinion, was the effect of thrombotic degeneration on the histological elements of tumors, and again, is it possible for clots to be converted into the tissue of the original tumor, as is asserted by some?

The President remarked that the case was of much interest from a clinical standpoint, in view of the possibility of surgical interference, and asked Dr. Osler whether the conditions, as found post-mortem, suggested any means by which such a tumor as this could be diagnosed

from a similar growth occupying the more usual position in the lumbar region.

Dr. Tyson, in connection with the clinical history, called attention to a retroperitoneal sarcoma, presented by him to the Society last winter, which had been mistaken by him and others for a tumor of the kidney.

Dr. Osler, in reply to Dr. Tyson's first question, stated that the only remnants of sarcomatous tissue were two or three small, but very distinct, portions of the lower attached part of the tumor; the remainder had wholly undergone this thrombotic change, and in the upper part had become converted into a blood cyst. This change was, no doubt, slow, with first a destruction of the sarcomatous elements by the blood-clot, and then a slow process of necrosis. There was no evidence in any part of the tumor of an invasion of the coagulum by the sarcomatous elements, as is not infrequent in thrombi in other regions, as he had seen in the portal and renal veins. The chief interest in the specimen lies in the remarkable extent of the thrombotic change. Looking at the clinical aspect, he had diagnosed the case as one of retroperitoneal sarcoma from its large size, the central position, the slight movability, the distinct separation from liver, kidney, and spleen, not being placed more on one side than on the other, and from the fact that palpation in the lumbar region gave no pain or other evidence of kidney lesion. It was firmer above the brim of the pelvis than any other tumor he had ever examined. One remarkable feature about these tumors is their painless character; this patient complained of no pain, and in two other similar growths, which he described at length, pain was not a symptom.

January 14, 1886.

Cirrhosis of liver; fatal hemorrhage from œsophageal varix.

David M., æt. 44 years, white, admitted to Philadelphia Hospital Surgical Wards on October 26, 1886, with an ulcer of the leg. Had been a hard drinker, but up to the present time had not been unwell for many years. He had had syphilis. Patient was very pale and tremulous. On the morning of the 27th he complained of nausea, and at 1 o'clock P.M. vomited a large quantity of blood. The vomiting continued at intervals through the afternoon and night, and he lost several pounds of blood. I saw him for the first time at noon on the 28th, when he was in a semicomatose state, could not be moved, was breathing deeply, and was evidently failing fast. The examination of the thoracic viscera was negative. In the abdomen there was notable diminution in the area

of liver dulness, and it was considered probable that this was the cause of the hemorrhage. The blood, which he had last vomited, had been kept, and was thickly clotted, dark in color, and not mixed with food; that first brought up was brighter, and contained part of his dinner. A stool, which he passed to-day, was dark and tar-like. He gradually sank, and died on the 29th, with no further bleeding.

The autopsy showed advanced cirrhosis of the liver of the ordinary atrophic form; the portal branches within the organ were very much contracted. The diaphragmatic veins were greatly distended and anastomosed freely with the œsophageal plexus. A rich network of vessels covered the kidneys, and the posterior and lateral folds of the peritoneum, particularly in the region of the descending colon. The stomach did not contain blood; mucosa was pale; no erosions. The veins about the cardiac end were greatly distended. The œsophagus presented in its lower half a network of dilated veins, some of which projected on the mucosa. One of these, the size of a quill, extended in a tortuous manner along the posterior wall, and at its upper part showed a grayish elevated spot, covered with a thrombus. This proved to be an erosion on the vein, and a probe passed freely from the veins through the orifice. This, doubtless, was the cause of the hemorrhage.

Remarks.—Bleeding from an œsophageal pile is a rare, but well recognized event in cirrhosis of the liver. It is by no means uncommon to find the veins of the gullet greatly distended in this disease, as their anastomosis with the gastric and the azygos vessels affords one important channel by which the portal blood reaches the general circulation. In cases of fatal hæmatemesis a careful inspection of the œsophagus should always be made, otherwise the cause of the bleeding may be overlooked.

February 24, 1887.

Aneurism of the larger cerebral arteries; twelve cases.

Aneurisms of the branches of the circle of Willis play an important part in the history of cerebral hemorrhage, ranking next to miliary aneurisms of the nutritive arteries. They are certainly more common than the statements of text-books would indicate, and unless a careful dissection is made they are very readily overlooked. Abstracts of twelve cases are appended, nearly all of which occurred at the General Hospital, Montreal. In eight, the aneurisms had burst and caused fatal hemorrhage; in four, they were found accidentally, and had not produced any symptoms.

A majority of the patients were young or middle-aged individuals. One was a child of 6, another a lad of 17, and a third a man of 20. In five the age was about 40. The early age at which they occur has been noted by several writers. Thus, of seventy-nine cases collected by Coats,[1] there were forty-two between the ages of 10 and 40. The case here reported, occurring in a boy of 6, is the youngest of which I can find any note. Eight were males and four females. The arteries involved were: Left internal carotid, Case I.; right Sylvian, Cases II. and V.; left Sylvian, Cases III., V., IX., and XI.; basilar, Cases IV., VII., and VIII.; anterior communicating, Cases VI. and X.; and anterior cerebral, Case XII. The aneurisms ranged in size from a small pea to a large cherry. With the exception of Case IV., they were sacculated, and communicated with the lumen of the vessel by an orifice smaller than the circumference of the sac. In Case V. there were two aneurisms, one on either Sylvian artery. In Case III. the aneurism was surrounded by thickened meningeal tissue; in the others the sac was free. In seven cases the hemorrhage was chiefly meningeal, and the laceration of brain substance was slight. In Case III. the hemorrhage was altogether into the substance, which, from Coats's account, seems not uncommon. The extravasation was usually basic, and beneath the arachnoid; the amount of blood considerable, except in Case I. In Case X. the hemorrhage extended along the right optic nerve and appeared as a subconjunctival ecchymosis.

In Cases III., VII., VIII., and IX. there was heart disease; in Case VIII., ulcerative endocarditis. In Cases I., V., VI., VII., IX., and XI. there were atheromatous changes in the branches of the circle of Willis.

Embolism, endarteritis, and atheroma are the chief causes of aneurism, and the cases in this series afford illustration of each. Although it was suggested by Ogle,[2] Church,[3] and others that embolism played an important part in the production of aneurism, the evidence was not very conclusive until the publication of Ponfick's observations in 1873.[4] In several of his cases, the connection of the embolus with the aneurism was very clearly demonstrated. Of the cases here recorded, four were associated with heart disease, but in only one, Case III., was the condition suggestive of the previous occurrence of embolism. In this patient, a lad of 20, with aortic valve disease, the aneurism projected directly into an oval cyst with reddish-brown contents, and there can be

[1] Glasgow Medical Journal, 1873.
[2] Medical Times and Gazette, 1866.
[3] St. Bartholomew's Hospital Reports, vol. vi.
[4] Virchow's Archiv, Bd. lviii.

little doubt that here, on a former occasion, a lesion of the vessel, most probably embolic, had occurred. Ponfick supposes the dilatation results from a weakening of the wall due to direct contact with the embolus. Recently, I have had an opportunity of studying an aneurism of the renal artery which had developed on one of the primary branches, and, indeed, involved to a slight extent the bifurcation. There were ulcerative endocarditis and a large infaret in the lower end of the righ kidney, with considerable fibroid change about it. The vessel going to this part was obliterated and fibroid in the greater part of its extent, but for one-fourth of an inch from the main division it was dilated and aneurismal. The walls were grayish-red in color, softer than normal, and the coats could be readily separated. Here the aneurism had developed on the proximal side of the obstruction in consequence, apparently, of interference with the nutrition of the coats of the vessel.

In the other cases associated with heart disease, there did not appear to be any trace of previous embolic lesion in the affected vessels. In six cases there were atheromatous changes in the vessels of the circle of Willis, and I think this process stands in more frequent connection with the formation of these aneurisms. Patchy atheroma, with fatty changes in the intima, is very common in the larger arteries of the brain, and I have met with instances in which the branches of the middle cerebral arteries were chiefly or alone involved. The occurrence of so many of these cases under the age of 40 has been urged in favor of the embolic theory, but atheroma, particularly in isolated foci, may occur in the young. A weak spot in one of the large cerebral vessels would be specially liable to yield, as the pressure in these branches is so directly communicated from the aorta.

In Case IV. the dilatation was due to local endarteritis, which was possibly associated with recent syphilis. There were subendothelial proliferation and infiltration of the media with leucocytes.

The clinical history of cases of cerebral aneurism is necessarily meagre, as they rarely cause symptoms prior to rupture. In six of the eight cases in which this took place, death occurred rapidly. In Case I. the hemorrhage was small, and the patient lived about six weeks; in Case XI. the duration of life after the rupture was ten days.

Case I. *Aneurism of left internal carotid.*—Female, æt. 53 years, admitted, under Dr. George Ross, December 24th, with headache and debility. Three days before she had had an epileptiform convulsion, followed by drowsiness, and in the succeeding forty-eight hours there were four other seizures. There was no paralysis, but the chief symptom was a rambling delirium, from which she could be roused, and then

would answer intelligently. Urine albuminous. She remained in this state nearly five weeks. On January 25th the right arm was flaccid. Insensibility supervened, and death about six weeks after admission. The post-mortem examination showed atheromatous arteries at the base of the brain, and on the left internal carotid artery, just before its division, a sacculated aneurism the size of a hazel-nut, which communicated with the lumen of the vessel by an orifice one by one and one-half lines in diameter. The sac contained a firm decolorized clot. In the course of the middle cerebral artery there was recently effused blood, beneath which the brain substance was lacerated to a slight extent. There was an atheromatous patch on the anterior segment of the mitral valve; otherwise the heart was healthy.

Case II. *Aneurism of right middle cerebral artery.*—Mrs. R., æt. 40 years, married, five children, patient of Dr. John Bell, was found speechless in her bed on May 29th. She had been a healthy woman, but had suffered with vertigo, and of late her memory had failed. There was left-sided hemiplegia, gradually deepening insensibility, and death occurred on the night of the 30th. At the autopsy, slight meningeal hemorrhage was found at the base and over the convolutions of the right side. The right Sylvian fissure contained a large clot, and the convolutions bounding it were considerably lacerated. At the main bifurcation of the right middle cerebral artery was an aneurism the size of a bean, about half an inch in length and a quarter of an inch in breadth. At its under surface was a rupture with a ragged orifice. There was no atheromatous change in the vessels at the base. No heart disease.

Case III. *Aneurism of left middle cerebral artery.*—A. R., æt. 20 years, a small, but well-built man, died suddenly on the evening of the 25th of March, and the body was brought to the hospital. No history could be obtained of any previous illness. Brain, on section, presented a large clot on the left side, which involved the lenticular nucleus, internal capsule and part of the thalamus, and reached almost to the convolutions of the insula. On carefully tracing the vessels in the left Sylvian fissure, one of the vessels was closely adherent in the angle between the insula and the parietal convolutions. The artery appeared to enter an oval mass the size of a large cherry, which, internally, was in direct contact with the clot, and on slitting up the vessel it expanded into a small aneurism the size of a pea, which occupied about one-third of the oval mass above referred to. The wall of the aneurism presented a rupture four millimetres in length. The chief part of the oval mass was made up of a cyst with firm walls and reddish-brown, pulpy contents. No communication existed between this and the aneurism, but at one

point the connection of the aneurism and the cyst was very rough and fibrous. A branch was given off just below the aneurism, which looked as if it had been formed at the fork of a vessel. Arteries of the circle of Willis were not atheromatous. Heart hypertrophied; fusion of two of the aortic cusps; no vegetations.

Case IV. *Aneurismal dilatation of left vertebral and first part of basilar arteries; endarteritis.*—James B., æt. 36 years, found dead in his bed. Eighteen months before had had secondary syphilis. Extensive coagulum at base of brain from optic commissure to medulla, and extending along the vessels into the fissures and filling the fourth ventricle. The left vertebral and first portion of the basilar much dilated, and in the latter vessel, close to its origin, there was a shallow dilatation, with a small perforation in the centre. The intima was smooth, but in places presented opaque atheromatous areas, which, about the centre of the basilar, very materially reduced the lumen. The carotids and Sylvian vessels normal. Heart healthy. No other regions of arterial disease.

Case V. *Aneurisms of right and of left middle cerebral arteries.*—Male, æt. 55 years, patient of Dr. Arthur A. Browne. Ill for eighteen months with obscure brain symptoms. Vessels at the base very atheromatous, and just beyond the first division of the left middle cerebral there was a sacculated aneurism the size of a pea. It had not ruptured. On one of the main branches of the right middle cerebral artery there was a second small irregular dilatation. In the left hemisphere there was an old apoplectic cyst, in the vicinity of which were numerous miliary aneurisms. No valvular disease of heart.

Case VI. *Aneurism of anterior communicating artery.*—Mrs. G., æt. 40 years, died suddenly in a shop, and was brought to the General Hospital. No history of previous illness. Clots in region of longitudinal fissure, and a uniform sheeting at the base from olfactory bulbs to cord, entirely beneath the arachnoid. One or two spots of atheroma on basilar and middle cerebral branches. Careful dissection of the circle of Willis revealed a small aneurismal pouch projecting from the anterior communicating artery, and on its under surface a slit-like rupture 1.5 millimetres in length. The sac was smooth-walled, very thin, and presented a spot of atheroma near the orifice. Heart normal. Aorta atheromatous. Kidneys a little granular.

Case VII. *Aneurism of basilar artery.*—J. S., over 75 years of age. Death from thrombotic softening in left hemisphere of brain. Vessels at the base atheromatous. An aneurism the size of a large pea was connected with the basilar artery, and lay imbedded in a shallow fossa in

the pons. The walls were thick, and did not contain thrombi. Heart hypertrophied. Aortic valves incompetent. Pericardium adherent.

Case VIII. *Aneurism of basilar artery.*—M. W., male, æt. 43 years. Had had syphilis. Admitted with pneumonia, and developed ulcerative endocarditis. An aneurism six by five millimetres projected from the upper wall of the basilar artery, about its centre, and had formed a bed for itself in the pons. It did not contain clots. Branches of circle of Willis not atheromatous. Heart a little hypertrophied. Recent ulcerations on aortic and mitral valves.

Case IX. *Aneurism of left middle cerebral artery.*—Female, æt. 40 years. Died of pneumonia. Vessels of circle of Willis slightly atheromatous. A patch in the basilar narrowed its lumen considerably. Just before the first bifurcation of the left Sylvian artery there was a sacculated aneurism the size of a pea. The wall of vessel about it not atheromatous; no clots in interior. Heart hypertrophied; vegetations on aortic valves.

Case X. *Aneurism of anterior communicating artery.*—G. E., a lad, æt. 17 years, admitted December 18th in an insensible condition. Three months previously had an epileptic fit, from which he quickly recovered. For eight days past had had severe headache. He remained unconscious and died on the 23d. Ecchymosis of right upper eyelid and conjunctiva developed while under observation. Extensive hemorrhage at base of brain, involving meninges and extending along the anterior cerebral arteries upon the corpus callosum. On separating the orbital plates of the frontal lobes, and carefully removing the clots, an aneurism (measuring 10 by 11 millimetres) was seen occupying the longitudinal fissure. It was partially imbedded in the adjacent brain tissue, which was a little lacerated. On dissection, it was found to spring from the anterior communicating artery by a very small orifice situated close to the right anterior cerebral. The sac was full of dark blood, walls very thin, and presented a rent of 2 millimetres in extent at the lower part. Other vessels of the brain healthy. No heart disease.

Case XI. *Aneurism of left middle cerebral artery.*—Woman, æt. 62 years. Admitted in a semiconscious state, with right hemiplegia, which came on after a fit three days before. Death occurred on the seventh day after admission. There was extensive hemorrhage in the meninges of the left Sylvian fissure, and thin clots also at the base. The inner and anterior part of the left temporal lobe was lacerated. A small sacculated aneurism the size of a pea was found on the left Sylvian artery, just within the fissure. The walls were extremely thin, and the

orifice of rupture large. The vessels of the circle of Willis were atheromatous. No heart disease.

Case XII. *Aneurism of anterior cerebral in longitudinal fissure.*—Boy, æt. 6 years, brought to hospital unconscious, with feeble pulse, pale face, eyes and head turned to right, and left hemiplegia. Death in six hours. He had fallen from a hay-loft three weeks before, but recovered rapidly from the effects. There was meningeal hemorrhage at base and in longitudinal fissure. On separating the median surfaces of the hemispheres, and clearing away the blood, a small nodular projection was seen on the right side, about the middle of the gyrus fornicatus. This proved to be an aneurismal sac imbedded in the calloso-marginal fissure just where it turns vertically upward. The rupture was on the meningeal surface, but there was hemorrhage into and slight laceration of the contiguous portion of the brain substance. The arteries were not atheromatous, and the heart was healthy,

Our knowledge of the subject of cerebral aneurism may be thus summarized:

1. The rupture of aneurism of the large arteries is a frequent cause of cerebral hemorrhage in persons under forty years of age; in the experience of some pathologists, the most common cause.

2. The hemorrhage is usually extensive, and may be exclusively meningeal or mainly into the brain substance and ventricles. (Coats.)

3. The aneurisms are caused in a few cases by embolism, in a large number by atheroma and fatty change, and occasionally by acute endarteritis.

May 13, 1886.

Aneurism of thoracic aorta; perforation into left pleura.

Mabel W., æt. 22 years, was admitted to the Philadelphia Hospital complaining of pain in the abdomen. She had been dissipated and had had syphilis. I saw her the next day at 4 P. M. She was a medium-sized well-nourished woman, anæmic, and looked as if she had been drinking; was extremely nervous and excitable. She complained of pain in the epigastrium and left side. I made a careful examination of the abdomen and thorax, without detecting anything abnormal. The heart sounds were clear. About 4 or 5 o'clock the next morning, she got out of bed complaining of agonizing pain in the abdomen and side, and in a few minutes fell dead on the bed.

Autopsy.—On opening the thorax, the mediastinum with the heart

was pushed to the right by an extensive hemorrhagic effusion into the left pleura, amounting to several pounds. The lung was collapsed. When the pericardium was opened, it was noted that the apex of the heart was not pushed beyond the middle line, and the oblique position of the organ was retained in spite of the dislocation of the mediastinum by the large effusion.

Heart: Right auricle contained about ℥j of blood and clot. Left auricle and ventricle empty. On further dissection valves normal, the arch of aorta smooth, muscle substance pale and flabby.

Aorta: The arch was small, and the lining membrane healthy. Thoracic aorta looked normal until level of the ninth vertebra; here there was an opening on the posterior wall an inch and a quarter in length by a half inch wide. The contiguous parts of the aorta looked infiltrated and swollen. This orifice communicated with a sac full of clots, which lay immediately in front of the tenth and eleventh vertebræ, and projected into the left pleura, where it was closely united to the diaphragm. At the point of greatest prominence, there was a transverse laceration a half inch in length. The sac was about the size of an orange. The bodies of the ninth and tenth vertebræ were eroded, the latter most deeply. The cartilages were not involved. No changes of note in the other organs. *November* 11, 1886.

Small aneurisms of arch of aorta; compression and perforation of trachea; death from suffocation.

Dr. Osler exhibited the specimen, and gave the following account of the case. Patient, an Englishman, æt. 32 years, had come to Philadelphia on his way to Colorado, as he had been advised to winter there by his English physicians, who suspected the existence of lung disease. He had been in Australia, where he had lived a very active life. Had had a chaneroid, and had taken alcohol in excess. For nine months before leaving England he had a cough, much worse at times. He came to the hospital August 31st, complaining of weakness and severe cough. Examination of the chest revealed no special areas of dulness, but many râles, mucous and sibilant, in front and toward the bases. At times the cough was very rough and hard, and there was much wheezing. There was irregular fever; the temperature on 14th reaching 102°. Remedies had very little influence on the cough. On the 17th he was found in a condition of stupor, and it was thought that he possibly had taken morphia, but the next day he was brighter. On the 21st there was blood with the expectoration. On the 24th he seemed as usual through the

day, though ever since the attack on the 17th he had looked bad. Toward evening he again became very heavy and drowsy, and he was suspected to have obtained whiskey. The breathing became much embarrassed, and he had great difficulty in expectorating the mucus. At midnight he seemed sleeping very naturally. At 6 A.M. he was found dead. The face was suffused and cyanotic. From facts ascertained afterward, it seems that he had secreted a bottle of whiskey, of which he had taken largely.

The autopsy showed the lungs to be crepitant, the bronchial tubes filled with thick mucus, not blood-tinged. Anterior margin of the middle lobe of the right lung, and a margin of the lower of the left, were airless, and the bronchi dilated and filled with very thick purulent exudation. On slitting up the trachea, the tube, just above the bifurcation, was greatly narrowed by the projection of a hemispherical tumor, at the lower part of which was a small opening, through which blood exuded. The heart was not enlarged; valves healthy; aortic semilunar a little thick. Sinuses above the valves dilated. Entire arch of aorta widened, and the intima atheromatous. On anterior surface, just at pericardial attachment, was an aneurismal dilatation the size of a walnut. The orifice of the innominate was also dilated. On the posterior wall of the transverse portion was an orifice not as large as a quarter dollar, leading into a sac the size of a large walnut, which directly compressed the trachea, and had eroded its wall. The sac was filled with firm clots. Just below the orifice of the subclavian were two shallow pouch-like dilatations, not lined with clots. The other organs presented nothing special.

Dr. Osler remarked that as he had not examined the case, he could not speak of the physical signs; the general symptoms were evidently those of severe pulmonary trouble. The compression of the trachea had caused the intense inflammation of the tubes, with exudation of thick mucus, and no doubt the fatal termination was due to plugging of the bronchi with secretion. The whiskey would, of course, hasten the suffocative process.

October 8, 1885.

Aneurism of arch of aorta, with rupture into the trachea in two places and perforation of the œsophagus.

W. J., æt. 54 years, colored, a teamster by occupation, and accustomed to do heavy work, was admitted to the University Hospital January 6, 1885. Had been healthy and strong; no history of syphilis. In

August, 1882, he began to suffer with pains in the chest and left shoulder, but he did not have any serious inconvenience until September, 1883, when he was attacked with cough and thoracic trouble, possibly pulmonary, which kept him in the house and in bed for several months. It was not until May of last year that he was able to work. Since July he has had at times attacks of shortness of breath, with wheezing, and often at night he has to sit up in bed. Within the past three weeks the pains in the shoulder and down the left arm have become very severe and the cough and shortness of breath have increased.

Note on admission was as follows: Well-built man, face thin, general musculature good. Inspiration rough and noisy, expiration long and harsh and often accompanied by a brazen, laryngeal cough. Respirations 18 per minute. Can rest in the recumbent position. On inspection, the left side of the neck is much flattened, especially above the clavicle, and the sterno-mastoid muscle on this side is evidently atrophied. Apex beat visible in normal position, no abnormal pulsation; slight visible pulsation in vessels of neck. Palpation in the ordinary way negative, but on firm pressure with one palm on the upper bone of sternum, and the other on the back, a decided impulse can be felt, and the second sound is accentuated; deep pressure reveals pulsation above sternum and behind the left sterno-clavicular joint. Percussion reveals a slight area of dulness in the left half of the manubrium sterni and beneath the left sterno-clavicular joint. Heart's dulness not increased. Auscultation: heart sounds clear. At sterno-clavicular joint, when the breath is held, there is a soft double murmur, the diastolic the loudest, and the second sound is markedly accentuated. These murmurs can be heard over the left carotid and on supra-sternal notch. Tugging at trachea is marked on elevating the larynx; pupils equal.

The left radial pulse is smaller than the right and is slightly retarded. Lungs negative; loud tracheal and bronchial stridor; no pressure signs on either bronchus. Patient expectorates much thin muco-serous fluid which is blood-tinged, and at times there are more consistent sputa containing much blood. He was ordered to take twenty grains of potassium iodide three times a day and rest quietly in bed. No restriction as to diet. On examination, laryngoscopically, the left cord was found immobile.

Within three weeks he was greatly benefited as regards the pains, the cough, and wheezing, and the blood had disappeared from the sputum. Throughout February he remained very well, having occasional attacks of spasmodic coughing at night which were relieved by spt. æther. co. His general health improved and he was allowed to go about the ward.

Sputum occasionally streaked with blood. On March 19th he was shown to the class, and the following changes noted: Slight increase in sub-sternal dulness on firm percussion; more marked accentuation of second sound over this region; persistence of the double murmur, which was now also to be heard just to the right of the sternum and at the aortic cartilage, and at this point it was the loudest. No increase in the pulsation, but in certain lights a slight impulse at the upper part of the sternum was visible.

At the beginning of the month he began to be more wheezy; the stridor was very marked and the dyspnœa became urgent, so that he had to sit up in bed. Sometimes these attacks would come on suddenly. On the 3d and 4th the dyspnœa was severe, and he got much weaker. On the 5th and 6th he spat up some bright blood, but not in any great amount, and gradually sank, dying at 9.30 P.M. The specimen removed by Dr. Hamaker shows an aneurism of the aortic arch which occupied a position between the first bone of the sternum and the spine, very firm, solid, and about the size of an orange. The entire arch is dilated, but the sac of the aneurism involves specially the upper and posterior part and is lined with dense yellow fibrinous laminæ. The orifices of the innominate and left carotid are free; that of the left subclavian is considerably narrowed by atheromatous ridges. The great veins are not compressed. The left recurrent laryngeal passes round the sac and is much stretched and looks thinned; the right is normal. The trachea is much compressed about the middle of its course, and the aneurism causes a marked bulging on the left side, and here two perforations can be seen. The upper one, about six centimetres from the bifurcation, is only two or three millimetres in diameter, and the tissue about it is puckered and dark, and the mucosa somewhat fibroid. The lower orifice is smaller and looks more recent. Neither of these leads directly into the sac proper, but into a small pocket situated between the dense laminæ of fibrin and the thinned tracheal wall. On inspecting the œsophagus, an oval perforation was found seven cubic centimetres from the cricoid cartilage, which communicated directly with the sac, but was partially blocked with fibrinous clots. The stomach was found distended with fresh clots, and there was much altered blood in the small intestine. Collapse and congestion at the bases were the only changes in the lungs. The heart was not hypertrophied; valves were normal; muscle substance flabby and in a state of fatty degeneration and brown atrophy.

The points of interest in this case were the repeated bleedings extending over several months, and the associated wasting of the muscles of the left side of the neck. At first the bleeding was looked upon as an

indication that erosion of the trachea had occurred, but subsequently it was thought more probable that it came from the swollen mucosa at the site of compression. No doubt the first supposition was the correct one, as the upper of the perforations had probably been the source of the bleeding, but the firm leathery clots effectually prevented any profuse hemorrhage. The final bleeding into the œsophagus also took place very slowly, probably during the last thirty-one hours of life, as there was dark, much altered blood in the ilium.

It is impossible to say upon what the atrophy of the neck muscles depended, as no careful dissection was made of the nerves in that region. Possibly the sympathetic was affected, but there were no differences in the pupils.

April 9, 1885.

Rupture of the posterior papillary muscle of the left ventricle of the heart.

B. P., æt. about 70 years, a large-framed negro, was in Ward 6 of the Philadelphia Hospital, four months, with symptoms of mitral valve disease and heart failure. When I first saw him, about a month before his death, the legs were swollen, and the urine scanty. There was orthopnœa, and slight effusion existed at right base. The apex beat was outside the nipple line; impulse forcible; and a systolic thrill could be felt in the apex region. There was a loud, rough systolic murmur heard well into the axilla. The pulse was irregular; superficial arteries very atheromatous. His history was not very clear. He had been a hard worker up to a few months before his admission to the hospital. His symptoms appear to have come on gradually, and throughout were those of mitral insufficiency. Three weeks prior to his death Cheyne-Stokes breathing came on, and persisted without intermission. During this time he was well enough to get out of bed for his dinner, and at this time he was repeatedly seen to wait for the urgency of the respiratory movements to pass away before taking a mouthful.

Body that of an elderly, well-built man. Œdema of legs, back of thigh. Abdomen contained a small amount of serous fluid. In thorax effusion into both pleural sacs. Pericardium contained a moderate amount of fluid. The pulmonary veins, arteries, and also the aorta, were filled with dark, firm clots. Right auricular appendix filled with an ante-mortem clot softened in the centre; several globular concretions in the neighborhood. The right auricle was much dilated. Tricuspid

orifice admitted four fingers to second joint with thumb between. Cusps thickened; ventricle dilated and hypertrophied, muscular columns large. The pulmonary semilunar valves thin and clear. Left auricle dilated, walls somewhat thickened. Mitral orifice as seen from auricle not stenosed. Left ventricle dilated. Chamber circular. Anterior segments of mitral thin and natural looking. Chordæ tendineæ smooth, not thickened or shortened; plates of atheroma at the base of this segment. The posterior segment was normal at the part where the anterior chordæ tendineæ were attached. From the posterior papillary muscle four or five chordæ passed to the portion of the posterior segment next the aortic ring. A group of six or eight chordæ were attached on the middle and under portion of this segment, and their papillary ends were twisted and attached to a yellowish-brown portion, looking like the apex of a papillary muscle. This portion of the valve flapped freely, and could be pushed into the auricle. There were no vegetations. On the posterior wall of the ventricle, near the main mass of papillary muscle, there was a flat, slightly roughened surface, from which the small papillary muscle had been torn. The aortic segments were a little thickened, but competent. Both coronary segments fenestrated; calcification at attached margin. Aorta atheromatous; orifices of coronaries large; the arteries much calcified. Muscular substance of heart of good color. Walls of the left ventricle were from a half to three-quarters of an inch in thickness. Weight of heart twenty-five ounces.

Remarks.—Careful microscopical examination showed the loose portion to which the central chordæ of the posterior valve were attached, to be undoubtedly the tip of a papillary muscle. Indeed, it represented one of the chief divisions of the muscle, torn off close to the heart wall. Here and there a muscle fibre could be seen imbedded in brown pigment and surrounded by fibrous tissue such as in elderly people so often supplants the proper tissue of the musculi papillares. The specimen is unique in my experience, and I do not remember to have noted an instance in literature. The absence of vegetations on the torn surfaces is interesting.

March 10, 1887.

Two cases of four leaflets to the pulmonary valve.

These two cases represent a not very uncommon anomaly of the pulmonary valve, in which a small space left between adjacent cusps is occupied by a fourth segment. The cases presented no points of clinical interest bearing upon the heart.

Case. I.—Between two cusps there is a space 3–7 mm. in width, which is occupied by a small semilunar valve. It has a well-marked curvilinear base of attachment, the free margin is 8 mm. in length, presents no corpus Arantii, and is anchored to the artery wall by a small narrow tag. The depth of the valve is 8 mm. The lateral attachments are to the adjacent cusps, not directly to the artery. Two or three fenestrations of the large cusps communicate directly with the pouch of the small one. The three segments are of equal size, and normal.

Case II.—Between two normal looking segments there is placed a small cusp 7 mm. in width, 8 mm. in depth, with a distinct crescentic margin of attachment and a curved free border. The lateral edges are united to the contiguous valve. The sinus is distinct and does not communicate with the adjacent ones. The adjacent cusps look a little smaller than the third. *November* 11, 1886.

Bicuspid pulmonary valve.

In a case of carcinoma ventriculi, with enormous secondary mediastinal growth, the pulmonary valve presented the following peculiarities. The orifice was guarded by two segments. The smaller measured 33 mm. along the free border, was 15 mm. across the face, presented two fenestrations, and there was no distinct corpus Arantii. The other segment measured 36 mm. and across the face 15 mm. The free border was thickened, presented no distinct corpus Arantii. The body of the leaflet was also a little thickened. At the attached margin there was a slight indication of separation into two segments. On the arterial face there was a small median raphe which passed from the arterial wall to the base of the segment. Here it expanded into a series of radiating fibres which extended along the inner surface. This median raphe separated two sinuses of about equal size. *December* 9, 1886.

Large phlebolith of long saphenous vein.

The specimen was obtained from G. H., an elderly man, who died in the Philadelphia Hospital of fatty and dilated heart. The tumor was noticed during life, but there is no note as to how long it had existed. There was no sign of a wound or of external injury, though the size and situation suggest that it may have resulted from traumatism.

Aorta smooth; common iliacs large; femorals present plates of atheroma. In Scarpa's space two inches below Poupart's ligament was a firm tumor the size of a large egg. On pressure it was elastic. Its relations on dissection were as follows: The femoral artery passed directly beneath it and was not involved. Femoral vein was free. Orifice of the long saphenous vein occluded about a quarter of an inch from orifice. The occlusion was at the tumor above mentioned, which occupied the upper end of the long saphenous vein. The vein was pervious from below, and entered the tumor directly at a distance of an inch and a quarter from the femoral vein. It seemed to terminate in the tumor by three or four small passages. On section, it presented externally a dense fibro-calcareous structure; the contents brownish, tolerably consistent, altered blood.

February 10, 1887.

On the morbid anatomy of pneumonia.

My post-mortem records include 105 cases of lobar pneumonia, all of which, with one or two exceptions, occurred at the Montreal General Hospital. For the purposes of this article, I shall exclude five cases, in which the data are incomplete. As is the case at most large hospitals, the death-rate from this disease is high, due, first, to the fact that, as a rule, only the severer cases are brought in; and, second, that a considerable proportion of the cases occur among enfeebled and dissipated paupers, who rapidly succumb to such an acute affection as pneumonia. In the statistical report of Dr. James Bell,[1] the mortality for a period of ten years was somewhat over 25 per cent., one-third of the deaths occurring within forty-eight hours of admission. As a contrast, it may be stated that the mortality of the cases of pneumonia in the practice of Prof. R. P. Howard, of Montreal, during a period of twenty years, was only 4.8 per cent.

The statistical details are as follows:

Sex.—Of the 100 cases, 70 were in males, and 30 in females.

Age.—In 94 instances the age was given: up to 10th year, 5 cases; between 10th and 20th, 6; from 20th to 30th, 12; between 30th and 40th, 18; between 40th and 50th, 21; between 50th and 60th, 12; and over 60, 20 cases.

Lung affected.—In 51 cases, the right; in 32 cases, the left; in 17,

As to the position of the inflamed region in the lung the figures

[1] Montreal General Hospital Reports, vol. i. Dawson Bros., 1880.

are: in the right, whole organ solidified (except, perhaps, narrow margin at apex and anterior border) in 17; lower lobe alone, in 18; upper alone, in 7; middle and lower, in 3; middle and upper, in 2; upper and lower, in 3. In the left lung, entire organ in 10; lower lobe, in 16; upper lobe, in 6. In the cases of double pneumonia, it was most often the lower lobes which were affected together, but in three instances the lower lobe of one lung and the upper of the other were affected; in three cases both upper lobes; and in Case LXIX. the most extensive inflammation of both lungs occurred—the left was in a state of uniform red hepatization, with the exception of the anterior border, and the right in the stage of gray hepatization, except still smaller portions of the corresponding regions. Altogether, in 39 instances a lower lobe was involved, in 19 an entire lung, and in 16 the upper lobe.

Weight of lungs.—To estimate the amount of solid exudation, the lungs were generally weighed. The heaviest was in Case XLVIII., a man æt. 40 years, whose left lung, uniformly solid, weighed 2303 grammes, and the right, very congested and œdematous, 900 grammes. (The normal lung weight is between 600 and 700 grammes.) In eight cases the affected lung weighed about 2000 grammes, representing rather more than three pounds of solid exudate.

State of lung tissue affected.—In about one-half the cases, the inflamed area was in a state of red hepatization. In 30 per cent. there were regions of gray hepatization with the red, and in 22 cases there was gray hepatization, either dry or passing into the condition of purulent infiltration.

State of uninvolved portions.—Usually the crepitant parts of the affected lung were greatly congested or intensely œdematous. The latter was invariably the case when the whole organ was involved, except the apex and anterior border, which then presented a condition of almost gelatinous œdema. The unaffected lung was generally congested and œdematous, particularly at the posterior part. It was not uncommon to find the anterior portions quite dry and bloodless, while the dependent regions were full of blood and serum. No doubt this is largely due to post-mortem subsidence. We do not always find extensive congestion or œdema in the uninflamed parts. Thus, in Case XXXII., in which the lower lobe of the right lung was hepatized, the upper and middle lobes were noted as "very dry and bloodless," whereas the left lung was œdematous, except at its anterior borders. So, also, in Case LVIII., a woman, æt. 50 years, with red hepatization of the left lower lobe, the upper lobe was crepitant throughout, dry on section, no redness, and no blood. The right lung was also crepitant (except a fibroid apex), dry, no œdema, and very little blood.

Air-passages.—The bronchi generally contained a frothy, serous fluid—not often the tenacious mucus characteristic of pneumonic expectoration. The mucous membrane was usually reddened, rarely swollen. In the affected regions the smaller bronchi very often contained fibrinous plugs, and in twelve instances these were noted as very abundant and extending into the larger tubes of the inflamed region, forming perfect casts of the bronchi.

The *bronchial glands* were invariably swollen and succulent, occasionally very soft and pulpy. In no instance was there suppuration.

The pleura.—When the inflammation reaches the surface of the lung the pleura is inevitably involved, with the result, commonly, of a thin sheeting of exudate, perhaps of such delicacy that it produces only turbidity of the membrane. In only two instances the pneumonia was deep-seated, and did not reach the pleura; in every other instance this membrane was involved in a greater or less degree. In some cases the fibrinous exudate was extraordinarily thick and extensive, as in Case V., in which the right lung was uniformly solid, weighing three pounds six ounces, and every portion of the pleura was covered by a creamy fibrinous layer an inch in thickness.[1] In several cases there was copious serous exudation amounting to three or four pints. In six cases there was extensive double pleurisy, with pneumonia on only one side. Case XV. illustrated how readily the inflammation could cross the anterior mediastinum and spread from the pleura of the left upper lobe to that of the right,

Among the more uncommon terminations of pneumonia, there were cases of abscess, gangrene, and fibroid induration.

Abscess.—When a lung in a state of purulent infiltration is examined, we wonder that softening and breaking down of the lung tissue is not a more frequent result of this process. In four instances there were definite small abscesses. In Case XXXIV., a woman, æt. 56 years, with gray hepatization of the right upper lobe, there was a small abscess cavity, the size of a walnut, with shreddy walls, in the interior portion of the lobe. The tissue about it was in a state of purulent infiltration. In Case XXXVI., male, æt. 69 years, with gray hepatization of upper half of left lung, there were in the central part of the upper lobe several spots of softening, the size of marbles, irregular, with ragged, uneven walls and purulent contents. In Case LXXVII., female, æt. 64 years, with almost uniform consolidation of left lung, the upper lobe was in a state of intense purulent infiltration, and there were in the middle por-

[1] Specimen in the museum of McGill College.

tion several large abscess cavities communicating with each other, with ragged walls and purulent contents.

Gangrene.—In three instances this termination was met with. Case LIV., female, æt. 35 years, a hard drinker, was admitted with pneumonia of the left lung, which had existed for some days, during which she had been neglected and much exposed to cold. The lower lobe presented at its apex and extreme base signs of consolidation, but in the rest of its extent was represented by a large gangrenous cavity, occupied by shreddy and necrotic lung tissue and blood clots, the whole forming a stinking mass.[1] The walls were not defined, except at the lower part, where a separation between the sloughing and firmer lung tissue could be plainly seen. In Case LX., male, æt. 63 years, with pneumonia of the left lung, there was a spot of gangrene at the apex surrounded by dark consolidated tissue. Case LXXIV., male, æt. 50 years, a hard drinker for twenty years, was admitted supposed to be suffering with delirium tremens; had had convulsions before admission. Rigidity of muscles of arms, coma, and death thirty-six hours after admission. At apex of right lung was a gangrenous mass the size of a hen's egg, surrounded by greenish-black consolidated tissue. Suppurative meningitis of cortex.

Fibroid induration.—The production of a chronic—so-called interstitial—pneumonia from the ordinary croupous form is, perhaps, the most rare termination of the disease. The following case is of special interest, from the fact that the man was under observation almost from the outset, and the induration was in patches and in an early stage: Louis Phillippe, æt. 58 years, a laborer, was admitted with cough and pain in the side. Had a chill five days before admission. Temperature 101° F.; pulse 106; respiration 26. Expectoration not bloody. Physical signs of pneumonia over right lower mammary, infra-axillary, scapular, and infra-scapular regions. During the first ten days in hospital patient made no satisfactory progress; temperature ranged from 99° to 103°; he was heavy and dull, not delirious; pulse weak, 100 to 120. Defective resonance in infra-clavicular regions on right side; in mammary region, a flat tympanitic note; behind, absolute dulness, feeble blowing-breathing; a few râles on deep inspiration. The note over right mammary was markedly tympanitic. Patient emaciating. No heart murmur; very little expectoration, muco-purulent, not bloody. On the twenty-sixth day he had a chill, and the temperature went up to 104°. No change in physical signs. Died at noon on the twenty-seventh

[1] Specimen in museum of McGill Medical Faculty.

day after admission. The right lung was uniformly solid, grayish in color, with recent pleuritic exudation, and the surface, on section, was bathed with serous fluid. On carefully inspecting the cut section, three features called for attention. In the first place, in certain regions the air-cells could be seen with their fibrinous plugs, of a very opaque white character, undergoing fatty change. This state existed in very considerable areas. Secondly, there were small localized areas densely infiltrated with pus, and breaking down into definite abscesses. The largest of these was about the size of a marble. And thirdly, in several areas of the lung there were spots which had a very translucent aspect, were firm, smooth, homogeneous, not granular, and had the look of recent connective tissue. In these areas a fibroid change was going on in the lung; the alveolar walls were thickened, and the fibrinous plugs filling the air-cells were undergoing transformation into a new growth of connective tissue.

State of the other organs.—Heart: Distention of the chambers, particularly the right, with very firm, tenacious coagula, is a very constant feature in pneumonia autopsies. The right auricle is usually very full, and a solid mould, capped usually with a buffy layer, can generally be removed with the extensions into the cava and many of its branches. I have seen a complete cast of the branches of the superior cava, even to the smaller vessels, and a mould of the inferior cava, including the hepatic and the iliac branches. From the pulmonary artery there can be withdrawn, by careful manipulation, a dendritic clot representing the vessels of quite small calibre. In no disease, I think, are we likely to meet with such solid coagula—so firm and fibrinous; and on several occasions, when I did not know the nature of the case, the preliminary incisions for the right chamber have enabled me to make a shrewd guess as to the existence of pneumonia. In many instances the engorged state of the right side and condition of general venous stasis, suggested the possibility that a copious venesection might have relieved the overloaded chambers—and I have in several cases acted with benefit upon this suggestion. In extensive red hepatization the circulation in the inflamed area must be very much impeded, and the work of the right ventricle greatly increased. If we may reason from the experiments of Welch,[1] the collateral œdema which we have so much dreaded under these circumstances, has no existence; for he seems to show very clearly that to produce pulmonary œdema the blood pressure must be raised to a point very much beyond that which can be induced by the cutting off of cer-

[1] Virchow's Archiv, lxxii.

tain territories of capillaries, however extensive, in a pneumonia. Yet there are difficulties in the way of explaining the œdema of the sound portions of the lung on the view which Prof. Welch holds—viz., that the left ventricle is first weakened or paralyzed and the continued action of the right gradually produces the engorgement and œdema. It seems natural to think that the engorged right ventricle would more quickly fail than the left, which is rarely found so full, and certainly has not to bear the strain and tension of the right chamber.

The left chambers usually contained coagula, but were rarely distended, never to the degree often met with in the right.

The tricuspid orifice was frequently found dilated, measuring from five to six inches in circumference.

Turbidity and moderate fatty change were sometimes noted in connection with the heart muscle. The endocarditis will be considered with the complications.

Spleen: Friedreich and others have called attention to the very general enlargement of this organ in pneumonia. The normal weight may be taken at about 170 grammes. In only 35 cases was the weight over 200 grammes—the heaviest, in Case LXXV., was 670 grammes. In 12 cases the weight was under the average; in Case LV. it was only 72 grammes. Usually the pulp was very soft; but in 4 cases the note is, "pulp firm, and cuts well." In many cases the weight was not recorded, but the note entered was either "normal" or "slightly enlarged."

Kidneys: In exactly twenty-five per cent. these organs showed signs of interstitial changes, being hard and fibroid, with adherent capsules and often small cysts. In eight cases there was marked parenchymatous swelling; in Case XXIII., chronic parenchymatous nephritis; in Case XXV., amyloid degeneration; and in Case XXXII., extensive fatty changes in the tubules.

Other diseases and injuries.—One case occurred in connection with diabetes and one with erysipelas. Three cases followed injuries, one a burn, and one came on in the course of a carbuncle. In all, the pneumonia was fibrinous and lobar. These cases of "contusion-pneumonia," as Litten terms this form,[1] are very interesting, and may come on after slight or severe injuries, or after operations.

Complications.—Pericarditis occurred in five cases. In two there was extensive double pleurisy with the pneumonia. In one there was endocarditis as well. Except in Case XCIII., a portion of lung contiguous to the pericardium was involved in each case.

[1] Zeitschrift für klin. Medicin., Bd. v.

Endocarditis: I have on several occasions called attention to our exceptional experience in this respect; though, indeed, a review of the literature shows that the occurrence of this complication in pneumonia is by no means infrequent. In 16 cases there was endocarditis, either of the simple or malignant types, most often of the latter. In five instances these were simple warty vegetations, and there was no special cardiac symptoms. In 11 cases the lesions were more extensive, usually of the ulcerative form, and the character of the disease was much altered, or even masked by this complication. Our cases bear out Bouillaud's suggestion that endocarditis most frequently complicates left-sided pneumonia, but in a review of 36 cases of endocarditis occurring in this disease, and in which the lung affected was mentioned, I find that in 20 it was in the right side and in only 10 the left, so that it seems doubtful if contiguity has anything to do with it.

Meningitis: In 8 cases there was meningeal inflammation, in 7 pia-arachnitis, and in 2 dura-arachnitis. In 5 of these cases there was also ulcerative endocarditis. Brief details of these cases may be given:

Case II., male, æt. 38 years. Red hepatization of upper lobe of right lung, extensive exudation at base of brain, in longitudinal sinus and along the Sylvian fissure.

Case LXVII., female, æt. 64 years. Gray hepatization of left lung, with small abscess cavity; the under surface of the dura mater of left hemisphere covered by a sheeting of recent lymph, which could be detached in flakes. No lymph beneath the arachnoid or at the base.

Case LXXXIV., male, æt. 50 years. Gray hepatization of right upper lobe and a spot of gangrene. Intense congestion of cortical meninges and exudation of lymph in patches over the frontal and occipital lobes; none at the base.

The following cases were associated with endocarditis:

Case XXVIII., female, æt. 29 years. Upper half of right lung hepatized. Mitral ulcerative endocarditis. Meningitis of the cortex. A thick flake in the neighborhood of the left fifth nerve, and another about the optic chiasm.

Case L., male, æt. 40 years. Lower lobe of right lung. Extensive endocarditis of mitral and aortic valves. Thick, creamy lymph over sides and upper surfaces of the hemisphere. None at the base.

Case LXXIX., male, æt. 43 years. Lower half of left lung affected. Endocarditis, mitral and aortic. Meningitis of the left hemisphere, with exudation of lymph over the frontal and parietal convolutions. None at the base or on the right side.

Case LXXXVII., male. Double pneumonia; right apex. Ulcer-

ative endocarditis of mitral. Cortical meningitis. No lymph at the base.

Case XCIX., female, æt. 19 years. Red hepatization of central part of right lung. Endocarditis of anterior segment of mitral valve. Meningitis of cortex—both hemispheres.

The complication of meningitis is one of the most serious that can occur in pneumonia, and it would appear, in a considerable proportion of the cases, to be associated with ulcerative endocarditis. We may suppose the inflammation of the heart and the meninges to be induced by a common cause, or, what would appear likely in many cases, the meningitis is embolic in origin, for it also occurs in malignant endocarditis, unassociated with pneumonia. In twenty cases of meningitis in this disease, only fifteen occurred with pneumonia. The infective material may possibly be derived directly from the infiltrated lung-tissue, and carried off by the pulmonary veins. We know that occasionally large emboli may be derived from this source, as in a case of pneumonia occurring at the General Hospital in 1879, in which, during the progress of the disease, and not associated with endocarditis, there was embolism of one femoral artery and gangrene of the leg, necessitating amputation above the knee.

The inflammation in these cases is almost always cortical, and the chief symptoms are initial delirium, then stupor and coma, sometimes rigidity of the muscles.

Croupous colitis: In Cases III., XXVIII., XLII., LXXXV., and XCIX., this unusual complication was met with. In Case III. the cæcum was covered with a thin layer of adherent lymph, and scattered throughout the colon and sigmoid flexure there were numerous elevated patches of lymph, about the size and shape of rupia-crusts, which on section were found firmly attached to the mucosa. In this instance, the process was very extensive and the patches much thicker than in any subsequent case. More often there is a thin, flaky exudation, involving only the surface of the mucous membrane. In none of the cases was there ulceration.

Croupous gastritis: In Case IV. the stomach and duodenum were found "greatly distended with gas. The mucosa was pale, except about the fundus, where, just to the left of the cardia, there was an extensive area of croupous inflammation, represented by a thick, adherent, grayish-white exudate, covering an area 12 by 8 cm. Beneath the mucosa the membrane was deeply injected."

This paper is meant to be merely a statement of facts, a record of observations upon a common and well-known disease. As opinion is

still divided as to the general or local nature of pneumonia, it is interesting to note how strongly the evidence from morbid anatomy tends toward the former view. The frequency of the occurrence of various consecutive inflammations finds a parallel only in some of the specific fevers.

While this paper has but a trifling value as a pathological contribution, to the writer, as doubtless to the students who performed the autopsies under his direction, the careful study and observation of the cases upon which it has been based have been of the greatest service. In the investigation of disease a knowledge of the morbid phenomena observed during life and of the organic alterations found after death are inseparable. The teaching of the post-mortem room must supplement and illustrate the lessons of the ward, and, as Bichat says, it is neither from the one nor the other, but from both, that "la veritable pathologie" can be gained.

April 23, 1885.

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2. *Aspergillus from the lung.*

The specimen was sent by Dr. Rogers, of Denver, Col., with the following history: "Mrs. H., æt. 29 years. In Colorado for two years. Mother died of phthisis when patient was eight months old. She is a robust and vigorous woman, and states that she has always enjoyed good health. When seventeen years old she began to cough up bodies similar to the accompanying one, but smaller, at intervals of about three months—never more than one at a time, and it was generally unbroken. The bodies have gradually increased in size, and the intervals have become shorter, until now the attacks recur every two or three weeks. The bodies, as you may see from this one, are now of the size and shape of a small, white bean, and present a soft downy outgrowth on all sides but one, which is flattened and smooth and has a small opening in the centre which leads to a little cavity. The color is of a light gray, but dark on the attached side. On examination, I found it to be a vegetable fungus, and send it to you for more accurate determination. Mrs. H. has no cough, except from one to three days before one of these bodies is expelled, and it is finally brought up by a very violent cough, and she describes it as coming with some force into the larynx against the vocal cords, where it sometimes lodges until another cough expels it. Shortly before it comes up she has a 'husky,' obstructed sensation on taking a deep breath, but no hoarseness or marked discomfort of any kind. For a short time she experiences a disagreeable, musty taste. After its expulsion she has no

further symptoms until the next attack. Her husband, who is a physician, has examined the lungs repeatedly, and can find nothing abnormal."

The specimen conforms to the excellent description of Dr. Rogers, and on examination is seen to be made up almost exclusively of the mycelium and spores of an aspergillus, most probably *A. glaucus*. There is no portion of lung or bronchial tissue with it, or any mucus or adherent cells.

Cases of so-called pneumonomycosis aspergillina are rare, not more than eight or ten cases having been reported. The literature is fully given by Furbringer, in Virchow's *Archiv*, lxvi. The majority of the specimens have been discovered post-mortem, in old cavities or spots of hemorrhagic infarction. The points of special interest in this case are: (1) the occurrence in a woman in apparently good health; (2) the remarkable duration of the affection; and (3) the recurring attacks of coughing which result in the expulsion of the fungus.

October 8, 1885.

Specimen from a case of tuberculosis of both lungs, with implication of the suprarenal bodies and tuberculous ulceration of the colon—symptoms of Addison's disease.

The specimens exhibited were removed from the body of a gentleman 38 years of age, married, and by occupation a physician. Family history bad; his mother, his paternal grandfather, and two uncles, having died of pulmonary consumption. The patient's health was fairly good until about two years ago, when he had well-characterized mild enteric fever, from which he made what was regarded by his physician as a good recovery. He did not, however, fully regain his strength, and an occasional cough, from which he had suffered for some years, began to be persistent and annoying. He was able, however, to resume his usual occupation. During the spring and summer of 1885 he began to lose flesh and strength, his appetite became irregular and capricious, his cough more troublesome. The cough was especially annoying on assuming a recumbent position and during the early hours of the night. Expectoration was rare and always mucoid in character. He suffered from occasional irregular chills which were regarded as malarial; night sweats from time to time annoyed him. After a cold contracted while driving in September, all the symptoms were aggravated and the patient began to experience more or less constant deep pain in the epigastric region.

This pain he described as of a tearing or dragging kind not aggravated by food and liable to paroxysmal exacerbations of considerable intensity. He now noticed that his complexion, always dark, was becoming deeply and somewhat irregularly pigmented. About this time he began to suffer from occasional vomiting, for which no cause could be ascribed. At intervals of five or six days the contents of the stomach were thrown up without pain or distress, and equally without relief to the ordinary symptoms of his malady. The bowels were moved with remarkable regularity once a day, the evacuations being fluid and containing small sponge-like masses. The urine, upon repeated examination, yielded no trace either of albumin or sugar. Notwithstanding his growing weakness and sufferings, the patient delivered a course of lectures in the institution with which he was connected during the winter, and devoted some hours each day to literary work in addition to the discharge of other professional duties. In March, however, he completely broke down and came to this city for treatment. The appearance of the patient, when he first came under observation here, was that of well-marked Addison's disease. The face was deeply pigmented, the discoloration being more marked about the brows, eyelids, and lips. The mucous membrane of the mouth was but slightly affected, the hands were much discolored, the finger-tips clubbed, the nails incurvated, the body and limbs were also much discolored, especially about the flexures. The pigmentation over the site of a former blister and in the neighborhood of an old injury near the left knee, was peculiarly intense.

Anæmia was of moderate degree, the number of red corpuscles, as counted by Dr. Osler, being 4,200,000.

The patient suffered from a sense of great weakness, which was increased and accompanied by dyspnœa and faintness upon exertion. His mental condition was clear.

The clinical phenomena relating to the digestive system remained the same, with the exception that the appetite curiously increased during the last weeks of the patient's life.

The pulmonary symptoms grew rapidly worse. Physical examination revealed dulness over the upper lobe of both lungs, more marked and more extended on the left side. There were also feeble bronchial respiration and occasional crepitant and subcrepitant râles.

The heart's action was regular, 90–110 per minute, very feeble; there were no adventitious sounds.

The area of liver dulness was somewhat increased; that of splenic dulness was normal.

The abdomen was neither distended nor retracted; it was resonant

upon percussion, with the exception of a limited area in the left iliac region, where there was diminished tympany and some obscure resistance on palpation. These signs were afterward found to correspond to thickening of the colon and enlargement of the glandulæ epiploicæ in the region of an ulcer.

There was slight epigastric tenderness upon pressure. Death took place May 22, 1886.

Autopsy, thirty-six hours after death.—Moderate emaciation. Pigmentation not so deep on trunk as it was some weeks before death; on face quite as intense.

In *abdomen*, no chronic peritonitis; membrane not dark colored. In the course of the colon were several thickened and congested portions, one of which, about the middle of the sigmoid flexure, was very firm, and the appendices epiploicæ, and adjacent mesocolon were greatly enlarged. There were several calcified lymph glands in the mesentery. Branches of portal system moderately full.

In *thorax* universal adhesions on right side; on left, at apex and postero-lateral regions.

Heart of medium size; chambers contained dark clots. Valves normal. Muscle pale, and showed fatty changes.

Lungs: Upper lobes extensively diseased, and in great part airless. Section showed many groups of tubercles in a fibroid and pigmented tissue. Here and there a small caseous nodule. No cavities. The smaller bronchi a little dilated. In the left lung, one of the large bronchi, passing to the apex, was plugged with firm, cheesy matter. Between the groups of indurated tubercles and at the margins the tissue was emphysematous. The process was most advanced in the left lung. In the middle lobe of the right and in the lower lobes there were a few groups of firm tubercle.

Spleen of normal size, and presented scattered cheesy tubercles, with firm capsules.

Stomach: Extensive post-mortem solution at cardiac end and in œsophagus. Mucous membrane pale; veins full.

Pancreas healthy.

Duodenum normal. Bile-ducts pervious.

Small intestine presented a few small tubercles in Peyer's patches, but no loss of substance. In large intestine five large areas of ulceration, evidently of long standing, as the bases of the ulcers were cicatrized, and in one or two the calibre of the bowel was reduced.

Kidneys, suprarenals, and aorta removed together for dissection. The tissue between the cœliac axis and the head of the pancreas was puckered

by the presence of three or four calcified lymph glands. The left splanchnic nerve entered a large, normal-looking semilunar ganglion, circular in form, which embraced a small accessory suprarenal about the size of a pea. The right splanchnic passed to a smaller ganglion, which also looked normal. There was no "matting" or thickening about these bodies, and the nerves passing from them could be readily traced. Just to the right of the cœliac axis the tissues were a little matted. The suprarenal capsules were small and flat, and had lost the normal shape. The left seemed lower than usual, and was separated by a distinct interval from the kidney. It presented two firm cheesy masses which occupied the greater portion of the gland. In the thinner, peripheral parts remnants of cortical substance could be seen as small islands of yellow-brown tissue imbedded in a gray fibrous stroma. The right gland was flatter and thinner, puckered on the surface, and presented no trace of normal tissue. A large, flat, cheesy mass occupied the greater part of the organ. The kidneys were large but normal; veins full. Microscopical examination of the capsules showed tubercle bacilli in scrapings of the cut surface. The section presents the usual character of the fibro-caseous change so often described in these glands. There was also marked atrophy of the cortical regions, due apparently to an increase in the interstitial tissue. The nerves passing to the glands and the semilunar ganglia presented no essential changes. There was the usual pigmentation of the nerve cells.

May 27, 1886

The hæmatozoa of malaria.

Our knowledge of the animal parasites infesting the blood has been of late enriched by observations which show that certain of these hæmatozoa, as they are called, are more widely distributed and more important than we had hitherto supposed. Parasites belonging to the sporozoa, and to the nematode and trematode worms, have long been known to occur in the blood of various animals. Recent investigations prove that the flagellate protozoa are also not uncommon blood parasites, and it is possible that they may be the pathogenic organisms of certain diseases. I propose in this communication to give an account of the hæmatozoa which have been found in persons suffering with the various forms of malaria.

Historical.—Our knowledge of the blood-changes I am about to describe, dates from the researches of Laveran, in Algiers, which were communicated to the Paris Academy of Medicine in 1881 and 1882,

and which were finally embodied in a large work on the malarial fevers, published in 1884.[1] He found, as characteristic elements in the blood of persons attacked with malaria, (1) crescentic pigmented bodies; (2) pigmented bodies in the interior of the red corpuscles, which underwent changes in form, described as amœboid; and (3) a pigmented flagellate organism. These forms were looked upon as phases in the development of an infusorial organism which he regarded as the germ of the disease. Richard[2] confirmed these observations. A more general interest in the question was aroused by the publications of Marchiafava and Celli,[3] who found in the blood of malarial patients at Rome the bodies described by Laveran. They figured carefully the alterations of the organism in the interior of the red corpuscles to which they gave the name Plasmodium malariæ. Councilman, of Baltimore, has more recently confirmed these observations.[4] The pigment granules so numerous in the interior of the red corpuscles in cases of "comatose pernicious fever," which appear to be included in a hyaline mass, are, according to Marchiafava and Celli, and Councilman (who had previously described them[5]), these amœboid parasites deeply laden with altered hæmoglobin.

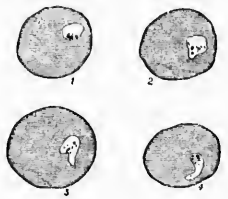
Technical details.—The finger pad from which the blood drop is taken should be thoroughly cleansed, and if the examination is made during a paroxysm, the sweat which may exude after the friction and drying should be removed. Attention to these, apparently trivial, details will secure specimens of blood free from small particles of dirt, and facilitate considerably the search for pigmented bodies. The layer of blood beneath the top cover should be very thin and uniform, the corpuscles, as far as possible, isolated and not aggregated in clumps or in rouleaux. It is well to surround the cover with paraffin if the examination is prolonged. No reagent of any kind should be added. Cover-glass preparations may be made and stained in methyl-blue or fuchsin, and mounted in balsam. Osmic acid preparations may also be employed. Although these bodies may be seen with a power of 500 or 600 diameters, it is essential for the satisfactory study of the changes to use higher powers. I have uniformly worked with the $\frac{1}{12}$ homo. immersion of Zeiss, and the $\frac{1}{15}$ im. of Reichert. Stricker's warm stage will be found useful.

Description of the Bodies. 1. *The forms which exist within the red corpuscle.*—(*a*) The most common alteration in the blood of malarial patients is presented by a pigmented structure inside the red corpuscle.

[1] Traité des Fièvres Palustres, Paris, 1884.
[2] Comptes Rendus, 1882.
[3] Fortschritte der Medicin, Nos. 14 and 24, 1885.
[4] Paper read before the Association of American Physicians, June, 1886.
[5] Councilman and Abbot: American Journal of the Medical Sciences, April, 1885.

The attention of the observer will most likely be first attracted by the presence of a few dark grains in the stroma, and a careful study of a suitable specimen will soon lead to the conviction that these are not scattered loosely, but are enclosed in a finely granular or hyaline body in the interior of the corpuscle (Fig. 1). The red disks in which they

FIG. 1.

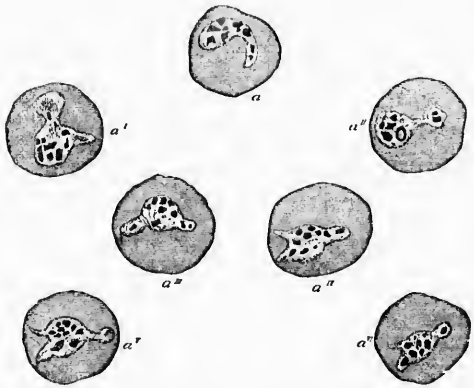


Amœbold body in red blood-corpuscles. The sketches were made at intervals of five minutes.

occur are usually larger, look flat, and are very often paler than normal; they may, indeed, exist only as colorless shells. The number of corpuscles so affected varies extremely in different cases. In some instances they are readily found after a search of a moment or two, but, in other cases, a prolonged examination may be necessary. Only one is usually present in each corpuscle, but two or three, or even four, may occupy the stroma. They vary greatly in size, the smaller ones not occupying a fourth of the corpuscle, while the larger ones may almost fill it. A delicate contour line can usually be seen separating the body from the stroma; at times this is very indistinct, particularly if the illumination is very bright. The substance appears hyaline, or very finely granular, and the pigment grains are scattered irregularly in it. They may be very numerous, and give a dark aspect to the body, or they may be scanty. They frequently present rapid Brownian movements. Occasionally a vacuole may be seen in the interior of the body. In several instances the bodies appeared to be enclosed in a clear space—vacuole—in the stroma. When first seen they are more or less spherical, but, as already stated, the outline may be indistinct. The pigment granules may be seen to alter their position in relation to each other. If the margin of the body is carefully observed, slow changes can be seen, which gradually bring about alterations in shape. These movements, which appear to be amœboid in character, can often be traced with great ease. They are well represented in Fig. 1, and, better still, in Fig. 2. Changes in position of the body of the corpuscle result from them. They are

decidedly slower than the amœboid movement of the colorless corpuscle. I have not seen any evidence of migration from the corpuscle. In dry

FIG. 2.



[1] Case VI. Pigmented body in red blood-corpuscle; outlined with camera (1-12 Zeiss, C eye-piece), by Dr. J. P. C. Griffith; illustrating some of the changes during an hour and a half's observation. *a*, at 11.45, slow alterations in outline, and the pigment-granules are in active dancing motion. *aI*, 12.15. *aII*, 12 25, body has rotated as well as altered its shape. *aIII*, 12.30. *aIV*, 12.40. *aV*, 1 o'clock. *aVI*, 1.02.

preparations these bodies stain deeply with gentian violet or fuchsin and present a granular stroma, in which the pigment grains are imbedded. (Fig. 3.)

FIG. 3.

Cover-glass preparation of blood stained with fuchsin. The amœboid bodies stain deeply in the corpuscles. Some of them are not pigmented.

(*b*) In seven cases peculiar hyaline structures existed in the interior of the red corpuscles, which differ from the bodies just described, in the absence of pigment and in the much greater activity of the changes. Fig. 4 illustrates the appearance and the alterations in outline. These bodies are devoid of structure, and the corpuscles in which they are present are not so pale as those with the pigmented forms. Marchiafava and Celli, who have given an excellent plate of these bodies,[1] regard

[1] Fortschritte der Medicin, No. 24, 1885.

them as the initial forms of the pigmented bodies. One does occasionally see appearances indicative of commencing pigmentation, but they have not, as a rule, the solid aspect of the pigmented bodies. In three cases I have seen the following remarkable changes. The hyaline body, while

FIG. 4.

Sketches of the alteration in form of one of the hyaline bodies; 1, at 7.8 P.M.; 2, at 7.12; 3, at 7.15; 4, at 7.20.

actively changing shape, suddenly burst from the stroma, and disappeared, or formed only a few granules. Thus, in a red corpuscle, there were, at 3.10 P.M., two hyaline, irregular-shaped bodies, which were changing rapidly in outline. The alterations were so marked that the physicians present at the time had no difficulty in seeing them. The stroma of the corpuscle was of full color. At 3.50 P.M., as I was carefully watching these forms, the corpuscle suddenly ruptured, and gave exit to two distinct masses, which quickly broke up into ten or twelve spherical bodies. No change took place in these after twelve hours, except that they became pale and indistinct. The stroma of the corpuscle became quite colorless. On two other occasions a similar phenomenon was witnessed, but in one no trace could be seen of the extruded material. This is evidently a physical change, and I think these very pale hyaline bodies must be carefully distinguished from the pigmented forms, though possibly associated with their early development.

(*c*) In seven cases there were vacuoles in the red corpuscles containing solid-looking bodies of various sizes and shapes. Certain of these structures resembled micrococci very closely (Fig. 5), and stained deeply in

FIG. 5.

Cover-glass preparation, showing corpuscle with solid, deeply stained bodies in small vacuoles.

aniline dyes; but others, often in the same corpuscle, were larger, more irregular, and altogether different in appearance (Fig. 6). The smaller ones were usually highly refractile, and, when two were together, the appearance suggested a diplococcus. In three instances these bodies

had a deep brown tint, as if composed of pigment. The larger bodies were homogeneous, very variable in size and shape. No movement was noticed in them, but the outlines of the spaces in which they lay sometimes changed actively. In Case XXIX. these bodies were very abundant, and for days formed the only noticeable alteration in the corpuscles.

FIG. 6.

1, 2, 3, larger solid bodies in the interior of vacuoles (?) which alter in outline. 4, a red corpuscle, with a small vacuole containing small pigment-granules of a deep brown-red color.

2. *The free forms.*—(*a*) Pigmented crescents. These bodies, which were found in eighteen cases, present remarkable features in appearance and structure. The form was usually that of a beautiful crescent (Fig. 7), with rounded or gently tapering ends; but the degree of curvature was variable, and many forms were almost straight. The length is about double that of the width of a red corpuscle, sometimes more. They are not attached, and they never show any motion. Joining the ends of the crescents—or, more correctly, at a little distance from the points—a narrow line can often be seen on the concave margin (Fig. 7, *e*). The body of the crescent appears made up of a structureless, homogeneous material, in the centre of which is a prominent collection of pigment granules. This, with the peculiar form, makes these bodies very easily

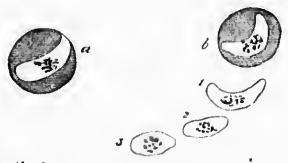
FIG. 7.

Crescents, *a*, *b*, *c*, show the slow alterations in the form of the pigment, as sketched at 9.20, 10.40, and 10.55 A.M. *e*, shows the narrow membrane sometimes present in the concave side.

recognizable in the blood, even when closely surrounded by the corpuscles. The pigment is very dark in color, distinctly granular, and varies somewhat in its arrangement. As a rule, it is central and aggregated, either in a heap, or assumes the form of a band placed transversely to the axis of the crescent. In some instances it is more scattered, but I have

never seen it at either end of the body. Although the most careful examination fails to detect any movement in the hyaline substance of the crescent, yet the existence of such may be inferred from the very positive movement which the pigment granules undergo. Fig. 7, *a*, *b*, *c*, represents these alterations; changes in form are exceptionally seen, as shown in Fig. 8 (1, 2, 3). A crescent became within an hour, an ovoid

FIG. 8.



a and *b* show crescents in the interior of red corpuscles; 1, 2, and 3, changes in a crescent.

body. Sketch 1 was made at 9.40, 2 at 10.10, and 3 at 10.30 P.M. The outline of these bodies is very clear and defined. Ovoid, elongated, and rounded forms of identical structure are also met with, but the crescents predominate. The number is variable, from one or two in a slide, to six or eight in the field of the 1–12th im. Though almost always free, they occur sometimes in the interior of a corpuscle, indicating, doubtless, the mode of development (Fig. 8, *a* and *b*).

(*b*) *The rosette form.*—In six instances there were rounded bodies, a little larger than red corpuscles, with a dimly granular protoplasm, and in the centre a rosette of pigment (Fig. 9). Some of these appeared to be enclosed in a delicate membrane, others were free. In six cases

FIG. 9.

Rosette form: 1 free; 2 within the shell of a red corpuscle.

remarkable changes were seen in these forms, of the nature of segmentation. Thus Fig. 10, *a*, represents one of these as seen at 6 P. M., September 4th. At 6.10 (*b*) there were distinct indications of segmentation in the finely granular protoplasm. At 6.30 (*c*) this had resulted in the formation of twelve or fifteen rounded bodies clustered about the central pigment, and still enclosed in the sheath. At 7.40 (*d*) the shell had burst, and given exit to the small corpuscles, which presented a tiny speck

at or about the centre. At 10.40 they had not undergone any material change. In Case LX., one of quartan ague, this phenomenon was repeatedly observed. The development of the rosette form can, I think, be traced from the intracellular pigmented bodies, which increase in

FIG. 10.

Segmentation of a rosette form: *a* at 6 P.M.; *b* at 6.10, segmentation proceeding; *c* 6.30, segmentation complete; *d* 7.40, small free bodies.

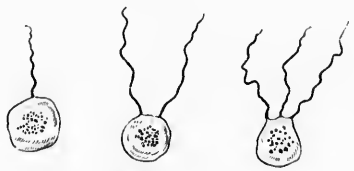
size until the entire corpuscle is filled. In some instances the body was surrounded by the remnant of the red corpuscle, in others there was no trace of it. The pigment granules gradually collect in the centre of the body in a more or less distinct rosette. I thought these changes had been overlooked by the writers on this subject, but I find that Golgi[1] has given a very full description of them, and has beautifully figured the development of the rosette form from the intra-cellular pigmented bodies. He has followed the process of segmentation with much greater detail than I have been able to do.

(*c*) *Flagellate organisms.*—Two or three years ago, when I first read Laveran's papers, nothing excited my incredulity more than his description of the ciliated bodies. It seemed so improbable, and so contrary to all past experience, that flagellate organisms should occur in the blood. The work of the past six months has taught me a lesson on the folly of a scepticism based on theoretical conceptions, and of preconceived notions drawn from a limited experience. Flagellate bodies were seen in seven cases, never in great numbers, usually only one or two in a slide. They are smaller than red blood-corpuscles, often not more than half the size. A specimen in one case was equal in one diameter to a red corpuscle lying near it. They are round, ovoid, or pear-shaped; the protoplasm finely granular, and in every instance contained pigment, usually central, which often displayed rapid Brownian movements (Fig. 11). The flagella are variable in number; one, three, and four were noted in different specimens. The length, as closely as could be estimated, was two or three times that of the body. They are exceedingly delicate, gently tapering, and, except in one instance, I could not determine the exist-

[1] Sulla Infezione Malarica, Archivio per le Scienze Mediche, vol. x. No. 4, 1886.

ence of a small terminal knob, figured by Laveran. The movement is exceedingly active, and the lashing of the long filaments may be sufficiently strong to drive away the corpuscles in the vicinity. The undulatory movement caused by the play of the filament over the surface of

FIG. 11.



Flagellate forms.

a group of corpuscles may attract the attention of the observer before he sees the cilia. The motion does not persist long; in none of the specimens which I examined, for more than half an hour. In one instance, the flagella disappeared in the short interval between two observations, but I could not determine what became of them. I have not seen the free-swimming cilia described by Laveran, but Dr. Councilman tells me that he has confirmed this observation. I have not been able to discover either nucleus or vacuoles in the flagellate organism. Slight, irregular changes in outline occur, due to slow movements in the protoplasm.

(*d*) Small round, pigmented bodies, from one-fourth to one-half the size of a red corpuscle, were not uncommon in some cases (Fig. 12).

FIG. 12.

Small free pigmented bodies, some of which show amœboid movements.

Usually, they remained unchanged, but in several instances they showed amœboid movements. The smaller ones about equal in size the products of subdivision of the rosette form.

Before proceeding to discuss the nature of these bodies and their relation, I will briefly refer to the condition of the blood corpuscles.

The red corpuscles showed no other notable alteration save that already described. The pigmented organism evidently destroys the vitality, and consumes the hæmoglobin, for the affected cells become pale, often spher-

ical, and, finally, are reduced to the condition of mere shells; except in cases of pronounced anæmia, the variations of the corpuscles in size and outline were not great. The colorless corpuscles were in some cases increased in number, and in very many instances contained dark granules. In several specimens they were observed to contain the pigmented organisms. In Case XL., a crescent had been included (Fig. 13), and, in Case LI., the process of inclusion of two free pigmented bodies was

Fig. 13.

A colorless corpuscle containing a crescent.

watched during half an hour. The blood plates were, as a rule, scanty, even when the anæmia was pronounced. No pigment was seen in them.

Types of malaria studied.—Of the seventy cases examined, a majority were instances of ordinary intermittent fever, chiefly quotidian and tertian, with two quartan cases. There was one case of remittent fever, one of comatose pernicious malarial fever, and the remainder were cases of malarial cachexia or chronic paludism, with occasional outbreaks of fever, with or without chills. In all of the cases, with the exception of seven, one or other of the forms above described was found in the blood.

Relation of the forms to the varieties of malaria.—The pigmented amœboid bodies are met with in acute and chronic cases, but they may be said to be specially characteristic of the more acute manifestation of the disease. In recent examples of quotidian or tertian ague which had not been under treatment, the amœboid intracellular forms were almost invariably present. I will refer subsequently in detail to the cases in which they were not found. The hyaline non-pigmented forms, and the vacuoles containing solid bodies, also occur in the acute cases; indeed, these latter forms were the only alterations noted in several instances. Thus, in Case XXIX., a man aged 48 was admitted to the Philadelphia Hospital September 27th, in a chill. He had had a paroxysm ten days before, and had suffered with malaria several years previously. The blood examined during the hot stage showed no pigmented bodies, but numerous corpuscles containing the vacuoles shown in Figs. 5 and 6. The chills occurred on the 28th, 29th, 30th, and October 1st; and each day the blood was carefully examined, without finding other bodies than those in the vacuoles or hyaline spaces. On October 1st, the patient

began with ten grains of quinine twice a day, which was continued for five days. He had no chill after October 1st. On the 7th there were crescents in tolerable numbers, which persisted until the 27th, the date of the last examination.

The crescents appear to be associated with the more chronic forms of malaria, or with acute cases which have been under treatment for some time. Of eighteen cases in which they were present, in twelve there was a history of infection lasting from six weeks to six months. In many, the cachexia was marked, and the spleen greatly enlarged. In six instances the attacks were recent—under a month; but in every one of these cases quinine had been taken. As a rule, the crescents occurred alone in the blood; but there were cases observed in which the pigmented amœboid bodies, the rosette form, and the flagellate organisms, were also present. I did not find the crescents in any recent cases of intermittent fever which had not been under treatment.

The rosette form, with its peculiar segmentation, occurred in six cases, and always in association with the amœboid intracellular bodies. Case XXXI.: tertian ague, examined in fourth attack; no medicine. Case XXXIII.: quotidian for seven days. Case XXXVII.: quotidian for six weeks, anæmic, and had a large spleen; took quinine one day. Case XXXIX.: quotidian for seven days. Case LVIII.: quotidian, on and off, for six weeks, then stopped; now daily chill for a week. Case LX.: quartan for three weeks. I have noted these details, as this form has not been much studied, and as Golgi seems inclined to ascribe to it an important connection with the development of the paroxysm. It was only observed in acute cases which had not been under treatment.

The flagellate organisms were present in seven cases, six of which were chronic forms, and one an acute case of three weeks' duration.

The small free pigmented bodies were very variable in numbers; they seemed more abundant in the chronic forms with cachexia.

Relation of those forms to the paroxysm.—Very many observations were made with a view of determining whether these organisms bore any definite relation to the remarkable periodic attacks which characterize acute malaria. For this purpose, in typical cases, examinations were made in the intervals of, just before, and in each stage of, the paroxysm. The results may be thus stated: there were instances, particularly if recent, in which the amœboid organisms were decidedly more numerous and larger before and during the paroxysms than in the intervals; there were others in which the number during the chill and hot stage was so small, that examples were very hard to find; in others again, slides taken before the attack and during each stage were negative, and yet in

subsequent paroxysms the bodies were present in the blood. I think, on the whole, that pigmented bodies in the red corpuscles are more numerous before and during an attack, but the difference is by no means striking, and I have repeatedly had to search long in slides prepared during a paroxysm for a single example. In acute cases which have lasted some weeks, and have had no medicine, the amœboid bodies have seemed to be quite as abundant at one time as another. Nor have I been able to see any special difference in the form of the bodies just before or during the chill, though in the early days of the attack they may be small and less distinctly pigmented, or, indeed, may present, as in Case XXIX., already referred to, the appearance of vacuoles containing small solid bodies.

The remarkable segmentation of the rosette form was in each instance met with during the paroxysms, and Golgi claims to have traced in five cases a series of changes corresponding to the stages of the attacks. In the intervals, the pigmented bodies gradually increase in size until they fill the affected red corpuscles, and, finally, the pigment collects in the centre, as shown at Fig. 9. The process of fission coincides with the onset and course of the paroxysm, and by the time of its conclusion the rosette forms disappear. In Case LX.—a quartan ague—an attempt was made to follow these changes, with the following result. The patient, a lad of 18, had had malaria, on and off, for a year, but for three weeks before admission the chills had been recurring with regularity. On Saturday, the 6th, the blood was examined in the chill. The red corpuscles contained many large pigmented bodies, and the rosette forms were numerous, many in process of subdivision. On the 7th and 8th, he was free from fever, and the most careful examinations of the blood failed to detect any forms but the ordinary pigmented intracellular bodies. They did not seem more numerous on the evening of the 8th than they were on the 7th. On the 9th, hourly examinations of the blood were made between 11 A. M., when the fever began, and 4 P. M. In the first two slides, there were very many pigmented bodies with the granules becoming concentrated, some with typical rosettes and a few in course of segmentation. In the specimens taken during the afternoon, the process of division was readily traced, and there were many of the small bodies in the field. On the 10th the note is: "No free bodies, all intracellular, tolerably numerous; no rosettes; no segmentation." On the 11th, several examinations were made, and the note reads, "absolutely none, save pigmented forms in the red." On the 12th, the slide at 8 A. M. showed large numbers of pigmented bodies, some with the granules irregularly arranged, other with distinct rosette. Fever began

at 12 A. M. Throughout the paroxysm, hourly examinations were made; rosette forms were abundant, and segmentation active. On the 13th and 14th, the ordinary forms were present, and in the paroxysm of the 15th, the segmenting bodies were again seen. The development of pneumonia interrupted the observations. It is worth noting that in this case the onset of the paroxysms was marked by an outbreak of the most intense urticaria. Blood and lymph from the wheals did not show any special changes.

Certainly the segmentation seems associated in some way with the paroxysm in these cases, but unless our observations have been faulty or very incomplete, there are many others in which there are no such changes in the attack. It is a point, however, to which the attention of observers should be carefully directed.

The crescents appear, as already stated, to be confined to the more chronic cases, or to those which have had treatment. They may persist for weeks or months. Thus, in Case LVI. a patient had irregular fever with what he called dumb chills, which had lasted for a month; for three weeks there was fever without chills, the temperature rising on some occasions to 103°. The crescents were numerous, and were not associated with other forms. With this his general condition was good, and he did not look anæmic. Under arsenic he improved, and the fever subsided, but the crescents were still in his blood six weeks from the date of the first observation.

Genuine paroxsyms may occur in these chronic cases without the development of other forms than the crescents. This observation was repeatedly made in Case XXV., a man with irregular malaria of many months' duration and occasional severe chills. The flagellate organisms did not seem to have any special relationship to the paroxysm, but they were so rarely seen that my observations on this point are not of much value.

Influence of medicines on the organisms.—Quinine invariably caused the pigmented bodies to disappear. In acute cases, which were usually studied during two or three paroxysms before the administration was begun, this observation was repeatedly confirmed. In a few days the corpuscles were entirely free; in several instances, the crescents appeared before the blood became normal. For example, Case XLVI. had his first chill on October 1st, and a daily recurrence until the 10th, when he came under observation. The pigmented bodies were abundant, and continued so on the 11th and 12th, when the temperature rose in the paroxysm to 105°. Quinine (twenty grains) was given on the morning of the 13th (which broke the chill), and repeated on succeeding days.

The bodies were present on the 13th, and a few on the 14th. They were not found on subsequent days. In less acute cases the action of the quinine did not seem to be so prompt, and the crescents did not disappear so rapidly under its use. Certainly, in recent cases this medicine acts as a positive specific against these organisms, just as it does against the malady itself. Arsenic does not appear to influence the pigmented intracellular bodies. In a chronic case, without chills, but with irregular fever, the crescents persisted for over five weeks, although the patient had improved in general health and vigor, and was no longer anæmic. Thallin and antifebrin were given in some cases without any noticeable results. As is well known to practitioners in malarial regions, there are cases of intermittent fever which subside without special treatment. I have had several patients in whom, without any quinine, the chills stopped or recurred very irregularly. In Case LXVI., the crescents appeared in the blood, which at first contained only the intracellular forms.

Cases examined with negative result.—As before stated, there were eight instances of apparently true malaria in which the organisms were not found, and to these I shall now briefly refer. I would remark, in the first place, that we cannot always rely upon one, or even two, examinations of the blood for these bodies. They may be very scanty, or they may be present at one examination and absent at the next. For example, Case XLI., a man, æt. 26, was admitted with a temperature of 104°. He had been cranberry-picking in New Jersey, and had been ill for a week with fever and [illegible]nite pains, but no chills. He was so very dull, that as the fever persisted, typhoid was suspected, although, as a cranberry-picker, malaria was first thought of. The blood was examined on three occasions with negative results, but on the fourth observation, five days after admission, and when the temperature had fallen to normal, crescents were found, which continued in the blood until he was thoroughly cinchonized. The cases are as follows:

Case X.—Child, æt. 5; chills and fever in Maryland nine months ago, occasional chills since, the last two weeks ago; spleen four inches vertical diameter; had taken quinine, none recently. One examination.

Case XI.—Man, æt. 19; never malaria before. Four distinct paroxysms. Slides examined from fifth and sixth, taken in cold, hot, and sweating stages. No quinine. I did not see the case subsequently.

Case XX.—Man, æt. 40. First attack six months ago. Chill on and off for past three months. Blood examined three days after last chill. Had taken quinine for two days. Spleen enlarged.

Case XXI.—Man, æt. 28. Examined on 17th, first chill on September 6th; four since. On 14th, took quinine gr. xxx, and has had gr. x t. i. d. since.

Case XXVI.—Man, æt. 35. Chills for three weeks, at first quotidian, latterly tertian. Had taken medicine, but did not know the nature of it. Was admitted on 24th. Two examinations, negative; pigment in white corpuscles. On 25th quinine was given. Three subsequent examinations, without result.

Case XXVIII.—Man, æt. 60. Admitted on 14th. Well-marked chills for eight weeks; had one when he came in, and four after. Blood examined on 28th, two slides. He had had quinine gr. xx each day since admission.

Case XXXVIII.—Man, æt. 70, resident of the almshouse for six years. First chill on 2d, second on the 5th, third on 6th, when blood was examined, two slides.

Case LII.—Man, æt. 25. Chills and fever for six days. Blood examined in chill, and on the following day. Had had quinine.

Thus, in five of these cases quinine had been taken, and they may be counted out. In Case X., the child was brought from the country, and only one examination was made. Case XI. was undoubtedly a case of quotidian ague, and the examination of slides taken from each stage of the fifth and sixth paroxysm was negative. I did not see the patient, and further examinations were not made. In Case XXXVIII., the bodies were not found on two occasions. This man also could not be followed, and I do not know his subsequent history.

The importance of excluding other causes for the paroxysmal chills was well illustrated by a case under the care of my colleague, Dr. J. H. Musser, which we regarded as one of malaria, but in which the pigmented bodies could not be found. The man had had chills on and off for several years; of late, the attacks had been more frequent and recurred more regularly. Quinine in medium-sized doses had no influence, but very large doses appeared to control the paroxysms. Their recurrence excited suspicion, and the discovery of pus in the urine, with decided pain on deep pressure in the lumbar region, indicated a more probable cause for the irregular chills.

Nature of the organisms.—It is very evident that we are dealing here with structures unlike any others which have been described in human blood, and with bodies which have no relation whatever to the spirilla, micrococci, and bacteria of certain acute diseases. I would call attention to the remarkable unanimity in the description of these parasites by Laveran, Richard, Marchiafava and Celli, Councilman, Golgi, and

myself. Laveran's original description is well-nigh complete, and subsequent workers have done little else than confirm his results, though to Marchiafava and Celli is due the credit of insisting upon the amœboid character of the intracellular form. Before discussing the relation of the forms to each other, it will be necessary to take a brief review of cognate organisms occurring in the blood, upon which recent investigations throw an important light.

It has been known for some years that hæmatozoa exist in the frog; one form, a flagellate organism, the Trypanosoma sanguinis, described by Gruby in 1843, is a well-recognized monad; a second, the Drepanidium ranarum, of Lankester, is evidently a gregarine, possibly a larval form, as he suggests.[1] Having been long familiar with these bodies,[2] which were very abundant during several winters in the frogs in my laboratory at Montreal, I was at once struck with an apparent similarity to them of the forms found in malarial blood. The crescent-shaped body in particular resembles strongly certain of the gregarines, and I thought it possible that we had here an instance of a sporozoon becoming flagellate at one stage of its development as Rivolta affirms may be the case. I soon discovered, however, that there were other observations on hæmatoza which bore more directly on the subject, and rendered possible a more likely explanation. Mitrophanow,[3] in 1883, announced the discovery, in the blood of the carp and of the mud-fish, of parasites belonging to the flagellate infusoria. A description of these forms need not detain us, further than to note that they were polymorphic, and one stage was represented by an amœboid body without flagella.

In a report published by the Punjab Government, December 3, 1880, and in the *Veterinary Journal*, London, 1881–82, my friend, Dr. Griffith Evans, described a new and very fatal disease known as *surra*, which prevailed among horses, mules, and camels in India, and in which he discovered a parasite in the blood during life. At first Evans believed it to be a spirillum, but subsequently came to the conclusion that it was a much higher organism. His observations have an important bearing on the question of the parasites in malaria. In 1885, Veterinary-Surgeon Steel published "An Investigation into an Obscure and Fatal Disease among Transport Mules in British Burma," which also proved to be *surra*. A careful clinical investigation of the disease led to the conclusion that it was a true relapsing fever, very similar to recurrent fever of man. Steel found the parasite described by Evans in all cases, and de-

[1] Quarterly Journal of Microscopical Science, vol. xxii.
[2] Canadian Naturalist, 1883.
[3] Biologisches Centralblatt, Bd. iii, p. 35

termined that it appeared as the temperature rose, and disappeared in the intervals between the paroxysms. He regarded it as a true spirillum, and named it Spirochæta Evansi. Both Steel and Evans found the disease readily communicable to dogs, horses, and mules, either by inoculation or by ingestion. Recently, on the return of Dr. Evans from India, he placed material from the *surra* disease in the hands of Dr. Crookshank, who has made an elaborate report,[1] confirming Dr. Evans's view that the organism is not a spirillum, and states that the parasite is morphologically identical with the hæmatoza described by Mitrophanow in the carp and mud-fish. In 1879, Lewis[2] described certain parasites in the blood of rats in India; and, again, in 1884,[3] he more fully discussed the question, and spoke of the identity of the organism with that found in the *surra* disease. Crookshank, in the paper just mentioned, gives the results of his investigations on the blood of European rats, twenty-five per cent. of which he finds infested with Lewis's parasite. It is a flagellate organism, with an undulating fin-like membrane, and is highly polymorphic. Crookshank has distinguished "globose, angular, non-filamentous, bi-flagellate, semicircular, and disk forms;" the latter represent the encysted stage. This organism is believed to be morphologically identical with the *surra* parasite and with Mitrophanow's hæmatozoa.

In the *Biologisches Centralblatt*, 1885, Professor Danielewsky, of Charkoff, makes an important contribution to the subject. He states that Trypanosoma, the well-known flagellate organism of frog's blood is polymorphic, and occurs in an amœboid form, and also produces spores; and, further, he has found in the red blood-corpuscles of birds a pigmented protoplasmic body, which subsequently appears in the plasma as a pigmented flagellate organism. In a later communication,[4] he suggests the identity of the pathogenic blood parasites of man with the hæmatozoa of healthy animals, and refers specially to the similarity of the forms which he has found in birds to certain of those described by Laveran in malaria.

With this information, we are in a better position to discuss the relation of the forms described to each other, and the zoölogical position of the organism. It is evidently closely allied to the hæmatozoa just spoken of, and the facts which we know of their life-history enable us to assert, with greater confidence, that we are here dealing with the

[1] Journal of the Royal Microscopical Society, 1886.
[2] Quarterly Journal of Microscopical Science, 1879.
[3] Ibid., 1884
[4] Centralblatt f. die medicinischen Wissenschaften, Nos. 41 and 42, 1886.

varieties of a highly polymorphic species, and not with two or three different organisms. The flagellate form is doubtless the adult condition; and it is interesting to note, in contrast to the hæmatozoa of the rat and of the *surra* disease, the comparative infrequency of its occurrence. Laveran met with it ninety-two times in four hundred and thirty-two cases, and Councilman eleven times in eighty cases. The steps in development remain to be worked out. It seems clear, however, that the pigmented amœboid form may become transformed into a sporocyst (represented by the rosette form and its changes), or into an encysted body (resting form), the crescent. The gaps in our knowledge relate specially to the form and manner of entrance of the parasite into the red corpuscle. Do the solid particles contained in the vacuoles (Figs. 5 and 6) represent the earliest stage? I think it highly probable that they do, and that they, with the hyaline unpigmented bodies, are the immature forms. The spore-like structures which result from the segmentation of the rosette form do not resemble the small solid bodies seen in the red corpuscles, but are rather like the tiny free pigmented forms which, in some cases, were abundant in the plasma. Of the latter, various sizes are found, and it is possible that from them the adult flagellate bodies arise. Golgi suggests that the spores, resulting from the segmentation pass to the spleen, and there attack the red corpuscles, in which they develop into amœboid forms. As at present the data are not available for a final decision, a further consideration of these points need not detain us. There is sufficient evidence to show that the various forms are only phases in the life-history of one, the flagellate protozoa, belonging to the order Flagellata-Pantostomata. Mitrophanow suggests a new genus, Hæmatomenas, to include the monad hæmatozoa; but Crookshank, who has carefully worked out the affinities of the parasites of the rat, the fish, and the *surra* disease, has referred them to the genus Trichomonas. The organism here described has not, however, the characteristic marks of a Trichomonas; for it lacks the undulating fringe on one side, and the caudal filament. Nor does it agree with the features of a Cercomonas; so that, meanwhile, until the true affinities are determined by an expert, its proper place seems to be the genus Hæmatomonas of Mitrophanow, which conveniently includes all monads parasitic in the blood. Thus: genus, Hæmatomonas; species, Hæmatomonas malariæ. Definition: Body plastic, ovoid, or globose, no differentiation of protoplasm, which contains pigment grains; flagella variable, from one to four. Highly polymorphic, occurring in (1) amœboid form; (2) crescents, encysted form; (3) sporocysts; (4) circular, free, pigmented bodies. The name designates the natural affinities of the

parasite, the habitat, and the conditions under which it occurs, on which grounds it seems preferable to that of Plasmodium malariæ, suggested by Marchiafava and Celli.

Relation of the parasites to the disease.—The same difficulty meets us here as in so many affections in which microörganisms have been found: Are they pathogenic, or are they merely associated with the disease, which in some way furnishes conditions favorable to their growth? As evidence of their pathogenic nature may be urged, with Laveran, the constancy of their presence, their absence in other individuals in malarial regions, the destructive influence upon the blood-corpuscles, and their abundance in the graver forms of the disease. But even these considerations, weighty as they may appear, will not carry conviction to all, in the absence of experimental demonstration such as can be afforded in the case of certain pathogenic schizomycetes. Attempts to isolate and grow these hæmatozoa outside the body have failed. Marchiafava and Celli have shown that the inoculation of healthy persons with blood taken from a case of malaria is followed in a variable time by genuine ague paroxysms, in which the blood contains the parasites; but in regions where malaria is prevalent such experiments are not wholly free from objections. A series of negative observations on undoubted cases of malaria would be convincing. I lay no special stress on the three cases in which I did not find the parasites, as the patients were not followed from day to day with the accuracy necessary to give any value to the observations. It must be borne in mind that hæmatozoa are not uncommon in animals, and, as in the rat, do not appear to interfere seriously with the health of their hosts. Under these circumstances, the association of a specific form with a definite disease in an animal makes it all the more probable that the species is pathogenic. A further study of the *surra* disease is particularly to be desired with the new light which Evans and Crookshank have thrown upon it. The conditions under which the disease occurs, combined with its paroxysmal character, are so similar to those of malaria, that a full explanation of its pathogeny would have a very direct bearing upon the present question.

To my mind, two facts in connection with these hæmatozoa point significantly to their etiological association with malaria. First, the positive anatomical changes which can be directly traced to their action, changes upon which one at least of the most marked symptoms of the disease depends. I refer to the destruction of the red blood-corpuscles, which can be followed in all its stages, and is as well defined an alteration of tissue brought about by a parasite, as any of which we know. The second fact is the action of quinine upon the parasites. The simul-

taneous disappearance of the symptoms of the disease and the hæmatozoa suggests that the specific influence of the medicine is upon the parasites, though it may be urged that the quinine, while curing the disease, simply removes the conditions which permit of their growth in the blood.

Practical considerations.—An interesting practical point is the diagnostic value of the presence of these bodies. There were six or eight cases in which the examination of the blood proved of great service in determining the existence of malaria. Some of these are worth mentioning. One of the first was a man æt. 37, who had been under observation on three or four occasions with anæmia and an enlarged spleen. He had had three attacks of hæmatemesis. There was no history of malaria, and, from the gravity of the case, I was led to regard it as one of severe splenic anæmia. On his fourth visit, however, a careful examination of the blood revealed the presence of the parasites, and I gave, in consequence, a more favorable prognosis in the case, which has since been justified. In an instance of pernicious malaria admitted to the Philadelphia Hospital, under the care of my colleague, Dr. J. H. Musser, the diagnosis rested on the discovery in the blood of the characteristic changes in the corpuscles. To a third case, XL., I have already referred, and there were four or five other instances of chronic malaria in which the nature of the disease was determined by an examination of the blood. On the other hand, in many cases of suspected malaria, the absence of these bodies led to a more careful examination, and to the discovery of the cause of the chills and fever. Four of these were cases of phthisis with ill-defined physical signs; in a fifth, after several negative blood-examinations, the ague-like paroxysms were found to be due to a septic pneumonia; in a sixth and seventh, renal disease was discovered. I feel confident that, in malarial regions, the examination of the blood will prove, in skilled hands, a most valuable aid in the diagnosis of many obscure cases.

Melanæmia.—These researches on malaria throw much light on the formation of pigment in the blood and various organs in these chronic cases. Evidently the primary change is in the red blood corpuscle, which is gradually destroyed by the amœboid form of the parasite. Every stage of this process can be readily traced, and these observations bear out the more recent views on the origin of the pigment in the blood itself. The pigmentary degeneration of the red corpuscles noticed long ago by Frerichs and Kelsch,[1] was no doubt the same as here described. The

[1] Archiv d. Physiologie, 1875.

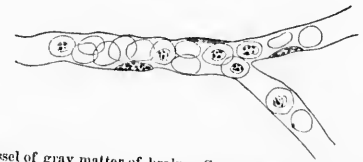
gradual accumulation of the granules in the spleen, liver, and bone-marrow leads to the characteristic melanosis of these organs. I sought carefully for evidence of active interference with these parasites on the part of the white blood-corpuscles, but on only two or three occasions

FIG. 14.

A colorless corpuscle studied for an hour and a half, during which time it had, as shown at 1, included a pigmented body, and was about to take another 2.

was this seen. Once a crescent was found inside a colorless corpuscle (Fig. 13), and again, as shown in Fig. 14, a corpuscle gradually enclosed two free pigmented bodies. The greater portion of the pigment resulting from the destruction of the monads is picked out by the cells of the spleen and bone-marrow, which also, no doubt, as in health, remove the effete red cells and their remnants. Pernicious malaria, common enough when Stewardson[1] wrote his well-known article, has now become very rare in Philadelphia. In these cases, Marchiafava and Celli have found the capillaries of the various organs filled with corpuscles containing pigment-grains which appear enclosed in a hyaline matrix. Councilman and Abbot[2] have described the same change, and I am indebted to Dr. Councilman for the specimen from which the accompanying sketch was taken (Fig. 15). It represents a small brain-

FIG. 15.



Sketch of a capillary vessel of gray matter of brain. Case of pernicious comatose malaria—Dr. Councilman. The red corpuscles are seen in outline, and in five there are pigmented bodies.

capillary filled with corpuscles, in many of which are pigmented bodies which stain deeply, and, so far as can be ascertained, are identical with the pigmented organisms met with in the red corpuscles during life.

[1] American Journal of the Medical Sciences, 1851.

[2] Ibid., 1885.

Only one instance of fatal malaria came under observation, a man æt. 70, admitted to Dr. Musser's wards on October 25th. He had been on the Isthmus of Panama and in Georgia, and had chills and fever in both places; last chill was three days before admission. He had also had hæmaturia. He was very anæmic, the spleen was slightly enlarged, the temperature 101.3°. There was great stupor, and he was roused with difficulty; the tongue was dry. The temperature became subnormal on October 27th and 28th. Examination of the blood showed many pigmented bodies in the red corpuscles, numerous free circular forms, a few crescents, and several flagellate organisms. The stupor deepened to coma, and he died on the night of October 28th. The spleen and liver showed typical pigmentation, and the bone-marrow was also very dark. The spleen-pulp contained free pigment and many large cells, some of which were filled with dark granules, while in others there were bodies identical with the small pigmented forms so abundant in the blood during life. The marrow presented similar changes. The number of red corpuscles containing the pigmented bodies was not great, nor were the capillaries of the liver or the brain stuffed with them, as in the instances of pernicious malaria just referred to. Probably this was an instance of severe malarial cachexia of many months' duration, and scarcely should be grouped with the pernicious comatose form.

To my colleagues, Drs. Curtin, Neff, and Musser, I am indebted for the privilege of examining the malarial cases in their wards; and to my resident physicians, Drs. Donohue, Albertson, and Westcott, for assistance which materially lightened my work. *October* 28, 1886.

Tænia echinococcus.

This rare parasite was reared experimentally by feeding a dog with hydatids from the liver of a pig. The animal was killed about seven weeks after the feeding when the intestine was found to contain many hundreds of the mature tapeworms. The portion of bowel exhibited had many adherent to the mucous membrane. From the small size of the worms, only a few lines in length, they were apt to be overlooked. Cobbold states that the only specimens procured in England have been experimentally reared. Dr. Leidy has never met the adult worm in this country. That it may occur here in the dog is very evident from the frequency with which echinococcus cysts (the larvæ) are met with in the hog and other animals. *September* 24, 1885.

Cysticercus cellulosæ of brain, heart, and voluntary muscles.

The "measle" or cysticercus of the Tænia solium is found very frequently in the hogs at the Berlin abattoir, and these specimens illustrate the extraordinary numbers which may exist in a well nourished and apparently healthy animal. The brain presents at least thirty or forty, all encysted, and very readily seen as opaque white bodies the size of large peas. It is remarkable that the animal does not, even with such numbers, have symptoms of brain disease. I suppose the slow growth of the parasites and the comparatively small size to which each one attains permits of the displacement of tissue without much disturbance of function.

In the heart the cysts are also very numerous and at least a dozen may be counted beneath the endocardium of the left ventricle. They were very generally distributed throughout the voluntary muscles and in this case the diagnosis of the condition could be made with half a glance. When scanty even the most careful examination may fail to detect them, and probably the chief danger is in these cases, as, of course, a single cysticercus taken in a slice of raw "schinken" or in "wurst" is sufficient.

In this case parasites were so numerous that I made a careful inspection of the mouth to see if their presence could not be determined in the lingual and buccal muscles. Beneath the tongue three or four could be distinctly seen, and the affection might really have been diagnosed during life in this way. As with the trichina, the hog appears to harbor the cysticerci with very little inconvenience and the symptom of the affection are very indefinite. In this country pork "measle" is not nearly so frequent as the veal and beef form—the larva of the T. mediocanellata.

September 24, 1885.

Liver, with dilatation and calcification of the bile-ducts, the effect of flukes.

The liver fluke, Distoma hepaticum, so common in Europe, is not very often met with in sheep and cattle in this country, and in my experience it is rare to find here the advanced changes described in works on parasites. When in Berlin, in 1884, I spent two afternoons of each week at the abattoir, which, owing to the elaborate system of inspection, both ante- and post-mortem, offers one of the best fields in Europe for the study of comparative pathology and helminthology, and

through the kindness of Dr. Hertwig I was enabled to secure a large number of interesting specimens.

The liver here shown represents a condition which may be seen almost any day. The organ was not much enlarged and externally did not look much altered, though here and there a gray-white spot could be seen. I have dissected the bile-ducts of the right lobe from the under surface, leaving intact the upper portion of the liver substance. The appearance is not a little remarkable. The ducts are uniformly enlarged and converted into rigid, calcified tubes. The primary branches are as thick as the thumb and the terminal ones toward the edge of the liver the size of pipe-stems. When broken the wall is from one to two lines in thickness, calcified, quite brittle, and without a trace of any tissue. Here and there are saccular dilatations. The inner surface is roughened and irregular, stained of a black or yellow-brown color, and in the larger tubes there were a few flukes. In other specimens I have found them in numbers, dead, broken up, and calcified. A bile-stained glairy mucus filled the tubes. The condition is one of chronic cholangitis due to the irritation of the flukes. It is interesting to note that the liver substance is not much changed, and is not to any extent cirrhotic. The animal from which this specimen came was fairly well nourished, sufficiently so to escape the vigilant inspectors. In sheep the changes in the liver may be much more advanced and the symptoms of the affection, known popularly as the "rot," closely resemble those of cirrhosis of the liver in man. *September* 24, 1885.

Hydatids passed with the urine.

The patient, George S., æt. 58 years, an Englishman, resident of Ontario for thirty-five years, at present a farmer, but formerly a butcher for fifteen years. Always enjoyed good health until about four years ago, when he had a severe attack of nephritic colic on the right side, lasting only a short time and quickly relieved. Had no further trouble until two years afterward, when a similar attack occurred, confining him to bed for several weeks; some days he was better, but always worse on exertion. After a period of improvement for several weeks, during which time he was able to attend to his farm duties, he felt pain and uneasiness over the right kidney, followed in a day or two by pain at the point of the penis, which continued for several hours, and was relieved by the passage of gelatinous-looking masses in the urine. These bodies—hydatid—he has continued to pass at intervals of from two to

four weeks. The discharge is always preceded by an uncomfortable feeling of fulness in the region of the kidney and pain or uneasy sensations at the penis. No tumor has at any time been discovered in the neighborhood of the kidney. With the exception of these attacks of pain and distress in the urinary organs, prior to the discharge of the hydatids, he enjoys good health. He lost no weight; appetite good; bowels regular.

The specimens, which were given to me for examination by Dr. Palmer Howard, of Montreal, consisted of ten or a dozen hydatid cysts, ranging in size from a pea to a grape, and contained in a small quantity of urine. They were evidently the daughter-cysts of a larger one which was in communication with the urinary passages. Several of the cysts contained smaller ones (grand-daughter cysts). On examination of a drop of the urine in which they were, numerous hydatids and the characteristic hooklets could be seen.

Echinococcus of the kidney or urinary passages is very uncommon. Statistics show that the left organ is more frequently affected than the right. The points of interest in this case are: the long duration, the absence of evident tumor, and the excellent condition of the patient. Here is evidently a cyst of considerable size, possibly in the right kidney, and which bursts at times into the pelvis with the discharge of the hydatids.

In 1882 Dr. Osler had reviewed the literature of American cases of echinococcus disease, and had made inquiries of the curators of the principal museums, the result of which was the collection of sixty-one instances of the disease (*American Journal of the Medical Sciences*, 1882). In not one of these was the cyst in the kidney. Since that date si other cases have been reported, by Carson (*St. Louis Courier*, 1884), cyst of liver; Schæffer (liver), *Transactions* of the Medical Society of Pennsylvania, 1884; liver (liver and mesentery), *New York Medical Journal*, 1885; Helen (cyst of liver, ruptured into intestine), *New England Medical Journal*, 1883–4: Welch (spleen), *Medical News*, 1884.

June 25, 1885.

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Extracted from the
American Journal of the Medical Sciences for April, 1886.

ATROPHY OF THE STOMACH,

WITH THE

CLINICAL FEATURES OF PROGRESSIVE PERNICIOUS ANÆMIA.

By Frederick P. Henry, M.D.,
Professor of Clinical Medicine in the Philadelphia Polyclinic, Physician to the Episcopal Hospital, Philadelphia,

AND

William Osler, M.D.,
Professor of Clinical Medicine in the University of Pennsylvania.

Although for many years past the attempt has been made to associate certain cases of profound anæmia with wasting and degeneration of the gastric tubules, the occurrence of a primary atrophy of the mucous membrane of the stomach is still doubted, and probably the majority of pathologists agree with the statement of Welch, in his recent article on this subject in Pepper's *System of Medicine*, "that the existence of atrophy of the stomach as a primary and independent disease has not been established."

The following interesting case is offered as a contribution toward the solution of the question:

Samuel I., white, male, æt. forty-two, was admitted to the Episcopal Hospital on June 15, 1885. Seven weeks before this date he began to complain of weakness, loss of appetite, and perverted sense of taste—"everything tasted like pepper." Dyspnœa was also a prominent symptom. On slight exertion he would be seized with vertigo, and be compelled to sit down. There is no record of hemorrhage from any part of the body. There was, and still is (at date of admission), a tendency to constipation, the bowels being moved every other day. In the autumn of 1860 he had an attack of tertian intermittent. After treating himself with domestic remedies, among which vinegar and salt seem to have occupied a foremost rank, he was cured by Peruvian bark and port wine. Twenty-four years ago he had a venereal sore, followed by two suppurating buboes, but without other secondary symptoms.

He was on the police force from 1872 to 1880, during which period and subsequently, up to December, 1884, he was in the habit of drinking freely—"twenty to thirty drinks daily," many of them before breakfast—and eating at irregular hours. After leaving the police he drove

an ice wagon, and was afterward a cab-driver. Eight years ago he had an attack of gonorrhœa. In 1876 he weighed 305 pounds, and was a prominent figure at a "fat-men's ball." His height is six feet two inches. In 1877 he began to grow thin, and continued to lose flesh at the rate of one, two, and three pounds daily. He was in the habit of weighing himself on the same scales in a shop in his district. He once during this period of rapid diminution of weight, lost seven pounds in twenty-four hours. This loss of flesh continued with intermissions for eight or nine months, until his weight was reduced to 147 pounds, when he began to regain, and in a year thereafter weighed 180 pounds. The patient's memory of the exact dates of these fluctuations in his bodily weight is not absolutely accurate, though sufficiently so for the purpose of this clinical history. He attributed his loss of flesh to indigestion. At the period referred to, he was in the habit of vomiting almost invariably after taking food, and was frequently obliged to leave the table hastily on this account. His weight at time of admission was 139 pounds.

His skin possesses the peculiar yellowish pallor that is almost pathognomonic of pernicious anæmia, and the ocular conjunctiva is of the characteristic yellow hue, which differs, however, from the tint of icterus. The palpebral conjunctiva is milky-white, apparently bloodless. The skin of the abdomen is flaccid, and easily gathered in folds by a grasp of the hand, which fact is corroborative of the patient's statement regarding his former obesity. This statement, however, is proved by the best possible evidence, that of photographs in his possession. His girth was once fifty-two inches, and is now thirty-two. The patient dates his illness from a period about eight weeks prior to his admission to hospital. It began with dizziness, nausea, palpitation of the heart, and a sense of great weakness. These symptoms have continued up to date of admission.

The results of physical examination are, for the most part, negative. The heart sounds are very feeble and distant, and unaccompanied by murmur or *bruit*. The lungs are free from any sign of disease. There is neither tenderness nor increased area of dulness on percussion over liver or spleen. There is decided tenderness over middle of sternum, and a tender spot was also found on one of the lower ribs when making percussion in the splenic region. There is no enlargement of the lymphatic glands. The tongue is exceedingly pale in the centre, with pink edges and tip, but without fur. The urine contains a minute trace of albumin; its reaction is acid; its specific gravity 1.020; it is free from sugar and bile pigment. On June 16, 17, and 18, the temperature rose above normal: on the first of these dates to 101°, and on the two latter to 102°, in the evening. After the 18th the temperature was normal, while in hospital.

June 17. First examination of blood. Number of red globules per cubic millimetre, 790,000. Proportion of white to red, 1 to 158. The percentage of red globules, as compared with the normal number (5,000,000), that is to say, the "hæmic unit," is 15.8.

The majority of the globules are larger than normal and many of them are pear-shaped and oval. Microcytes present in considerable quantity. Schultze's granule masses scantily present. The color, as tested by Gowers's hæmoglobinometer, is 16 per cent.; therefore, the amount of hæmoglobin is relatively normal. This is a cardinal feature

of pernicious anæmia. In all other forms of anæmia, the percentage of hæmoglobin is lower than that of the red globules. In pernicious anæmia, it generally equals, frequently exceeds, and has been observed by Laache to be double, that of the blood globules.

18th. An ophthalmoscopic examination was made by Dr. Albert G. Heyl, one of the ophthalmic surgeons to the hospital: "Both optic disks free from swelling, margins clear and distinct. In R. E. arteries of normal calibre, veins of increased calibre, at least double the size of arteries. A large hemorrhage, for the most part decolorized, was seen above the disk, and a more recent one upward and inward, in some places quite dark, in others of a raspberry-red. In L. E. the main upper vein was very full and inclined to be tortuous. The corresponding artery was abnormally full. A hemorrhage was seen below the disk. The media were quite clear. The condition is that of engorgement of the retinal vessels, with hemorrhages such as occur in anæmia."

24th. Number of red globules per c. m., 1,195,000. Hæmic unit, 23.9. Color, 20 per cent. No white seen. The red globules vary greatly in size and shape, being oval, pear-shaped, and generally of irregular outline. Some of them are four times the normal size. There is a moderate number of microcytes.

The date on which the patient left the hospital is not preserved, but there are notes of a visit to him at his own home on June 26th, so that his stay in hospital did not exceed two weeks.

July 2. Came to have his blood examined, walking a distance of nearly two miles. Was not fatigued, but complained of a slight "numbness" in the legs. Number of red globules per c. m., 1,215,000. No white seen. Hæmic unit, 24. Color, 28. Globules abnormally large and irregular.

6th. Patient had an attack of diarrhœa, which began the day before (Sunday), although he had felt uneasiness in bowels since Friday, and had stopped his medicine in accordance with directions. He had been taking Fowler's solution, and had reached eight drops thrice a day, when diarrhœa set in.

7th. Sent for. He had five watery stools the day before, and one large, liquid, very offensive stool to-day. During the night, about 1.30, he had a decided chill. Pulse full and bounding, 112; skin hot and perspiring slightly; temperature 103.2°. Ordered 2½ grs. quiniæ sulph. every three hours, and suppository of half a grain extract. opii aq. every three hours until diarrhœa is checked.

8th. Has had thirteen stools since 12 M. the day before, but feels decidedly better, owing to subsidence of the fever. Pulse 80; temperature 99.8°. Wishes to get up.

10th (Friday). Sitting up and looking worse. Has had forty watery, offensive stools since Tuesday morning, five between 4 and 9 A. M. None since 9, when last suppository was used.

12th. Came to have his blood examined. Not so much fatigued as when he came on July 2d, which, considering the recent attack of diarrhœa, is remarkable. Number of red globules per c. m., 1,635,000. Globules, for the most part, much larger than normal, and of irregular shapes. No white in specimen. Hæmic unit, 32.5. Color, 40.

20th. Number of red globules per c. m., 1,605,000. Globules mostly very large, some of them three times the normal size, and very irregular in shape; a few microcytes. Hæmic unit, 32. Color, 30. The count is

almost the same as the last, although the patient feels decidedly better, and walks considerable distances without fatigue, in spite of the intense heat now prevailing; the thermometer to-day reached 100° F., in the shade. His appetite is good, and the bowels are moved once daily. Ordered ferri pyrophosphat., gr. iiss *ter in die*.

Aug. 2 (Sunday). On Thursday patient came to have his blood examined, but it could not be done at that time. On his way home he drank a glass of buttermilk and soon after swallowed a plate of mock-turtle soup and a glass of lemonade. The consequence was an attack of cholera morbus the same evening. He treated himself with laudanum and blackberry brandy, and by next day the attack had ceased. On Friday he weighed 135 pounds. Number of red globules per c. m., 1,640,000. Hæmic unit, 32.8. Color, 36. Average size of corpuscles still decidedly above normal. Very few microcytes. No granule masses. Shape of globules less irregular. No white cells seen.

10th. About the same. Blood not examined. Hydroleine prescribed.

15th. Feels much better. Weighs 140 pounds. Talks of getting to work—cab-driving. Has walked a distance of two miles without fatigue during the past week. Appetite good and bowels regular. Did not take hydroleine, but, by advice of an officious friend, took elix. ferri, quiniæ, et strychniæ phosphat., instead. Number of red globules per c. m., 1,805,000. Hæmic unit, 36. Color, 32. No white seen. Patient looks very pale and ghastly.

Sept. 2. Has been working as a street-car conductor for a week, getting up at 3.30 A. M., and working until late at night. Got along very well until two days ago, when an attack of diarrhœa compelled him to stop work.

12th. Working again as car conductor. Rises at 4 A. M. and does not get to bed until one o'clock next morning. He has, therefore, if his statement is correct, only three hours in bed. "Never felt better in his life," but looks exceedingly pale and thin. No. of red globules per c. m., 1,470,000. Hæmic unit, 29.4. Color, 35.

Oct. 21. No. of red globules per c. m., 1,255,000. Hæmic unit, 25. Color, 20. White corpuscles to red as 1 to 500. Globules large and irregular. Patient complains of great weakness in legs on walking short distances. Has been continuously at work as car conductor, though not on full time.

Nov. 19. Sent for, and found him lying down though dressed. Has not worked for a month and is exceedingly feeble. Has followed no regular treatment whatever, being incorrigible in this respect. Has taken lately some pills called "tree of life," which purged him freely and reduced his little remaining strength. He complained of difficulty in passing water, and stated that some years ago he had been treated for stricture by the late Dr. Maury. Passed a No. 15 (French) catheter and drew off a little limpid urine. No blood followed passage of instrument. (About ten days later No. 21 was passed without difficulty.) His quarters are very confined and dark, and exceedingly noisy from continual passage of Pennsylvania R. R. trains almost directly overhead.

Dec. 10. Sent for late at night on account of alarming dyspnœa. When visited he was relieved, the relief having succeeded the belching of large quantities of wind.

17th. About the same. He had apparently sent to inquire whether

there was any prospect of his recovery. Ordered vin. ferri amar., ʒss, and liq. potass. arsenit., ♏iiss. *ter in die.*

21st. Worse. Diarrhœa began during the night and has weakened him considerably. This has been the invariable result of attempts to administer arsenic. The diarrhœa, which amounted to seven or eight watery stools, was checked by fifteen drops of laudanum. Ordered liquor ferri dialysat., gtt. v *ter in die*, to begin to-morrow, if diarrhœa does not return.

28th. Exceedingly pale and feeble. No conveniences at house for examination of blood. Taking ten drops of solution of dialyzed iron thrice daily.

On Jan. 5th, through the kindness of Dr. S. Weir Mitchell, he was admitted to the Summer St. Hospital. For several days before, he had been exceedingly weak, unable to sit up, and complaining of a sense of utter prostration.

10th. He lay in a semi-comatose condition, from which he could be partially roused, but was unable to recognize any person. The pulse eighty, very small, soft, and compressible, and the respirations deep and sighing.

Number of red globules per c. m., 315,000. Owing to the extremely pale tint of the blood, the color test could not be employed. The count was made at three o'clock. At half-past four, Dr. T. G. Morton injected into the left internal saphenous vein, at about the junction of the middle and lower thirds of the leg, fifteen fluidounces of a solution of sodium chloride, 100 grains to the quart of distilled water. Present: Drs. Hunt, Cantrell, T. S. K. Morton, and Orville Horwitz. Toward the close of the operation, which, it is needless to say, was performed with the greatest skill, the patient became restless, and opened his eyes, but could not reply to questions. Pulse before and after transfusion unchanged in frequency (80), but somewhat fuller after the operation. 8.30 P. M., patient in condition of heavy stupor; pupils moderately dilated; pulse extremely weak, but still 80 per minute; respiration labored and sighing, but not stertorous. Died at 12.30, four hours later.

Autopsy, eleven hours after death. Rigor mortis present. Considerable emaciation. Cicatrices on glans penis. Panniculus not more than half an inch in thickness; fat of a deep yellow color. Great pallor of skin and all organs. *Muscles* of a light red tint. In *abdominal cavity*, peritoneum smooth; small amount of a dark yellow serum; the intestines distended with gas. In *right pleura* general adhesions. *Pericardium* covered with a moderate amount of mediastinal fat; slight excess of fluid in cavity. *Heart* large, right chambers full; walls flaccid; preliminary incisions show in right auricle much pale serum, with a large yellow clot; in right ventricle a colorless clot, infiltrated with serum, closely adherent to trabeculæ and chordæ; ten ounces of a watery blood were collected from these chambers. The left chambers were nearly empty; small thin clots blocked the mitral orifice. On further dissection of the heart, walls of normal thickness; muscle very anæmic, and evidently fatty; right chamber looks dilated; valves normal. *Aorta* not atheromatous; coronary arteries healthy. *Lungs* pale, crepitant throughout; the lower lobes very œdematous, and the infiltration extends to the adhesions which exist between the lobes; frothy mucus in bronchial tubes and trachea.

Spleen is slightly enlarged, moderately firm; pulp of a deep purple-

red color; the Malpighian corpuscles not evident. *Kidneys* of normal size; capsules detach readily, surfaces a little rough; on section, cut with increased resistance; cortical portions pale; small arteries at bases of pyramids very prominent. The *suprarenal capsules* are of average size, firm; cortical portions of a deep yellow color. *Bladder* contains several ounces of clear urine.

Stomach looks natural, contains gas and about an ounce of dark fluid; pyloric orifice firmly contracted, and the ring seems thickened; cardiac orifice normal; length of organ eleven inches; breadth, when opened, eight inches. Walls not increased in thickness; at fundus two to three millimetres, at middle of anterior wall two and a half to three millimetres, and at pyloric zone, ten centimetres from the ring, eight to nine millimetres. General surface of mucosa pale; mucus covers the pyloric region; there are a few dilated venules in several places. At the fundus the mucous membrane is very thin, smooth, grayish-white in color, tough, and tears with difficulty. No trace of superficial softening. In the middle zone it has the same pale gray aspect, is smooth, and there is an entire absence of the velvet-like appearance of the healthy mucosa. About the middle of the lesser curvature there is an old cicatrix, plainly shown by four or five radiating lines. In the pyloric zone, the mucosa is more vascular and decidedly thicker. Scattered over the surface of the membrane, particularly in the central zone, are numerous small, grayish-white elevations the size of a pin's head, most of them isolated, others in groups, and contiguous ones are joined by narrow lines of tissue projecting half a millimetre above the surrounding surface. Toward the pylorus there are larger, more flattened elevations, separated from each other by shallow areas of a pale gray aspect. With a low-power lens small orifices can be seen in these flattened elevations, and here and there in the smaller nodular projections little orifices and tiny cysts can also be seen. The general surface of the mucosa as examined with a hand lens, has a smooth cuticular appearance; the thin mucosa is readily movable on the muscularis; the submucosa does not appear thickened; and, with the exception of the pyloric region, there is no thickening of the muscular coat.

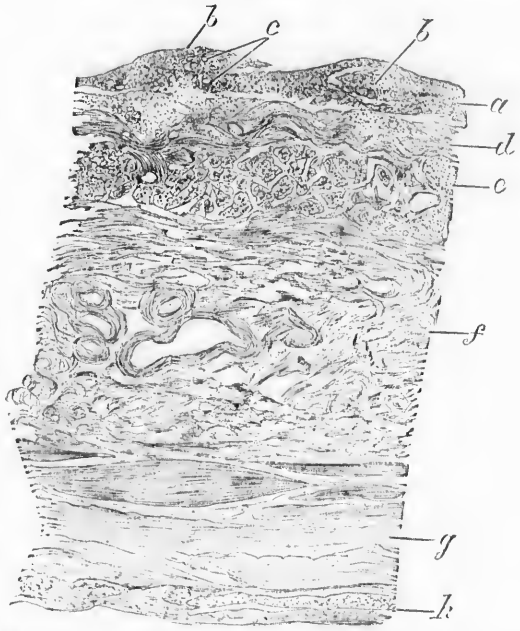
The œsophageal mucous glands are unusually distinct. *Duodenum* contains a bile-stained mucus. Bile flows freely from the orifice of the duct on compression of the gall-bladder. *Small intestines* contain a thin mucus. The walls of the jejunum look of average thickness; those of ileum thin. Peyer's gland, in the portions examined, normal. The large bowel was not opened. *Liver* looks large, is of a light yellow-brown color; capsule presents patches of thickening. Tissue cuts easily, and contains very little blood. Gall-bladder distended with pale bile. *Pancreas* very large, weighs more than 100 grammes; looks natural, lobules distinct; on section, presents a very normal appearance. *Thoracic duct* normal. The *thoracic* and *semilunar ganglia* have a natural appearance. No enlargement of the *bones*. *Marrow* of ribs and sternum of a deep purple-red color. That of lower portion of right tibia lymphoid, the cancellæ at the end of the bone contained fat.

Brain not examined.

Histological Examination.—*Stomach*. Portions were taken from four different parts and hardened in alcohol. (1) From fundus, where the mucosa looked thinnest and had a very smooth, cuticular appearance. Entire thickness of section about 3.5 millimetres, of which

scarcely one-half is made up of the muscular coat. Neither glandular nor epithelial elements of the mucosa occur in the section, but immediately upon the muscularis mucosæ there is a narrow layer (Fig. 2, *a*) of flattened and small round cells, embedded in an indifferent matrix. In the stained preparation the nuclei of these cells are distinct, but the outlines are feebly marked. The muscularis mucosæ shows a remarkable alteration. There are two distinct layers, in the innermost of which the cells are cut longitudinally and form a prominent wavy band of fibres, which are marked even under low powers (Fig. 1, *d*, Fig. 2, *b*). From twelve to fifteen muscle cells can be counted in this band, which varies somewhat in thickness in different places. Below it, forming a much thicker and not so sharply defined layer, are the transverse fibres of the muscularis mucosæ, seen in cross-section, arranged in bundles and groups, separated by more or less connective tissue (Fig. 1, *e*, Fig. 2, *c*). They

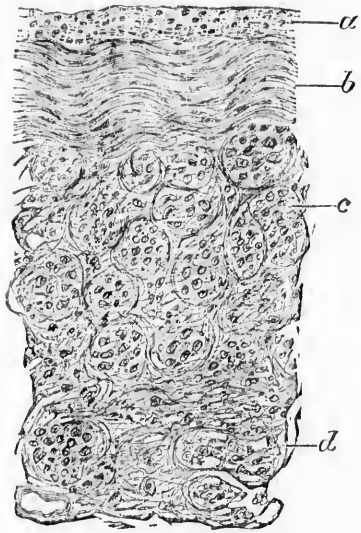
FIG. 1.



Section through mid-zone under low power, showing relations of the layers. *a*, mucous membrane with two of the nodular projections, *b*, *b*; *c*, remnants of tubules; *d*, muscularis mucosæ, fibres cut longitudinally; *e*, muscularis mucosæ, fibres cut transversely; *f*, submucosa; *g*, inner, *h*, outer layers of muscular coat. Low power. Ocular A. Obj. one and one-half inches.

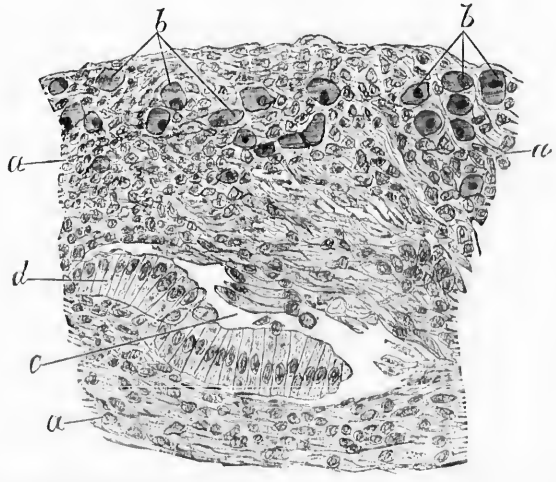
extend for some distance into the submucosa, and in places there are alternate layers of transverse and longitudinal fibres below the distinct band above mentioned. The submucosa (Fig. 1, *f*) presents coarse fibre

FIG. 2.



Section of mucosa of fundus. *a*, remnants of glandular layer; *b*, inner band of muscularis mucosæ, fibres cut longitudinally; *c*, outer layer of muscularis mucosæ, fibres cut transversely and arranged in bundles; *d*, beginning of submucosa. Ocular A. Obj. one-fifth inch.

FIG. 3.



Portion of one of the nodular projections of mucosa, under high power. Ocular A. Obj. No. 8. *a*, the small-celled infiltration; *b*, large spheroidal cells with eccentric nuclei, the remnants of the peptic cells; *c*, portion of a tubule with cylindrical epithelium; at *d*, the cells were displaced.

cells and is loosely connected to the muscular coat. The bloodvessels are numerous and large and the walls of the arteries are much thickened. The muscular layers (Fig. 1, *g* and *h*) appear normal. The muscle cells do not look so large, nor are they as well stained or well defined as those in the muscularis mucosæ.

(2) Portion of the middle zone of the stomach in which are the nodular projections. The sections, which are from three to four millimetres in thickness, present essentially the same features as those from the fundus, but the small projections offer special features of interest. They are in reality remnants, or islets, of mucous membrane left in the general atrophy, and in them can be seen fragments of gland tissue. Even on inspection of the fresh organ with a low-power lens this seemed apparent, for in these portions and nowhere else could the orifices of tubules be seen. These portions are flattened, mushroom or pear-shaped, pyramidal or even pedunculated. Three tissue elements can be seen in them: (1) a basis or matrix of small round cells (Fig. 3, *a*) which stain deeply and give a very pronounced color to these parts; (2) large rounded epithelioid cells with eccentric nuclei, resembling, though somewhat larger than the normal gland cells of the peptic tubules (Fig. 3, *b*, *b*); (3) remnants of the tubules (Fig. 3, *d*), chiefly of the uppermost portions, with columnar epithelium. In many sections these tubules are represented as empty spaces (Fig. 1, *e*) from which the cells have fallen, in others they are still present. A normal-looking tubule was not seen, only portions; in places cystic dilatation seems to have occurred. At the base of the projections the small-celled infiltration is very dense and abuts directly in the longitudinally cut band of fibres of the muscularis mucosæ. Between two of these nodules, the mucosa has the appearance described in section 1.

(3) Flattened elevations in the pyloric region 5 or 6 centimetres from the ring, which were 5 or 6 millimetres in diameter, and stood out distinctly surrounded by areas of pale gray mucosa. With the low-power lens the orifices of peptic tubules can be plainly seen. On section, the columnar epithelium of the surface is seen in a few places. The tubules are distinct, particularly in the central portion of the patches, but the amount of small-celled intertubular growth is very great, and toward the margins it becomes the preponderating tissue, and a peptic tubule is only here and there noticeable. The cells of the tubules look normal in the central portion of these elevations, but toward the periphery they can be seen in all stages of atrophic degeneration.

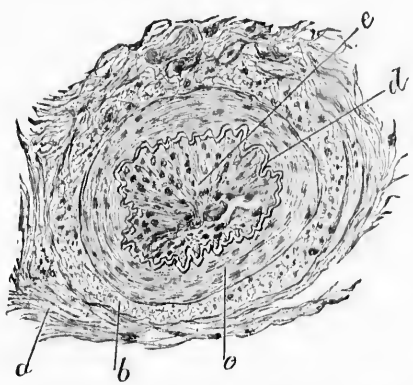
(4) Portion from the neighborhood of the pylorus. Thickness of section nearly six millimetres. Epithelium not apparent on the surfaces. The tubules are numerous and large, with normal-looking epithelium. There are groups of closely set glands, but in most places the tubules are separated by the small-cell infiltration, which in certain regions, corresponding doubtless to the interspaces between the mammillations, occupies the entire thickness. Small cysts also occur in this region. The muscularis mucosa is thicker here than in the sections described under (3).

The arteries in the submucosa presented thickened walls, particularly the muscular coat, and in almost every section vessels could be seen in process of obliteration by subintimal proliferation, as represented in Fig. 4.

Bits of the fresh mucosa from various parts were teased carefully in salt

solution. Except in the pyloric zone, no tubules or cylindrical epithelium were found. In some of the nodular projections remnants of gland tissue and a few columnar cells were seen. Gentle scrapings of the surface and the teased bits show a large number of flattened cells, unlike anything

FIG. 4.



Section of a small artery in submucosa. *a*, stroma; *b*, adventitia; *c*, muscularis; *d*, elastic lamina of intima; *e*, proliferation of subendothelial connective tissue, resulting in almost complete obliteration of the lumen of the vessel.

met with in the normal mucosa. They are irregular in shape, longer than broad, with granular protoplasm and central nuclei. The average measurements of a number gave $\frac{1}{1280}$ to $\frac{1}{853}$ of an inch in length, and $\frac{1}{2560}$ to $\frac{1}{1280}$ of an inch in breadth. Some of these are remarkably long; measurements of four gave $\frac{1}{2133}$, $\frac{1}{3200}$, $\frac{1}{2844}$, and $\frac{1}{2560}$ of an inch, and from $\frac{1}{800}$ to $\frac{1}{1000}$ of an inch in breadth. Many of the cells, particularly in the pyloric region, look like swollen glandular epithelium of the peptic follicles. Flat ribbon-like muscle cells are numerous in all the portions examined, and there is a distinct fibrous stroma thickly beset with cells. Throughout this there are in places groups of rounded, translucent bodies, resembling the amyloid corpuscles met with in degenerating tissues.

Sections of the *duodenum* show many normal-looking tubules, but here, too, the amount of intertubular tissue seems excessive. Brunner's glands look healthy.

Unfortunately, by an oversight, portions of the jejunum and ileum were not reserved for examination.

Pancreas. Cells of the acini very granular, but otherwise normal; in places there are dark brown pigment grains. The interacinous connective tissue is slightly increased.

Heart muscle very fatty, but the degeneration is unequally distributed, as is evident, indeed, macroscopically. The brown pigment granules are very abundant in many fibres.

Liver. Cells distinct, moderately fatty. Small brown-red pigment

grains very abundant both in the gland cells and in the connective tissue elements.

Kidneys. Epithelium of cortical portions swollen, and in places very fatty. The reddish pigment granules are very numerous, both in the convoluted tubes and in the epithelium of the loops of Henle, and in some of the collecting tubules.

The *bone marrow* presents the usual constituents of this tissue. There is very little fat; the marrow cells of various sizes make up the chief part, but the ordinary red corpuscles are abundant, and many of them are very large (megalocytes) Nucleated red corpuscles occur in numbers. There is no essential difference between the marrow of rib, sternum, and tibia, except that in the last-named bone the cancellæ at the end contained fat.

Sections of the *semilunar ganglia* show deeply pigmented nerve cells and an excess of connective tissue.

SUMMARY.—*Clinical.* History of drinking habits for many years. Ten years ago severe gastric symptoms with great loss of flesh. For more than nine months severe symptoms of anæmia, with nausea, occasional diarrhœa, and irregular fever. Corpuscles greatly reduced, sinking to 315,000 per cubic millimetre. Transfusion; death.

Anatomical. Extreme anæmia, with the usual fatty changes in the organs and hyperplasia of the marrow of long bones. Atrophy of mucous membrane of the stomach, with complete destruction of the secretory tubules in the larger part of the organ. Hypertrophy of the muscularis mucosæ.

REMARKS.—The patient with the foregoing clinical history presented a vivid picture of progressive pernicious anæmia. Every symptom was present in bold relief: the excessive pallor and prostration, the anæmic fever, the retinal hemorrhages, and, above all, the extreme reduction in the number of the red globules, with, at the same time, a normal *proportion* of hæmoglobin, the alterations in the size and shape of the globules (poikilocytosis), and the presence of microcytes in abnormal amount. The most prominent symptoms were those of profound gastric disturbance, due to the prolonged abuse of alcohol, and the rapid diminution of weight. In less than one year the patient lost more than one hundred and fifty pounds. This is by no means the first case of pernicious anæmia to which gastric disorder stands in causative relation. Similar cases have been reported by Fenwick,[1] Quincke,[2] and Nothnagel,[3] through which a bright light has been thrown upon the pathology of this hitherto obscure disease, and it is for this reason that exception is now taken to the indiscriminate application of the term "idiopathic" to cases of progressive pernicious anæmia. The rapid loss of flesh may be regarded from another point of view than that of symptomatology. It is a well-attested fact that fevers, inflammatory and essential, are of more serious import in fleshy, so-called plethoric individuals, than in those of sparer habit, and, in explanation, von Recklinghausen[4] sug-

[1] Atrophy of the Stomach, 1881.
[2] Volkmann's Sammlung Klin. Vorträge.
[3] Deutsches Archiv für klin. Med., Bd. xxiv.
[4] Deutsche Chirurgie, 1883, Bd. i. p. 180.

gests that the rapid absorption of fat and the products of fatty metamorphosis may give rise to a qualitative change in the composition of the blood.

The conservation of the muscular strength is also worthy of notice in this and other cases. On August 15 the patient walked two miles without fatigue, when there were less than 2,000,000 red globules per cubic millimetre. A patient of Laache, of Christiania, walked three kilometres (more than two miles), the entire distance being *up hill*, when his blood contained less than 1,000,000 globules per cubic millimetre.[1] Such facts acquire additional significance when taken in connection with the deep red color of the muscles in these cases. It would appear that the muscles in pernicious anæmia are nourished at the expense of the other tissues.

All attempts at treatment in this case were rendered nugatory by the irritable state of the intestinal tract and by the patient's wilfulness and perversity in regard to matters of diet. Leaving out the blood examinations in which he always took a keen interest, it was impossible to secure his coöperation in any diagnostic or therapeutic procedure. Although repeatedly requested to save the urine secreted during the whole twenty-four hours, in order that its percentage of urea might be estimated, he only managed to do so once. On this occasion (June 26) the amount was 45 oz.; sp. gr., 1.012; percentage of urea, 2.05 (normal). There was no albumen.

The only special lesion in the case was the atrophy of the mucous membrane of the stomach. This was evident to the naked eye in the thin, cuticular appearance, and was abundantly confirmed by the microscopical examination, which showed that the peptic glands had been destroyed over the greater portion of the organ. The numerous small elevations which existed in the middle zone, represented areas of the mucosa less advanced in degeneration, and are comparable to the nodules of relatively normal tissue which beset the surface of a cirrhotic liver. Toward the pylorus, where the atrophy was less advanced, the various stages of the process could be traced, consisting essentially in a small-celled infiltration between the tubules, such as occurs in all forms of slow interstitial inflammation; and we may reasonably conclude that this process, extending over many years, ultimately led to the condition here described. The only other alternative is the supposition that a creeping ulceration had at one time involved the greater part of the mucosa, with the exception of the little islets of tissue already mentioned, and in healing had left the membrane in this state. The radiating cicatrix at the lesser curvature no doubt indicates that the patient had had, at one time, probably in 1877, when the gastric symptoms were so marked, an

[1] Die Anämie, S. Laache, Christiania, 1883, p. 147.

ulcer in this region, but the uniform, smooth appearance of the membrane, the absence of puckering, and the condition of the muscularis mucosæ, are not consistent with the view that there had been extensive ulcerative destruction, such as in rare cases does involve the stomach. In these instances, the process is not confined solely to the layer of tubules, but involves the muscularis mucosæ, which is infiltrated with round cells, and in healing the mucosa and submucosa are closely united to each other. Except at the site of the cicatrix, the mucous membrane was in this case freely movable on the muscular coat. The remarkable hypertrophy of the muscularis mucosæ is an associated condition not easy of explanation, but we call to mind in this connection the increase in the unstriped muscle elements in other conditions associated with irritation or degeneration, as notably in the lung of the cat affected with the nematoid parasite Ollulanus; and in the bronchial tubes of man in some cases of chronic bronchitis.

The recorded cases of atrophy of the stomach with clinical features of pernicious anæmia are not very numerous. Fenwick[1] describes four cases, Quincke[2] one, Nolen[3] two, and Brabazon[4] one; and in all of these the mucous membrane was affected without special alteration in the thickness of the walls of the stomach, or any diminution in its capacity. Nothnagel's case was one of cirrhotic contraction of the stomach and atrophy of the peptic glands, with the clinical features of pernicious anæmia. In some of these cases the histological examination was very defective, and the exact condition remains doubtful. In Fenwick's cases the interstitial connective tissue was greatly increased, and the gland tubules atrophic, but there was not the extensive destruction of the glandular layer which was so marked a feature in our case. The histological account in Nothnagel's case, by W. Müller, makes it clear that there was complete atrophy of the tubules in the entire organ, with the exception of the pyloric region. There was great thickening also of the muscularis mucosæ.

It seems natural to conclude that in the case we have described, the abuse of alcohol, extending over many years, played a part in the causation of the atrophy. Certainly he had chronic dyspepsia, and had suffered from a gastric ulcer; but while these not uncommon conditions may lead to moderate wasting of the mucous membrane, such extensive destruction of tubules is rarely seen. In the cases narrated by Fenwick there was no history of alcoholism. In connection with the extensive endarteritis of the smaller gastric vessels, and the existence of scars on the glans penis and in the groins, the possibility of a syphilitic process may be considered, but we know as yet very little of the influence of syphilis on the stomach, and the recent attempt of Gaillard[5] to connect

[1] Loc. cit. [2] Loc. cit. [3] Centralblatt f. d. med. Wissenschaften, Bd. xx.
[4] Brit. Med. Journal, 1878, ii. [5] Archives Générales, January, 1886.

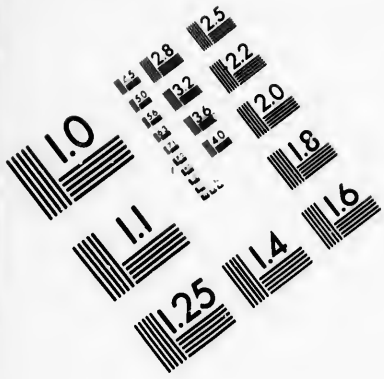
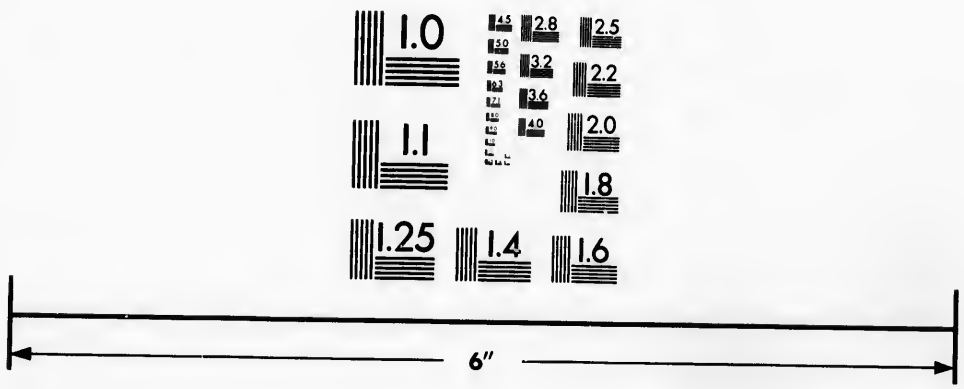
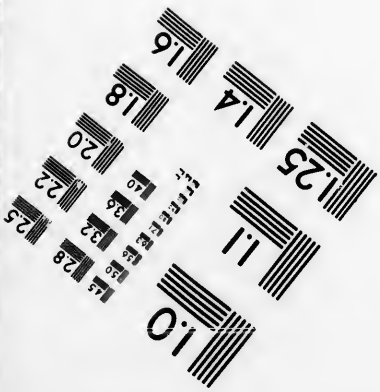
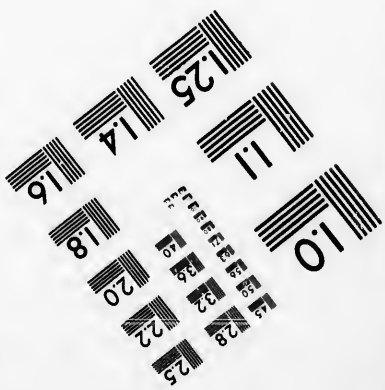


IMAGE EVALUATION TEST TARGET (MT-3)







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certain forms of gastritis with this disease cannot be regarded as in any way successful. It is quite possible, however, that the state of the small arteries may have had something to do with the production of the atrophy. We have learned of late years to connect indurative processes in other organs with arterio-sclerosis and the endarteritis of the nutritive vessels of the mucosa may really have played an important part in inducing the wasting. In a recent review of this subject, Martin[1] suggests that certain lesions of the mucosa may be due to these end-arterial changes, but acknowledges that, with regard to the stomach, the facts are as yet too few to warrant any conclusions.

To the other anatomical features of the case we do not propose to refer. The reader will doubtless have noted the identity of the conditions with those in pernicious anæmia, even to the hyperplasia of the bone marrow and the pigmentation of the cells in the organs. One point, however, is worthy of note, viz., the large size and healthy appearance of the pancreas. This organ varies greatly in size, but we regard it as certainly hypertrophied in this case, and we may see here possibly a compensatory effort to supply the defects in gastric digestion.

A careful study of this case justifies, we believe, the conclusion that a primary atrophy of the mucous membrane of the stomach does occur; and it further bears out the original suggestion of Flint, confirmed by Fenwick, Nothnagel, and others, that certain of the cases of progressive pernicious anæmia depend upon profound alterations in the gastric tubules.

For the sections and drawings we are indebted to the skill of Dr. J. P. Crozier Griffith.

[1] Revue de Médecine, January, 1886.

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CARTWRIGHT LECTURES.

ON CERTAIN PROBLEMS IN THE PHYSIOLOGY OF THE BLOOD CORPUSCLES.

Delivered before the
Association of the Alumni of the College of Physicians and Surgeons, New York, March 23d, 27th, and 30th, 1886.

BY

WILLIAM OSLER, M.D.,

FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS, LONDON; PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

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LECTURE I.

THE BLOOD PLAQUE.

Introduction.—Around the blood corpuscles still centre some of the most interesting questions in physiology and pathology, and though amid microbes and cultures we may have forgotten them for the moment, they are nevertheless still calling for solution, and perplexing this quite as much as any one of the six or seven generations which have passed away since Loeuwenhoek first detected the red corpuscles in the human blood.

The origin and life history of the corpuscles of the blood have been, and still are, among the great secrets of physiology. Strange, indeed, is it to think of the thousands of able observers who have gazed long and ardently, with rude and with perfect instruments, vainly endeavoring to solve the riddle constantly propounded by these common objects of study. In no department of physiology has so much labor been spent with so little apparent result. While in other lines we have penetrated to the centre of certain biological mysteries, the progress here seems painfully slow, and the discovery by Wharton Jones, in 1846, of the amœboid power of the colorless corpuscles, the rediscovery by Cohnheim of their migratory power, and the discovery of the blood-forming function of the marrow, may be said to be the most important additions to our knowledge in this generation.

The activity of research during the past decade has had, however, a perceptible influence, and there are signs of breaking in the heavy clouds which ove.hang the origin of these corpuscles, and the darkness is certainly less dense than it was.

A peculiarity of these perennial problems is that cer-

tain phases for the time engage the attention of observers, and the laboratory activity the world over seems centred upon them, with the result, in a few years, of an enormous increase in the literature. After the question has been thoroughly fought out and quiet is resumed, we are thankful if only an outpost has been gained in the struggle and we are a step nearer to the citadel of truth.

As regards the blood corpuscles, the work of the past few years has been largely in two directions—toward the determination of the existence or non-existence of a third corpuscle in the blood, and in the study of the histological processes attending degeneration and regeneration of the corpuscles in disease, and upon these subjects I shall hope to engage your attention during this course.

I propose, therefore, in the first lecture to consider the much debated third corpuscle, or hæmatoblast of Hayem, which, so far as I know, has not yet received systematic consideration before any American or English audience. In the second I shall discuss certain histological problems connected with the degeneration and regeneration of the blood corpuscles; and in the third I shall present a statement of recent views on the relation of the corpuscles to coagulation.

THE THIRD CORPUSCLE OR BLOOD PLAQUE.

Definition.—A colorless protoplasmic disk, constant in mammalian blood, measuring from 1.5 to 3.5 micromillimetres. The number per cubic millimetre in the blood of a healthy adult is about 250,000, but their number varies greatly at different periods of life and with varying conditions of health and disease. The ratio to the red is about 1 to 18 or 20. They are delicate elements, and, like the red corpuscles, tend on the withdrawal of the blood to adhere to one another, when they form the irregular granular clumps which have long been known as Schultze's granule masses.

Name.—It will be necessary, at the outset, to refer to the names which observers have given to this corpuscle. Unfortunately they are rather numerous, and no one of them entirely satisfactory. Donné,[1] whose description

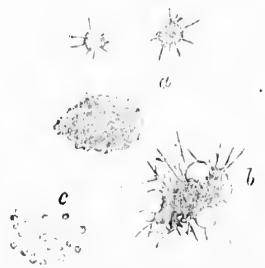
is the earliest, called them *globulins*. Zimmerman[2] spoke of them as *elementary corpuscles*. Later, the collected groups were referred to as "*granular débris*" or Schultze's[3] *granule masses*. Among the more recent observers, Hayem[4] gave the name of *hæmatoblast*, and Bizzozero[5] that of *blutplattchen—blood-plate*. Various writers refer to this element as the *third corpuscle*, while in the research of Kemp,[6] just issued from the Biological Laboratory of Johns Hopkins University, the term *plaque* is used and has received the sanction of Prof. Martin. To the terms *third corpuscle* and *hæmatoblast* there is the serious objection that these names have been applied to other bodies which have nothing to do with the elements in question. The former, to the so-called invisible corpuscle* of Norris, and the latter to the nucleated red corpuscle of the bone marrow. The name hæmatoblast, moreover, carries with it certain theoretical conceptions regarding the functions of these bodies which may or may not be true. I am inclined to favor the name which Bizzozero has adopted, partly because we are indebted to the distinguished Turin Professor for a series of able researches which hav awakened the liveliest interest in these corpuscles, and partly because usage of late has confirmed the name. Blood-plate, the English equivalent of the word *blutplattchen*, is by no means euphonious, while the French *plaque*, adopted by Kemp, is perhaps more convenient and might be employed in the future by American and English writers.†

* Shortly after the publication of Bizzozero's paper, Norris claimed that the corpuscles described in it were the same as the barely visible corpuscles of his "fugitive group," but a study of the beautiful photographs in his book, will, I think, convince anyone with a practical knowledge of the blood plates of Bizzozero, that they are separate elements. The granules which he figures (Fig. 45) as resulting from the breaking up of the younger or fugitive corpuscles are in reality the disintegrated blood-plates. Moreover, the corpuscles which he figures are uniformly larger than the blood-plates.

† I did think of suggesting the word *disklet* as very suitable for these *little disks*, but I had not the courage to add another to the already long list; moreover, as my own name has been used in connection with these bodies, I felt absolved from further sponsorial duties on their behalf.

Methods of Study.—Let us first consider the plaques in blood examined in the usual manner, without the addition of any reagent; and let us suppose the blood to be taken from a case of consumption or cancer, or from a newborn animal, as in these states these corpuscles are abundant. We then find, in addition to the red and colorless corpuscles, many grayish-white granular masses of various sizes and shapes. Examined at once, and if too much pressure is not exercised by the top-cover, the edges of these masses are clearly defined and they form compact aggregations. With a power of 500 diameters, the composite structure is well seen and the granular character is plainly discernible to be due to

FIG. 1.



a. Aggregations of plaques in human blood, forming the so-called *granule masses* of Max Schultze. *b.* Disintegration of the plaques, with fibrin filaments and mucin-like spheres adhering to the mass. *c.* Isolated plaques.

the agglutination of numerous small bodies of uniform size. At the edges, isolated or partially free corpuscles can usually be noticed. The fibrin filaments, as coagulation proceeds, seem to radiate from the masses as centres. This remarkable conglutination of the plaques and a tendency to undergo rapid change have retarded greatly the recognition of the corpuscles as veritable elements of the blood. Observers have, as a rule, seen in them nothing more than a granular débris of no special significance. Nor is this to be wondered at, as they so quickly undergo change that the clusters, in the course of a short time, really present the appearance

of disintegrating protoplasm (Fig. 1, *b*). The size and shape of the groups are most variable; the more abundant, as a rule, the plaques the larger and more numerous the aggregations; the smaller ones, composed of two or three plaques, may not equal in size a red corpuscle, while the larger ones may be ten or fifteen times this size. A tendency to adhere to foreign particles is very noticeable, and they will collect in numbers upon a fine thread of cotton or linen. In the normal blood of the adult the plaques are not very numerous, and so do not form very large collections. In some individuals, however, in health the groups are always of considerable size. There are conditions of the blood in which, from some cause, the attraction of the plaques to each other appears diminished, and instead of forming large masses, they adhere to the slide either isolated or in scattered groups of from two to ten in number (Fig. 1, *c*). Possibly this may be an accident of preparation, but I am inclined to think it not, from the fact that I have noted it in cases of malignant fever, smallpox, scarlet fever,—the very states in which the normal process of nummulation of the red corpuscles may be so altered that the cells aggregate into compact clumps. In fact, the red corpuscles and the plaques in normal blood have each their peculiar mode of aggregation, the red in series and the plaque in masses. I have never seen any appearance which would suggest that the plaques have the slightest tendency to adhere by their flat surface, and to form roulcaux, as the red. It will be found too, I think, that just as there are, apart from modes of preparation, peculiarities which interfere with the normal nummulation of the red, so there are conditions in which the plaques present variations in their usual method of aggregation.

It was a consideration of the relative size of the masses, and the impossibility of their passing through the capillaries, which led me in 1873, in University College Laboratory, London, to the discovery of their corpuscular nature; and it was found that while in the blood of the young rat, when withdrawn, the masses were numerous and large, in the bloodvessels the collections, as such, never occurred, but innumerable small corpuscles, similar in character to those seen at times so plainly at the edge of the masses.

To study the plaques properly, the blood must be allowed to pass directly into a solution which, while preventing conglutination, does not materially alter their form or characters. Or they may be, perhaps, more satisfactorily observed while still within the bloodvessels.

Various solutions have been employed by different observers. Zimmerman, whose study of these corpuscles was really very complete, allowed the blood to flow directly into a solution of a neutral salt which prevented coagulation, and then in the supernatant fluid he found small colorless cells in extraordinary numbers. I have repeatedly confirmed this observation in the case of horses' blood, when demonstrating the common experiment of preventing clotting, by letting the blood flow into sodium sulphate. The plaques abound in the clear serum, and if the solution is not too concentrated they are very little altered. In using the hæmatocytometer (Gowers), the sulphate of soda with which the blood is mixed acts in the same way, although in the counter it is more common to find the plaques aggregated than isolated, but the individual plaques are unusually distinct. More suitable solutions for histological purposes are osmic acid 1 per cent., the fluids of Pacini, modified by Hayem, and of Bizzozero. Pacini's solution, as used by Hayem, consists of sodium chloride 1 part, sodium sulphate 5 parts, corrosive sublimate 0.5 part, in 200 of distilled water. Bizzozero employs the ordinary salt solution, ¾ per cent., to which methyl-violet has been added. Afanassiew[10] recommends strongly the use of salt solution to which 0.5 per cent. of dried pepsin has been added, and 1 to 1000 of methyl-violet, and a small amount of sublimate or carbolic acid to prevent decomposition. I find that the Pacini fluid and osmic acid answer every purpose, and in them the plaques undergo very little change. The examination is made in the following way: Upon the thoroughly cleansed finger-pad a single drop of the solution is placed, and with a sharp needle, or pricker, the skin is pierced through the drop, so that the blood passes at once into the fluid, which is then received upon a slide and covered. The withdrawal of the corpuscles into the solution prevents the plaques from aggregating, and they remain as isolated and distinct elements. The amount of blood allowed to flow into the drop must not be large, and should be quickly mixed.

In many respects the most suitable medium is osmic acid, ½–1 per cent., which has the advantage that by its use permanent preparations can be obtained. The various cells are at once fixed, and the plaques are, by this method, very well preserved. Good preparations may also be obtained by spreading rapidly a thin film of blood on a top cover, and then placing it at once in the osmic acid. Still another method is to dry the blood in the thinnest possible layer, and then fix with osmic acid or stain with methyl-violet, and mount in balsam. Kemp recommends placing the blood drop on a top cover, rapidly moving it about, and then washing off the superfluous blood with salt solution. The plaques adhere to the cover, while the red cells are swept away. The cover is then quickly put in osmic acid.

For the study of the plaques in the circulating blood, the mesentery or omentum plate must be employed, and similar measures adopted to those used in the study of the circulation of the blood in mammals. The half-grown rabbit, white rat, or guinea-pig will be found best adapted for this purpose. The chief difficulties arise from the amount of fat which, in some instances, obscures the vessels, and the rapidity of the current may render it hard to see the plaque. But when, as in the omentum, a small transparent vessel is found, in which the current is slow, then with the red and colorless corpuscles the smaller plaques are also seen (Fig. 2). In Bizzozero's paper, and in the recent communication of

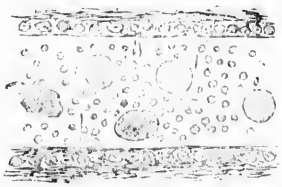
FIG. 2.

Plaques in circulating blood, omentum of guinea-pig. 18, 1, '83.

Eberth, full directions are given for the study of the plaques in the circulating blood. They are modifications of the original Sanderson-Stricker method (*vide*

Sanderson's *Handbook*), which answers every purpose in the case of the guinea-pig, the omentum of which is a peculiarly suitable object. In the rapidly flowing current no plaques are distinguishable, but when the stream is slow they can be seen here and there in the still layer with the white corpuscles, while if the current becomes very feeble they tend to collect at the periphery with the leucocytes. In a small venule, where the stream is slow, and only a few corpuscles passing, the best opportunity is afforded of seeing the plaques. They may be well studied within the vessels in the recently killed animal, or in man, in portions of tumors, etc., recently removed. The subcutaneous tissues of the newborn rat afford perhaps the very best situation in which to study the plaques while within the vessels. The rat is killed with a snip of the scissors through the spine, and then portions of the mucoid connective tissue spread thin upon the slip, either with or without saline solution. In the thin transparent vessels, the plaques are very distinct, and they remain unchanged for hours. Perhaps there is no better mode of studying these forms, as the thin walls offer no impediment to the view, and the plaques are in their natural medium. In the subcutaneous tissue of man I have had several opportunities of examining the plaques in this way, and Fig. 3 represents

FIG. 3.



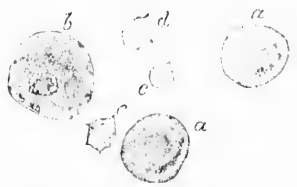
Plaques in small artery from subcutaneous tissue of scrotum of man, one hour after removal. Case of elephantiasis. 20, 11, '85. They had collected in numbers at this portion of the vessel.

them in a vessel of the tissue of the scrotum an hour after its removal. In the smaller vessels of the pia mater they may also be seen.

General Characters and Structure.—The plaques are minute elements circulating in the plasma with the other

corpuscles, and possessing such specific and distinct characters that they must be reckoned among the normal histological constituents of the blood.

FIG. 4.



Isolated plaques in normal blood. Osmic acid 1 per cent.; one-twelfth im. (Zeiss). *a*. Red corpuscles. *b*. A white corpuscle. *c. c*. Plaques with slightly irregular margins. *d*. Plaque with faint granular appearance in centre as if nucleated.

The plaque is colorless, with a uniform grayish-white appearance, homogeneous or very finely granular, and presents no differentiation in the delicate protoplasm of which it is composed. So far as my observation goes, it is always colorless.

The *size* is variable. In man they may be said to measure from 1.5 to 3.5 micromillimetres, or from about one-sixth to one-half the size of a red blood-corpuscle. The majority of them are from 1.5 to 2.5 μ. Occasionally a plaque may be seen measuring as much as 5 micromillimetres, but this is exceptional. When they are abundant, remarkable gradations in size may be measured between the smallest and largest forms. They have not the constancy in size of the red corpuscle. I think in man, when very abundant, the average size is slightly less than when they are not so numerous. They are stated to bear in size some relation to the size of the red corpuscle of the animal, but we need a more elaborate series of measurements to determine this. In the white rat they are slightly smaller than in man.

The shape of the normal plaque, as seen in the vessels, is a circular disk with smooth, well-defined margin. When slightly tilted it has naturally an ovoid appearance, and when seen in profile is as a narrow, straight rod or staff. Whether they are flat disks, or biconcave,

as the red corpuscles, is really not easy to determine. I should say that the majority do not show a bilateral depression, but forms are sometimes seen which resemble in outline very closely miniature biconcave disks. Alterations in form quickly occur when the blood is withdrawn; but the natural shape, as seen in the vessel, and also, as a rule, in Pacini's fluid, or osmic acid, is as here stated.

The plaque consists of a homogeneous, smooth, structureless protoplasm of a light gray color. In the unaltered condition no nucleus can be seen, but in the fluids used to conserve them the appearance is in the form of a collection of distinct granules, which may look like a nucleus. This will sometimes, in dried preparations, stain a deeper color in the hæmatoxylon than the remainder of the plaque, and it is regarded by Hayem as a nucleus.

Changes in the Plaques.—Outside the vessels the plaques are characterized by two peculiarities which have been a serious hindrance to their recognition as special elements of the blood, viz., the rapidity with which the protoplasm alters and the tendency to adhere to one another and to any substance with which they may come in contact. Within the vessels, however, they do not seem to be more prone to rapid decay than the red or white corpuscles, and in the young rat, kept at ordinary

FIG. 5

a

a. Changes in appearance of the plaque, due to separation of its protoplasm into a darker and clearer portion. *b* Alterations in form of plaques examined in blood serum and watched for three hours.

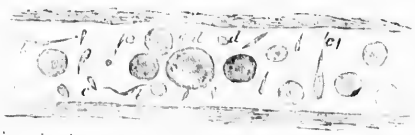
temperature, I have seen them in the vessels quite distinct and clear twenty-four hours after death. So also I have found them unaltered in the vessels of the pia mater in man, some hours after death; and, as I shall have occasion to show in the third lecture, they may in masses remain apparently unchanged for some time.

The substance composing the plaque appears homo-

geneous when first seen, but soon a change occurs, and the plaque presents a darker, more highly refractile portion and a clearer substance. Usually this darker portion is peripheral, but it may be central, and then is not unlike nucleus. It is as if a material had separated from the stroma or bases of the plaque, just as the hæmoglobin of the red corpuscle may do under the influence of reagents. The plaques undergo the most curious changes in shape, to the study of which I devoted much time in 1873. Within the vessels they are circular, but when at rest they not unfrequently become ovoid or prolonged, or slightly angular and crenated. These angular processes may increase greatly in length, and give a stellate appearance to the plaque. The changes in form are very fully described and figured in my original paper. These alterations are probably induced by changes in the external conditions, and are not amœboid or vital in character. The addition of serum to the blood drop, and the examination in a warm stage, afford the best means of studying the variations in form. Even within the vessels they may show these changes, and in the course of a few hours alter in a remarkable manner so as to be scarcely recognizable.

A very common change is the separation from the plaque of a mucin-like (?) material in the form of a pale sphere, which may remain attached to the cell or separate from it. When aggregated in masses, as in a slide

FIG. 6.



Alterations in the plaque while within the bloodvessels, sketched after three hours on the warm stage. 6, 4, '73.

of fresh blood, this process can be readily seen at the margin, and the field in the vicinity may be covered with these pale globular bodies. They result, doubtless, from the separation of some material from the substance of the plaque, and are identical with the spheres so often seen attached to spermatozoa in urine.

In marked contrast to the stability of the plaques within the vessels is their rapid disintegration when withdrawn. At a low temperature this does not occur so quickly, and of this Hayem took advantage in his researches; but at the ordinary temperature, and in the examination of the blood without any reagent, the plaques unite with each other and undergo rapid change —a viscous metamorphosis, as Eberth[11] terms it. As I shall have occasion to point out, this is associated with the separation of fibrin which seems to arise first about the groups of plaques, as Ranvier noted in 1873, and he spoke of these little granulations—*grains sarcodique* of Vulpian—as centres of coagulation.

Action of Reagents.—This has already been referred to in the consideration of the best modes of examining and preserving the plaques. Water reacts upon them as upon the colorless elements, causing a swelling of the protoplasm and a rapid production of the pale spheres already described Dilute acid and saline solutions act in the same way. In three-fourths per cent. salt solution, or in the sodium sulphate solution for blood counting, they retain their outlines and do not so rapidly coalesce and disintegrate. Dilute potash solution causes speedy dissolution.

The aniline dyes stain the plaques as other protoplasmic bodies, and Bizzozero's fluid has the advantage of tinting them and making them more distinct. In preparations by Ehrlich's method, the tint of the central portion of the plaques may be deeper than the periphery. Carmine appears to have no effect. For permanent preparations the dry method is the best, and they may be stained with hæmatoxylon, fuchsin, Bismarck-brown, or methyl-violet. The blood in osmic acid may be kept for some days if the cover-glass is carefully surrounded with paraffine. A solution of corrosive sublimate 1 : 1000 is also suitable for their preservation. The precise chemical composition of the plaques has not been determined, but from the similarity in most points of their reaction and behavior with dyes to the nuclei of cells, we may suppose their composition to be of a similar nature.

The Number.—The numeration of the plaques presents serious difficulties, on account of their extraordinary adhesiveness and the numbers now given may be sub-

ject to revision when better methods are devised. In my own case the numbers range from 250,000 to 300,000 in the cubic millimetre, figures which correspond to those of Hayem. Full-blooded, plethoric individuals have rarely more than 250,000 per cubic millimetre. The variations in the same individual may be considerable during the day, and they seem increased after a full meal. Age has an important influence—in the infant and young child the number may be double that of the adult. In the newborn of all the mammals I have examined they were specially abundant. In advanced age they seem more numerous, particularly if the individual is weak and debilitated.

Until more extensive and more reliable counts are announced, we may say that the plaques in health number between 200,000 and 300,000, the ratio to the red being about 1 to 18 or 20, and to the white corpuscles 35 or 40 to 1. The numeration of the plaques is a much more tedious matter and requires far more patience than counting the red and white corpuscles. Rapidity is essential to success. I find the *compte globule* of Malassez rather more adapted than the Gower's apparatus, as the mixture can be more thoroughly and quickly made. The blood is got from a deep puncture and aspirated into the tube of the Potain mixer and then the Pacini's fluid or osmic acid is immediately drawn in. Frequently it will be found that, with the greatest care, the plaques have run together and the process must be repeated. It is essential, too, in the first aspiration of the blood, to reach the line at once; if the blood column goes beyond, it must be discarded and a fresh attempt made, as the time lost in accurately adjusting the column would be sufficient to allow the plaques to coalesce.

The Plaques in Disease.—In health the plaques are relatively scanty, and they aggregate into such small, scattered groups, that they do not necessarily excite the attention of the student, but every constant observer of the blood in states of disease must have marvelled again and again at the extraordinary number and size of the granule masses met with in certain cases. Led away by their constancy and peculiar character, writers have regarded them as specific and distinctive elements in certain affections (leukæmia, phthisis). From the able

and comprehensive paper of Riess to the more recent one of Afanassiew, there have been very many observations on the frequency and significance of these bodies in disease, but we still lack careful and painstaking enumerations in the various acute and chronic diseases. A rough estimate of their increase or diminution may be made by any one well accustomed to their observation, but for scientific accuracy the hæmatocytometer must be used, and means must be devised to overcome the present serious source of error.

My own observations have been very numerous, and I have for years been in the habit of noting the paucity or abundance of these elements. In the absence, however, of systematic and reliable counts the notes are not worth much. The general results I may state as follows:

1. The plaques are increased in all chronic wasting maladies—cachexiæ—with or without fever.

This is very evident by examining in rotation the various patients in a hospital ward. The debilitated individuals, the subjects of phthisis, cancer, or other chronic wasting diseases, present a marked increase. In phthisis the number per cubic millimetre may reach 500,000 or more, and the ratio of the plaques to the red may rise as high as 1 to 5.

2. In acute sthenic fevers the plaques are not increased in the early stages, but as the disease advances, and the patient becomes weaker and more debilitated, the increase is usually marked. This is well seen in typhoid fever, in which the number of plaques during the first week may not rise above normal, while in the third and fourth week there is usually a notable increase.

3. In the so-called blood diseases the number of the plaques is variable. Many observers have remarked the great numbers in certain cases of leukæmia, but in others the increase is not apparent. So, also, in lymphatic anæmia. In some cases of Hodgkin's disease I have seen the plaques in extraordinary numbers. In profound anæmia the plaques may be very scanty. I have long noted, in cases of pernicious anæmia, that the clusters of plaques may be almost absent, or much more scanty than in health.

Distribution of the Plaques in Animals.—So far as our present knowledge goes, the plaques are constant con-

stituents of the blood in mammals, and, with the exception of slight variations in size, the general features are the same in the various orders. My observations on this point have not been extensive, but I can speak of their presence in the blood of the dog, cat, mouse, guinea-pig, rabbit, sheep, ox, horse, pig.

They also occur in the ovipara, and here they are nucleated. Kemp states that in the blood of oviparous animals there is a nucleated corpuscle which is physiologically analogous with the plaque in the blood of mammals, and which behaves like it when the blood is drawn.

Origin.—Various explanations have been given to account for the origin of the plaques, and Kemp enumerates no less than seven different views. Perhaps the most prevalent idea, particularly among clinical physicians, is that they result from the disintegration and degeneration of the blood corpuscles, especially the leucocytes. This is really not unnatural, for the irregular clumps of plaques in blood examined in the ordinary way look very like—and, indeed, are—protoplasmic débris. But we know of no such process of rapid disintegration in the colorless corpuscles, which are remarkably stable elements, and even in their death and decomposition never, so far as I can make out, produce structures similar to the groups of plaques. The fact that the formation of the *granular débris*, as the groups of plaques are called, can be prevented by drawing the blood directly into a drop of osmic acid (or Pacini's fluid), in which the elements are fixed instantly, should be sufficient to convince the most sceptical; but if it does not, the study of the plaques in the newborn rat will satisfy, I think, the most obdurate. The abundance and large size of the groups of plaques in a blood drop examined in the ordinary way, and the ready demonstration of the individual elements in the blood-vessels of the subcutaneous tissue, and the identity of these with the corpuscles at the edges of the groups, and with those in the osmic acid drop, render the conclusion irresistible that we are dealing with something quite independent of the colorless corpuscle.

I am unaware of a single observation corroborative of the view that the plaques result in any way from the degeneration of the red corpuscles. We need not con-

sider the views that the plaques represent fibrin particles, or are depositions of globulin.

A majority of observers regard the plaques as independent elements in the blood, others agree with Hayem that they are young red corpuscles—hæmatoblasts—and a further discussion of this point will be best considered in the next lecture, when I speak of the regeneration of the corpuscles.

Historical.—I do not propose to enter into the literature of the blood plaque. This has already been done very fully by several German observers, and quite recently by Kemp, whose paper in the "Studies from the Biological Laboratory of Johns Hopkins University," will be readily accessible to all American and English students. In my original paper I have also given pretty fully the older references. We may conveniently divide the work which has been done in this department into three periods The first embraces the time prior to the publication of Hayem's researches in 1877. The masses had been observed frequently, and the corpuscles had been studied, notably by Donné, Zimmerman, and Max Schultze. In 1874 I demonstrated the corpuscular nature of the granule masses, and showed that the bodies of which they were composed "were present as separate elements in the vessels, and showed no tendency to adhere together." In 1873 Ranvier[9] called attention to their possible association with fibrin formation. Riess and others had called attention to their increase in disease. The second period dates from the publication by Hayem, in 1877–78, of his researches, and to him really belongs the credit of establishing the histological position of these corpuscles as constant blood elements. It is curious that his careful observations met with very slight recognition among physiologists. The interest in the question had almost died out when, in 1882, Bizzozero, of Turin, published an exhaustive article in Virchow's *Archiv* upon the *Blutplattchen*, and their relation to fibrin formation. From this we date the third period, during which there have been already published eighteen or twenty essays, chiefly in Germany, and the most intense interest seems to have been aroused in the subject. The weight of histological evidence is strongly in favor of the views which I have here laid before you, but there still re-

mains the greatest diversity of opinion as to the function of these bodies in blood development, and of their relation to the formation of fibrin, and upon these questions I shall have more to say in the second and third lectures.

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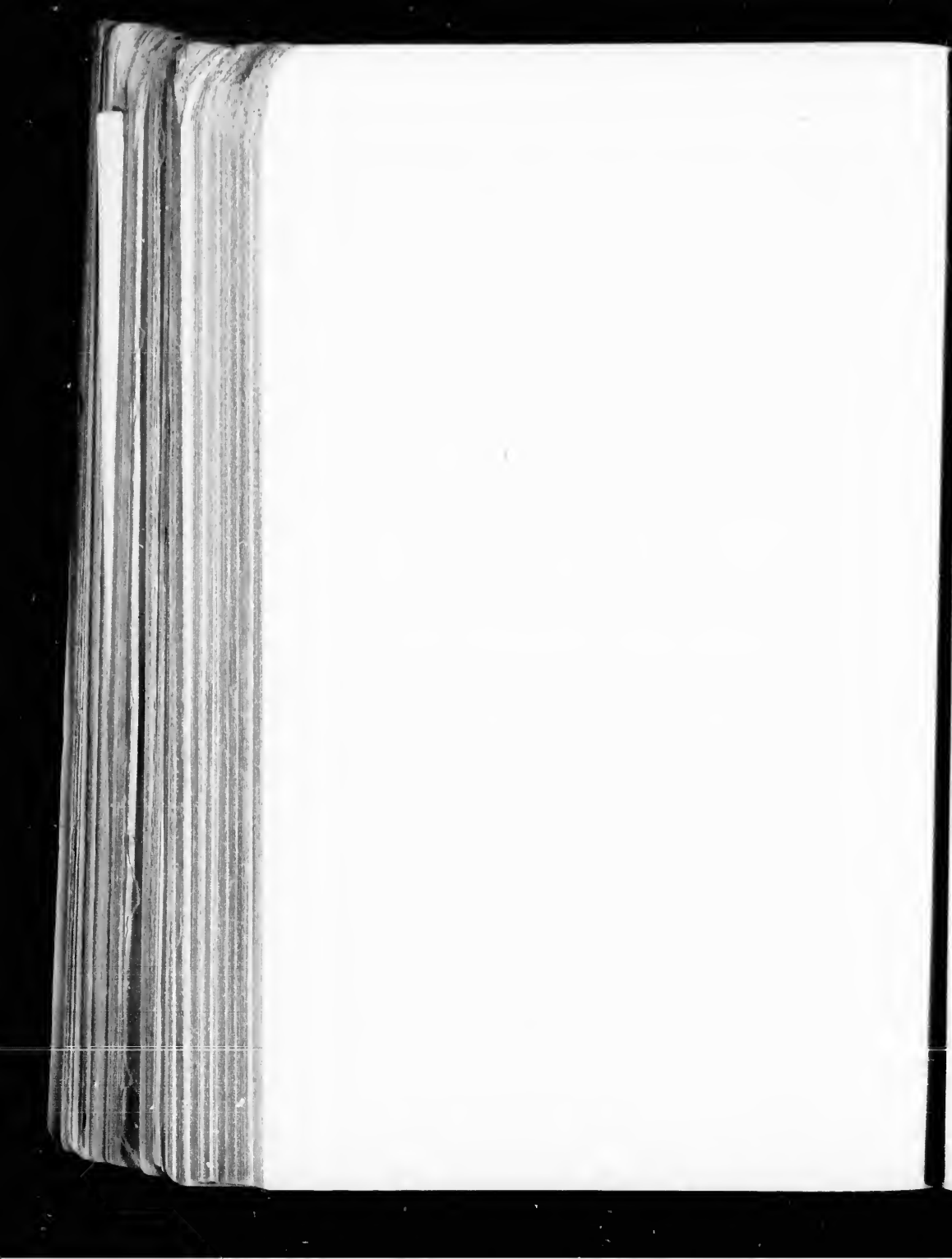


LECTURE II.

DEGENERATION AND REGENERATION OF THE CORPUSCLES.

THE conception of the blood as a fluid tissue, the corpuscles representing the cells and the plasma the matrix, is not a very happy one, as both cell elements and matrix present peculiarities unknown in any other tissue. Rather is it to be regarded as an internal medium, to use Bernard's phrase, bearing the same relation to the constituent tissues as the external medium does to the individual.

In spite of local variations, the composition and characters of the blood present a remarkable uniformity, the result of the combined action of the receptive, excretory, and formative tissues, which are concerned in the digestion and absorption of food, in the discharge of waste, and in the renewal of worn-out elements.

The maintenance of the histological uniformity of the blood is absolutely dependent upon the integrity of these processes. In health the waste and repair of the corpuscles are not accompanied by any striking or obvious phenomena. The corpuscles present a remarkable sameness, and we cannot pick out with readiness the old elements ready to die, or the new ones which have just made their appearance. This it is which makes the blood such a puzzle, for the corpuscles, so far as observation goes, neither die nor are born in the circulating fluid, but appear to enter it as perfect elements and are removed from it before they are so changed as to be no longer recognizable.

That the red corpuscles in health are constantly degenerating and as constantly being reproduced, is uni-

versally acknowledged, though the facts upon which this belief is based are not very numerous. There is evidence that the coloring matters of the bile and of urine are derived from the hæmoglobin, and to supply their daily amount many corpuscles must be destroyed, and to replace which new ones must be formed. The variations in number at different times and under different conditions, indicate that waste and repair are ceaseless processes. Moreover, there is the direct evidence in the presence of degenerating red corpuscles in certain organs, spleen and bone marrow. Our very imperfect knowledge of the details of degeneration and regeneration of the corpuscles in health has been supplemented to some extent by experiment and by the study of the blood in disease, and I propose in this lecture to touch upon the salient features of these processes so far as we at present understand them. As it is difficult to separate the two conditions, which in many instances coexist, I shall first take up the consideration of the state of the corpuscles in anæmia, as induced either by increased destruction or loss of the corpuscles, or as it results from scanty production. The loss may be sudden, as from hemorrhage or acute poisons, or be a slow gradual process, as in fever and chronic poisoning. Anæmia from imperfect production of cells may result from primary changes in the cytogenic tissues, or be a secondary effect of imperfect nutrition, but in either case the reduction in the number of the red corpuscles is by far the most important [illegible] and upon this the symptoms mainly depend.

In health the red corpuscles present a remarkable uniformity in size, or perhaps it is more correct to say that the variations which occur are within very narrow limits. The large proportion of the corpuscles have a diameter of 7.5 μ, but there are a few to be found which measure a micromillimetre less or more, 6.5 or 8.5 μ. These slightly smaller and slightly larger forms are not numerous in normal blood, not so numerous, I think, as Hayem's[1] researches would indicate, for he places the medium-sized at 75 per cent., the smaller forms at 12 per cent., and the larger at 12 per cent. Gram,[2] who

[1] Leçons sur les modifications du Sang. 1882.

[2] Fortschritte der Medecin, 1884.

has made a number of careful observations on this point, finds the average diameter to be a little more than 7.5 μ (7.8 μ), but the percentage of corpuscles of less or greater diameter varies greatly in different individuals. In the newborn, and for some time after birth, the maximum and minimum diameter of the red corpuscle presents a much wider range, the variations being from 10.3 μ to 3.3 μ. One of the most striking alterations of the red corpuscles in certain diseased states is a reversion to this embryonic or infantile condition, with a variation in the size of individual corpuscles to a degree which is truly remarkable. Instead of an extreme variation of 2 μ as in health, the range between the smallest and largest forms may be from 8 μ to 10 μ, or even more. Thus, minute corpuscles may be measured from 2.5 μ to 3.5 μ while contiguous cells may be as much as 10, 12 or even 14 μ. To these abnormal forms the terms microcytes and megalocytes have been appropriately given.

Microcytes occur normally in the blood of the embryo (Fig. 10, *b*) and newborn, but are rarely to be seen in a healthy adult. In disease they are most abundant

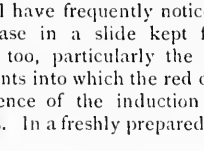
FIG. 1.

Outlines of red corpuscles in a case of profound anæmia. 1, 1. Normal corpuscles. 2. Large red corpuscle—megalocyte. 3, 3. Very irregular forms—poikilocytes. 4. Very small, deep red corpuscles—microcytes.

in anæmia, whether from hemorrhage or as a result of changes in the cytogenic organs, or secondary to disease of important viscera. When the attention of observers was first directed to these bodies it was thought that they might be of diagnostic import in certain forms of anæmia, but we know now that they

occur—in variable numbers, it is true—in all forms, in chlorosis, splenic anæmia, pernicious anæmia, leukæmia, Hodgkin's disease, and in the anæmia of cancer, phthisis, and other chronic affections. I must say, however, that so far as my personal experience goes I have not met with them so uniformly or so abundantly in any condition as in those cases which we designate by Biermer's name of progressive pernicious anæmia. In what may be called the primary anæmias they are almost invariably to be found, while in the secondary form they are variable and may be absent. There is unfortunately a difference of opinion as to the nature and origin of the microcytes, some regarding them as disintegrated remnants of corpuscles, others as young forms in process of development. Possibly both views may be correct. The small, spherical bodies of a deep red color, 1.5–2.5 μ in diameter, should, perhaps, be distinguished from the forms slightly larger, more distinctly discoid, and less deeply tinted. That they may result from changes in the ordinary red corpuscles is, I think, certain. I have frequently noticed that they appeared to increase in a slide kept for observation. They resemble, too, particularly the small deep red ones, the fragments into which the red cells disintegrate under the influence of the induction stream and of various solutions. In a freshly prepared slide of anæmic

FIG. 2.



Extreme poikilocytosis in blood from anæmic patient, examined in Pacini's fluid. It illustrates also a possible mode of origin of the microcytes.

blood firm pressure on the top cover will sometimes be sufficient to produce a large number of microcytes which result from the destruction of the red corpuscles by pressure. They may, indeed, be observed in process of formation as shown at Figs. 2 and 3.

Normal blood in Pacini's fluid does not often show special changes in the form of the corpuscles, but the corpuscles, in cases of profound anæmia, may become in it very irregular in outline and deeply fissured as sketched at Fig. 2, and portions may separate and appear in the field as microcytes. In the bone marrow, too, I have often noted a somewhat similar process (Fig. 3),

FIG. 3.

Origin of microcytes from red corpuscles by process of budding and fission. Specimen from red marrow.

and by a sort of budding and fission many small forms may arise. These microcytes are not always to be regarded as a result of post-mortem change, they may be seen in blood examined with the greatest possible rapidity after removal. Whether the slightly larger form of microcytes from 2.5 to 5 μ, and which are often less deeply tinted, arise in the same way is still an unsettled question. They occur with the others, but are regarded, as I shall point out later, by many good observers as developing forms.

The *megalocytes* have attracted less attention than the smaller forms, but are equally curious. The term may be applied to forms above 8.5 μ or 9 μ in diameter. They may reach an extraordinary size, 12, 14, and even 15 μ. They are very constant elements in cases of pernicious anæmia, and also occur in chlorosis and leukæmia. Gram[1] has made the interesting observation, which I have been able to confirm, that these forms occur in numbers in cases of icterus. He also states that ordinary red corpuscles placed in icteric serum (of ascites in cirrhosis) seem to increase somewhat in size. We may call to mind in this connection the peculiar lemon or subicteroid tint of the skin in many cases of pernicious anæmia, and possibly

[1] Fortschritte der Medicin, Bd. ii.

there may exist in the blood-serum some element—the product of destruction in the hæmoglobin—which may act upon the red cells and cause them to assume a more flattened form. These megalocytes often show the most eccentric changes in outline, to which I shall shortly refer. When I speak of the development of the corpuscles, I shall return again to these forms.

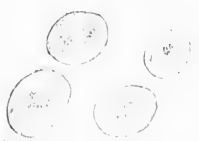
In the normal red corpuscles regularity in outline is not less constant than uniformity in size, but in the blood of the various anæmias we now recognize the loss of this character as a very distinctive feature. Here, also, many of us erred in supposing this condition to be peculiar to pernicious anæmia, the disease in which these irregular forms were first accurately described. Quincke called them *poikilocytes*, a term which has been very generally adopted. At Figs. 1 and 2 this condition is represented. The corpuscles may present the most remarkable shapes, ovoid, elongated, pyramidal, balloon-shapes, with indented edges, or rods, either straight or bent at right angles. Many of these bizarre forms are scarcely recognizable at first as red corpuscles. I still hold that we meet with these forms in a more extreme degree in cases of pernicious anæmia than in any other disease, but they occur also in the anæmia of phthisis, cancer, and inanition. This is a physical change depending probably upon alterations in the blood serum. It is not induced in the healthy corpuscles by dilution of the serum or slight grades of concentration or by any of the reagents which tend to produce crenation. In Pacini's fluid the corpuscles of anæmic blood may sometimes be observed to become much more irregular in form (Fig. 2).

Percentage of Hæmoglobin.—We know as yet little or nothing of the processes associated with the production of the coloring matter of the corpuscles. In a state of health the percentage of hæmoglobin in each cell is tolerably definite, varying within very slight limits. In diseased conditions we have learned to recognize two remarkable changes in the relation of the coloring matter of the corpuscles. One is the observation made some years ago by Duncan (1867) that the hæmoglobin in chlorosis was reduced out of proportion to the reduction of the corpuscles, so that the individual worth of each red corpuscle in coloring matter might

be very greatly lowered. The true anæmia might be much greater than the number of red corpuscles per cubic millimetre might indicate. Subsequent researches have fully borne out this fact, for which, however, we have as yet no suitable explanation. The pallor of the corpuscles may even be recognized with the microscope. In ordinary anæmia from hemorrhage or organic disease, the average worth in hæmoglobin of each corpuscle usually remains unaltered and the percentage of coloring matter corresponds closely with the percentage of the corpuscles, but in certain cases of pernicious anæmia the interesting fact has been ascertained that the percentage of hæmoglobin in each corpuscle is increased, and the anæmia in reality may not be so great as the reduction in the number of red corpuscles would appear to indicate. The individual worth of each corpuscle in hæmoglobin may be actually doubled and the heightened color be evident on microscopic examination. These two facts, intensely interesting and suggestive, may be said to comprise our knowledge of the changes in hæmoglobin percentage in the corpuscles in disease, and they serve as a background against which to display our ignorance of this most essential feature in hæmatogenesis.

Nucleated Red Corpuscles.—In anæmic states there may be present in blood, nucleated red corpuscles such as normally occur in the blood of the embryo, and such as are present in the red marrow of the bones. I have not met with these elements so frequently as the statements of certain observers (Ehrlich) would lead us to

FIG. 4.



Nucleated red blood-corpuscles from blood in case of leukæmia.

suppose. Certainly they do not occur in all cases of profound anæmia. I have met with them in leukæmia in larger numbers than in any other state. (Fig. 4.) They present characters identical with the nucleated

red cells, which I shall speak of shortly in connection with the regeneration of the corpuscles. They are usually a little larger than the ordinary red corpuscles, and the tint may be slightly paler. The nucleus may be seen in process of division, and I have seen corpuscles in process of fission, identical in appearance with those long ago described and figured by Kölliker, as occurring in the blood of the embryo. They may be not infrequently found in groups of three or four, close together, or even in contact, as if the group had resulted from the division of a single corpuscle. I was particularly struck with this feature in one case of leukæmia in which they were very abundant, and I regard the explanation just given as a very likely one in the light of the recent observations of Bizzozero, upon the rapidity of the process of division in these forms. That they originate in the bone marrow there can be no doubt, and in my experience it is just in those conditions in which this tissue is hyperplastic, that they occur in the blood.

A rare and odd element in the blood is the *corpuscle containing red blood corpuscles*. Several observers have noticed the presence of red cells inside colorless corpuscles in the circulating blood. It is very uncommon, and the sketches at Fig. 5 represent the only examples

FIG. 5.

Corpuscles containing red blood-corpuscles. 1. From blood of child at term. 2, From blood of a leukæmic patient.

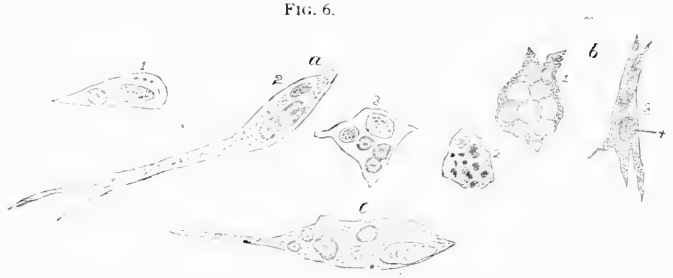
which I have met with. Considering the abundance of these cells in the marrow, spleen, and lymph glands in certain states, it is surprising that we do not find them more often in the blood. It is quite possible, however, that the colorless corpuscle circulating in the blood may itself take up a red cell into its interior just as it may an oil drop or a particle of pigment. I have a sketch of a colorless corpuscle of the blood of the frog, with three or four human red corpuscles in its interior, which it had *eaten*. I have sought in vain in

chronic malaria, for evidence that the leucocytes in the blood take the corpuscles entire into their interior in the formation of the black pigment. They would appear to take in the disintegrated particles, possibly in the spleen and liver, but not the entire cells.

It is interesting to compare with the sketch I have thus given of the state of the corpuscles in anæmia with the condition of the blood in the acute anæmia following a profuse hemorrhage, either accidental or experimentally induced. With our present knowledge, there is a really serious difficulty in deciding just what features of the blood indicate degeneration and what a process of regeneration. Thus, the microcytes, as I have stated, are regarded by some as evidence of a retrograde process, by others as indicating repair of the waste. In an animal deprived of one-third of the amount of blood, or in an individual after a severe prostrating hemorrhage, the changes noted are almost identical with those already described. 1st. The red corpuscles display irregularity in size and shape. The microcytes are numerous and resemble in all respects those of chronic anæmia. The larger forms of red corpuscles are not so constant. Poikilocytes also occur. As the percentage of red cells approaches the normal, these irregularities diminish in a marked manner. 2d. The colorless corpuscles are relatively, and may be even absolutely increased in number. This doubtless is the result, in part, of a relatively smaller loss in white corpuscles in consequence of their adhesive, wall-loving property, and in part, to the flooding of the blood current with leucocytes poured in with the copious flow of lymph which takes place to make up the volume of blood. 3d. The nucleated red corpuscles may appear. In the experimentally induced anæmia in animals (dogs) they are more abundant than after profuse hemorrhage in man (cirrhosis, hæmoptysis). 4th. There is a marked increase in the number of the blood plaques.

Regeneration of the Corpuscles.—There is probably no subject in physiology upon which opinions differ more widely than in the mode of formation of the corpuscles—particularly the red—after birth. The possibility of a solution of the question seems to have been offered in the discovery of the blood-forming function

FIG. 6.



a. 1, 2, 3. Spleen cells containing red blood-corpuscles. *b*. From marrow; 1, cell containing nine red corpuscles; 2, cell with reddish granular pigment; 3, fusiform cell containing a single red corpuscle. *c*. Connective tissue corpuscle from subcutaneous tissue of young rat, showing the intracellular development of red blood-corpuscles.

of the red marrow by Neumann and Bizzozero, and the positive assertions of Hayem regarding the blood plaque and its connection with regeneration, have served to arouse again the interest in this important question.

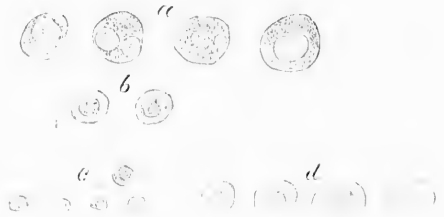
I propose to lay before you briefly a statement of the current views, as interpreted in the light of more recent investigations, and I shall first direct your attention to the study of the formation of red corpuscles in the *bone marrow*.

I begin with this, as I here feel more at home, having for some years been an observer of this tissue in various states, and having arrived at certain conclusions which appear to me justifiable. The red marrow which in the newborn and young child occupies the bone cavities of the entire body, is confined in the adult to the cancellæ of the short and flat bones, but even with this limitation the entire bulk is very great, and if massed as one organ would exceed considerably the volume of the spleen. Without entering into preliminary histological details on the structure of the marrow, which are now incorporated in the text-books, I shall proceed at once to the consideration of the cell elements of this tissue. With a fine capillary pipette a small quantity of the soft red marrow is placed upon a slide without any reagent and a thin cover applied with gentle pressure so as to procure a layer of uniform thinness. The plasma of the marrow is usually quite sufficient, and there is serious objection to the addition of any reagent, as the delicate colored stroma of many of the cells may be at once altered. I feel sure that neglect of this precaution, so strongly emphasized by Neumann, has time and again prevented observers from seeing the very objects they were in search of, and they have ended with a denial of their existence (Rutherford, *Histology*). Examined in this manner we can usually see the following elements: 1. Ordinary marrow cells, (*a*) with coarsely granular protoplasm (Fig. 7, *a*), coarser-looking than that of a colorless blood-corpuscle. The nuclei may not be apparent at first, but they gradually become distinct, two or three in number, oval, round, or reniform in shape and vesicular in character. On the warm stage these elements display feeble amœboid movements.

b. Smaller cells about the size of colorless corpuscles

with more solid nuclei and less granular body protoplasm; they are not so numerous as the larger cells and some of them may be colorless blood-corpuscles.

FIG. 7.



Cell elements of red marrow. *a*. Large granular marrow cells. *b*. Smaller, more vesicular cells. *c*. Free nuclei, or small lymphoid cells, some of which may be evenly surrounded with a delicate rim of protoplasm. *d*. Corpuscles with clear, translucent protoplasm.

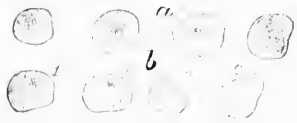
2. Marrow cells (9 to 12 μ in diameter) with smooth homogeneous protoplasm (Fig. 7, *d*) and finely granular nuclei, indistinct on first examination, but becoming more apparent in a few minutes. The protoplasm surrounding the nucleus is translucent, homogeneous, colorless, and variable in amount. There may be a single large nucleus surrounded by a narrow rim, or there may be a dumbbell-shaped nucleus, or it may be divided into two, or even three. The process of indirect division of the nucleus can be well traced in these forms. Certain of the cells may present the faintest possible tint of color, and as they are carried about among the other corpuscles they show a peculiar flexibility.

3. Small lymphoid elements, resembling free nuclei; solid-looking, homogeneous, 2.5–5 μ in diameter, Fig. 7, *c*. They resemble the smallest lymph corpuscles, but about many of them no distinct rim of protoplasm can be seen. In others there is a faint border of protoplasm. These bodies are variable in number but they may be regarded as constant elements of the red marrow. Identical structures may be found in the spleen, Fig.

11, 4. They are well described by Norris as the "primary lymph cell."

4. Nucleated red corpuscles, which we may regard as the special element of the red marrow, and which are present at all periods of life, Fig. 8, *a*. They range in

FIG. 8.



Nucleated red cells of marrow, illustrating mode of development into the ordinary non-nucleated red corpuscle. *a*. Common forms of the colored nucleated cells of red marrow. *b*. 1, 2, 3. Gradual disappearance of the nucleus. *c*. Large non-nucleated red corpuscle resembling 2 and 3 of *b*, in all respects save in the absence of any trace of nucleus.

size from 6 μ to 12 μ, and are circular or slightly ovoid in shape. When freshly examined the protoplasm is homogeneous, clear, and the nucleus indistinct. The color is of all grades up to the intensity of an ordinary red corpuscle. As they float about in the current they show the flexibility and elasticity of the ordinary colored forms. The nucleus may be single and large, and is frequently seen in all stages of division. It is not colored. In certain cells there are appearances which indicate that the nucleus undergoes changes prior to

FIG. 9.

Nucleated red corpuscles, illustrating the migration of the nucleus from the cell, a process not infrequently seen in the red marrow.

disappearing, becoming granular and indistinct. In some specimens the nucleus can be seen adherent to the edge of the cell as if in process of migration from it (Fig. 9), and bodies of a similar appearance may be seen in the immediate vicinity of the red cells.

5. Red corpuscles of ordinary form and appearance. Upon their abundance or paucity depend the color of the marrow. In addition to the usual biconcave disks there are commonly megalocytes, especially if the marrow is hyperplastic, and a variable number of microcytes. The larger corpuscles are, I think, more frequent than the smaller ones.

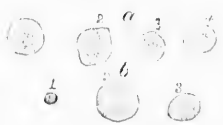
6. Myeloplaques or giant cells, the description of which need not detain us, and

7. Corpuscles containing red blood cells (Fig. 6, *b*, 1). Some of these are evidently collections of red corpuscles undergoing disintegration to form the cells containing granular pigment (Fig. 6, *b*, 2), while others, resembling rather the giant cells (Fig. 6, *b*, 3), may possibly bear a different interpretation.

The chief interest centres in the nucleated red corpuscle of the marrow and of the spleen. From what does it originate? What is the process of its conversion into the ordinary red disk? All are agreed as to its importance in blood-making. It is the earliest red corpuscle in the embryo; it is constant in the cytogenic tissues of all animals, and it would be unreasonable in the highest degree to suppose that in the red marrow of the adult it was present for any other purpose. Moreover, in states of anæmia and after bleeding, the nucleated red corpuscles increase in the bone marrow and even appear (overflow) in the blood; and lastly, Bizzozero has watched the process of division, which may occur with remarkable rapidity, within fifteen minutes. My observations lead me to regard the nucleated red corpuscle as the product of transformation of the clear-bordered homogeneous marrow cell, as all grades of tint can be seen, between cells with scarcely a trace and strongly colored forms. There is no essential difference apparent in the body protoplasm, in both it is smooth, flexible, and translucent. It is not difficult to outline corpuscles in series from those without a trace of color to forms well and clearly tinted. The colorless marrow cells with clear-bordered protoplasm appear to be the descendants of the solid lymphoid cells—the primary lymph corpuscles—the protoleucocyte—which gradually becomes surrounded by a zone of homogeneous protoplasm. Certainly intermediate gradations can be seen between the forms figured at Fig. 7, *c*, and the

smaller corpuscles at Fig. 7, *d*. The process of transformation of the nucleated red into the ordinary forms, occurs, I believe, by the gradual disappearance of the nucleus, as shown at Fig. 8, *b*, 1, 2, and 3. It seems impossible to draw any other conclusion from a study of such cells, and the small granular remnants which they contain may be the sole means of distinguishing them from ordinary red corpuscles. Very many observers have recorded the fact of the migration of the nucleus from the cell, and it may be seen in all stages of the process as represented at Fig. 9, but I have not been able to convince myself that this is anything but a post-mortem change. Certainly in the fresh marrow there are not nearly so many corpuscles with nuclei partially extruded, as in a specimen kept for twenty-four hours. Rindfleisch regards this as the normal mode of transformation, and we need additional careful observation on the point. In favor of the view that the nucleus undergoes disintegration is the fact that a similar process may be traced in the nucleated red blood cells of the embryo, as shown at Fig. 10, *a*, and as the cells are identical in appearance and probably

FIG. 10.



Blood of embryo, four months. *a*. 1, 2, 3, 4. Nucleated red corpuscles. In 4 the same granular disintegrated appearance of the nucleus as in marrow cells. *b*. 1, microcyte; 2, megalocyte; 3, ordinary red corpuscle.

in origin, this may be regarded as strong confirmative evidence. Bizzozero, whose careful study of this question entitles his opinion to the greatest consideration, regards the nucleated red corpuscle as a fixed and constant element derived, by fission, from preëxisting forms of the same kind, and not by any process of development from colorless cells of the marrow.

The nucleated red corpuscles are slightly larger than

ordinary blood-corpuscles, and in size resemble the megalocytes which are usually abundant in the bone-marrow. Such a cell as is represented at Fig. 8, *b*, 4, differs in appearance from those at *b*, 1, 2, 3, solely in the absence of nuclear remnants. In the further process of development into the ordinary red corpuscle, we must suppose condensation of the stroma and a change from a flattened cell to a biconcave disk. In anæmia the megalocytes which may be so abundant in the blood are to be regarded as imperfectly formed corpuscles, which, from causes as yet unknown to us, have not attained their proper form.

Possibly in other ways the spleen and marrow elements may participate in blood formation. I have already referred to the process of budding which may be seen in certain of the red cells of the marrow (Fig. 3) and of the spleen, and Malassez looks upon these gemmæ as capable of development into ordinary red forms.[1] The difficulty is one of interpretation; the process can be readily followed, but, as I mentioned, it is probably a physical change.

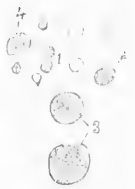
Within the large myeloplaques and also in the elongated cells of the stroma of the marrow, there can be seen, occasionally, red corpuscles, which suggest *development* not *disintegration;* inasmuch as the corpuscles are in smaller number and show no traces of degeneration. They are figured at *6 a*, 1, 2, 3, from the spleen, and at *6 b*, 3, from the marrow. I have been struck with the close resemblance of such cells to those in the subcutaneous tissue of the young rat, in which the process of intracellular development of red corpuscles can be readily traced, as shown by Mr. Schäfer. Fig. *6 c*, represents one of these connective tissue corpuscles with four developing red cells in its protoplasm. It is quite possible that in the reversion to the embryonic or fœtal state of the bone-marrow, these cells may resume their hæmatogenous function, which seems to be

[1] Creighton has described the formation of colored corpuscles in blood cysts by budding from embryonic cells lining their walls, and a few years ago Johnstone maintained (Seguin's Archives, vol. vi.) that the red cells developed by budding from the granular protoplasm of the adenoid reticulum of the spleen and lymph glands.

a widely distributed property in the protoplasm of mesoblastic (parablastic?) elements.

The relation of the plaque to blood formation is still undetermined, and the most diverse views prevail among those who have studied the question. Hayem argues that they are the true *hæmatoblasts*, and the red corpuscles arise directly from them, basing his opinion upon the following grounds: 1. The shape of the plaque is discoid, resembling a miniature blood cell; 2. The faint tint of color which he says may be observed in them; 3. The remarkable gradations in size which they present, so that a complete series of forms may be traced from the smallest plaque to a common blood disk; 4. Their paucity in the healthy adult, their abundance in the young, and in all conditions in which blood formation is rapidly going on; 5. Their occurrence in the cells of the blastoderm. These views of Hayem have met with active opposition from a large majority of the observers who have studied the blood plaque. I have never been able to detect coloration in the plaque, but in the larger forms the pale gray-white aspect of the protoplasm seems most distinct. I cannot see any connection between the blood plaque and the ordinary microcyte, which is of a deep red tint, even when as small as the smaller plaques. The larger microcytes, 4–5 μ, which are usually paler in tint, have a homogeneous and distinctly colored stroma, precisely similar to the red corpuscle, and unlike plaques of the same size. Fig. 11 gives a representation of a

FIG. 11.



From spleen. 1. Blood plaques, colorless and varying a little in size. 2. Microcytes of a deep red color. 3. Two ordinary red corpuscles. 4. A solid, translucent, lymphoid cell or free nucleus.

group of elements from the spleen with the blood plaques, five or six in number: 1, are of various sizes, and presented a pale, faintly granular protoplasm; at 2, were seen two microcytes, resembling more closely miniature blood disks than the form represented at Figs. 1 and 4, but though resembling in size the larger plaques, the appearance is totally different, and forms intermediate between them are not seen. A strong point in Hayem's theory is the abundance of the plaques under the very conditions in which the corpuscular production goes on rapidly: (1) in the embryo and newborn, (2) after hemorrhages, (3) in the stage of convalescence from acute diseases. So, also, in chronic wasting diseases, and in certain forms of anæmia, their prevalence may be reasonably explained by failure to develop into more mature forms. We enter here the region of hypothesis, and it must remain for future observers to determine the precise position of the plaque in the development of the corpuscles. There is remarkable unanimity of opinion among those who have lately worked at the subject, to the effect that the evidence is at present altogether insufficient. Afanassiew is an exception, but he holds that the plaque develops into the nucleated red blood-corpuscle, the nucleus of which is in turn extruded and becomes a plaque.

The observations of the past ten or twelve years have led us away from the old view that the red cells are derived from the colorless corpuscles. Except in the mode I have indicated in the marrow, there is no evidence in favor of the conversion of the colorless corpuscles into colored forms, and the opinion is gaining ground daily that the corpuscles constitute separate elements with important functions quite apart from regeneration of the red cells. They constitute so many masses of primitive or basis-protoplasm which may be called upon in the repair and reproduction of tissues and in the healing of wounds. They act as scavengers—*phagocytes*—in the removal of dead parts, or enclose injurious particles in their interior, and so render them inert. The leucocytes of the body have been compared to a standing army ready to resist invasion, and inflammation, in which they play such an important part, is but a battle by which they protect the organism against injurious agents, such as microörganisms. The researches

of Metschnikoff, Lavdowsky, and others, have so materially widened our conception of the functions of the colorless corpuscles, that we can regard with equanimity their displacement from the duty so long attributed to them of acting as progenitors of the red corpuscles.

After all, the most solid acquisition to our knowledge of the process of regeneration of the corpuscles is the participation in the adult of the bone marrow, and the development of the red corpuscles from its nucleated colorless cells. Here we seem to tread on a firm pavement of carefully observed and well worked-out facts. There are minor details yet in dispute, which the next few years will see settled. Doubt and uncertainty still exist as to how far, in the adult, the spleen shares in the process, and some good observers (Neumann) would deny altogether the post-natal formation of red corpuscles in it, but I think the evidence is sufficient to show that it shares this important function with the marrow.

We shall find, as our information on the subject deepens, that the regeneration of the corpuscles follows the laws governing the regeneration of tissues in general. In the adult body there are permanent and transitory tissue elements, and to the latter the blood corpuscles undoubtedly belong. The nutrition of the former is entirely interstitial, and does not involve any change in the element, when once fully developed. Of transitory elements the epidermic tissues are the best examples. The epithelium is in constant process of regeneration, and the shedding of the superficial cells is analogous to the destruction of the older red corpuscles. The new growth takes place by the constant fission and multiplication of the cells of the deeper part of the *rete mucosum* and if the entire thickness of a portion of the epidermis is removed by accident, the remnant of the cells adherent to the corium repair the loss. Just so, in the life history of the blood corpuscles, which are fleeting structures, like the epithelial cells, the hæmatogenous tissues—spleen, bone marrow, lymph glands—contain as permanent elements cells which, by fission, multiply and pass into the blood current, more or less modified, as the red and white corpuscles.

The recent increase in our knowledge of the changes in the corpuscles in disease, and of the processes of reproduction, is an earnest of fuller information in

the near future. A key to the solution of many problems in pathology, will, I doubt not, here be found, but in seeking it let us not forget that the corpuscles float in the blood plasma, the pathological relations of which await investigation, and offer a field for research which should be equally fruitful in advancing our knowledge of the ultimate processes of nutrition and of those deviations from it which lie at the very root of so many chronic diseases.

LECTURE III.

THE RELATION OF THE CORPUSCLES TO COAGULATION AND THROMBOSIS.

I PROPOSE, in this lecture, to consider the question of the relation of the corpuscles to the processes of coagulation and thrombosis, and I will first call your attention to the action of the *colorless corpuscles*. Our knowledge of the connection between these elements and coagulation dates from the observations of Buchanan in 1831. He attributed the action of what he called washed blood-clot, in inducing clotting, to the colorless blood corpuscles included in the meshes, and which he said acted as a sort of ferment, comparing the action to that of rennet. These views have been greatly elaborated by Schmidt, of Dorpat, and his pupils, to whose researches we are indebted for an important extension of our knowledge in this department of physiology.

According to these well-known observations, the colorless corpuscles furnish the fibrinoplastin or paraglobulin, and the ferment, while the third element, the fibrinogen, exists naturally in the blood plasma. Schmidt and his pupils hold that, in furnishing these two elements to make up the fibrin, the colorless blood corpuscles undergo disintegration and destruction. Part of the evidence which they bring forward in proof this is as follows: The blood plasma of the horse may be readily collected by keeping the blood at a low temperature and allowing the red blood corpuscles to subside, when a clear layer remains, consisting of plasma with a few red and many colorless corpuscles. Now, if a portion of this plasma is taken and whipped with twigs, the difference between the number of colorless corpuscles remaining in the serum and those in the original plasma represents the number of

colorless corpuscles which have undergone destruction in the process of the formation of fibrin, and Schmidt and his pupils estimate that at least seventy per cent. of the colorless corpuscles undergo destruction in this way. They found that, instead of 15,000 colorless corpuscles in a cubic millimetre of the plasma before it is whipped —*i. e.*, before the fibrin is extracted—there were subsequently not more than 4000 per cubic millimetre remaining in the serum. Examining the clot so obtained, it is stated that the colorless corpuscles have largely, if not entirely, undergone destruction in the formation of fibrinoplastin and the fibrin ferment. This is, perhaps, the most convincing experiment which any one of Schmidt's pupils has brought forward to sustain the view, that colorless corpuscles undergo destruction in the process of coagulation. There are many other points urged by Schmidt to which I need not refer, as they are readily accessible in the works on physiology.

The researches of Wooldridge[1] have also shown that the colorless corpuscles play an important part in the formation of fibrin. He has been able to procure leucocytes from lymph glands in a tolerably pure condition, by means which he has described at length in his paper. These leucocytes when added to an equal volume of a ten per cent. solution of common salt seem to be converted into a material resembling very closely ordinary fibrin. By experimenting with what is known as peptone plasma he has obtained very striking results which would appear to indicate still more clearly that leucocytes play an important part in this process. Peptone plasma is obtained by injecting peptone into the bloodvessels and then bleeding the animal. Coagulation is prevented entirely by the influence of peptone, and the red blood corpuscles may be entirely removed from the serum by the centrifugal machine. This plasma shows no special inclination to coagulate, and is, of course, particularly suitable for experimental purposes. If the leucocytes prepared from the lymph glands be added to this plasma, coagulation at once occurs. If a small quantity of leucocytes is added, the amount of fibrin produced is small; if a larger quantity is added, more fibrin is pro-

[1] Proceedings of the Royal Society of London, 1881.

duced. In fact, Wooldridge has shown that the amount of fibrin produced in the peptone plasma is directly proportionate to the leucocytes added. The leucocytes seem themselves to form the fibrin—perhaps the entire mass, for the weight of the fibrin produced is the same as the weight of the leucocytes added. Moreover the albumins in the peptone plasma, after coagulation, can be shown not to have undergone any change, but remain the same, quantitatively and qualitatively; and a third point is that the leucocytes appear to have undergone disintegration.

There are other points in Wooldridge's researches to which I shall not have time to refer at length, but he concludes that it is only the dead plasma which converts the cells into fibrin, as the injection of leucocytes into the blood of the living dog produces no effect.

Such facts appear to show very conclusively that the corpuscles do undergo disintegration, and yet if the blood plasma of the horse is examined after it has been whipped leucocytes may be found in the serum and also in the clot which has been produced, so that all the leucocytes have not undergone destruction. The existence of a certain number of the leucocytes after clotting has occurred has caused one of Schmidt's pupils, Heyl,[1] to divide the leucocytes into two sets: the alpha-leucocytes, which undergo destruction during clotting; and the beta-leucocytes, which remain. From observation, I do not believe that the number of the leucocytes which undergo disintegration in the clotting of the horse's blood is anything like so extensive as Heyl states.

Although the evidence in favor of the destruction of the colorless elements seems conclusive, yet, if the fibrin formation is studied under the microscope, it appears to take place without any disintegration of colorless corpuscles, and it is extremely difficult to demonstrate their participation in the process. As is well known, it can be studied in a blood-drop examined in the ordinary way, or, better still, in the moist chamber. The time which elapses before coagulation begins is variable in different individuals and under different conditions. Usually, however, from fifteen seconds to two or three minutes elapse before the first appearance

[1] Dorpat Dissertation, Fortschritte der Medicin, 1883.

of the fibrin filaments is noticed. A slide can be prepared in a very few seconds, and there is sufficient time before clotting begins to examine the colorless corpuscles, the red corpuscles, and the blood plaques. I must say that, in a very careful examination of the process of the formation of fibrin in this way, I have never seen any appearance in the leucocytes which would indicate that, as the fibrin was formed, they underwent disintegration or dissolution. On the contrary, they seem most stable elements, and the amœboid movements persist long after the fibrin network is thick and dense in the field. Certainly in the microscopical examination of the ordinary slide, or in the examination of the blood-drop in a moist chamber, I do not think anyone has seen the direct disintegration of leucocytes in the production of fibrin. An interesting and instructive experiment is to draw the blood of a frog, or of the horse (in which Schmidt and his pupils hold that the colorless corpuscles so rapidly undergo disintegration), into a fine capillary tube in which the process of clotting can be watched under the microscope. At first, the entire tube is filled with corpuscles; but, before long, it is seen that the clot contracts, and there is a peripheral layer of serum squeezed out. In a short time, leucocytes can be seen emerging from the clot in numbers, either squeezed out or migrating from it. This experiment, which can be readily demonstrated, forms an admirable mode, as Schäfer showed some years ago, of studying the process of coagulation.

A study of the histogenesis of fibrin as seen in the moist chamber, in the capillary tube, and on the ordinary slide, affords, I think, no evidence in favor of the destruction of the colorless corpuscles, but, on the contrary, is directly opposed to this view. In a certain number of instances the aggregations of blood plaques, to the connection of which with the process of coagulation I shall shortly refer, have possibly been mistaken for colorless corpuscles.

The relation of the *red corpuscles* to coagulation is not regarded as very important; they play a more passive part. But Landois and others have described a process which can be readily seen in the blood of the frog and in mammalian blood, examined in serum. If we take the blood of the frog and examine it in the

serum of the blood of the rabbit, it will be seen that the red corpuscles of the frog crowd into columns, and in a short time the hæmoglobin leaves the corpuscles, which become granular, and fibrin filaments form in their vicinity, and, according to Landois, the red corpuscles break down into a material which resembles granular fibrin very closely, indeed. These observations were made ten or eleven years ago by Landois, and they have been confirmed by others; but whether the corpuscles undergo transformation into the fibrin filaments, or whether fibrin only clots about these groups of corpuscles under the influence, perhaps, of a ferment which they extrude, it is impossible to say.

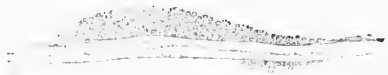
The relation of the *blood plaques* to coagulation is particularly interesting, and is, at present, attracting a great deal of attention.

In the study of fibrin formation, as seen under the microscope, it has long been noticed that the fibrin filaments spread out as distinct rays from the minute aggregations which have been known as Schultze's granular masses. Schultze noticed these, as did also Ranvier, in 1873, who regarded these masses as centres of coagulation. That the fibrin sets in a thick, dense network about the plaques is readily seen, but it can also be noticed, particularly if healthy blood is examined in which the plaques are not very numerous, that the fibrin also appears quite independently of the plaques. It forms as distinct little needle-shaped bodies presenting an appearance not unlike that of crystals. That these crystal-like portions of fibrin appear in regions of the field quite apart from the blood plaques, is well seen in studying the process of coagulation in the moist chamber. Although the fibrin needles when first formed may appear in portions of the field unoccupied by blood plaques, yet the network is usually most dense in their neighborhood, and when the entire field is covered with fibrin filaments, the disintegrated blood plaques look like centres from which the filaments radiate.

The relation of the blood plaques to coagulation, as examined experimentally, is even more interesting. If an ordinary ligature is passed through the femoral vein of a dog and allowed to remain for five or six minutes, or even less, the threads become coated with the

plaques, as represented in Fig. 1. It is well to separate slightly the filaments of the thread, and if exposed to the blood stream for as long as ten minutes they become uniformly beset with the plaques. A few white corpuscles may be entangled among them, but un-

FIG. 1.



Aggregation of plaques on a thread of cotton passed through femoral vein of dog and allowed to remain ten minutes.

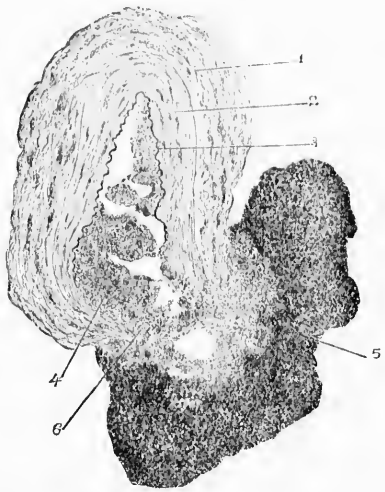
doubtedly the plaques are the first elements to aggregate about such a foreign body. The outlines are usually distinct, but if allowed to remain long in the vein those nearer the threads become more granular, and the distinct corpuscular nature is less evident. If a small brush of thread is tied to the end of pen-handle, or any suitable object, then whipped in the blood, as freshly drawn, for four or five minutes, and then examined, the brush of threads will have precisely the same appearance, and are uniformly covered with blood plaques. The colorless corpuscles are adherent here and there, but the blood plaques form the striking elements. They adhere to the filaments of the thread, and several of the finer fibres of the thread may be entirely agglutinated by the aggregation of the blood plaques about them. I can fully confirm these original observations of Bizzozero and Hayem, and the experiments have now been repeated by a number of observers. If the threads, after having been whipped in the blood, are carefully washed in a saline solution, all the red corpuscles can be washed away, so that few, if any, can be seen, and then if these threads are dipped into a coagulable solution, clotting will occur. This experiment was performed by Bizzozero in 1882, and has been repeated by other observers. It has been urged against it that possibly the threads beating about in the blood have absorbed some of the fibrin ferment. This is, of course, possible, but certainly in such threads the chief elements to be seen are the blood plaques, and the leucocytes are very scanty; besides, the greater the number of the blood plaques adherent to the thread the denser the coagulum

will be, as if the blood plaques furnished the material for the production of the fibrin or the ferment in large quantity.

Still more conclusive evidence of the participation of the blood plaques is their relation to thrombi, as experimentally produced.

The femoral artery of a dog is exposed and a linear slit made in the vessel, through which the animal is allowed to bleed to death. This portion of the vessel is

FIG. 2.



Section of femoral artery of dog at the site of longitudinal incision through which the animal bled to death. (Cut rather obliquely, low power.) 1, 2, 3. Adventitia, media, and elastic lamina of intima. 4. Aggregations of blood plaques in enormous numbers about the intima and the cut margins of the vessel. 5. Clot composed chiefly of red corpuscles. 6 ×. The cut end from which Fig. 3 was sketched.

rapidly excised and placed at once in alcohol, or, still better, first in osmic acid, and then sections carefully cut through the part where the incision was made, when such an appearance as seen in Fig. 2 will be found. Occupying

the cut edges, and filling in places the lumen of the vessel a finely granular material is seen under a low power. Surrounding it, to the outside, as represented at 5 in the figure, there is a darker material made up largely of dark clots composed of red blood corpuscles. In the central portion, in immediate contact with the cut edges of the vessel, in contact with the elastic lamina of the intima, and occupying the interstices of the ragged surfaces, are the blood plaques. This was so stated by Bizzozero in 1882, and it has been confirmed in an elaborate investigation from the laboratory of Langhans,[1] in Berne. My own observations are in harmony with these, and we may say that the plaques are the elements which first settle on the edges of a wounded vessel and which form the basis of the thrombus.

Fig. 3 represents the end of a portion of the adventitia indicated by a cross (×) in Fig. 2. The sketch

FIG. 3.

End of small portion of adventitia indicated at × in Fig. 2. The fibres are everywhere surrounded with granular disintegrating plaques.

shows the blood plaques in a condition of granular disintegration, but under a high power the outlines can be distinctly defined, and any one with a knowledge of these elements and of the changes they undergo has no difficulty in recognizing them. If the cut ends of the vessel are examined when fresh, in osmic acid or Pacini's fluid, the elements are still more clearly seen and are readily determined to be identical with those in the circulating blood and in the granule masses. The elaborate investigations of Eberth, published in the January

[1] Lubnitzky, Archiv f. Exp. Path. u. Pharm., 1883.

number of Virchow's *Archives*, 1886, clearly demonstrate that the plaques are the first elements to settle and lodge on the lacerated portion of the vessel or on a portion of vessel destroyed by acid or by caustic.

The relation which the blood plaques bear to the so-called white thrombi is particularly interesting. Zahn[1] appeared to prove by his observations that white thrombi are composed exclusively of colorless corpuscles, and the current idea is that to a lacerated portion of a vessel the colorless corpuscles adhere and undergo disintegration, become granular, and form in this way a white

FIG. 1

Plaques from thin clot on warty endocarditis.

thrombus. Bizzozero, Hayem, and Eberth have shown, I think pretty conclusively, that if a needle is passed across a vessel in the omentum or in the mesentery, so as to injure it, the first elements which are collected at the site of the injury are not the colorless corpuscles, or the red corpuscles, but the blood plaques, which form distinctly aggregated masses—white thrombi. There may be colorless corpuscles as well, but the chief bulk of the thrombus, which has formed at the site of the injury, is undoubtedly made up of blood plaques.

A study of white thrombi as met with in man leads us to the same conclusion. These structures have been long recognized, and have been supposed to be made up largely of colorless corpuscles. We find them on atheromatous ulcers, forming thrombi in the femoral veins, in the auricles and ventricles, on the valves in endocarditis and as the lining of aneurismal sacs. The examination of the superficial part of a white thrombus in osmic acid, Pacini's fluid, or even salt solution, reveals the fact that it is composed of blood plaques. In the peripheral part where they have not undergone disintegration, such thrombi are, so far as my observation goes, without exception, made up of small circular, disk-like elements which any one familiar with the blood

[1] Virchow's Archiv, Bd. 62.

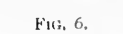
plaques will readily recognize as such. Fig. 5 represents two or three white thrombi in the aorta immediately above the bifurcation. The case was one of cancer of the

FIG. 5.

White thrombi composed almost entirely of blood plaques. Abdominal aorta. Woman dead of cancer of the stomach. From specimen in Museum of McGill Medical Faculty, Montreal.

stomach, and when the aorta was slit open these masses were seen looking as if a neoplasm from the retroperitoneal glands had perforated it. They were grayish-white in color, soft, and on examination were seen to

FIG. 6.



Plaques from specimens illustrated in Fig. 5.

be composed of the elements shown at Fig. 6. There could be no doubt as to their nature; they were blood

plaques, presenting the circular appearance, and on profile, the narrow linear aspect of these bodies. This was the first specimen in which I was able to demonstrate that the white thrombi were made up of the blood plaques. Since then many specimens have fallen under my observation, particularly in connection with vegetations on the valves of the heart, the thrombi in aneurisms, and upon atheromatous ulcers. I would ask those specially interested in the question carefully to observe the white thrombi, more particularly the superficial parts of them in contact with the blood current. I think they will find that, without exception, they are composed not of colorless corpuscles, nor of a reticulated fibrin network, but almost exclusively of these plaques which, in the deeper parts, have undergone granular disintegration, but in the superficial parts still retain their normal shape and appearance.

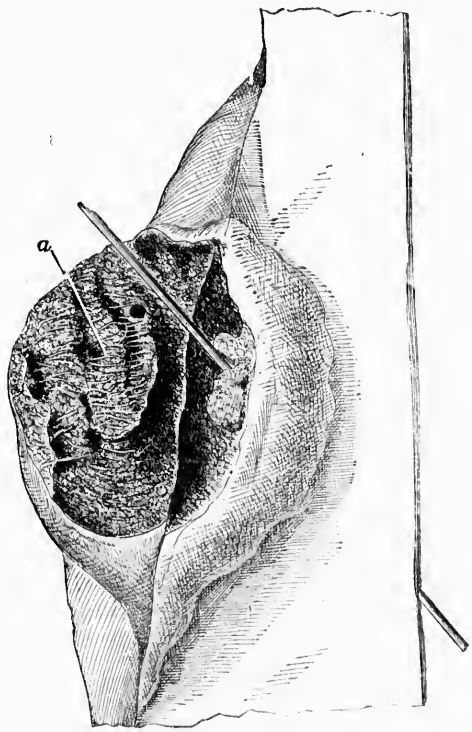
The observation that these white thrombi consisted of blood plaques was confirmed in 1882, by Bizzozero, and, in the same year by Hayem, and since then it has been noted by a number of observers.

Fig. 7 represents a small aneurism of the thoracic aorta, which shows on its lining membrane a number of soft grayish-white curvilinear elevations, such as all observers have noted. On examination these will be found to be made up of elements similar to those which compose the white thrombi, namely, distinctly circular, disk-like blood plaques. The changes which these bodies undergo are very peculiar. As I mentioned in my first lecture, they appear in masses as soon as they are withdrawn, and then undergo remarkable transformation, whereby they lose their outline and become converted into a granular material in which the individual plaques become unrecognizable. That change occurs in the blood plaques as they form these white thrombi. In the deeper portion of the thrombus, represented in Fig. 5, the blood plaques had disintegrated and become granular and were no longer distinctly recognizable; but at the superficial part they were distinct, their outlines were well marked, and in osmic acid, in teased preparations, distinctly made out and readily preserved.

Eberth's researches are of special value in this connection, and appear to place the experimental evi-

dence of this important point on a firm basis, and explain the production of white thrombi. In the

FIG. 7.



Small aneurism of thoracic aorta, showing the internal wall of the sac covered with numerous curvilinear elevations, grayish-white in color, and composed of blood plaques. Specimen in Museum of McGill Medical Faculty, Montreal.

rapidly circulating blood, the central portion of the vessel is represented by a dark line in which you see

no corpuscles whatever; nothing but a red streak, on either side of which there is the so-called still layer, with an occasional leucocyte. This represents the blood current in its active rapid condition. If the circulation becomes slower, then it is seen that, in addition to the leucocytes which collect in the still layer, the blood plaques appear; but in the rapidly circulating blood, as seen in the mesentery or the omentum of the guinea-pig or the rabbit, the still layer, the peripheral portion, contains no blood plaques, and only occasionally a leucocyte—in fact, the corpuscles are separated from the wall of the bloodvessel by a distinct tube of plasma.

Eberth brings forward these facts in explanation of the development of white thrombi. So long as the circulation is active the plaques remain central, and adhere neither to each other nor to the vessel wall; but when, from any cause, the current is slow, this natural disposition of the corpuscles is disturbed, and the plaques tend to collect at the periphery, and aggregate in groups at any point which has been injured, or which has been deprived of the endothelium. Slowing of the blood stream is then, on this view, one of the essentials in the formation of white thrombi, and this is entirely in accord with what we know of the pathology of these structures. It is not alone the presence of intact endothelium which prevents the formation of thrombi in the vessels, for we frequently find in aneurisms, on the heart valves, and on the aorta, denuded and rough regions upon which thrombi do not form. Indeed thrombi are not often found on atheromatous ulcers, which would offer the favorable localities for their formation if it is the epithelium alone which prevents it. The other condition would appear to be slowing of the blood stream, which has long been known to play such an important part, and the true significance of which is well seen in the light of these observations of Eberth.

What I contend is, that the white thrombi are composed chiefly of plaques, and that the colorless corpuscles play an altogether insignificant part in their formation, and the experimental evidence which has been offered is borne out completely by a study of morbid anatomy.

The further development of the thrombus results from the disintegration of the plaques, and the forma-

tion of a finely granular material in which there may be no fibrin filaments. We must recognize a granular or stroma fibrin, as Landois call it, and a fibrillar or plasma fibrin. The former is a granular material which develops when cells undergo the peculiar metamorphosis described by Weigert as coagulation-necrosis, and it is this in reality which goes on in the white thrombi. There may be no trace of fibrin filaments, but the chief mass is made up of a granular matrix in which the outlines of the plaques are no longer visible. The stages of this transformation I have traced in thrombi of the femoral vein, and it is well seen in passing from the superficial parts to the deeper parts. The plaques on the surface of a white thrombus, as at Fig. 5, may be intact, or they may show signs of disintegration and conversion into a granular débris. The central softening of a white thrombus results from the liquefaction of the plaques, and is a result possibly of the presence of fluid in greater abundance than is necessary for the process of coagulation-necrosis. Quite recently in a case of typhoid fever, I had an opportunity of studying the histological characters in thrombi in the femoral veins. In both they were mural, and had originated behind the valves. The attached portion was a light brown-red color, but the upper half was of a dead-white color, and the extension into the iliac was of the same character. The line of demarcation between the two parts was pretty clearly defined. At the thickest portion the superficial white thrombus had softened to an opaque milky liquid, but at the prolongation it was firm and consistent. A few colored and colorless corpuscles were scattered through the white thrombus, but the great mass of it was composed of blood plaques, and a study of the softened milky region showed clearly that the granular detritus was composed of the altered plaques. In the deeper parts the plaques became less and less distinct, until a point was reached at which the individual cells were no longer visible, and there was nothing but an indifferent matrix. The contrast in color between the outer and inner portions indicated a difference in age, possibly in mode of formation, though in the outer portion of the brown and the inner part of the white, close to the line of demarcation, the structure seemed identical.

In the light of these new observations on the connection

of the blood plaques with thrombi, the entire question may be restudied with advantage, particularly the relation of the white and mixed thrombi, and the mode of formation of the clot in aneurisms. Of the truth of the statements here made regarding the connection of the plaques with thrombosis, I feel assured from careful observation on the structure of the white thrombi, (1) on atheromatous ulcers, (2) on the valves of the heart, (3) in aneurisms, and (4) in thrombi of the veins. I have not lately had an opportunity of examining a "globular vegetation" of an auricle or ventricle, but I venture to state that they are composed originally of similar structures.

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THE BICUSPID CONDITION OF THE AORTIC VALVES.

BY

WILLIAM OSLER, M.D., F.R.C.P. LOND.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

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By WILLIAM OSLER, M.D., F.R.C.P. Lond.,
PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

Definition.—A condition of the arterial valves in which two of the cusps are more or less perfectly fused, so that the orifice is guarded by only two segments.

Frequency of the Occurrence.—It is usually referred to as a common abnormality, and Dilg[1] has tabulated 64 cases in the pulmonary, and 23 in the aortic, valves. A careful study of the anomaly has recently been made by Martinotti and Spernio,[2] and again by Martinotti,[3] who remarks that the list given by Dilg of the condition in the aortic valve might be greatly extended. In over eight hundred autopsies, I have met with it in 18 cases, 17 in the aortic valves, and in 1 case in both aortic and pulmonary valves. A detailed account of the cases is given in the appended table. In 110 cases of valvular disease of all kinds, there were 57 in which the aortic segments were affected, either alone or in conjunction with the mitral and tricuspid valves; so that this condition was present in over thirty per cent. of all the cases of aortic disease, a proportion which I am inclined to regard as exceptional.

Description of the Valves.—The coronary[4] segments are usually affected. In 16 of the 18 cases this was the order, and it may also have been so in Case VII., but I have no note of the fact. This point, previously overlooked, may prove of interest in the etiology, and should be carefully noted in future observations. The united

[1] Virchow's Archiv, xci. [2] Atti della R. Academia di Medecina di Torino, 1881, reprint.
[3] Gazzetta delle Cliniche, 1886, reprint.
[4] In speaking of the aortic cusps it seems preferable to use the term *coronary* to describe the segments behind which the right and left coronary arteries are given off, the third being called the intercoronary. This obviates the confusion which at present results from the description by some anatomists of two posterior and one anterior cusp, and by others of two anterior and one posterior.

cusps may have a perfectly normal appearance (Cases 7 and 10), but in adults they are almost invariably thickened and the seat of sclerotic or, in some cases, ulcerative changes. In Case 7, a fœtus of seven months, the tissue of the valves showed no trace of thickening or inflammatory processes. In Case 10 the united segments were practically healthy; in the others there were sclerotic changes more or less marked, and in several distinct losses of substance. Unless seriously stiffened, or the seat of erosion, the bicuspid segments seemed capable of closing the aortic orifice, and in several instances the valves held water when poured into the aorta. In 13 cases the valves were carefully measured. For purposes of accurate comparison, 6 of these may be excluded on account of incompleteness or extensive disease of one cusp. Of the 7 cases, in 1 the two cusps were of equal size, in 2 the single curtain was the larger, while in 4 the fused segments were larger than the single one. The average measurement along the free margin in these 7 cases gave for the fused cusp 3.93 centimetres, and for the single cusp 3.45 centimetres, so that the former was, as a rule, larger than the latter.

In the conjoint valve there are three points to be noted. The free border was usually straight, oftentimes curled, and in no instance was there any nodular thickening indicative of the presence of a corpus Arantii. The attached border presented, from the ventricular aspect, either the normal contour of a semilunar valve, or, more commonly, a shallow groove, indicative of the junction of two cusps. The aortic side of the valve presented in all the cases a more or less distinct raphé, or frænum, dividing, or indicating a division into, two sinuses. This raphé, the representative of the bands which in the normal segments unite them to the aortic wall, was present either (*a*) as a narrow elevated ridge confined to the aortic wall; (*b*) as a single band passing for a variable distance on to the valve; or (*c*) was divided into two distinct portions, which passed out the inner aspect of the valve and were ultimately lost. The sinuses of Valsalva, thus incompletely marked, were usually of equal size, and in sixteen of the cases they gave origin to the coronary arteries.

Of associated lesions in this condition of the valves, hypertrophy of the left ventricle is the most important. This existed in a majority of the cases. In Nos. 10 and 14 it was scarcely noticeable. The state of the other organs, when of interest, is mentioned in the tables.

CLINICAL FEATURES.—In two of the Cases (2 and 14) the condition was found after death and there was no evidence that the persons had suffered from cardiac symptoms. Cases 5 and 10 died suddenly, and in Case 4 death was also sudden but resulted from the rupture of a cerebral aneurism. Excluding Case 7, a fœtus, the remaining twelve cases presented the clinical features of heart disease. In eight there was ulcerative endocarditis, in Cases 7, 9, 13, and 18 of a very severe type. Cases 1, 11, 15, and 16 were examples of gradual heart failure with the usual symptoms of disturbed compensation. Thus in fifteen[1] of the cases the cause of death could be attributed directly or indirectly to the existence of this anomaly. Whether the result of fœtal endocarditis or a primary failure in development, the condition thus plays an important part in the history of aortic valve disease. The special proneness of malformed structures to disease is well known, and the conjoint segments are rarely, in the adult, free from sclerotic changes, while in nearly half of my cases there was also ulceration. Doubtless, the strain upon the fused curtains is more severe than upon normal cusps, and though in the fœtus, and even in the adult, the tissue of the valve may have the natural thinness and mobility, yet, as a rule, there are induration and thickening. I have elsewhere[2] called attention to the frequency with which ulcerative endocarditis attacks sclerotic valves. Indeed, it is exceptional for normal segments to be affected. The recent investigations in experimental endocarditis by Orth[3] (which are confirmed by the beautiful demonstration of Prudden at this meeting) would indicate that the micrococci cannot lodge on the normal valve, but the slightest abrasion suffices to permit of their entrance. Although Ribbert[4] has been able to induce endocarditis by injecting cultures of the microörganisms without any previous lesion of the valves, particularly if the material was associated with rougher particles, these recent experiments support the experience of the post-mortem room that a damaged valve is the most likely to become the seat of ulcerative changes.

[1] In Case 4, a lad of twenty, in which rupture of a cerebral aneurism was the immediate cause of death, there was evidence of the connection of the aneurism with a previous embolic process, which might reasonably be associated with the valve lesion.

[2] British Medical Journal. Gulstonian Lectures, 1885, vol. i.

[3] Tageblatt der 58 Versammlung Deutscher Naturforscher zu Strassburg, 1885.

[4] Deutsche med. Wochenschrift, 1885, No. 42.

Of the eighteen cases here reported, all save one were in adults. In Dilg's table of twenty-three cases the ages of nineteen are given, and of these only nine were adults. Seven were under five years of age. My experience has been in a general hospital in which the great majority of the patients were adults. Dilg's paper is on various cardiac anomalies, so that his search in the literature has tended in the direction of pædiatrics, which may account for the large number of children in his list.

ORIGIN.—Whether the condition is the result of a fœtal endocarditis or is an anomaly of development cannot be finally settled until we have fuller knowledge of the details of formation of the semilunar valves. The advocates of the inflammatory view urge that indications of the original separation invariably exist and that the valves as constantly present evidences of endocarditis. To this view Virchow has given the weight of his authority and has recently[1] stated that an examination of the question has convinced him that a majority of the cases show signs of a "secondary fusion of two cusps." This certainly may be so in some cases, but the following considerations lead, I think, to the conclusion that in many there is a faulty arrangement at the time of the development of the segments.

First. The greater frequency of the anomaly at the pulmonary orifice and its association with other cardiac defects. In the sixty-four cases collected by Dilg[2] there were fifty with imperforate ventricular septum. Errors of development occur more frequently in the right heart and involve the pulmonary artery more often than the aorta. Fœtal endocarditis, however, shows the same preference, and undoubtedly plays a part in the production of stenosis of the pulmonary orifice and narrowing of the conus. So far as we know, the development of the segments occurs at a very early period, eighth to tenth week, and it is really difficult to conceive of an inflammatory process so extremely limited, in an embryo not more than a few millimetres in length.

Second. A careful study of the united valves throws light on the question.

(*a*) In Case 7, a fœtus at the eighth month, the curtains at both arteries were involved, but the conjoint cusps were natural in appear-

[1] Virchow's Archiv, Bd. 103.

[2] Loc. cit.

ance and without a trace of inflammatory changes. Surely we can lay special stress on such an observation—which does not stand alone—for it is scarcely conceivable, if the fusion was inflammatory, that the edges of the cusps would be so thin and the points of attachment free from induration.

(*b*) The measurements of the valves are strongly confirmative of this view. In thirteen cases the average length of the single segment was 3.36 centimetres, and that of the conjoined cusp 3.67 centimetres. In seven of these, free from ulceration and circumstances interfering with the accuracy of the measurement, the figures were 3.45 centimetres for the single and 3.93 centimetres for the fused cusp. In one case the cusps were of equal size and in two instances the single curtain was the larger. An endocarditis, however early, could scarcely equalize the size of the curtains in this way. Such a circumstance points to a developmental error occurring at the time of the formation of the segments and not subsequent to it. The single segment, in its average measure, is also, I think, considerably larger than usual.

(*c*) The condition of the ventricular face of the fused segment in cases free from ulceration or extreme induration, seems inconsistent with an inflammatory origin. The surface may be smooth and without a trace of the extensive tissue changes which must take place in the process of union of two cusps. The slight indentation usually present at the attached border has been, in most of my cases, without a trace of puckering and without any special thickening of the ring immediately below it. If we consider the extent of the space existing between two segments and the nature of the endocardial changes which cause curling, shortening, or other deformity of the segment, it is almost impossible to suppose that a fusion, caused in this way, could leave the ventricular face of the valve smooth and natural-looking.

Third. A study of other anomalies of the valves has an important bearing on the subject. Without any fusion of the cusps, there are certain deviations from the normal mode of attachment to the aortic wall. Usually the line of attachment of each cusp remains separate and distinct, but the two may join at a lower level and at an anterior plane and be attached to the aorta by a single band. It will be seen in most of these cases that the anomaly is the result of a junction of the free borders of the cusp, from four to five centimetres of that part

furthest from the corpus Arantii. The condition is not very uncommon. In a recent specimen two of the aortic valves had partially united and were a good deal thickened. They were united to the aorta by a median raphé, similar to that so often seen in the conjoint valves, but in addition there were three strong chordæ tendineæ, seven millimetres in length, which united the edge of the valve to the aorta, to which they were attached at the normal level. These cords were thin and free from any trace of inflammatory thickening. The condition was unquestionably a defect in development and was of a similar character, though not so extensive, as that under consideration.

Fourth. If it turns out to be correct, as my cases indicate, that the affected valves are usually those behind which the coronary arteries are given off, this would point to some error associated especially with the development of these cusps. It would appear from the observations of Tonge,[1] that two of the segments are formed before the division of the primitive *truncus arteriosus* is complete, while the third arises later after the pulmonary artery and the aorta have divided. It is not at all improbable that we may have here a clew to an explanation of this anomaly, but this is conjectural until we have fuller details of the process of the development of the sigmoid valves in mammals.

[1] Proceedings of Royal Society, 1868, xvi.

TABLE OF EIGHTEEN CASES OF FUSION OF TWO SEGMENTS OF THE AORTIC VALVES.

No.	Sex and age.	Cause of death.	State of heart.	Aortic valves.	Other cardiac valves.

TABLE OF EIGHTEEN CASES OF FUSION OF TWO SEGMENTS OF THE AORTIC VALVES.

No.	Sex and age.	Cause of death.	State of heart.	Aortic valves.	Other organs.	Remarks.
1	M. 42	Cardiac dropsy.	Hypertrophied; weight 750 grms.	Incompetent. Coronary segments fused. The single valve measures 4 cm. along border. Cuspoint segment incomplete. A Vellapeau is absent from one side. Measures 3 cm. along edge. Fraenum distinct. Both valves sclerotic. Three coronary arteries.	Aorta dilated; pulmonary apoplexy.	No history of rheumatism. Duration of heart symptoms only five months.
2	M. 40	Typhoid fever.	Moderate hypertrophy and dilatation of left ventricle.	Do not hold water. Posterior segments fused. Measure 4 cm. along border. Slight indication of separation on ventricular face. Distinct raphe on aortic surface. A little roughening with sclerotic change. Only one coronary segment involved in this case. Single segment measures 3.3 cm.; is thin and natural looking.	Typhoid lesions.	Never complained of heart trouble.
3	M. 20	Cardiac dropsy.	Hypertrophied; 690 grms.	Coronary segments fused. 2.5 cm. along border. Recent ulceration and destruction of one end. From ventricular surface a depression which indicates the separation. Raphe small. Sclerotic changes; no vegetations. Intercoronary segment 3.5 cm.; a little opaque.	Aorta atheromatous in places.	No rheumatism. A thrill with systolic obstruction. Symptoms lasted over a year.
4	M. 29	Rupture of cerebral aneurism.	Considerable hypertrophy.	Coronary segments united. Measure 3.2 cm. along border. Edge curled and thickened. A prominent raphe separates two distinct sinuses. Recent vegetations. Intercoronary cusp measures 3.3 cm., also sclerotic, and presents a narrow perforation.	Aorta normal; infarcts in spleen.	No history. Death sudden.
5	M. 42	Heart failure.	Hypertrophy, particularly of left ventricle.	Coronary cusps fused; measure 4.6 cm. along edge. Slight sclerotic changes. Raphé distinct, but does not extend up the segment. Intercoronary segment measures 3.6 cm. Aortic ring large, 9.6 cm. in circumference.	Aorta normal.	Sudden death. A blacksmith.
6	M. 45	.....	Great dilatation and hypertrophy.	Incompetent. Coronary cusps united; measure 4.5 cm. Two aneurisms the result of recent ulcerative changes. Edge rough, and raphé calcified. Intercoronary cusp torn across almost to its attachment; very atheromatous.	Aorta normal; pulmonary apoplexy; no infarcts.	
7	Fœtus at 8 mos.	.....	Hypertrophied.	Vessel from left chamber only two valves, one 9 mm. in width, the other 8 mm. Both thin and translucent; no trace of endocarditis; median raphe distinct. The artery of the right ventricle presents two valves, each measuring 10 mm. They do not meet, but leave a space of 2 mm. which is occupied by an imperfect valvular fold.	Umbilical hernia, spina bifida, hydrocephalus, talipes varus.	The descending aorta and left subclavian were given off from right ventricle; the innominate and left carotid from the left ventricle.
8	M. 50	Pneumonia and ulcerative endocarditis.	Hypertrophy and dilatation of left ventricle.	Coronary segments fused; measure 2.5 cm.; much thickened. Raphé distinct, but sinuses unequal in size. The intercoronary cusp measures 3.7 cm., also sclerotic and presents recent vegetations.	Ulcerative (mycotic) aneurisms of aorta; infarcts in spleen; resolving pneumonia.	Patient known to have had aortic valve disease for some time.

No.	Sex and age.	Cause of death.	State of heart.	Aortic valves.	Other organs.	Remarks.
9	M. 45(?)	Ulcerative endocarditis.	Much hypertrophied; weight 600 grms.	Coronary segments united; measure 4.5 cm. Sinuses of equal size. Raphé small. Shallow groove on ventricular surface at attachment of valve. Moderate sclerosis. Intercoronary segment covered with vegetations, and presents a perforation 2 by 1 cm	Infarcts in spleen.	In hospital four days. Malignant endocarditis.
10	F. 25	Sudden death; heart failure.	Little, if any, hypertrophy.	Coronary segments united; very little thickening. Raphé divides sinuses of equal size. The single cusp normal in appearance. The valves held water when poured into aorta.	No other lesions.	Patient was known to have heart disease, and had had rheumatism three years before. Died in a shop
11	M. 35(?)	Ulcerative endocarditis.	Much hypertrophy.	Coronary segments united and sclerotic. Behind them a recent aneurism which projects into, and communicates with, left auricle. Vegetations on ventricular face. Intercoronary segment much thickened, and presents recent vegetations.	Great enlargement of spleen; weight 500 grms.	Patient ill several months.
12	F. 60	Gradual heart failure	Hypertrophy and dilatation.	Coronary segments united; measure 3.5 cm. Very sclerotic, and at middle of cusp a calcified mass fixes it in the diastolic position. The raphé at its attachment is split into two portions. Intercoronary segment sclerotic.	Septum ventriculorum, near apex, fibroid.	Extreme cyanosis and dyspnœa.
13	M. 38	Ulcerative endocarditis.	Hypertrophy and dilatation.	Coronary segments fused. Edge much thickened. Sinuses large, and the raphé scarcely visible. Intercoronary segment presents many recent vegetations, and is a little thickened.	Extensive recent disease of mitral valve; infarcts.	Marked typhoid symptoms.
14	M. ?	Phthisis.	.....	Coronary segments fused; measure 5 cm.; a little thickened. Single cusp 4 cm.	No other changes.	No heart symptoms
15	F. 40	Heart failure.	Moderate dilatation and hypertrophy of left ventricle.	Coronary segments fused; measure 3.7 cm. Calcified nodule at point of junction of the valves which holds the united cusps 1 cm. from aortic wall. Raphé divided where it joins the segment. Normal segment 3 cm.	No other changes.	
16	F. ?	Cardiac dropsy.	Hypertrophy and dilatation.	Coronary segments fused and rigid, covered with recent vegetations. Single segment sclerotic, and at the edge calcified. The two segments from their position obstruct and narrow the orifice.	Aorta not atheromatous.	
17	M. 40	Ulcerative endocarditis.	Hypertrophy.	Coronary segments united. Ulceration (with vegetation) of the fused cusps. Old sclerotic changes. Intercoronary segment thickened.	Vegetations in mitral.	
18	M. 26	Ulcerative endocarditis, apoplexy.	Hypertrophy of left ventricle.	Fusion of coronary segments. Sclerotic changes. Vegetations on ventricular face. Perforation of valve. Vegetations on intercoronary cusp.	Infarcts.	Case simulated typhoid fever.

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17	M. 40	Ulcerative endocarditis.	Hypertrophy.	Coronary segments united. Ulceration (with vegetation) of the fused cusps. Old sclerotic changes. Intercoronary segment thickened.	Vegetations in mitral.	
18	M. 26	Ulcerative endocarditis, apoplexy.	Hypertrophy of left ventricle.	Fusion of coronary segments. Sclerotic changes. Vegetations on ventricular face. Perforation of valve. Vegetations on intercoronary cusp.	Infarcts.	Case simulated typhoid fever.

ON THE USE OF ARSENIC

IN

CERTAIN FORMS OF ANÆMIA.

IN an address last year, Dr. Wilks remarked that in therapeutics we do not so much need new remedies as a fuller knowledge of when and how to use the old ones. I do not know a more striking illustration of this than is afforded by arsenic, a good old remedy, for which an almost new use has arisen in certain cases of pernicious anæmia. The attention of the profession was directed to the subject by Bramwell in 1877, and although various reports bearing witness to the value of this drug have appeared from time to time, the knowledge of its efficacy does not appear to be very wide-spread, and there are still points in connection with its employment upon which we need information. These, I trust, discussion may bring out, and render clear the direction which future observation should take.

In treating a case of anæmia, it is of the first importance to ascertain, if possible, the cause. For convenience, and until the present complex pathology is simplified, we may classify the anæmias into secondary and primary; the former induced by causes acting upon the blood itself, the latter the result of disturbance in the blood-making organs. This distinction, not always clear, serves to separate two clinical and pathological groups of cases.

The secondary anæmias are the most common, and arise from a variety of causes, as hemorrhage, prolonged drain of albuminous material in chronic disease, and the action of toxic agents on the blood. In very many of these conditions a return to the normal state follows naturally upon removal of the cause, and the regeneration of the corpuscles may take place with extraordinary rapidity, as after a copious bleeding or a sharp fever; but, as a rule, iron in some form will be found useful or indispensable. In three of these secondary anæmias I have found arsenic very beneficial.

1. *The Anæmia of Heart-Disease.* — In chronic valvular trouble we not infrequently meet with an impoverished condition of the blood, which materially aggravates the cardiac distress. The comfort of such patients is in direct proportion to their corpuscular richness, and without any apparent increase in the valve mischief, a reduction in the ratio of the corpuscles is followed by shortness of breath, palpitation, and signs of heart-failure. The value of iron in this condition is well known, and its combination

with digitalis a universal practice. Arsenic is also indicated in these cases, particularly in children, or if, as sometimes happens, iron does not agree. In June of this year I saw a lad, J. W., æt. 14, who had had chronic valve-disease for four years. He had been wintering in the South, and went afterwards to the Arkansas Hot Springs. When I saw him the anæmia was very marked, and he suffered from breathlessness on the slightest exertion. There was no cardiac distress, and the compensation was not seriously disturbed. At the Hot Springs he had several chills, with fever, for which he had taken quinine. He was ordered Fowler's solution of arsenic, beginning with ♏iii, three times a day, and increasing to ♏vi, if well borne. He had been taking an iron and strychnine pill for several weeks, and had with him a boxful, which he was advised to finish. Digitalis was prescribed, but was not to be taken unless there were signs of heart-failure. The diet was carefully regulated. The lad improved rapidly, and within six weeks had a good color, and had gained several pounds in weight. He had not needed the digitalis. The arsenic was well borne. The improvement had continued on the 3d of this month. Possibly here there was a malarial taint; but, in any case, if medicinal agents had anything to do with the rapid improvement, the credit is due to the Fowler's solution.

2. *In Malarial Anæmia.*—The value of arsenic in chronic ague-poisoning is so well recognized that I need scarcely detain you with the narration of cases in support. There

have been several at my clinic during the past year in which the improvement in the blood condition, as tested by the hæmacytometer, has been very remarkable. One case in particular, from Cape May, I may refer to, as the patient, with enlarged spleen, had on two occasions hemorrhage from the stomach. The arsenic in this case was pushed for several months in increasing doses. At one time he took ♏xxxvi of the Fowler's solution daily. When last heard from, in July, he was at work, and had gained in flesh and strength. On May 12, the date of the last blood count, the percentage was over eighty (it had been scarcely fifty), and the spleen had diminished materially in volume. In certain of these cases the ratio of the corpuscles may increase rapidly without any essential change in the volume of the spleen. In the case of M. D., a girl of 15, who has been in the University Hospital on several occasions for the past two years, the arsenic, which was very persistently employed, does not appear to have reduced the spleen in the slightest degree, and yet under its use the corpuscles rose to eighty-five per cent. In this instance, with a history of malaria, there is evidence also of congenital syphilis, to which may possibly be due the splenic enlargement. Injections of arsenic into the substance of the organ were tried without benefit.

3. *Certain Anæmias of Gastric Origin.*—As a tonic in debilitated states of the stomach, arsenic has long been a favorite remedy with many practitioners. It is sometimes also of great service in the anæmia of chronic gastric catarrh, particularly in alcoholic patients.

A good illustration of this was under my care at the Philadelphia Hospital this spring. W. G., aged 25; waiter; hard drinker; history of dyspepsia for several years. Admitted April 5 with anæmia and attacks of giddiness. Ill for ten days; vomiting, pain in stomach, and fainting spells on attempting to stand. Had been failing in strength for some time and getting pale. Had suffered from palpitation, and said he had vomited blood. He was profoundly anæmic, and could not stand without danger of fainting. Tongue coated; great irritability of stomach; vomiting on the slightest provocation; great throbbing of abdominal aorta. He was kept at rest, given a milk diet, and Fowler's solution in 3-drop doses. The red corpuscles were not more than twenty-five per cent., and the coloring matter about the same. The improvement was rapid, and by the 21st the corpuscles had risen to over forty per cent., and the gastric irritation had almost disappeared. The arsenic was well borne, and was gradually increased to ♏vii t. i. d., and on May 4 he was ordered small doses of nitro-muriatic acid. On May 17 he left the hospital with a fair digestion and, for him, tolerably good color. On June 24, when readmitted with extensive pleuro-pneumonia, he stated that he had recovered strength rapidly, and had been at work. Possibly, in this case, there was ulceration of the stomach in addition to the chronic catarrh; but, whatever the condition, it was one in which the arsenic seemed to be highly beneficial, and, as he received no other medication, we may reasonably attribute to it the stimulation of the

blood-making function. As we shall see, there are anæmias of gastric origin in which this drug is powerless. These are some of the secondary anæmias which have, in my experience, been apparently benefited by the use of arsenic.

Turning now to the primary group, we have here again for convenience to make a division of the cases. There is, first, a large section of what may be called cytogenic anæmias, in which the reduction and alteration in the corpuscles is associated with evident changes in the hæmatogenous tissues,—the spleen, lymph-glands, and bone marrow. Sometimes these changes are accompanied by an increase in the colorless corpuscles of the blood ; and, depending on the organ involved, we then speak of splenic, lymphatic, or medullary leukæmia. If there is no marked increase in the white corpuscles we call the cases splenic anæmia, lymphatic anæmia (Hodgkin's disease), and medullary anæmia. The pronounced leucocytosis in certain of the cases, which gives a special character to the blood, is probably not such an important factor as we have hitherto supposed, and there are such insensible gradations between the cases that in a strict classification they may be appropriately grouped together. Secondly, there is the curious primary anæmia known as chlorosis, characterized by well-marked etiological and anatomical peculiarities ; and, thirdly, we have the much-discussed affection, pernicious or essential anæmia.

The anæmias of this primary group offer a remarkable therapeutic study, embracing cases of the most hopeful and the most hopeless

character. A clearer knowledge of the etiology and pathology of certain of these forms may give a clue to lines of treatment more fortunate than those we now possess; for, if we except chlorosis, the majority of the cases of this class of anæmias prove fatal. Leukæmia, splenic anæmia, when non-malarial, Hodgkin's disease, are considered incurable affections, and very many of the cases of pernicious anæmia prove obstinate to all treatment.

The relation of arsenic, as a remedy, to this group of primary anæmias is worthy of our closest study, more particularly as of late years remarkable results have been reported from its use. Chlorosis may here be excluded from our consideration, as it would only be in a strangely obstinate case that a practitioner would require to employ arsenic. The specific action of iron in increasing the defective hæmoglobin of the corpuscles, and doubtless, also, in stimulating the formation of new ones, is one of the few instances in therapeutics in which definite tissue-changes, under the influence of a drug, may be followed with scientific accuracy from day to day and from week to week.

In *leukæmia* and *Hodgkin's disease* arsenic has been extensively tried, occasionally with temporary success. We must bear in mind in these affections that there are natural periods of improvement without any special medication. I have met with this in leukæmia, and it must be taken into account in our estimation of the effect of a remedy. Personally, I have not seen any benefit from the use of arsenic in this disease. It was given in several of the eleven cases which I saw in

Montreal, all of which were fatal. In Hodgkin's disease the report is more favorable. In 1883 I had two cases, both in women, in which the large glands of the neck and armpits reduced materially under the prolonged use of Fowler's solution, but I do not know the subsequent history of the cases. Several writers have reported most satisfactory results. Karewski* had three recoveries, and of eleven cases treated at the Stockholm Hospital five were benefited.† The persistent use of it in full doses for many months is probably the most efficacious remedy we possess in this disease.

In cases of *splenic anæmia* of non-malarial origin, I cannot say that I have seen any special benefit from arsenic.

We come now to *pernicious anæmia*, in which so much has been gained by the judicious use of this drug. Pernicious anæmia includes cases of very diverse etiology. Any severe anæmia tending to a fatal termination may well be termed progressive and pernicious. In a considerable proportion pregnancy and parturition appear to have been determining factors, while others can be directly traced to defective food, as in many of the Zurich and Bern observations. Excluding these, we have a group of cases of which the etiology is obscure, and to which, in our present knowledge, the terms *idiopathic* of Addison and *essential* of Lebert are applicable. Every year, however, we are reducing the number of cases which we can strictly call

* *Berliner Klin. Wochenschrift*, 1884, 17 and 18.
† Abstract in Year-Book of Treatment for 1884.

idiopathic. It is reasonable to suppose that the extensive changes in the bone marrow found in certain instances are directly related to the profound disturbance in blood formation, just as is the case in hyperplasia of the spleen or of the lymph-glands. An anæmia medullaris is now very generally recognized. Then, there are the cases of pernicious anæmia in which the primary disturbance seems to be in the gastro-intestinal canal, and the condition of the blood the direct consequence of the impaired nutrition. There remain cases in which none of these conditions prevail, and neither during life nor after death do we find any clue to the origin of the anæmia. To such, for the time, the designation idiopathic is applicable. Clinically, it may be impossible to distinguish between these various forms, and the etiology is often very obscure and gives us no help. The cases which come on during or after pregnancy, or which result from inanition, are readily recognized, and offer, as a rule, a more hopeful prognosis; but we cannot yet with any accuracy separate during life the cases in which there is atrophy of the mucous membrane of the stomach, or extensive medullary changes, from those in which these conditions are absent. A more careful study may in the future enable us to do so, and I have laid stress upon these differences in etiology and pathology because in them will possibly be found the explanation of the success or failure of certain remedies.

Prior to 1877 arsenic was not systematically employed in pernicious anæmia, and to Bramwell is undoubtedly due the credit of its intro-

duction. Neither Müller* nor Eichorst,† in their elaborate monographs published in 1877 and 1878, speak of its use. Padley,‡ in an interesting review of the question, has carefully analyzed the cases in which arsenic was not employed, and finds that of forty-eight, forty-two were fatal, while of twenty-two cases treated with arsenic sixteen recovered, two improved, and four proved fatal; and he remarks, that "in the whole list there is not, with one exception, a single authentic case of recovery in which arsenic did not form the chief part of the treatment." Certainly the reports of this affection since 1880 have been much more encouraging, and it need not necessarily be regarded as "almost invariably fatal," to use the words of a leading text-book. Of three cases of pernicious anæmia which I have seen this year two have already proved fatal, and one is in a fair way to recovery.

Case I.—A man, aged 42, I saw with Dr. Henry. We reported it in full in the April number of the *American Journal of Medical Sciences*, and it is remarkable as an instance of pernicious anæmia, with advanced atrophy of the mucous membrane of the stomach. Arsenic was given during the course of the disease, but not for any length of time, as it seemed to bring on diarrhœa.

Case II.—A woman, aged about 45, I saw with Dr. Weir Mitchell on January 20. She had been the subject of dyspeptic attacks

* De Progressive Perniciose Anæmie. Zurich, 1877.
† De Progressive Perniciose Anæmie. Leipzig, 1878.
‡ *Lancet*, 1883, ii.

for some years, and had become very pale, and during last year the anæmia reached an extreme degree. With rest, systematic feeding, iron, and arsenic she improved, and was able to go home and attend to her household duties. I saw her in January on her way South. She returned in March very much worse; was again placed on the plan of treatment which had proved so successful in the first attack, but the stomach was so irritable and the digestive power so enfeebled that she sank, and died on the 18th of April. The improvement in her first attack was attributed by Dr. Mitchell to the careful feeding and rest as much as to the medicine.

Case III.—An active business man, aged 43; seen March 4. History of dyspepsia, and for the past six months failure in strength. Shortness of breath on the slightest exertion, and at times attacks of agonizing pain at the heart resembling angina. He had not lost much flesh; indeed, as is usual in these cases, the subcutaneous fat was well developed. When first seen, the anæmia was marked; lips and tongue very pale, and sclerotics pearly. The general surface did not look so pale, on account of his dark color and a decided saffron-yellow, sub-icteroid tint of the skin. The temperature was a little elevated; pulse 100, and of moderate volume. With the exception of heart-murmur, there were no symptoms elicited in the examination of thoracic and abdominal viscera. The blood showed in a marked manner the corpuscular changes of advanced anæmia. The blood count could not be made at the time, but when I next saw him, two weeks later, there

were only 700,000 red corpuscles to the cubic millimetre, and the color percentage was only about twenty. He was put to bed, absolute rest, given a milk diet, ordered massage once a day, and as medicines bismuth and carbonate of sodium, with Fowler's solution ♏v, three times a day, to be increased one minim daily at the end of a week. He had been taking, by the advice of his physician, an elixir of iron and strychnine, which was continued. For two months there was not much apparent change, though the ratio of the colored corpuscles increased to over 1,500,000 per cubic millimetre. The arsenic had been pushed to 15 drops three times a day, when puffiness of the eyelids and forehead came on, and it was omitted for a week, and started again with ♏v. On reaching ♏xiii a slight red rash appeared, and it was stopped, and, after beginning at ♏v again, he reached ♏xx t. i. d. On these large doses he seemed to improve more rapidly, and he bore them for two weeks or more, when gastric irritation supervened, with diarrhœa. The drug was then stopped for ten days, and pills of $\frac{1}{100}$ of a grain of arsenious acid ordered. On January 31 he was allowed to get up. By June 13 he was able to move to Cape May. The blood condition has rapidly improved, and at the last count the corpuscles were nearly 4,000,000 to the cubic millimetre. When seen on September 7 he looked remarkably vigorous, had a good appetite, was at business, and feeling very well. It would be incorrect to attribute the success in this case entirely to the arsenic, but rather to the plan of treatment, in which it was a

very important factor. It will be found, I think, that absolute rest in bed, with daily massage, and the strictest attention to feeding, are most important features in the successful management of these cases.

Arsenic has been spoken of as a specific in pernicious anæmia. This is a mistake. The disease, as I have indicated, is so varied, and results from the operation of such diverse causes, that we cannot expect any one remedy to be uniformly active. In a majority of the cases iron is useless, but it sometimes succeeds after arsenic has failed absolutely. Such a case was reported by Finlay* last year, which was cured by iron after a thorough and but ineffectual use of arsenic. I do not think we understand fully the conditions in which it is most serviceable, and for the time we must be content to employ it empirically, on faith of the success which has attended its administration in so many cases. Ultimately, we may hope to be able to discriminate between the cases which call for iron and those in which arsenic is indicated, and with this object in view the cases which come under observation should be carefully studied.

Mode of Administration.—I usually give the liquor arsenicalis (liquor potassii arsenitis), beginning, in an adult, with ℥v three times a day. Occasionally this is found too much, and I reduce the amount to 2 or 3 minims. After ten days, if well borne, I order an increase of a minim each day, so that by the end of the second week the patient is taking

* *Lancet*, 1885, i.

10 or 12 minims three times a day. This is kept up for a week, and then gradually increased until the physiological effects are obtained. The amount which will induce these varies with different individuals, and those who bear it best seem to improve the most rapidly. I have thought sometimes that the small doses are not so well borne as larger ones, and are more likely to cause gastric irritation. Young people bear it remarkably well. Within the physiological effects there is no special limit to the quantity, and, as in chorea, I make them my guide in the administration. A very important point is the continuous use for many weeks or months, omitting for a few days if unpleasant effects arise. Even after apparent recovery I advise the continuance of the drug. When the liquor arsenicalis is not well borne, the arsenious acid in pills may be tried, or the solution may be given hypodermically. In these cases of severe anæmia I never care to use hypodermic injections systematically, as I have seen ecchymosis of the tissues follow, and in several instances distressing small abscesses. By the rectum, it is usually well borne.

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DUODENAL ULCER.

CLINICAL AND ANATOMICAL CONSIDERATIONS BASED ON NINE CASES.

By William Osler, M.D.,
Professor of Clinical Medicine in the University of Pennsylvania.

(Read before the Philadelphia County Medical Society.)

The solitary ulcer occurs more frequently in the duodenum than in any other portion of the intestine, and in its ætiology and morbid anatomy is almost identical with the gastric ulcer. It is rarely met with below the bile papilla, at which point the acid chyme is neutralized. Blood stasis in a circumscribed area of the mucous membrane is the condition which permits of erosion by the gastric juice. Although the cases are few in number in which actual disease of a vessel has been discovered, they confirm in a striking manner this view. Thus Merkel* found an embolus in a duodenal vessel at the base of an ulcer, and there were emboli in other organs; similar cases have been reported of plugging of the arteries at the base of ulcers of the stomach. Thrombosis is also a cause, leading first to hemorrhagic infiltration and inducing a condition which permits of erosion. The experimental production of gastric ulcer by Cohnheim and others lend additional support to the embolic view. The following case suggests that in the duodenum there is possibly another mode in which ulcers may arise :—

* Wiener Med. Presse, 1866.

CASE I.—*Phthisis; small ulcers in ileum; ulcers in cæcum and colon; an ulcer in duodenum half an inch outside pyloric ring; cyst of Brunner's gland.*

J. I., middle-aged man, died of phthisis in Montreal General Hospital. No special symptoms. The lungs showed cavities; the heart valves were normal. There were a few small ulcers in the lower patches of Peyer, and a number of small ulcers in cæcum and colon. Just outside the pyloric ring there was a loss of substance in the posterior wall of the duodenum 1.5 cm. in diameter. The base was smooth, the edges overlapped so that the actual diameter of the ulcer was much greater than was apparent. Not far from this there was a small dark spot, with a little depression leading into a definite cyst-like cavity in the submucosa the size of a large pea, which contained a thick turbid fluid. Brunner's glands were very distinct, but not more so than is often seen when the mucosa is thin, and not deeply congested.

The open ulcer with undermined edges had possibly resulted from the rupture of a cyst of a Brunner's gland similar to the one which existed in its vicinity. One can readily understand that under such circumstances the thin mucosa covering the cyst, undermined and separated from its blood supply, might be eroded, or, after bursting, the acid gastric juice might dissolve the thin edges. In debilitated persons, or in conditions of portal congestion, such a small erosion might not readily heal, but rather increase, and be the starting point of an ulcer. Brunner's glands are not often found diseased, but they belong to the racemose variety in which cystic dilatation of acini is not uncommon. They exist most abundantly on the first portion of the duodenum, the region most prone to the disease.

Duodenal ulcer is not so frequent as the ventricular. I am sure, from my own experience, that it would be oftener found if the stomach and duodenum were opened together, *in situ*, and the mucous membrane examined. If, as is so commonly done, the stomach is cut away just beyond the pyloric ring, the chances are that, if an ulcer is present, the incision passes through it. I have found nine cases in about one thousand dissections.

Males are more subject to ulcer of the duodenum than females.

Thus the combined statistics of Krauss,* Chvostek,† Lebert ‡ and Trier (quoted by Chvostek) give 171 cases in males and 39 females. Of the nine cases which I have noted, seven were males and two females. It occurs most frequently in middle age. One of my cases was in a child of twelve.

There are no constitutional peculiarities which predispose to duodenal ulcer. Chlorosis, which seems to favor the production of the gastric ulcer, has no special influence.

In the following case the ulcer may have been tuberculous, as there was extensive affection of ileum and cæcum:—

CASE II.—*Phthisis; extensive ulceration of ileum, cæcum and colon; single ulcer in duodenum; slight jaundice.*

E. G., aged 23, died in the Montreal General Hospital with the usual symptoms of chronic phthisis. There were diarrhœa and abdominal tenderness, but no special features indicating ulceration in the upper part of the intestine. The autopsy showed cavities in both lungs. Extensive tuberculous ulceration of ileum, cæcum and colon, with recent peritonitis due to extension from the bases of the ulcers. In the anterior wall of first part of duodenum was a circular ulcer, a third of an inch in diameter, with clean cut edges and smooth base. It looked of recent origin. It did not involve the bile duct. There was congestion of the mucous membrane of the duodenum. There were no tubercles in the vicinity and no ulcers in the upper part of jejunum.

The ulcers in intestinal tuberculosis sometimes reach very high, and in a recent case at the Philadelphia Hospital there was an ulcer the size of a ten-cent piece at the upper end of the jejunum, not two inches from the duodenum. In *Case II*, although there were no signs of tubercle in the base of the ulcer, it may have been of this nature. In Krauss' 64 cases there were seven instances of ulcer in connection with phthisis.

Chronic valvulitis and atheroma of the aorta were present in only one of the nine cases.

* Das Perfor. Geschwur im Duodenum, Berlin, 1865.
† Medizinische Jahrbucher, Wien. 1853.
‡ Die Krankheiten des Magens, 1878.

I have not met with a duodenal ulcer in death from extensive burns.

In all of the cases the ulcer was solitary, and occupied the first or horizontal part of the gut. The form was round in all, and the diameter ranged from half an inch to an inch and a half. The base was either the submucosa, the head of the pancreas, or thickened connective tissues. In *Cases III* and *IV* the ulcer had cicatrized. The edges were usually rounded and not undermined. Perforation into the peritoneum, which occurs so frequently, was not met with. Perforation of a duodenal artery occurred twice with fatal hemorrhage.

Two of the cases illustrate healing of the ulcer, one with and the other without alteration in the lumen of the tube.

CASE III.—*Typhoid fever; illness of fourteen days; perforation; peritonitis; cicatrix of ulcer in duodenum.*

A. B., aged 40, night-porter at Montreal General Hospital, had been ill for two weeks with typhoid fever, when perforation took place, and death followed in eighteen hours from acute peritonitis. The post-mortem showed extensive typhoid lesions and a perforated ulcer one foot from the ileo-cæcal valve. In the first portion of the duodenum, an inch from the pylorus, on the anterior wall, was a stellate cicatrix about three-quarters of an inch in diameter. There was slight puckering in the vicinity, but no narrowing of the gut. The heart and valves were normal. A few patches of atheroma on the aorta.

This illustrates the most favorable termination of an ulcer. Such cicatrices, according to some authors, are not uncommon. They have been so in my experience.

CASE IV.—*Phthisis; healed ulcer of duodenum, with stenosis of first portion; dilatation and hypertrophy of stomach.*

S. F., aged 35, had been in medical wards Philadelphia Hospital for six months with symptoms of advanced phthisis. He had on several occasions complained of gastric pain, and at times vomiting was a troublesome symptom; but attention was no specially directed to the abdomen.

Post-mortem.—Extensive pulmonary tuberculosis. Stomach moderately dilated; mucous membrane thick; muscular walls at least twice the normal diameter. Pyloric ring of normal size, a little firmer and thicker than usual. Duodenum, for three-fourths of an inch beyond the ring, normal and had a circumference of two and a half inches. Beyond this, at a distance of about one inch from the ring, there was a stricture admitting the top of the little finger. When slit open, it extended one and three-fourths inches, and measured one inch in circumference. The narrow portion reached nearly to the bile papilla. There was not much thickening of the coats at this part, indeed in places it was very thin, and the texture of the pancreas could be seen through the thin wall. Towards the stomach there was puckering and greyish-white cicatricial tissue. The ulcer appeared to have completely healed except at one small spot. There was pigmentation of the tissues of this portion of the bowel; not much thickening of the contiguous parts attached to the stenosed portion. There had evidently been an extensive ulcer, which had healed and produced stenosis just as happens not infrequently in gastric ulcer when near the pylorus.

Cases are reported in which the ulcer has perforated the liver or eroded the portal vein or the hepatic artery. The following case, in which I performed the autopsy for Dr. Rodger, is remarkable, inasmuch as the ulcer perforated the gall-bladder, eroded the tissues in the hilus, and ultimately divided the right branch of the hepatic artery, from which the patient bled to death. There are four other instances in literature in which this occurred, and in the first published case of duodenal ulcer by Broussais (quoted by Chvostek) the hepatic artery was eroded:—

CASE V.—*Jaundice for more than three months; repeated hæmorrhages from stomach and bowels; large ulcer of duodenum; perforation of gall-bladder; erosion of right branch of hepatic artery.*

Mrs. R. S., aged 48 years, a stout, well-nourished person. The following notes have been furnished by Dr. Rodger, under whose care the patient was:

"She had been married upwards of twenty-four years, but never had been pregnant; menstruation had been regular, but had ceased about three years ago.

"The only illness of consequence that she ever had was about fifteen years ago, when she was laid up in bed for about six weeks, with what was called an attack of inflammation of the liver. No jaundice was perceptible at that time. Ever since, however, she has been troubled with dyspepsia, obstinate constipation, and more or less pain or feeling of discomfort in the region of the stomach. Her condition to-day (March 18th, 1879) is that of a person suffering from a well-marked attack of jaundice; skin and conjunctivæ deeply tinged; urine dark, and stools pipe-clay in color; tongue coated; loss of appetite; no increase of temperature. She states that she has not felt well all winter, but was always able to attend to her household duties.

"Patient came to my office for about four weeks, at the end of which time the symptoms had not improved.

"On April 24th, visited the patient at her house. Examination revealed no enlargement of the liver, and only slight tenderness on firm pressure over the organ. Heart and lungs healthy.

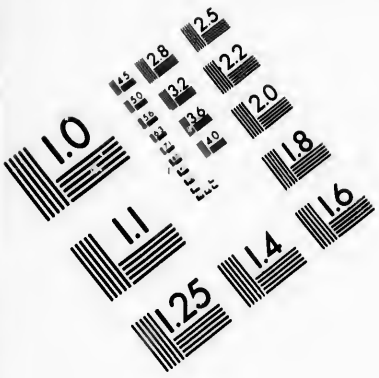
"Has noticed considerable blood at stool during the past few days, and fæces still pipe-clay in color. No hæmorrhoids. Dr. G. W. Campbell saw the case in consultation, and gave a very unfavorable prognosis, though the exact nature of the disease was doubtful.

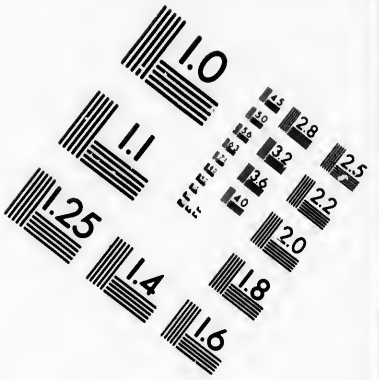
"All treatment adopted proved of no avail; the patient rapidly became emaciated, and continued deeply jaundiced. Several severe attacks of epistaxis have occurred lately, and to-day (May 30th) has passed more blood than usual by stool.

"At 3 p.m., May 31st, commenced vomiting blood, and continued to do so frequently all afternoon, in spite of treatment. The hemorrhage from stomach and bowels became excessive, and death followed in a few minutes."

Autopsy.—Body that of a well-nourished, moderately stout woman. In abdomen, coils of intestines dark-colored from staining of mucosa; peritoneal layer smooth. Liver dark-colored; the ascending colon, the stomach and duodenum are closely ad-

herent to the under surface of its anterior margin. Stomach, duodenum, pancreas and liver removed together. Stomach dilated and contains dark-colored cl[illegible] and remnants of food; mucosa dark and blood-stained, ot[illegible]se unaltered. Pylorus normal. Immediately outside its well-marked ring, in the upper and back part of the duodenum, is a large orifice 3·5 cm. in length and 1·5 cm. in breadth. It is partially blocked with clots, on the removal of which an oblong cavity is disclosed, occupying the under surface of the liver, in the position of the gall-bladder. The edges of the orifice are smooth and round, and the two fingers can be inserted into the cavity as far as the second joint. A good deal of thickening exists about the duodenum, where it is attached to the gall-bladder. Mucous membrane is not, however, puckered, and in the rest of its extent is normal. The following is the condition of the tissues in the hepatico-duodenal ligament: Portal vein uninvolved, normal in size. Common bile duct pervious, and can be traced down to the upper margin of the ulcer, where it appears to open; at least the probe-pointed scissors cut down freely and exposed the orifice at this situation, and it could not be further traced. It has probably been cut across by the ulcer. Walls are thickened. Branches in the liver normal. The cystic duct joins it by a small orifice, into which the probe can pass for 1·2 cm., and then meets with an obstruction on the wall of the sac. The hepatic artery, when slit up, is natural-looking; on following the branches, a probe inserted into the main division of the right branch, which passes backwards and outwards, enters the upper end of the gall-bladder, and on slitting it open the wall is seen to be ulcerated through in a space 3 by 2 m., and the vessel communicates freely with the sac. The gall-bladder was then exposed, and is found in a condition of ulceration. Only towards the upper part is there any trace of mucous membrane; in the rest of its extent the wall is rough, ulcerated, and, in places, sloughing. There is a deep prolongation towards the hilus of the liver, the tissue of which at this part is exposed and sloughing. It is here where the ulceration of the artery has taken place. The ascending colon, close to the flexure, is adherent to





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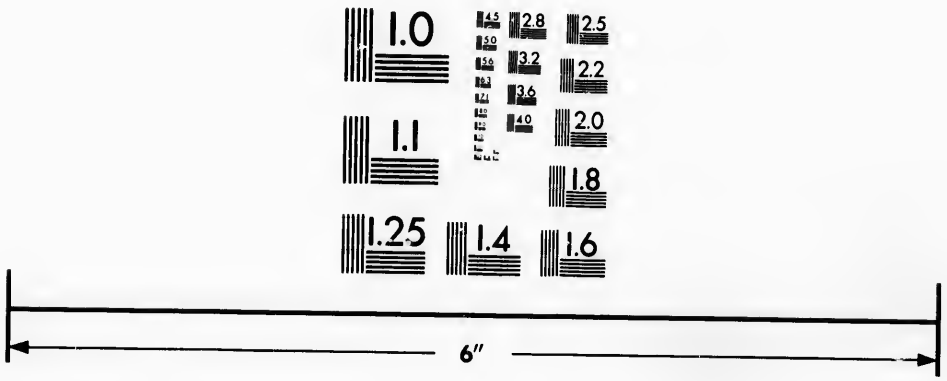

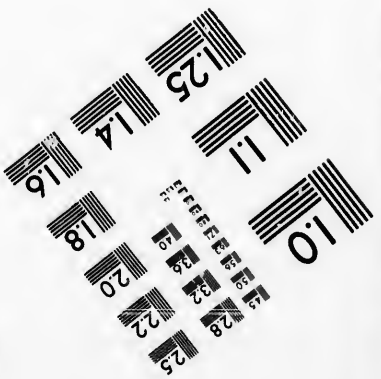

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the gall-bladder, and between the two there exists a circular orifice of communication, 7 m. in diameter, with rounded edges.

Death not uncommonly takes place by gradual exhaustion, consequent upon repeated vomiting.

CASE VI.—*Symptoms of gastric ulcer for many months; progressive emaciation; large irregular ulcer just outside pyloric ring.*

W. W., aged 72, patient of Dr. Wilkins. Well-marked symptoms of ulcer, supposed to be gastric. Death took place slowly, after many months illness.

Autopsy.—Body much emaciated. In abdomen, peritoneum dull and lustreless; two pints of turbid fluid, mixed with lymph, removed. Stomach appears dilated. Œsophagus presents in its terminal part an oval area, 3·5 by 1·2 cm., from which the mucous membrane has been completely removed by the action of the gastric juice. In the centre a thin external layer alone remains. Stomach moderately dilated, and contains a dirty-looking, highly acid fluid. Mucous membrane pale; that of the fundus thin, owing to post-mortem solution. At the pyloric end it is thick, and present numerous mammillations. The pylorus is greatly narrowed, admitting only the top of the little finger as far as the root of the nail. On slitting open the ring and the duodenum, the following condition is observed: Pylorus not thickened; ring prominent, but not more so than is often seen. Immediately external to it is an irregular ulcer extending round the greater part of the circumference of the gut, and presenting an imperfect division into two portions, the larger of which occupies the lower part of the tube, resting upon the pancreas, the other being placed above and to the right. The extreme length of the ulcer is 3·7 cm., the breadth ranges from 6 to 13 m. The edges are round and somewhat undermined. The base is formed of firm fibrous tissue of a greyish-white color. Close to the lower edge there is seen, on the floor, a small nodular body, looking like the end of a closed artery. The mucous membrane of the duodenum near the ulcer is greatly puckered, particularly the upper part. The bile papilla is about 5 cm. below the ulcer.

Nothing of special note in the other organs beyond the atrophy of extreme emaciation.

The symptoms of duodenal ulcer are extremely variable and rarely distinctive enough to make the diagnosis more than probable. In very many cases the process is latent, and the first symptom may be hemorrhage or peritonitis from perforation. In others the ulcer is accidentally found post-mortem, and has had no apparent influence in the course of the disease from which the individual has died, as in the following instance :—

CASE VII. — *Spinal curvature; bronchitis, pulmonary collapse; ulcer in first portion of duodenum; no symptoms.*

M. G., a boy aged 12, admitted to the Montreal General Hospital in March, 1877, with bronchitis. He had great deformity of the spine, with contraction (vertical) of the thorax. He became very cyanotic, and died in about a week. There was intense bronchitis, with splenization of lower lobes of the lungs. The right ventricle was large and the walls thick. The valves on both sides were normal. The mucous membrane of stomach and intestines was congested; in the jejunum the edges of the valvulæ conniventes were in places ecchymosed. In the first part of duodenum, one and a half inches from the pylorus, there was a punched out ulcer in the posterior wall, about 1·5 centimetres in diameter. The edges were well defined, the base made up of the muscular layer, and there was no special thickening in the neighborhood.

In essential details the symptoms of the duodenal are identical with those of the gastric ulcer. There are, however, certain peculiarities. Dyspepsia is not so constant a feature in duodenal ulcer, and may not amount to more than a slight feeling of uneasiness some time after eating. In Chvostek's list of cases collected since 1865, there were 44 in which this symptom was specially referred to, and of the entire number only 16 had loss of appetite and uneasiness after eating.

Vomiting is a variable symptom, and was only present in one-fourth of Chvostek's list of cases. Usually it occurs at the end of attacks of severe pain.

Hemorrhage is a common symptom, occurring in a third of the cases, and the blood may be either vomited or passed in the stools, or appear in both.

CASE VIII.—*Gastric symptoms for seven or eight years; attacks of severe gastralgia; prolonged periods of freedom: hemorrhage from stomach and bowels.*

M. I., aged 40, patient of Dr. F. W. Campbell. This case was remarkable for the long duration of the symptoms, the severe gastralgic attacks, and the remarkable periods of freedom from troublesome symptoms. He had on several occasions hemorrhage from the bowels without hæmatemesis, and this feature of the case led Dr. F. W. Campbell and Dr. R. P. Howard to suspect that the condition was one of duodenal, not gastric, ulcer.

Autopsy.—Moderate emaciation. In abdomen, stomach appears a little dilated; lower coils of small intestine dark-colored. Nothing special in thorax. Stomach somewhat dilated; walls of moderate thickness. Mucous membrane pale; at the cardiac end, thin. Pyloric orifice is narrowed, admitting the little finger to the second joint. When slit open, there is no special thickening; but the mucosa is puckered, and presents an elevated ridge. Duodenum: Part immediately outside the ring much narrower than adjacent regions, measuring only 3·7 cm. About 10 m. from the pylorus there is an oval ulcer 2·5 by 1·8 cm., extending in direction of axis of gut, and occupying chiefly the posterior section of the tube. It is deep, with rounded edges, which, toward the upper and back part, are undermined for about 6 m. In places the floor of the ulcer is quite 6 or 7 m. below the level of the mucosa, and presents a tolerably smoth, fibrous appearance. The head of the pancreas forms the base of the lower three-fourths, the upper part is protected only by the thin muscular walls of the first piece of the duodenum, the peritoneal surface of which, at the site of the ulcer, is puckered and cicatricial. Immediately in the centre of the floor is a small, dark, blood-stained elevation, consisting chiefly of fibrin. On injecting water through the hepatic artery, small clots are washed out at this point, and the water flows freely into the ulcer through an

opening in the gastro-epiploica dextra, 2 m. across, and with smooth edges. The papilla of the bile duct is 6 cm. below the ulcer. Nothing else of note in intestines.

CASE IX.—*Severe gastralgic attacks for six months; slight dyspeptic symptoms; hemorrhage from stomach and bowels.*

J. G., aged 45, seen with Dr. Whiteside June 13th, 1885. Patient was a large, stout man, who had been strong and healthy. He had taken alcohol freely, and of late has had business worries. No history of syphilis. He had suffered at times with dyspepsia, but, as a rule, he had a good appetite and good digestion. In February he began to have pains in the abdomen. The first attack came on suddenly one night, and was so severe that he got no sleep. They have recurred on and off ever since, most frequently at night, lasting from one to three hours. He described the pain as starting in the epigastric region and passing to the back and round the sides. He would frequently sit on the edge of the bed for hours doubled with the pain. In the intervals of the paroxysms there was a dull, heavy sensation in epigastrium. There was never any vomiting with these attacks. Food, he insisted, had no special influence one way or the other in inducing or aggravating the pain. Sometimes there was a sense of oppression after a full meal. Pressure often gave relief during the paroxysm. Since February he has not been a week free from attacks, and has lost between 30 and 40 lbs. in weight.

Inspection showed a stout, well-nourished man. Face pale, tongue lightly furred; pulse 104, tension increased. The abdomen large and fat, and in the epigastric region there was a remarkable throbbing, most distinct about two inches and a half from the ensiform cartilage, but a large wave of pulsation passed over the whole abdomen from this point. The shock, indeed, of the pulsation was unusually forcible, and was perceptibly communicated to the bed. The heart impulse was not very marked. On palpation, there was a sense of deep resistance between navel and ensiform cartilage, but no distinct tumor could be felt, no thrill. The thick panniculus, however, made the examination

very difficult. The throbbing was very violent with each systole, but the pulsation which could be felt was trifling in comparison with the visible pulsation. This I underlined in my notes. The spot where it was most distinct corresponded to a point a little more than two inches from the ensiform cartilage. There was no expansile movement; no dullness. There was no dilatation of stomach. On auscultation, a systolic murmur was heard at ensiform cartilage and for one and a half inches below it, also audible in 7th and 8th left costal cartilages. In these positions it was a distant but very distinct murmur. In the genu-pectoral position the throbbing was less marked, but no tumor could be felt. No murmur could be heard at the back, and there was not special tenderness over spines. The liver and spleen were normal. There was a soft systolic murmur at apex of heart, and the second aortic sound was very sharp and clear.

I only saw the patient on this occasion and a positive diagnosis was not reached. Three possibilities were discussed—ulcer of stomach, aneurism of abdominal aorta, and deep-seated tumor lying upon the aorta. The cardialgic attacks, so pronounced, and of a character so similar to those which occur in ulcer, seemed to point to this condition, but the entire absence of vomiting and the tolerance of food seemed inconsistent with this view. The remarkable throbbing and the systolic murmur suggested aneurism, in which, also, there may be, as in Stokes' celebrated case, the most intense paroxysms of pain, but in the absence of a positive tumor, throbbing and a bruit do not suffice to establish the diagnosis of aneurism.

Dr. W. L. Morris has kindly furnished me with the notes of the case subsequent to my visit. On the evening of the 13th he had most excruciating pain, lasting two hours; no vomiting. On the 14th he vomited in the morning; no gastralgic attack. On the 15th he vomited two quarts of thin fluid, in which there was a blackish sediment. On the 16th, vomited a great deal. For the next week he had repeated attacks, bringing up dark material like altered blood, and passed dark stools. He gradually sank and died on the 24th.

Autopsy, twenty-hours after death.—Skin blanched; much

subcutaneous and omental fat. The heart was flabby and soft. The mitral curtains a little thickened at edges; aortic cusps also thickened about the corpora Arantii. The aorta presented advanced atheromatous changes, particularly in arch and its branches. The abdominal aorta was also roughened by numerous irregular projections. The lungs presented no special changes. The stomach was distended with gas, and contained about a pint of dark fluid. Mucosa towards pylorus thickened; no other changes. Duodenum, half an inch from the pyloric ring, presented a round ulcer the size of a half-dollar piece (3 cm.), the base formed partly by head of pancreas and partly by thickened omental tissue. A small orifice existed in the wall of the superior pancreatico-duodenal artery which ran along the floor of the ulcer. There was thickening about the head of the pancreas, and the subjacent tissues were matted together.

Pain is a very variable symptom in duodenal ulcer, and is absent in at least one-half of the cases. There may be for years agonizing gastralgic attacks recurring at irregular intervals, usually worse at night, and coming on from two to six hours after taking food. As in *Case VIII*, there may be prolonged periods of freedom from the attacks. The diagnosis of duodenal from gastric ulcer is rarely possible, as there are no distinctive features. The gastralgic attacks recurring at intervals for many years appear to be more common in duodenal disease, and was the symptom, I believe, which led a distinguished American clinician to make the diagnosis in his own case.

LXXVI

LAVERAN.

A.[1]

Très honoré Confrère

Je vous remercie d'avoir bien voulu m'envoyer le tirage à part de votre article sur les hématozoaires de la malaria et j'y avoir joint vos très remarquables leçons sur différents problèmes de la physiologie du sang. Je vous remercie également d'avoir pris la peine d'écrire à M. Councilman pour le prier de m'envoyer

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[2] *Traité des Fièvres Palustres*, Paris, 1884.
[3] *Comptes Rendus*, 1882.
[4] *Fortschritte der Medicin*, Nos. 14 and 24, 1885.
[5] Paper read before the Association of American Physicians, June, 1886.
[6] Councilman amd Abbot, *American Journal of Medical Sciences*, April, 1885.

Autopsy, twenty-hours after death.—Skin blanched; much

LXXV

cerebral aneurysm.

An original drawing illustrating this [illegible] missing paper, and found in 1928, I have put in the pasted book, no. 7666 [illegible] W. W. F.

LXXVI

SS

MALARIA.[1]

ıfesting the blood has ıow that certain of these y distributed and more

Parasites belonging to the spirozoa, and to the nematode and trematode worms, have long been known to occur in the blood of various animals. Recent investigations prove that the flagellate protozoa are also not uncommon blood parasites, and it is possible that they may be the pathogenic organisms of certain diseases. I propose in this communication to give an account of the hæmatozoa which have been found in persons suffering with the various forms of malaria.

Historical.—Our knowledge of the blood-changes I am about to describe, dates from the researches of Laveran, in Algiers, which were communicated to the Paris Academy of Medicine in 1881 and 1882, and which were finally embodied in a large work on the malarial fevers, published in 1884.[2] He found, as characteristic elements in the blood of persons attacked with malaria, (1) crescentic pigmented bodies; (2) pigmented bodies in the interior of the red corpuscles, which underwent changes in form, described as amœboid; and (3) a pigmented flagellate organism. These forms were looked upon as phases in the development of an infusorial organism which he regarded as the germ of the disease. Richard[3] confirmed these observations. A more general interest in the question was aroused by the publications of Marchiafava and Celli,[4] who found in the blood of malarial patients at Rome the bodies described by Laveran. They figured carefully the alterations of the organism in the interior of the red corpuscles to which they gave the name Plasmodium malariæ. Councilman, of Baltimore, has more recently confirmed these observations.[5] The pigment granules so numerous in the interior of the red corpuscles in cases of "comatose pernicious fever," and which appear to be included in a hyaline mass are, according to Marchiafava and Celli, and Councilman (who had previously described them[6]) these amœboid parasites deeply laden with altered hæmoglobin.

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[1] An address delivered before the Pathological Society of Philadelphia.
[2] *Traité des Fièvres Palustres*, Paris, 1884.
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[5] Paper read before the Association of American Physicians, June, 1886.
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Autopsy, twenty-hours after death.—Skin blanched; much

AN ADDRESS

ON

THE HÆMATOZOA OF MALARIA.[1]

Our knowledge of the animal parasites infesting the blood has been of late enriched by observations which show that certain of these hæmatozoa, as they are called, are more widely distributed and more important than we had hitherto supposed. Parasites belonging to the spirozoa, and to the nematode and trematode worms, have long been known to occur in the blood of various animals. Recent investigations prove that the flagellate protozoa are also not uncommon blood parasites, and it is possible that they may be the pathogenic organisms of certain diseases. I propose in this communication to give an account of the hæmatozoa which have been found in persons suffering with the various forms of malaria.

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Technical Details.—The finger pad from which the blood drop is taken should be thoroughly cleansed, and, if the examination is made during a paroxysm, the sweat which may exude after the friction and drying should be removed. Attention to these, apparently trivial, details will secure specimens of blood free from small particles of dirt, and facilitate considerably the search for pigmented bodies. The layer of blood beneath the top cover should be very thin and uniform, the corpuscles, as far as possible, isolated and not aggregated in clumps or in rouleaux. It is well to surround the cover with paraffin if the examination is prolonged. No reagent of any kind should be added. Cover-glass preparations may be made and stained in methyl blue or fuchsin, and mounted in balsam. Osmic acid preparations may also be employed. Although these bodies may be seen with a power of 500 to 600 diameters, it is essential for the satisfactory study of the changes to use higher powers. I have uniformly worked with the $\frac{1}{12}$ homo. immersion of Zeiss, and the $\frac{1}{18}$ im. of Reichert. Stricker's warm stage will be found useful.

Description of the Bodies.

1. *The Forms which Exist within the Red Corpuscle.*—(*a*) The most common alteration in the blood of malarial patients is presented by a pigmented structure inside the red corpuscle. The attention of the observer will most likely be first attracted by the presence of a few dark grains in the stroma, and a careful study of a suitable specimen will soon lead to the conviction that these are not scattered loosely, but are enclosed in a finely granular or hyaline body in the interior of the corpuscle (Fig. 1). The red discs in which

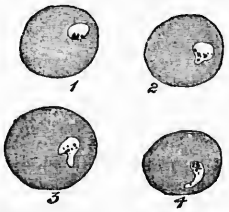

Fig. 1.—Amœboid body in red blood-corpuscles. The sketches were made at intervals of five minutes.

they occur are usually larger, look flat, and are very often paler than normal; they may, indeed, exist only as colourless shells. The number of corpuscles so affected varies extremely in different cases. In some instances they are readily found after a search of a moment or two, but, in other cases, a prolonged examination may be necessary. Only one is usually present in each corpuscle, but two or three, or even four, may occupy the stroma. They vary greatly in size, the smaller ones not occupying a fourth of the corpuscle, while the larger ones may almost fill it. A delicate contour line can usually be seen separating the body from the stroma; at times this is very indistinct, particularly if the illumination is very bright. The substance appears hyaline, or very finely granular, and the pigment grains are scattered irregularly in it. They may be very numerous, and give a dark aspect to the body, or they may be scanty. They frequently present rapid Brownian movements. Occasionally a vacuole may be seen in the interior of the body. In several instances the bodies appeared to be enclosed in a clear space—vacuole—in the stroma. When first seen they are more or less spherical, but, as already stated, the outline may be indistinct. The pigment granules may be seen to alter their position

in relation to each other. If the margin of the body is carefully observed, slow changes can be seen, which gradually bring about alterations in shape. These movements, which appear to be amœboid in character, can often be traced with great ease. They are well represented at Fig. 1, and, better still, at Fig. 2. Changes in position of the body in the corpuscle result from them. They are decidedly slower than the amœboid movement of the colourless corpuscle. I have not seen any evidence of migration from the corpuscle. In dry preparations these bodies stain deeply with gentian violet or fuchsin, and present a granular stroma, in which the pigment grains are imbedded. (Fig. 3.)

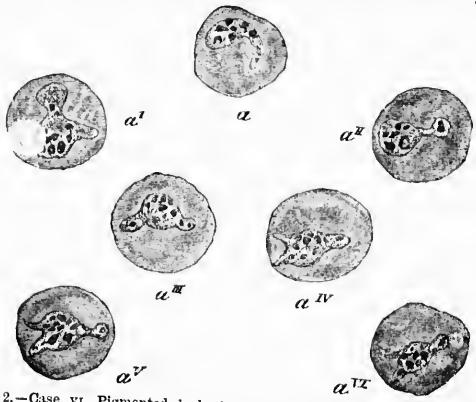

Fig. 2.—Case vi. Pigmented body in red blood-corpuscle; outlined with camera ($\frac{1}{12}$ Zeiss, C eye-piece), by Dr. J. P. C. Griffith; illustrating some of the changes during an hour and a half's observation. a, at 11.45, slow alterations in outline, and the pigment-granules are in active dancing motion. a^{i}, 12.15. a^{ii}, 12.25, body has rotated as well as altered its shape. a^{iii}, 12.30. a^{iv}, 12.40. a^{v}, 1 o'clock. a^{vi}, 1.02.

Fig. 3.—Cover-glass preparation of blood stained with fuchsin. The amœboid bodies stain deeply in the corpuscles. Some of them are not pigmented.

(*b*) In seven cases peculiar hyaline structures existed in the interior of the red corpuscles, which differ from the bodies just described, in the absence of pigment and in the much greater activity of the changes. Fig. 4 illustrates the appearance and the alterations in outline. These

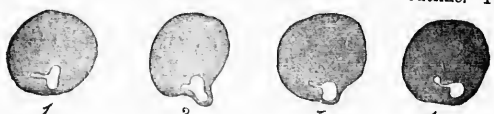

Fig. 4.—Sketches of the alteration in form of one of the hyaline bodies; 1, at 7.8 P.M.; 2, at 7.12; 3, at 7.15; 4, at 7.20.

bodies are devoid of structure, and the corpuscles in which they are present are not so pale as those with the pigmented forms. Marchiafava and Celli, who have given an excellent plate of these bodies,[7] regard them as the initial forms of the pigmented bodies. One does occasionally see appearances indicative of commencing pigmentation, but they have not, as a rule, the solid aspect of the pigmented bodies. In three cases I have seen the following remarkable changes. The hyaline body, while actively changing shape, suddenly burst from the stroma, and disappeared, or formed only a few granules. Thus, in a red corpuscle, there were, at 3.40 P.M., two hyaline, irregular-shaped bodies, which were changing rapidly in outline. The alterations were so marked that the physicians present at the time had no difficulty in seeing them. The stroma of the corpuscle was of full colour. At 3.50 P.M., as I was carefully watching these forms, the corpuscle suddenly ruptured, and gave exit to two distinct masses, which quickly broke up into ten or twelve spherical bodies. No change took place in these after twelve hours, except that they became pale and indistinct. The stroma of the corpuscle became quite colourless. On two other occasions a similar phenomenon was witnessed, but in one no trace could be seen of the extruded material. This is evidently a physical change, and I think these very pale hyaline bodies must be carefully distinguished from the pigmented forms, though possibly associated with their early development.

(*c*) In seven cases there were vacuoles in the red corpuscles containing solid-looking bodies of various sizes and shapes. Certain of these structures resembled micrococci very closely (Fig. 5), and stained

Fig. 5.—Cover-glass preparation, showing corpuscle with solid, deeply stained bodies in small vacuoles.

deeply in aniline dyes ; but others, often in the same corpuscle, were larger, more irregular, and altogether different in appearance (Fig. 6.)

Fig. 6.—1, 2, 3, Larger solid bodies in the interior of vacuoles (?) which alter in outline. 4, A red corpuscle, with a small vacuole containing small pigment-granules of a deep brown-red colour.

The smaller ones were usually highly refractile, and, when two were together, the appearance suggested a diplococcus. In three instances these bodies had a deep brown tint, as if composed of pigment. The larger bodies were homogeneous, very variable in size and shape. No movement was noticed in them, but the outlines of the spaces in which they lay sometimes changed actively. In Case 29, these bodies were very abundant, and for days formed the only noticeable alteration in the corpuscles.

2. *The Free Forms.*—(*a*) Pigmented crescents. These bodies, which were found in eighteen cases, present remarkable features in appearance and structure. The form was usually that of a beautiful crescent (Fig. 7), with rounded or gently tapering ends ; but the degree

[7] *Fortschritte der Medicin.* 1885. No. 24.

of curvature was variable, and many forms were almost straight. The length is about double that of the width of a red corpuscle, sometimes more. They are not attached, and they never show any motion. Joining the ends of the crescents—or, more correctly, at a little distance from

Fig. 7.—Crescents, *a*, *b*, *c*, show the slow alterations in the form of the pigment, as sketched at 9.20, 10.40, and 10.55 A.M. *e* shows the narrow membrane sometimes present in the concave side.

the points—a narrow line can often be seen on the concave margin (Fig. 7, *e*). The body of the crescent appears made up of a structureless, homogeneous material, in the centre of which is a prominent collection of pigment granules. This, with the peculiar form, makes these bodies very easily recognisable in the blood, even when closely surrounded by the corpuscles. The pigment is very dark in colour, distinctly granular, and varies somewhat in its arrangement. As a rule, it is central and aggregated, either in a heap, or assumes the form of a band placed transversely to the axis of the crescent. In some instances it is more scattered, but I have never seen it at either end of the body. Although the most careful examination fails to detect any movement in the hyaline substance of the crescent, yet the existence of such may be inferred from the very positive movement which the pigment granules undergo. Fig. 7, *a*, *b*, *c*, represents these alterations; changes in form are exceptionally seen, as shown at Fig. 8 (1, 2, 3). A crescent became, within an hour, an ovoid body.

Fig 8.—*a* and *b* show crescents in the interior of red corpuscles; 1, 2, and 3, changes in a crescent.

Sketch 1 was made at 9.40, 2 at 10.10, and 3 at 10.30 P.M. The outline of these bodies is very clear and defined. Ovoid, elongated and rounded forms of identical structure are also met with, but the crescents predominate. The number is variable, from one or two in a slide, to six or eight in the field of the 1-12th im. Though almost always free, they occur sometimes in the interior of a corpuscle, indicating, doubtless, the mode of development (Fig. 8, *a* and *b*).

(*b*) *The Rosette Form.*—In six instances there were rounded bodies, a little larger than red corpuscles, with a dimly granular protoplasm, and in the centre a rosette of pigment (Fig. 9). Some of these appeared to be enclosed in a delicate membrane, others were free. In

Fig. 9.—Rosette-form: 1 free; 2 within the shell of a red corpuscle.

six cases remarkable changes were seen in these forms, of the nature of segmentation. Thus Fig. 10, *a*, represents one of these as seen at

Fig. 10.—Segmentation of a rosette-form: *a* at 6 P.M.; *b* at 6.10, segmentation proceeding; *c* 6.30, segmentation complete; *d* 7.40, small free bodies.

6 P.M., September 4th. At 6.10 (*b*) there were distinct indications of segmentation in the finely granular protoplasm. At 6.30 (*c*) this had resulted in the formation of twelve or fifteen rounded bodies clustered about the central pigment, and still enclosed in the sheath. At 7.40 (*d*) the shell had burst, and given exit to the small corpuscles, which presented a tiny speck at or about the centre. At 10.40 they had not undergone any material change. In Case 60, one of quartan ague, this phenomonon was repeatedly observed. The development of the rosette form can, I think, be traced from the intra-cellular pigmented bodies, which increase in size until the entire corpuscle is filled. In some instances the body was surrounded by the remnant of the red corpuscle, in others there was no trace of it. The pigment granules gradually collect in the centre of the body in a more or less distinct rosette. I thought these changes had been overlooked by the writers on this subject, but I find that Golgi[a] has given a very full description of them, and has beautifully figured the development of the rosette form from the intra-cellular pigmented bodies. He has followed the process of segmentation with much greater detail than I have been able to do.

(*c*) *Flagellate organisms.*—Two or three years ago, when I first read Laveran's papers, nothing excited my incredulity more than his description of the ciliated bodies. It seemed so improbable, and so contrary to all past experience, that flagellate organisms should occur in the blood. The work of the past six months has taught me a lesson on the folly of a scepticism based on theoretical conceptions, and of preconceived notions drawn from a limited experience. Flagellate bodies were seen in seven cases, never in great numbers, usually only one or two in a slide. They are smaller than red blood-corpuscles, often not more than half the size. A specimen in one case was equal in one diameter to a red corpuscle lying near it. They are round, ovoid, or pear-shaped; the protoplasm finely granular, and in every instance contained pigment, usually central, which often displayed rapid Brownian movements (Fig. 11). The flagella are variable in

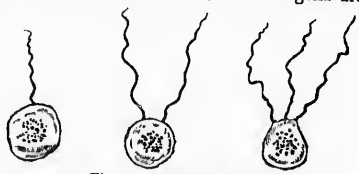

Fig. 11.—Flagellate forms.

number; one, three, and four were noted in different specimens. The length, as closely as could be estimated, was two or three times that of the body. They are exceedingly delicate, gently tapering, and, except in one instance, I could not determine the existence of a

[a] Sulla Infezione Malarica, *Archivio per le Scienze Mediche*, vol. x. No. 4, 1886.

small terminal knob, figured by Laveran. The movement is exceedingly active, and the lashing of the long filaments may be sufficiently strong to drive away the corpuscles in the vicinity. The undulatory movement caused by the play of the filament over the surface of a group of corpuscles may attract the attention of the observer before he sees the cilia. The motion does not persist long; in none of the specimens which I examined, for more than half an hour. In one instance, the flagella disappeared in the short interval between two observations, but I could not determine what became of them. I have not seen the free-swimming cilia described by Laveran, but Dr. Councilman tells me that he has confirmed this observation. I have not been able to discover either nucleus or vacuoles in the flagellate organism. Slight, irregular changes in outline occur, due to slow movements in the protoplasm.

(*d*) Small, round, pigmented bodies, from one-fourth to one-half the size of a red corpuscle, were not uncommon in some cases (Fig. 12).

Fig. 12.—Small free pigmented bodies, some of which show amœboid movements.

Usually, they remained unchanged, but, in several instances, they showed amœboid movements. The smaller ones about equal in size the products of subdivision of the rosette form.

Before proceeding to discuss the nature of these bodies and their relation, I will briefly refer to the condition of the blood-corpuscles.

The red corpuscles showed no other notable alteration save that already described. The pigmented organism evidently destroys the vitality, and consumes the hæmoglobin, for the affected cells become pale, often spherical, and, finally, are reduced to the condition of mere shells; except in cases of pronounced anæmia, the variations of the corpuscles in size and outline were not great. The colourless corpuscles were in some cases increased in number, and in very many instances contained dark granules. In several specimens, they were observed to contain the pigmented organisms. In Case 40, a crescent had been included (Fig. 13), and, in Case 51, the process of inclusion

Fig. 13.—A colourless corpuscle containing a crescent.

of two free pigmented bodies was watched during half an hour (Fig. 14). The blood-plaques were, as a rule, scanty, even when the anæmia was pronounced. No pigment was seen in them.

Types of Malaria Studied.—Of the seventy cases examined, a majority were instances of ordinary intermittent fever, chiefly quotidian and tertian, with two quartan cases. There was one case of remittent fever, one of comatose pernicious malarial fever, and the remainder were cases of malarial cachexia or chronic paludism, with occasional outbreaks of fever, with or without chills. In all of the cases, with the exception of seven, one or other of the forms above described was found in the blood.

Relation of the Forms to the Varieties of Malaria.—The pigmented amœboid bodies are met with in both acute and chronic cases, but they may be said to be specially characteristic of the more acute mani-

festations of the disease. In recent examples of quotidian or tertian ague which had not been under treatment, the amœboid intra-cellular forms were almost invariably present. I will refer subsequently in detail to the cases in which they were not found. The hyaline non-pigmented forms, and the vacuoles containing solid bodies, also occur in the acute cases; indeed, these latter forms were the only alterations noted in several instances. Thus, in Case 29, a man aged 48 was admitted to the Philadelphia Hospital September 27th, in a chill. He had had a paroxysm ten days before, and had suffered with malaria several years previously. The blood examined during the hot stage showed no pigmented bodies, but numerous corpuscles containing the vacuoles shewn in Figs. 5 and 6. The chills occurred on the 28th, 29th, 30th, and October 1st; and each day the blood was carefully examined, without finding other bodies than those in the vacuoles or hyaline spaces. On October 1st, the patient began with ten grains of quinine twice a day, which was continued for five days. He had no chill after October 1st. On the 7th there were crescents in tolerable numbers, which persisted until the 27th, the date of the last examination.

The crescents appear to be associated with the more chronic forms of malaria, or with acute cases which have been under treatment for some time. Of eighteen cases in which they were present, in twelve there was a history of infection lasting from six weeks to six months. In many, the cachexia was marked, and the spleen greatly enlarged. In six instances the attacks were recent—under a month; but in every one of these cases quinine had been taken. As a rule, the crescents occurred alone in the blood; but there were cases observed in which the pigmented amœboid bodies, the rosette form, and the flagellate organisms, were also present. I did not find the crescents in any recent cases of intermittent fever which had not been under treatment.

The rosette form, with its peculiar segmentation, occurred in six cases, and always in association with the amœboid intra-cellular bodies. Case 31: tertian ague, examined in fourth attack; no medicine. Case 33: quotidian for seven days. Case 37: quotidian for six weeks, anæmic, and had a large spleen; took quinine one day. Case 39: quotidian for seven days. Case 58: quotidian, on and off, for six weeks, then stopped; now daily chill for a week. Case 60: quartan for three weeks. I have noted these details, as this form has not been much studied, and as Golgi seems inclined to ascribe to it an important connection with the development of the paroxysm. It was only observed in acute cases which had not been under treatment.

The flagellate organisms were present in seven cases, six of which were chronic forms, and one an acute case of three weeks' duration.

The small free pigmented bodies were very variable in numbers; they seemed more abundant in the chronic forms with cachexia.

Relation of those Forms to the Paroxysm.—Very many observations were made with a view of determining whether these organisms bore any definite relation to the remarkable periodic attacks which characterise acute malaria. For this purpose, in typical cases, examinations were made in the intervals of, just before, and in each stage of, the paroxysm. The results may be thus stated: there were instances, particularly if recent, in which the amœboid organisms were decidedly more numerous and larger before and during the paroxysms than in the intervals; there were others in which the number during the chill and hot stage was so small, that examples were very hard to find; in others again, slides taken before the attack and during each stage were negative, and yet in subsequent paroxysms the bodies were present in the blood. I think, on the whole, that the pigmented bodies in the red corpuscles are more numerous before and during an attack, but the difference is by no means striking, and I have re-

peatedly had to search long in slides prepared during a paroxysm for a single example. In acute cases which have lasted some weeks, and have had no medicine, the amœboid bodies have seemed to be quite as abundant at one time as another. Nor have I been able to see any special difference in the form of the bodies just before or during the chill, though in the early days of the attack they may be small and less distinctly pigmented, or indeed may present, as in Case 29, already referred to, the appearance of vacuoles containing small solid bodies.

The remarkable segmentation of the rosette form was in each instance met with during the paroxysm, and Golgi claims to have traced in five cases a series of changes corresponding to the stages of the attacks. In the intervals, the pigmented bodies gradually increase in size until they fill the affected red corpuscles, and finally the pigment collects in the centre, as shown at Fig. 9. The process of fission coincides with the onset and course of the paroxysm, and by the time of its conclusion the rosette forms disappear. In Case 60—a quartan ague—an attempt was made to follow these changes, with the following result. The patient, a lad of 18, had had malaria, on and off, for a year, but for three weeks before admission the chills had been recurring with regularity. On Saturday, the 6th, the blood was examined in the chill. The red corpuscles contained many large pigmented bodies, and the rosette forms were numerous, many in process of subdivision. On the 7th and 8th, he was free from fever, and the most careful examination of the blood failed to detect any forms but the ordinary pigmented intra-cellular bodies. They did not seem more numerous on the evening of the 8th than they were on the 7th. On the 9th, hourly examinations of the blood were made between 11 A.M., when the fever began, and 4 P.M. In the first two slides, there were very many pigmented bodies with the granules becoming concentrated, some with typical rosettes and a few in course of segmentation. In the specimens taken during the afternoon, the process of division was readily traced, and there were many of the small bodies in the field. On the 10th the note is: "No free bodies, all intra-cellular, tolerably numerous; no rosettes; no segmentation." On the 11th, several examinations were made, and the note reads, "absolutely none, save pigmented forms in the red." On the 12th, the slide at 8 A.M. showed large number of pigmented bodies, some with the granules irregularly arranged, other with distinct rosette. Fever began at 12 A.M. Throughout the paroxysm, hourly examinations were made; rosette forms were abundant, and segmentation active. On the 13th and 14th, the ordinary forms were present, and in the paroxysm of the 15th, the segmenting bodies were again seen. The development of pneumonia interrupted the observations. It is worth noting that in this case the onset of the paroxysms was marked by an outbreak of the most intense urticaria. Blood and lymph from the wheals did not show any special changes.

Certainly the segmentation seems associated in some way with the paroxysm in these cases, but unless our observations have been faulty or very incomplete, there are many others in which there are no such changes in the attack. It is a point, however, to which the attention of observers should be carefully directed.

The crescents appear, as already stated, to be confined to the more chronic cases, or to those which have had treatment. They may persist for weeks or months. Thus in Case 56—a patient had irregular fever with what he called dumb chills, which had lasted for a month—for three weeks there was fever without chills, the temperature rising on some occasions to 103°. The crescents were numerous, and were not associated with other forms. With this his general condition was good, and he did not look anæmic. Under arsenic he improved, and the fever subsided, but the crescents were still in his blood six weeks from the date of the first observation.

Genuine paroxysms may occur in these chronic cases without the development of other forms than the crescents. This observation was repeatedly made in Case 25, a man with irregular malaria of many months' duration and occasional severe chills. The flagellate organisms did not seem to have any special relationship to the paroxysm, but they were so rarely seen that my observations on this point are not of much value.

Influence of Medicines on the Organisms.—Quinine invariably caused the pigmented bodies to disappear. In acute cases, which were usually studied during two or three paroxysms before the administration was begun, this observation was repeatedly confirmed. In a few days the corpuscles were entirely free; in several instances, the crescents appeared before the blood became normal. For example, Case 46 had his first chill on October 1st, and a daily recurrence until the 10th, when he came under observation. The pigmented bodies were abundant, and continued so on the 11th and 12th, when the temperature rose in the paroxysm to 105°. Quinine (twenty grains) was given on the morning of the 13th (which broke the chill), and repeated on succeeding days. The bodies were present on the 13th, and a few on the 14th. They were not found on subsequent days. In less acute cases the action of the quinine did not seem to be so prompt, and the crescents did not disappear so rapidly under its use. Certainly, in recent cases this medicine acts as a positive specific against these organisms, just as it does against the malady itself. Arsenic does not appear to influence the pigmented intra-cellular bodies. In a chronic case, without chills, but with irregular fever, the crescents persisted for over five weeks, although the patient had improved in general health and vigour, and was no longer anæmic. Thallin and antifebrin were given in some cases without any noticeable results. As is well known to practitioners in malarial regions, there are cases of intermittent fever which subside without special treatment. I have had several patients in whom, without any quinine, the chills stopped or recurred very irregularly. In Case 66, the crescents appeared in the blood, which at first contained only the intra-cellular forms.

Cases examined with Negative Result.—As before stated, there were eight instances of apparently true malaria in which the organisms were not found, and to these I shall now briefly refer. I would remark, in the first place, that we cannot always rely upon one, or even two, examinations of the blood for these bodies. They may be very scanty, or they may be present at one examination and absent at the next. For example, Case 41, a young man, aged 26, was admitted with a temperature of 104°. He had been cranberry-picking in New Jersey, and had been ill for a week with fever and indefinite pains, but no chills. He was so very dull, that as the fever persisted, typhoid was suspected, although, as a cranberry-picker, malaria was first thought of. The blood was examined on three occasions with negative results, but on the fourth observation, five days after admission, and when the temperature had fallen to normal, crescents were found, which continued in the blood until he was thoroughly cinchonised. The cases are as follows:

Case 10. Child, aged 5; chills and fever in Maryland nine months ago, occasional chills since, the last two weeks ago; spleen 4 inches vertical diameter; had taken quinine, none recently. One examination.

Case 11. Man, aged 19; never malarial before. Four distinct paroxysms. Slides examined from fifth and sixth, taken in cold, hot, and sweating stages. No quinine. I did not see the case subsequently.

Case 20. Man, aged 40. First attack six months ago. Chills on and off for past three months. Blood examined three days after last chill. Had taken quinine for two days. Spleen enlarged.

Case 21. Man, aged 28. Examined on 17th, first chill on September 6th; four since. On 14th, took quinine grs. xxx, and has had gr. x t. i. d. since.

Case 26. Man, aged 35. Chills for three weeks, at first quotidian, latterly tertian. Had taken medicine, but did not know the nature of it. Was admitted on 24th. Two examinations, negative; pigment in white corpuscles. On 25th quinine was given. Three subsequent examinations, without result.

Case 28. Man, aged 60. Admitted on 14th. Well-marked chills for eight weeks; had one when he came in, and four after. Blood examined on 28th, two slides. He had had quinine gr. xx each day since admission.

Case 38. Man, aged 70, resident of the almshouse for six years. First chill on 2nd, second on the 5th, third on 6th, when blood was examined, two slides.

Case 52. Man, aged 25. Chills and fever for six days. Blood examined in chill, and on the following day. Had had quinine.

Thus, in five of these cases quinine had been taken, and they may be counted out. In Case 10, the child was brought from the country, and only one examination was made. Case 11 was undoubtedly a case of quotidian ague, and the examination of slides taken from each stage of the fifth and sixth paroxysm was negative. I did not see the patient, and further examinations were not made. In Case 38, the bodies were not found on two occasions. This man also could not be followed, and I do not know his subsequent history.

The importance of excluding other causes for the paroxysmal chills was well illustrated by a case under the care of my colleague, Dr. J. H. Musser, which we regarded as one of malaria, but in which the pigmented bodies could not be found. The man had had chills on and off for several years; of late, the attacks had been more frequent and recurred more regularly. Quinine in medium-sized doses had no influence, but very large doses appeared to control the paroxysms. Their recurrence excited suspicions, and the discovery of pus in the urine, with decided pain on deep pressure in the lumbar region, indicated a more probable cause for the irregular chills.

Nature of the Organisms.—It is very evident that we are dealing here with structures unlike any others which have been described in human blood, and with bodies which have no relation whatever to the spirilla, micrococci, and bacteria of certain acute diseases. I would call attention to the remarkable unanimity in the description of these parasites by Laveran, Richard, Marchiafava and Celli, Councilman, Golgi, and myself. Laveran's original description is well-nigh complete, and subsequent workers have done little else than confirm his results, though to Marchiafava and Celli is due the credit of insisting upon the amœboid character of the intra-cellular form. Before discussing the relation of the forms to each other, it will be necessary to take a brief review of cognate organisms occurring in the blood, upon which recent investigations throw an important light.

It has been known for some years that hæmatozoa exist in the frog; one form, a flagellate organism, the Trypanosoma sanguinis, described by Gruby in 1843, is a well recognised monad; a second, the Drepanidium ranarum, of Lankester, is evidently a gregarine, possibly a larval form, as he suggests.[9] Having been long familiar with these bodies,[10] which were very abundant during several winters in the frogs in my laboratory at Montreal, I was at once struck with an apparent similarity to them of the forms found in malarial blood. The crescent-shaped body in particular resembles strongly certain of the gregari- and I thought it possible that we had here an instance

[9] *Quarterly Journal of Microscopical Science*, vol. xxii.
[10] *Canadian Naturalist*. 1883.

of a sporozoon becoming flagellate at one stage of its development as Rivolta affirms may be the case. I soon discovered, however, that there were other observations on hæmatoza which bore more directly on the subject, and rendered possible a more likely explanation. Mitrophanow,[11] in 1883, announced the discovery, in the blood of the carp and of the mud-fish, of parasites belonging to the flagellate infusoria. A description of these forms need not detain us, further than to note that they were polymorphic, and one stage was represented by an amœboid body without flagella.

In a report published by the Punjab Government, December 3rd, 1880, and in the *Veterinary Journal*, London, 1881-82, my friend, Dr. Griffith Evans, described a new and very fatal disease known as *surra*, which prevailed among horses, mules, and camels in India, and in which he discovered a parasite in the blood during life. At first Evans believed it to be a spirillum, but subsequently came to the conclusion that it was a much higher organism. His observations have an important bearing on the question of the parasites in malaria. In 1885, Veterinary-Surgeon Steel published "An Investigation into an Obscure and Fatal Disease among Transport Mules in British Burma," which also proved to be *surra*. A careful clinical investigation of the disease led to the conclusion that it was a true relapsing fever, very similar to recurrent fever of man. Steel found the parasite described by Evans in all cases, and determined that it appeared as the temperature rose and disappeared in the intervals between the paroxysms. He regarded it as a true spirillum, and named it Spirochœta Evansi. Both Steel and Evans found the disease readily communicable to dogs, horses, and mules, either by inoculation or by ingestion. Recently, on the return of Dr. Evans from India, he placed material from the *surra* disease in the hands of Dr. Crookshank, who has made an elaborate report,[12] confirming Dr. Evans's view that the organism is not a spirillum, and states that the parasite is morphologically identical with the hæmatozoa described by Mitrophanow in the carp and mud-fish. In 1879, Lewis[13] described certain parasites in the blood of rats in India; and, again, in 1884,[14] he more fully discussed the question, and spoke of the identity of the organism with that found in the *surra* disease. Crookshank, in the paper just mentioned, gives the results of his investigations on the blood of European rats, 25 per cent. of which he finds infested with Lewis's parasite. It is a flagellate organism, with an undulating fin-like membrane, and is highly polymorphic. Crookshank has distinguished "globose, angular, non-filamentous, bi-flagellate, semi-circular, and disc forms;" the latter represent the encysted stage. This organism is believed to be morphologically identical with the *surra* parasite and with Mitrophanow's hæmatozoa.

In the *Biologisches Centralblatt*, 1885, Professor Danielewsky, of Charkoff, makes an important contribution to the subject. He states that Trypanosoma, the well known flagellate organism of frog's blood is polymorphic, and occurs in an amœboid form, and also produces spores; and, further, he has found in the red blood-corpuscles of birds a pigmented protoplasmic body, which subsequently appears in the plasma as a pigmented flagellate organism. In a later communication,[15] he suggests the identity of the pathogenic blood parasites of man with the hæmatozoa of healthy animals, and refers specially to the similarity of the forms which he has found in birds to certain of those described by Laveran in malaria.

With this information, we are in a better position to discuss the

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[11] *Biologisches Centralblatt*, Bd. iii, p. 85.
[12] *Journal of the Royal Microscopical Society*. 1886.
[13] *Quarterly Journal of Microscopical Science*. 1879.
[14] *Quarterly Journal of Microscopical Science*. 1884.
[15] *Centralblatt f. die Medicinischen Wissenschaften*, Nos. 41 and 42. 1886.

relation of the forms described to each other, and the zoological position of the organism. It is evidently closely allied to the hæmatozoa just spoken of, and the facts which we know of their life-history enable us to assert, with greater confidence, that we are here dealing with the varieties of a highly polymorphic species, and not with two or three different organisms. The flagellate form is doubtless the adult condition; and it is interesting to note, in contrast to the hæmatozoa of the rat and of the *surra* disease, the comparative infrequency of its occurrence. Laveran met with it ninety-two times in four hundred and thirty-two cases, and Councilman eleven times in eighty cases. The steps in development remain to be worked out. It seems clear, however, that the pigmented amœboid form may become transformed into a sporocyst (represented by the rosette form and its changes), or into an encysted body (resting form), the crescent. The gaps in our knowledge relate specially to the form and manner of entrance of the parasite into the red corpuscle. Do the solid particles contained in the vacuoles (Figs. 5 and 6) represent the earliest stage? I think it highly probable that they do, and that they, with the hyaline unpigmented bodies, are the immature forms. The spore-like structures which result from the segmentation of the rosette form do not resemble the small solid bodies seen in the red corpuscles, but are rather like the tiny free pigmented forms which, in some cases, were abundant in the plasma. Of the latter, various sizes are found, and it is possible that from them the adult flagellate bodies arise. Golgi suggests that the spores, resulting from the segmentation, pass to the spleen, and there attack the red corpuscles, in which they develop into the amœboid forms. As at present the data are not available for a final decision, a further consideration of these points need not detain us. There is sufficient evidence to show that the various forms are only phases in the life-history of one of the flagellate protozoa, belonging to the order Flagellata-Pantostomata. Mitrophanow suggests a new genus, Hæmatomonas, to include the monad hæmatozoa; but Crookshank, who has carefully worked out the affinities of the parasites of the rat, the fish, and the *surra* disease, has referred them to the genus Trichomonas. The organism here described has not, however, the characteristic marks of a Trichomonas; for it lacks the undulating fringe on one side and the caudal filament. Nor does it agree with the features of a Cercomonas; so that, meanwhile, until the true affinities are determined by an expert, its proper place seems to be the genus Hæmatomonas of Mitrophanow, which conveniently includes all monads parasitic in the blood. Thus: genus, Hæmatomonas; species, Hæmatomonas malariæ. Definition: Body plastic, ovoid, or globose, no differentiation of protoplasm, which contains pigment grains; flagella variable, from one to four. Highly polymorphic, occurring in (1) amœboid form; (2) crescents, encysted form; (3) sporocysts; (4) circular, free, pigmented bodies. The name designates the natural affinities of the parasite, its habitat, and the conditions under which it occurs, on which grounds it seems preferable to that of Plasmodium malariæ, suggested by Marchiafava and Celli.

Relation of the Parasites to the Disease.—The same difficulty meets us here as in so many affections in which micro-organisms have been found: Are they pathogenic, or are they merely associated with the disease, which in some way furnishes conditions favourable to their growth? As evidence of their pathogenic nature may be urged, with Laveran, the constancy of their presence, their absence in other individuals in malarial regions, the destructive influence upon the blood-corpuscles, and their abundance in the graver forms of the disease. But even these considerations, weighty as they may appear, will not carry conviction to all, in the absence of experimental demonstration such as can be afforded in the case of certain pathogenic schizomycetes.

Attempts to isolate and grow these hæmatozoa outside the body have failed. Marchiafava and Celli have shown that the inoculation of healthy persons with blood taken from a case of malaria is followed in a variable time by genuine ague paroxysms, in which the blood contains the parasites; but in regions where malaria is prevalent such experiments are not wholly free from objections. A series of negative observations on undoubted cases of malaria would be convincing. I lay no special stress on the three cases in which I did not find the parasites, as the patients were not followed from day to day with the accuracy necessary to give any value to the observations. It must be borne in mind that hæmatozoa are not uncommon in animals, and, as in the rat, do not appear to interfere seriously with the health of their hosts. Under these circumstances, the association of a specific form with a definite disease in an animal makes it all the more probable that the species is pathogenic. A further study of the *surra* disease is particularly to be desired with the new light which Evans and Crookshank have thrown upon it. The conditions under which the disease occurs, combined with its paroxysmal character, are so similar to those of malaria, that a full explanation of its pathogeny would have a very direct bearing upon the present question.

To my mind, two facts in connection with these hæmatozoa point significantly to their etiological association with malaria. First, the positive anatomical changes which can be directly traced to their action, changes upon which one at least of the most marked symptoms of the disease depends; I refer to the destruction of the red blood-corpuscles, which can be followed in all its stages, and is as well-defined an alteration of tissue brought about by a parasite, as any of which we know. The second fact is the action of quinine upon the parasites. The simultaneous disappearance of the symptoms of the disease and the hæmatozoa suggest that the specific influence of the medicine is upon the parasites, though it may be urged that the quinine, while curing the disease, simply removes the conditions which permit of their growth in the blood.

Practical Considerations.—An interesting practical point is the diagnostic value of the presence of these bodies. There were six or eight cases in which the examination of the blood proved of great service in determining the existence of malaria. Some of these are worth mentioning. One of the first was a man aged 37, who had been under observation on three or four occasions with anæmia and an enlarged spleen. He had had three attacks of hæmatemesis. There was no history of malaria, and, from the gravity of the case, I was led to regard it as one of severe splenic anæmia. On his fourth visit, however, a careful examination of the blood revealed the presence of the parasites, and I gave, in consequence, a more favourable prognosis in the case, which has since been justified. In an instance of pernicious malaria admitted to the Philadelphia Hospital, under the care of my colleague, Dr. J. H. Musser, the diagnosis rested on the discovery in the blood of the characteristic changes in the corpuscles. To a third case, No. 41, I have already referred, and there were four or five other instances of chronic malaria in which the nature of the disease was determined by an examination of the blood. On the other hand, in many cases of suspected malaria, the absence of these bodies led to a more careful examination, and to the discovery of the cause of the chills and fever. Four of these were cases of phthisis with ill-defined physical signs; in a fifth, after several negative blood-examinations, the ague-like paroxysms were found to be due to a septic pneumonia; in a sixth and seventh, renal disease was discovered. I feel confident that, in malarial regions, the examination of the blood will prove, in skilled hands, a most valuable aid in the diagnosis of many obscure cases.

Melanæmia.—These researches on malaria throw light on the forma-

tion of pigment in the blood and various organs in the chronic cases. Evidently the primary change is in the red blood-corpuscle, which is gradually destroyed by the amœboid form of the parasite. Every stage of this process can be readily traced, and these observations bear out the more recent views on the origin of the pigment in the blood itself. The pigmentary degeneration of the red corpuscles noticed long ago by Frerichs and by Kelsch,[16] was no doubt the same as here described. The gradual accumulation of the granules in the spleen, liver, and bone-marrow leads to the characteristic melanosis of these organs. I sought carefully for evidence of active interference with these parasites on the part of the white blood-corpuscles, but on only

Fig. 14.—A colourless corpuscle studied for an hour and a half, during which time it had, as shown at 1, included a pigmented body, and was about to take another 2.

two or three occasions was this seen. Once a crescent was found inside a colourless corpuscle (Fig. 13), and again, as shown at Fig. 14, a corpuscle gradually enclosed two free pigmented bodies. The greater portion of the pigment resulting from the destruction of the monads is picked out by the cells of the spleen and bone-marrow, which also, no doubt, as in health, remove the effete red cells and their remnants. Pernicious malaria, common enough when Stewardson[17] wrote his well-known article, has now become very rare in Philadelphia. In these cases, Marchiafava and Celli have found the capillaries of the various organs filled with corpuscles containing pigment-grains which appear enclosed in a hyaline matrix. Councilman and Abbot[18] have described the same change, and I am indebted to Dr. Councilman for the specimen from which the accompanying sketch was taken (Fig. 15). It represents a small brain-capillary filled with corpuscles, in many of which are pigmented bodies which stain deeply, and, so far as can be

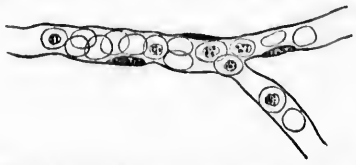

Fig. 15.—Sketch of a capillary vessel of grey matter of brain. Case of pernicious comatose malaria—Dr. Councilman. The red corpuscles are seen in outline, and in five there are pigmented bodies.

ascertained, are identical with the pigmented organisms met with in the red corpuscles during life. Only one instance of fatal malaria came under observation, a man aged 70, admitted to Dr. Musser's wards on October 25th. He had been on the Isthmus of Panama and in Georgia, and had chills and fever in both places; last chill was three days before admission. He had also had hæmaturia. He was very anæmic, the spleen was slightly enlarged, the temperature, 101.3°. There was great stupor, and he was roused with difficulty; the tongue was dry. The temperature became subnormal on October 27th and 28th.

[16] *Archiv. d. Physiologie*, 1875.
[17] *American Journal of Medical Sciences*, 1851.
[18] *American Journal of Medical Sciences*, 1885.

children, and hundreds of cases may be treated without

Examination of the blood showed many pigmented bodies in the red corpuscles, numerous free circular forms, a few crescents, and several flagellate organisms. The stupor deepened to coma, and he died on the night of October 28th. The spleen and liver showed typical pigmentation, and the bone-marrow was also very dark. The spleen-pulp contained free pigment and many large cells, some of which were filled with dark granules, while in others there were bodies identical with the small pigmented forms so abundant in the blood during life. The marrow presented similar changes. The number of red corpuscles containing the pigmented bodies was not great, nor were the capillaries of the liver or the brain stuffed with them, as in the instances of pernicious malaria just referred to. Probably this was an instance of severe malarial cachexia of many months' duration, and scarcely should be grouped with the pernicious comatose form.

To my colleagues, Drs. Curtin, Neff, and Musser, I am indebted for the privilege of examining the malaria-cases in their wards; and to my resident physicians, Drs. Donohue, Albertson, and Westcott, for sistance which materially lightened my work.

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ANTIFEBR

A FEW months ago Drs. Cahn and Hepp announced from Kussmaul's clinic the discovery of a new antipyretic, which they named antifebrin. A full account of their observations has more recently appeared in the *Berliner Klinische Wochenschrift*, Nos. 1 and 2, 1887.

The drug is known chemically as phenyl-acetamide or acetanilide ($C_6H_5C_2H_3OHN$), and is formed by the action of heat upon aniline acetate. It is a neutral body, and in this respect it differs from all other antipyretics, which are either phenols, like salicylic acid and resorcin, or bases of the chinoline series, as thallin, antipyrin, and quinine. It is a white crystalline powder, insoluble in cold water, but readily dissolving in hot water or alcoholic solutions. The taste is not unpleasant. The dose is from 8 to 12 grains. In larger amounts it is not poisonous, though it is advisable not to exceed 30 grains in the day. Usually 8 grains will be found an effective dose. It is conveniently given in spirit and

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CASE XVIII. (Chart IV.).—F. H., aged 31, was trephined for mastoid disease in Philadelphia Hospital January 15. On the 20th he was attacked with erysipelas. On the 23d, at 10 A.M., the temperature was 106⅖°; at 11, 103⅖°.

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During the past three months I have used it in my wards at the Philadelphia Hospital and at the Hospital of the University of Pennsylvania in the following 29 cases: typhoid fever, 7; pneumonia, 6; phthisis, 8; erysipelas, 4; pleurisy, 1; peritonitis, 1; rheumatism, 1; intermittent fever, 1. As a rule, 8 grains were given when the temperature rose above 103⅖°, and hourly observations were made for six or eight hours. In several cases of phthisis 4 grains were given four or five times a day. The maximum amount given in one day was 32 grains (Case II.). For brevity, the effects of the drug may be noted under the following heads:

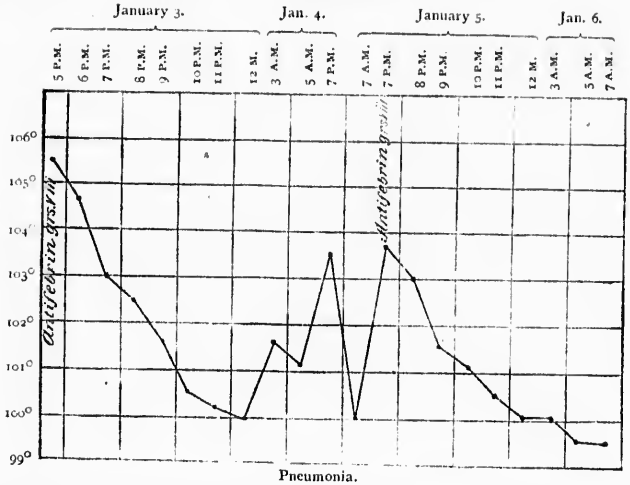
1. *Reduction of Temperature.*—This is the most marked and characteristic action, beginning usually within an hour. In eighteen administrations the fall was over 2° in this time; in three instances a fall of 3°, on two occasions a fall of 4°. In thirteen instances the temperature was reduced 4° in two hours, in sixteen administrations 3°, and on four occasions 5°. The greatest drop within this time was in Case XXIV., in which the fall was 6⅖°. The greatest reduction was in the following: Case I., 8° in five hours; Case X., 6⅗° in five and a half hours; Case XVIII., 7⅗° in two and a half hours; Case XX., 7° in seven hours; Case XIX., 7⅗° in ten hours.

In seven administrations the temperature was unaffected by the eight grains. Cases VII. and XIII., both of pneumonia; Case XXIII., peritonitis; and Cases IX. and XVIII., erysipelas.

The duration of the reduction was variable, usually from three to six hours. The following cases illustrate well the antipyretic action of this drug:

CASE XI. (Chart I.).—Man, aged 32, admitted to the drunkards' ward of the Philadelphia Hospital. A few days after admission he was noticed to be a little short of breath, and, on examination of the lungs, there was dulness, with râles and feeble blowing breathing at the right base. On January 3, at 5 P.M., the temperature was 105⅖°. Antifebrin, gr. viii, was given, and the fever gradually fell, as the chart shows, until midnight, reaching 100°. By 3 A.M. it had risen to 101¼°. At 7 P.M. on the 5th the temperature was nearly 104°, and another dose of the antifebrin was given with good effect.

CASE XI.

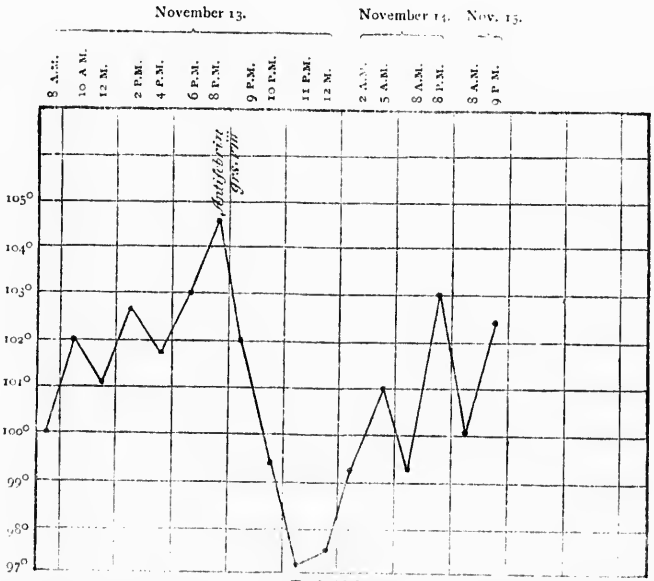


Pneumonia.

CASE IV. (Chart II.).—Rachel C., aged 21, admitted November 3 with typhoid fever. On the 4th the temperature was 104°, but from this date until the 13th it did not rise above 103°. At 8 P.M. on the 13th the temperature was 104$\frac{1}{5}$°. Antifebrin, gr. viii, was given. By ten o'clock there was a fall of 5°, with profuse sweating. At 11 P.M. the temperature was 97°. At 12 A.M. it began to rise, and by 2 A.M. was 99.4°. Between eleven and twelve o'clock she complained of slight chilliness, but the general condition was good, and there was no collapse. The thermometer did not again register above 103$\frac{2}{5}$° in her case.

CASE X. (Chart III.).—J. B., aged 35, with chronic phthisis and high fever. The chart shows how rapidly the antifebrin in three successive days reduced the temperature from 4° to 7° in from two to three hours.

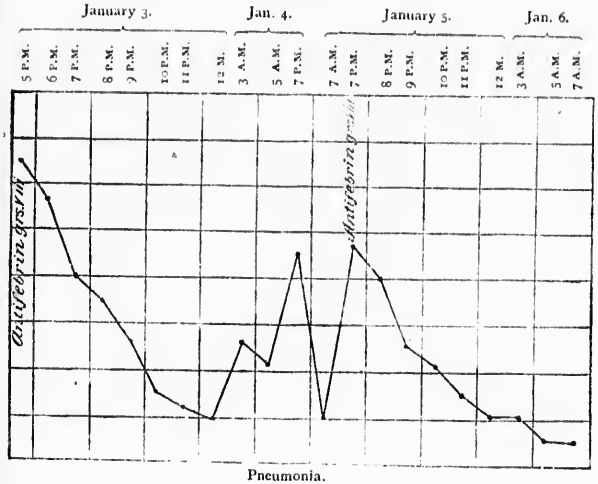
CASE IV.



Typhoid fever.

CASE XVIII. (Chart IV.).—F. H., aged 31, was trephined for mastoid disease in Philadelphia Hospital January 15. On the 20th he was attacked with erysipelas. On the 23d, at 10 A.M., the temperature was 106$\frac{2}{5}$°; at 11, 105$\frac{2}{5}$°.

CASE XI.



Pneumonia.

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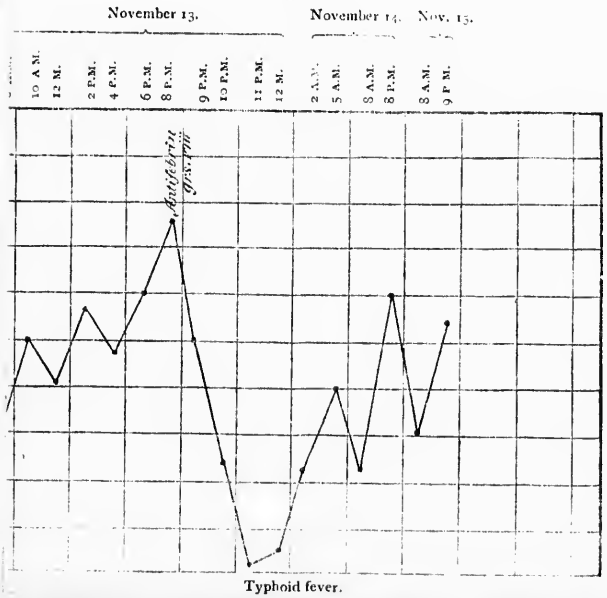
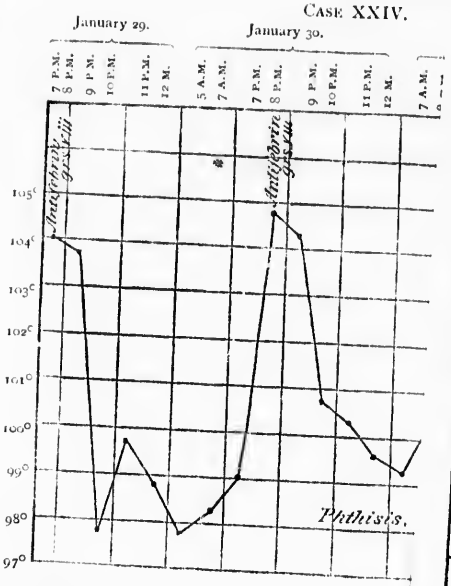


Typhoid fever.

CASE XXIV.



He was given antipyrin, gr. xv, and quinine, gr. xx. At 3 P.M. the temperature was still above 103°, and a second dose of antipyrin was given. At 5 P.M., quinine, gr. xx. He had had also quinine, gr. v, every four hours. At 8 P.M. the temperature had fallen to 100½°, at 11 P.M. to 99°, and at 3 A.M. to 98°. On the 24th the fever was again 105°, and antipyrin and quinine were given, with a reduction of 4° in five hours. On the 25th antipyrin and quinine were twice given, without any effect. He was transferred to the medical ward, and the antifebrin was used as shown by the chart. The last dose caused a fall of 7⅞° in two and a half hours. The patient subsequently did well. The chart is of interest, as it affords a comparison between the action of antipyrin with quinine, and that of a

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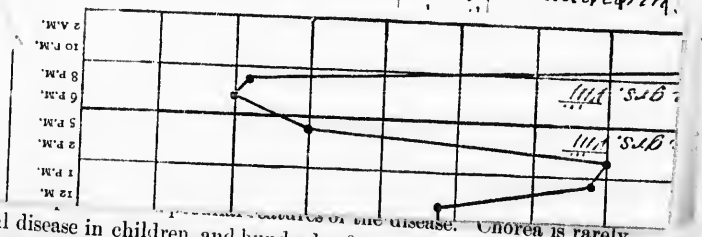

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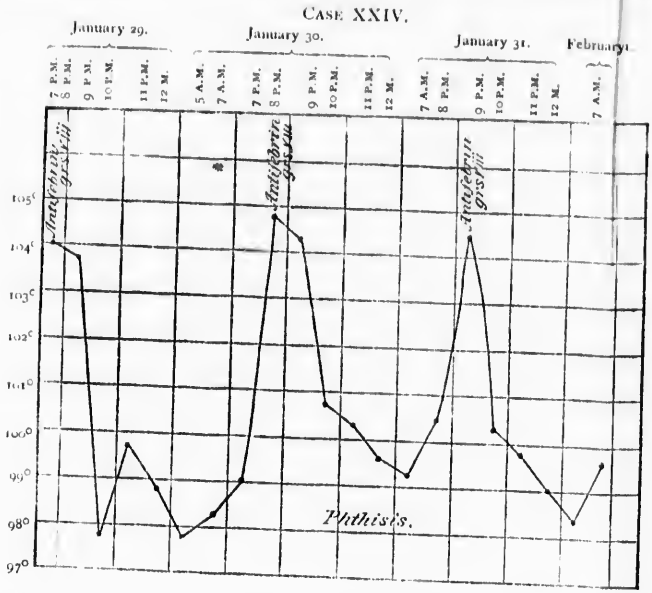

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In several cases the dose of gr. viii did not seem sufficient. In seven administrations little or no effect followed. This was particularly noticeable in the pneumonia cases. In Case XIII., with almost complete involvement of the right lung and affection of the left base, the temperature from the 5th to the 10th ranged from 102° to 105°. Antifebrin was given six times, thrice without effect, and on three occasions it only reduced the fever a degree or a degree and a half. Thallin, gr. iv, twice brought the temperature down 3° and 4°; but the most effective agent in this case seemed to be the cold pack, which reduced the temperature from 105° to 98⅘°. This patient had delayed resolution, and the fever did not subside until the thirty-ninth day from the initial chill. In other instances, a second dose repeated an hour or more after the first produced the full effect, as in Cases XI. and XVIII.

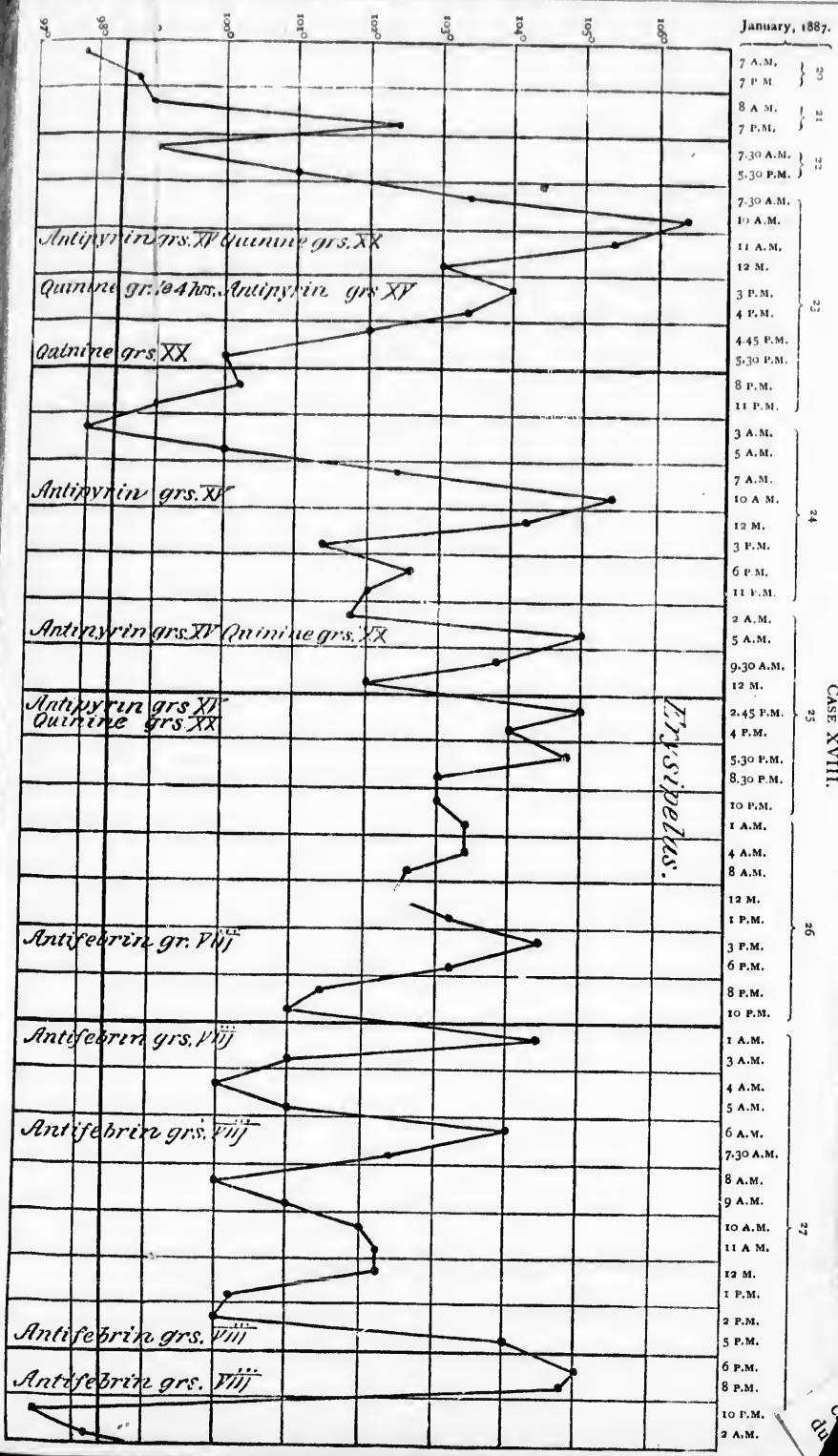
In typhoid fever the action was usually prompt and satisfactory. In Case II., a young man, aged 25, with persistently high temperature and marked nervous symptoms, the drug was given on fourteen occasions, and after each dose there was a drop of from 3° to 5°. In the milder cases the effect was more striking, as in Case IV.

In the erysipelas cases the action was in each instance most decided.

In phthisis, with high fever, the drug was usually given in a single powder of gr. viii, when the temperature was above 103°, but in three cases the plan was tried of giving gr. iv four or five times a day. This did not seem very successful, and the patients did not feel so comfortable as with the single dose.

In a remarkable case of quartan ague antifebrin in 8-grain doses given before or during the paroxysm seemed to be without effect. One curious circumstance, however, is worth mentioning. The lad had always with the fever the most intense general urticaria, which the antifebrin seemed to prevent, much to the patient's comfort.

2. *Action on the Circulatory System.*—Usually with the reduction of the fever the pulse would fall, and a drop of 20 or 30 beats in two or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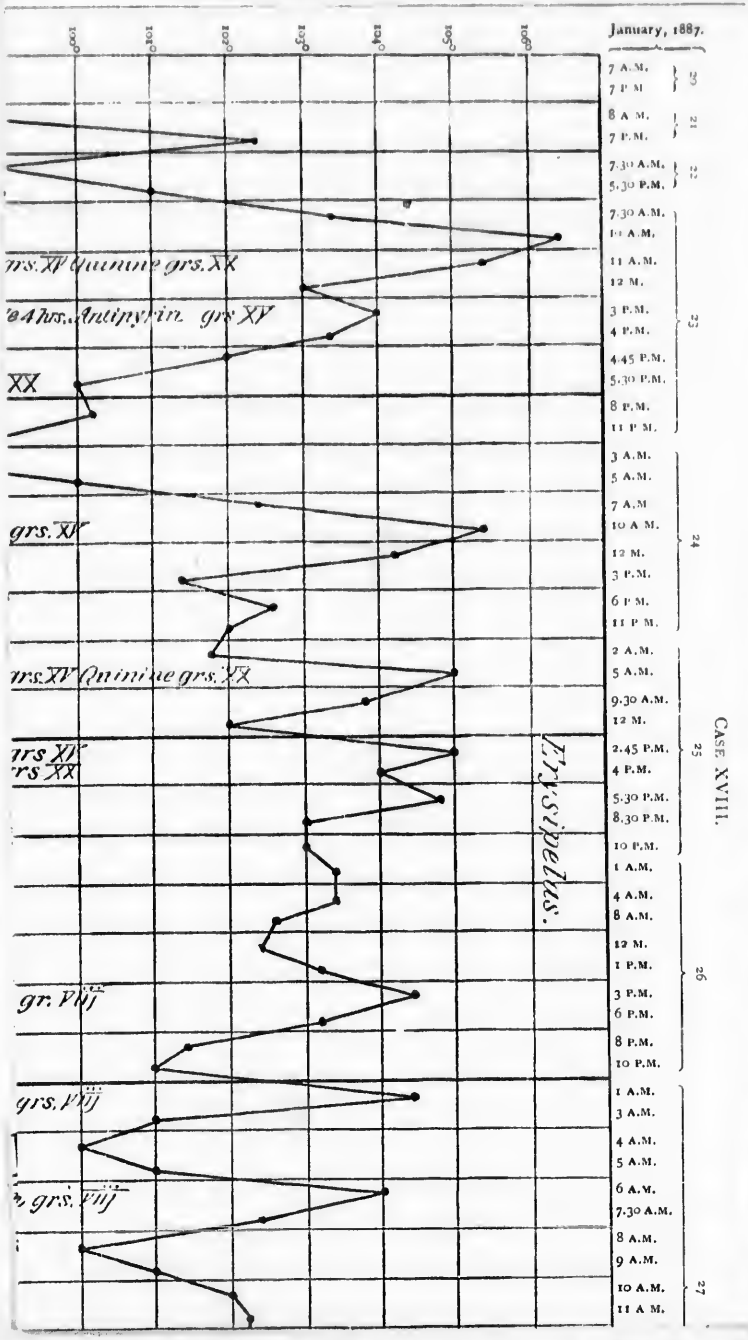
CASE XVIII.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CASE XVIII.
Erysipelas.

January, 1887.

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CASE XVIII.

three hours was frequently noted. Thus, in Case II., with a pulse-rate of 112 per minute, and the temperature at 105°, the pulse fell to 84 in four hours. In another case the pulse fell from 130 to 90 in four hours. A marked increase in the pulse-tension was observed in several cases. Even with a rapid fall of from 5° to 7° in two or three hours, there was no evidence of heart-weakness. Slight cyanosis, which is mentioned by one or two German writers, did not occur in any instance.

3. *Sweating.*—As with thallin and antipyrin, the action of antifebrin is almost invariably accompanied with profuse perspiration, which is often the first effect of the drug. Repeatedly I have seen the forehead beaded with sweat half an hour after the administration of 8 grains. This is sometimes a most unpleasant feature in the employment of the drug, and is the only one of which the patients have complained. In several instances the drug was combined with atropine, but without much effect. It does not seem to increase the night-sweats in cases of phthisis; indeed, under its use, one patient, who sweated much with the afternoon dose, had drier and, in consequence, more comfortable nights. In

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4. *On the Urine.*—The only change noted was a marked increase in the amount in some of the cases. This is probably a direct result of the increased arterial tension.

5. The effect on the general condition seemed usually beneficial. A quiet sleep often followed an hour or so after its administration. The phthisical patients expressed themselves more positively than the others in this matter.

There were none of the disagreeable effects which we sometimes see follow the use of antipyrin and thallin. There was no instance of vomiting; and, with the exception of Case IV., there was no shivering or chilliness, such as is so common after antipyrin.

These limited observations confirm those of Cahn and Hepp and others, and I think that we have in antifebrin a prompt and powerful antifebrile agent, easy to take, and free from unpleasant effects. It has the advantage also of cheapness. Merck's article, which I have used, is only sixty cents an ounce, wholesale.

LXXVIII

In the third case, a more severe example of the disease than either of the preceding, there was general improvement, with diminution of violent pulsation in the thyroid and over the neck and face, but the pulse-rate of 144 was not reduced to less than 96 to the minute, varying between this and 108. This patient suffered from continual fine tremor of the muscles, especially in the limbs; while taking spartein this tremor remained absent, but returned if the drug was left off. She has improved in strength and feels well whilst she is taking it. She has now been taking one-quarter of a grain ever four hours for six months.

I gave spartein for periods varying from two weeks to six months in daily quantities of one-third of a grain to twelve grains, the latter large dose was continued in one case for a month with benefit. It is best to begin with one-sixteenth of a grain every four hours, and gradually increase up to two grains, if necessary until the desired effect on the circulation is obtained. When the dose is given less frequently the result does not seem so good; sometimes a large dose may be gradually reduced without loss of effect. There is no fear of accumulation. The signs of an overdose are palpitation, præcordial pain, small, rapid pulse of high tension, and a feeling of great weakness, or even trembling.

Spartein begins to act in about thirty minutes after it has been taken by the mouth, and its action lasts from about five to six hours. This rapidity of action, at first consisting in a stimulation of the heart, rise of arterial tension not occurring until a little later, indicates the use of spartein in asystolic conditions of valvular disease, where a speedy effect is desired, giving it superiority over more slowly acting drugs.

In these conditions, too, a small dose should be employed (one-sixteenth to one-quarter of a grain), since in these doses spartein seems powerfully to stimulate and regulate the heart with the smallest rise of arterial tension, perhaps not more than is the normal accompaniment of increased cardiac force.

Diuretic effect is most marked with fairly large doses, half a grain to two grains; with small it is not so evident, but is often present. Flushing of the surface of the body occurred in from one to two hours after administration in most cases.

THE CARDIAC RELATIONS OF CHOREA.

By William Osler, M.D.,

Professor of Clinical Medicine in the University of Pennsylvania; Physician to the University Hospital, to the Philadelphia Hospital, and to the Infirmary for Nervous Diseases.

The heart symptoms of chorea demand special consideration as among the most important and peculiar features of the disease. Chorea is rarely a fatal disease in children, and hundreds of cases may be treated without

a death. By far the most serious fact in the clinical history of the disease is the occurrence of endocarditis; but here the danger is remote, not immediate, and lies in the changes which an acute valvulitis may initiate.

A satisfactory study of the cardiac relations of chorea must embrace the condition during the attack, and the subsequent heart history after a period of years. The first question has engaged the attention of many workers, and an attempt is here made to work out the second on a scale not hitherto attempted.

I. Condition of the Heart during the Attack.

Oftentimes the extreme jactitation renders the examination of a choreic child difficult or even impossible. I make it a rule to examine the bare chest. Auscultation through the clothing is not trustworthy, as soft murmurs, readily audible with the stethescope, may easily escape detection. It is a good plan to let the child lie quietly on a lounge for some time, and make the first examination in the recumbent position when the heart's action is less rapid. Subsequently the effect of exercise and of the erect posture may be tested.

In chorea, as in rheumatism, the evidences of cardiac disease must be sought for, as it is rare to hear complaints of either palpitation, pain, or other symptoms which would direct attention to the heart.

The cardiac disturbance is indicated by the presence of murmurs, alteration in the rate or rhythm of the heart's action, and by pain.

A murmur at one or other of the cardiac areas is by far the most common sign and is present in a considerable number of all cases. Of 410 cases in the records of the Infirmary for Nervous Diseases, there were 120 which presented a heart murmur at the time of examination. In at least 40 cases there was either no note or an imperfect one, and in very many the exigencies of out-patient work prevented a very thorough examination. It can safely be said that in over one-third of the cases a heart murmur was detected, and I have no doubt that this number would have been much increased had each child been stripped and special attention given to the auscultation of the heart.

Of the 120 cases, 113 presented the apex systolic or mitral murmur, in 7 a basic, and in 3 both apex and basic. In 15 cases the heart's action was noted as rapid, and in 6 as irregular. Pain was not a frequent complaint and was noted in only 6 or 7 cases.

It is common experience that the special indication of heart trouble in chorea is the presence of a soft systolic bruit, heard best at the apex or over the body of the ventricles and not often propagated to or beyond the mid-axilla. Basic systolic murmurs are usually associated with anæmia or debility. Diastolic and presystolic murmurs rarely, if ever, occur in acute chorea.

Before discussing the probable nature of these murmurs it will be well to study the anatomical condition of the heart in fatal cases. Fortunately these are rare. I have inspected three cases.

Case I.—S., a girl, aged eleven; had had acute rheumatism. Admitted to the Montreal General Hospital, under Dr. George Ross, with acute chorea, and died of an intercurrent pneumonia. The movements had almost ceased under hypodermics of arsenic. The autopsy (No. 465 post-mortem records Montreal General Hospital) showed slight hypertrophy of the heart, somewhat thickened mitral curtains with numerous irregular warty vegetations just inside the auricular margins. Two of the aortic segments also presented bead-like vegetations below the corpora Arantii.

Case II.—T. B., a boy, aged eleven, had chorea in May, 1880, and a second severe attack in July of the same year. No rheumatism. No heart murmur. About the 20th of February, 1881, there was a recurrence, and on March 3d he again came to the general hospital to see Dr. Molson. About the 10th he began to get feverish and extremely restless. On the 14th the temperature rose above 104° F., and he became comatose. The left arm seemed powerless, the right arm and leg were constantly twitching. On the 15th the temperature reached 105° F., and there were cutaneous ecchymoses. He died on the morning of the 16th. The autopsy showed very extensive mitral valvulitis, the vegetations large, soft, grayish-white in color. No chronic affection of the valves. The spleen and kidneys contained many recent infarcts. The brain and membranes healthy, with the exception of a spot of grayish-red softening in the right corpus striatum (lenticular nucleus) about the size of a cherry. It was no doubt embolic, though the arteries of the perforated space were carefully examined for emboli without success.

Case III.—Emma M., aged eighteen, admitted to the Montreal General Hospital, under Dr. George Ross,[1] and died in five days of exhaustion. There was no rheumatism, and the attack had followed a fright five days before admission. Here, too, the only important lesion was on the mitral valves—a row of soft warty vegetations on the auricular face just within the free margins.

The statistics of fatal cases of chorea have been collected by Sturges[2] and Raymond.[3] Of eighty cases, representing the combined experience of Guy's, Bartholomew's, St. George's, and St. Thomas's Hospitals, Sturges states that there were only five with the heart valves and pericardium reported healthy.

Excluding the London cases from Raymond's table of 79 cases, there are left 34, in only 19 of which there were specific statements as to the condition of the heart, and in every one of these endocarditis was present. I have found the reports of 15 additional cases,[4] which, with the three

[1] Canada Medical and Surgical Journal, vol. xi.

[2] Chorea. London, 1881.

[3] Dictionnaire encyclopédique des Sciences Médicales.

[4] Mackenzie (Trans. Infer. Med. Congress, 1881), six cases, five of endocarditis. Donkin and Hebb, 1 case, valves normal (Med. Times and Gaz., 1884, ii.). Baxter (Brain, vol. ii.) one case. Morell-Lavellée (Revue des Maladies de l'Enfance, 1884), one case. Frank (Allg. Wiener med. Zeitung, 1879), one case. Maixner (Med.-Chir. Centralblatt, Wien, 1882), one case. Koch (Deutsches Archiv f. klin. Med., Bd. xl.), four cases

here given makes 18, in 16 of which there was mitral endocarditis. We may say that of 115 fatal cases of chorea, with notes of the state of the heart, in not more than 10 was this organ found normal, and in the great proportion of the cases the lesion was acute mitral valvulitis.

One other point must be considered before we speak of the nature of the heart murmur. In what proportion of the cases is there a history of rheumatism? In 35 of the 120 cases, 29.1 per cent., there was a note of articular affection, either acute or subacute, or of pains which might be regarded as rheumatic.

Much has been written in explanation of the heart murmur of chorea: an idea of how much may be gathered from the fact that a discussion of the theories which have been advanced occupies twelve pages in Hayden's work on *Diseases of the Heart*. We are concerned chiefly with the apex systolic murmur, universally recognized as the most frequent and characteristic sign of implication of the heart in chorea. Speaking generally, we meet with such a murmur in mitral endocarditis, or in relaxation of the ventricular walls, such as occurs in anæmia and fevers, and it is attributed to regurgitation through the mitral orifice, owing either to absolute insufficiency, in consequence of the endocarditis, or to relative insufficiency when the normal valves are unable to close an orifice enlarged as a result of relaxation of the heart muscle. In chorea a special theory of musculo-papillary spasm has been advanced to account for the mitral murmur.

It would be fruitless to re-discuss, in all its aspects, a subject so well and ably presented in various works, particularly in those of Hayden and Sturges. That there is such a condition as spasm of the papillary muscles resulting in a "want of correspondence between the fibres of the ventricle, which obliterate the cavity and those which close the valve," is a plausible hypothesis unsupported, so far as I know, by any clinical or anatomical facts, while the general immunity of involuntary muscular organs in chorea speaks strongly against it.

Sturges thinks that there may be a fatigue paresis of the papillary muscles, similar to that which sometimes involves the limbs, and this weakness and relaxation prevent accurate adaptation of the valve segments. He urges in support the inconstant character of the murmur, appearing and disappearing without apparent cause, and states that it may be synchronous both in its time of arrival and duration with the paresis of the voluntary muscles. I have not been able to trace any such connection, nor have I found in the paretic cases any special tendency to variability in the murmur. Indeed, so far as my experience goes, the *apex* systolic bruit of chorea is by no means an inconstant murmur. If muscular incompetency has anything to do with the production of the choreic bruit, it is more likely to be of a similar character to that which occurs in anæmia, debility, and fevers. Here it is the relaxation of

the walls, and particularly the so-called mitral muscle, which induces a condition of relative insufficiency of the segments and permits of regurgitation. There may be in chorea, as is well known, a high degree of anæmia, and in a certain proportion of the cases this explanation of the murmur may hold good, but in the great majority of instances the bruit is detected early when there is neither anæmia nor debility.

I am strongly of the opinion that the apex systolic bruit of chorea is, in at least nine out of ten cases, associated with endocarditis:

1. The extraordinary frequency with which mitral valvulitis is met with in fatal cases. *There is no known disease in which endocarditis is so constantly found, post-mortem, as chorea.* As the figures above quoted show, it is exceptional to find the heart healthy. I do not know of statistics of any very large number of fatal cases of acute articular rheumatism to place beside these figures, but I doubt if even this disease, so prone to endocardial complication, can be compared with chorea in this respect. Dickinson has raised the question whether these beads of fibrin are not rather the consequence than the cause of the valvular defect, and Sturges holds that this appearance does not represent a true inflammation of the endocardium. Whether a true inflammation or not, I think it must be conceded that the lesion is identical, microscopically as well as macroscopically, with simple or warty endocarditis as we see it in other diseases.

2. The character and location of the murmur are such as experience in other affections has taught us are associated with inflammation of the mitral segments. I speak of the apex bellows-murmur. Why this should be so generally associated with the presence of a row of small warty vegetations just within the auricular margins of the curtains, not, one would think, seriously interfering with their functions, is a problem to be solved. The condition certainly does not necessitate regurgitation, and the bruit may perhaps, as has been suggested, be due to friction of the roughened faces of the segments.

3. The inconstancy of the murmur and its disappearance on the subsidence of the chorea have been urged against this view. Now we must acknowledge that the bruit may be variable and, indeed, does not necessarily accompany mitral endocarditis. Kirkes, years ago, insisted upon this, and there have been two autopsies in carefully studied cases of chorea in which the vegetations were found post-mortem, and careful examination failed to reveal a murmur (Baxter: *Brain*, vol. ii.; *Frank. Allg. Wiener med. Zeitung*, 1879.) The facts which I shall subsequently give suggest that we may during the attack have an endocarditis, not manifest even by a murmur, but which has laid the foundation of future trouble. The disappearance of the apex murmur of chorea—and of rheumatism too—has been repeatedly followed, and if caused by the small vegetations, this is a natural sequence of the changes which go on

in them. At first a soft granulation tissue, they become in time firmer, smaller, and ultimately smooth flat elevations mark the spots. It is not improbable that if we could follow accurately the auscultatory history of a valve affected with acute endocarditis, we should find in many cases that the murmur of the fresh attack disappeared, to reappear when the changes, which it is the misfortune of the acute disease to initiate, have reached a point of interfering with the competency of the valve.

4. In its sequel the cardiac affection of chorea has been supposed to differ from that of other diseases, "as none of the injurious after-consequences which attend endocarditis in its other relations . . . are found to ensue here" (Sturges). A study of any large number of choreics some years subsequent to the disease tells, as I shall show, a sad tale to the contrary and proves that the primary heart trouble is, in a majority of cases, at least, endocarditis.

II. The Condition of the Heart in Choreic Patients some Years after the Attack.

Owing, doubtless, to the difficulties inherent to such an investigation, this line of inquiry has not been followed by many workers. Indeed, so far as I know, Dr. Stephen Mackenzie's paper, at the London International Congress, is the only one which has dealt with the subject, and he has examined thirty-three patients at periods from one to five years subsequent to the attack. Postal cards were sent to all the choreic patients, in sets of twenty-five, who had been in attendance at the Infirmary since 1876, asking them to return for the purpose of having the heart examined. One hundred and ten came back, a number much exceeding our expectations.[1] All the more recent cases in attendance at the clinics have been excluded—all, indeed, after March, 1885, so that the study is based upon 110 cases in which the examination was made *more than two* years subsequent to the attack of chorea. In each case, as it came, reference was made to the original notes, questions asked concerning subsequent attacks, and rheumatism, and the heart examined in the recumbent and erect postures, at rest and after exertion.

The results summarized, are as follows: In 43 cases the heart was normal, in 54 there were signs of organic disease, and in 13 there was functional disturbance.

The tables which I have prepared are too full for publication, but the following abstracts of the cases affected will be of interest:

1871 (sixteen years). Two cases.

Case I.—Laura C. R., aged twenty-five. Several attacks subsequent to 1871. Never had rheumatism until February, 1887. No note of

[1] It speaks well for the stability of the artisan class in Philadelphia that so many of the postal cards reached their destination. Comparatively few were returned from the Post-office with the comment—*Removed; cannot find.*

heart condition in previous attacks. Has attacks of shortness of breath. *Status præsens:* Impulse is forcible. Dulness increased. Apex systolic murmur heard to posterior axillary fold. Second left accentuated.

CASE II.—Kate L., aged twenty-one. Two or three attacks after 1871; bad one in 1878. In 1882, had inflammatory rheumatism, never any joint trouble before this time. In 1878, note is "impulse strong; apex murmur." She has had attacks of shortness of breath. *Status præsens:* Feeble thrill; localized purring presystolic murmur. Loud apex systolic transmitted to posterior axillary fold. Second left accentuated.

1872 (fifteen years). One case. No heart affection.

1874 (thirteen years). Three cases.

CASE IV.—Annie M., aged twenty-five. Second attack in 1883, third in 1885. Had rheumatism just before the first attack. No note of heart in first or second; in 1885, an apex systolic murmur. *Status præsens:* Loud apex systolic transmitted to axilla; second left accentuated; transverse dulness increased; impulse forcible.

CASE V.—Bertha G., aged twenty-five. A second attack in 1880. No rheumatism. In 1880, a soft systolic murmur. *Status præsens:* Impulse not forcible. Loud apex systolic murmur propagated to axilla. Very ringing and accentuated second left. Has palpitation and attacks of shortness of breath.

CASE VI.—Charles M., aged twenty-eight. Second attack in 1880. Had pains in joints before second attack. No note of heart. Is strong and well, no subjective symptoms. *Status præsens:* Soft apex systolic murmur, not heard in axilla or in pulmonary area. No increase in dulness. Second left accentuated.

1875 (twelve years). Two cases; one normal.

CASE VII.—Hester G., aged twenty. Original attack very severe; a second in 1879, and one since. No rheumatism. No note of heart in attacks. For two years has had attacks of palpitation and dyspnœa. *Status præsens:* Impulse forcible. Presystolic thrill; rough presystolic murmur. Loud accentuated second left.

1876 (eleven years). Eight cases; one normal.

CASE IX.—Annie T., aged seventeen. Since 1876 three attacks, last in 1885. No rheumatism. In 1885, a soft systolic murmur. Complains that she does not lie comfortably on left side. *Status præsens:* Impulse forcible, outside nipple. Apex systolic loud, heard well in axilla. Second left accentuated.

CASE X.—Robert P., aged twenty-one. Second attack in 1879. No rheumatism. No previous note of heart. *Status præsens:* Action rapid, impulse diffuse. Dulness not increased. Blowing systolic murmur just above apex, not heard in axilla; disappears on exertion. Second left accentuated.

CASE XI.—Lizzie H., aged sixteen. Many attacks since 1876, two of them severe. Had rheumatism when four years old. In 1878, second left was reduplicated. *Status præsens:* No evident enlargement of heart; impulse feeble; no thrill. At apex double murmur, presystolic short, not rough. Systolic not loud, not transmitted to axilla. On

exertion louder. Both very distinct. Second left very loud. Has occasional attacks of palpitation.

Case XII.—Ida L., aged eighteen. Three attacks since 1876. No rheumatism. No note of heart in 1879. No symptoms. *Status præsens:* Beat forcible; dulness increased. Loud apex systolic murmur, heard at angle of scapula and very distinct along left margin of sternum. At aortic cartilage a soft systolic bruit. Second left ringing and accentuated.

Case XIV.—Jennie A., aged twenty. Second attack in 1878, third in 1879. No rheumatism. In 1879, sound, stated to be normal. *Status præsens:* Impulse not forcible, no apparent enlargement. In fourth left space a rough presystolic murmur; limited in area. At apex a systolic bruit, transmitted to axilla, and heard at angle of scapula. Second left very accentuated. Sounds at apex booming. No symptoms, always good health.

Case XV.—Annie L., aged twenty-four. Two attacks since, last one in 1882, when for the first time she had rheumatism. No note of heart. *Status præsens:* Apex an inch outside nipple. Impulse forcible. No thrill. Presystolic murmur, not rough, in fourth space; apex systolic, heard in axilla and at angle of scapula. Loudly accentuated second left. Has had palpitation and shortness of breath on exertion for three years.

Case XVI.—Miriam C., aged nineteen. Two attacks since. Never had rheumatism. Has had heart disease for some years; is now in bed with it.

1877 (ten years). Seven cases; three affected.

Case XVII.—Andrew G., aged twenty-one. The attack followed acute rheumatism. In 1878, a soft systolic murmur. No symptoms. *Status præsens:* When recumbent sounds clear. Erect and after exercise well-marked apex systolic, not transmitted. Second left ringing, accentuated, and reduplicated. No enlargement of the heart.

Case XX.—Mamie L., aged fifteen. Rheumatism (acute) four weeks before onset of chorea in 1877. No attack since. In 1877, "mitral murmur." No symptoms. *Status præsens:* Impulse forcible, beat outside nipple line. Transverse dulness increased. Loud apex systolic murmur, propagated to posterior axillary fold. Second left very accentuated.

Case XXIII.—Rose McF., aged twenty-four. Attack in 1877 prolonged and severe; none since. No rheumatism. In 1877, a faint apex systolic murmur. *Status præsens:* Heart's action violent; impulse forcible; apex outside nipple. Marked presystolic thrill. Presystolic murmur in fourth interspace. Systolic murmur in fifth space, and heard as far as posterior axillary fold. Second sound accentuated at the second left cartilage, and also heard loudly in axilla. Patient is at times very short of breath; has attacks of palpitation and has fainted.

1878 (nine years). Two cases; one affected.

Case XXIV.—Minnie C., aged fifteen. Attacks also in 1879, '80, and '85. Rheumatism in 1885, never before. In 1878 an apex systolic murmur. No symptoms. *Status præsens:* Impulse forcible; apex outside nipple-line; transverse dulness increased. Apex systolic murmur

heard to posterior axillary fold. Double murmur at aortic cartilage; diastolic heard also on sternum. Second left not accentuated.

1879 (eight years). Four cases; all affected.

CASE XXVI.—Fannie N., aged fifteen. Second attack in 1885. Has had rheumatic pains, but no swelling of joints. In 1879 had pain about the heart, and since then has had occasional attacks of palpitation on exertion. *Status præsens:* Impulse in fifth a little out. Transverse dulness increased. Presystolic thrill, most marked at apex. Rough presystolic murmur at and just above the apex. Soft systolic at and outside apex beat. Second left much accentuated, and is also very ringing and loud in axilla and at angle of scapula.

CASE XXVII.—Lizzie R., aged twelve. Three subsequent attacks, 1880, '83, and '86. Those of 1879, '80, and '83 very severe. No rheumatism. No previous note of heart condition. Has had no heart symptoms. *Status præsens:* Forcible, diffuse impulse. Apex a little outside nipple. Systolic murmur at apex transmitted to axilla and heard feebly at angle of scapula. Second left very accentuated.

CASE XXVIII.—Rose F., aged thirteen. Second attack in 1881. Heart normal in 1879. Has been short of breath, particularly on exertion. *Status præsens:* Impulse strong. Transverse dulness increased. Rough presystolic thrill. Very rasping presystolic bruit. Maximum intensity in fifth, just within nipple. Second left accentuated and reduplicated. Aortic sounds feeble.

CASE XXIX.—Mary G., aged thirteen. Several attacks since 1879; in 1885 a bad one, and now, May, 1887, is in infirmary with a severe attack. Rheumatism in 1885 with chorea, not before; and this time has had swollen joints. In 1885 had systolic apex murmur. *Status præsens:* Impulse in fifth and sixth, outside nipple. Dulness increased. Loud apex systolic bruit propagated to axilla and scapula. Second left much accentuated. Has had attacks of cardiac dyspnœa in which she could not lie down. At times severe pain at heart.

1880 (seven years). Five cases; three affected.

CASE XXXII.—Ellen McG., aged twenty-three. No rheumatism. No note of heart in 1880. Is anæmic; has palpitation, shortness of breath, and at times severe pain at heart. *Status præsens:* Action rapid and forcible; dulness increased. Presystolic thrill all over mitral area. Rough presystolic murmur. Soft systolic bruit just outside apex. Second left is loud but not specially accentuated. Examined again some weeks after a course of iron and arsenic, which had relieved the anæmia; murmurs unchanged.

CASE XXXIII.—Angela W., aged eighteen. Four attacks since the first in 1880. No rheumatism. Heart, in 1884, said to be normal. Has had pain at heart, and is at times short of breath. *Status præsens:* Impulse forcible. Soft apex systolic, heard as far as middle axilla, and increased on exertion; not altered by position. Second left a little accentuated.

CASE XXXIV.—Florence B., aged twenty. Rheumatism six months before the attack. In 1880 an apex systolic murmur. Has had since then occasional attacks of palpitation. *Status præsens:* Impulse forcible; apex a little out, but no special enlargement. Apex systolic murmur, heard well to middle axilla. Marked accentuation of second left.

1881 (six years). Sixteen cases; nine affected.

CASE XXXVI.—Louis O., aged seventeen. At least five attacks since 1881. No rheumatism. No note of heart. No symptoms. *Status præsens:* Apex beat in fourth space in nipple line, heaving and forcible; dulness increased. Loud systolic murmur at apex heard to posterior axillary fold, but not above fourth space. When recumbent it is heard in second and third spaces as well. Second left very accentuated.

CASE XXXIX.—Frank N., aged thirteen. A second attack in 1884. No rheumatism. Heart said to have been normal in 1884. For some time has been very short of breath, and gets tired on exertion. *Status præsens:* Precordia bulges. Impulse diffuse; dulness increased. Presystolic thrill in fourth interspace. A blubbering presystolic murmur. Maximum intensity in fourth space. Loud blowing systolic bruit; heard also in axilla. Very accentuated second left. Aortic second feeble.

CASE XL.—William P., aged twelve. Second attack in 1883, third in 1885. No rheumatism. Condition of heart not noted. Has no symptoms. *Status præsens:* Diffuse apex beat in nipple line, in fourth and fifth spaces. Transverse dulness increased. In erect posture sounds clear. Recumbent, distinct apex systolic murmur transmitted along anterior axillary fold. In third and fourth interspaces double murmur, the diastolic not rough. Second left very much accentuated.

CASE XLI.—Joseph M., aged thirteen. First attack January, 1881; second, October, 1881. No rheumatism. In 1881 a soft systolic murmur. Has had vertigo and rushes of blood to head. *Status præsens:* Impulse not forcible; dulness slightly increased. No thrill, but loud shock of first sound. Rumbling presystolic murmur, maximum in fifth space in nipple line, is well heard to anterior axillary fold. Loudly accentuated second left. No systolic murmur even when recumbent.

CASE XLII.—Carrie B., aged ———. Second attack in 1884; third in 1886, all severe. No rheumatism. In 1881 heart normal. No symptoms. *Status præsens:* Visible, somewhat forcible, pulsation in third, fourth, and fifth spaces. Erect posture, no murmur; recumbent, systolic bruit at second left, localized. Second sound here loud, sharp, and reduplicated.

CASE XLIII.—Mary B., aged sixteen. Three or four slight attacks since 1881. In 1881 pains in joints, no swelling. In 1881 an apex bruit. Has had no heart symptoms. *Status præsens:* No enlargement. When erect, sounds clear; recumbent, systolic bruit at second left, with marked accentuation of second sound.

CASE XLV.—Marcus Van A., aged eleven. None since. No rheumatism. In 1881 a somewhat loud musical bruit. No symptoms. *Status præsens:* Apex beat in nipple line, fifth space. Impulse not specially forcible. Loud blowing systolic bruit at apex, propagated to axilla and heard well at scapula. Second left accentuated and reduplicated.

CASE XLVI.—Alice W., aged seventeen. Second attack in 1882. Pains in knees in 1882, and lately in shoulders. Heart normal in 1881 and 1882. *Status præsens:* Soft apex systolic murmur, not heard in axilla. Second left accentuated. No enlargement of heart. Has at times palpitation and shortness of breath.

CASE XLIX.—Jessie J., aged nineteen. Three attacks since. Rheumatism with attack in 1883, and again in 1885. Heart said to be

normal in 1885. *Status præsens:* Beat in fifth space outside nipple. Dulness increased. At apex a soft systolic bruit, not heard in axilla, except after exertion. In fourth space, in localized region, a soft diastolic murmur, not increased toward sternum, not heard at aortic or pulmonary cartilages; it also is intensified by exertion. Has "attacks at the heart," faints, and gets cold. Has much pain at times and is short of breath.

1882 (five years). Thirteen cases; ten affected.

CASE L.—Tillie M., aged fifteen. Attacks also in 1883 and 1886. No rheumatism, but lately has had pains in shoulders. No note of heart. Has had at times pain at heart and palpitation. *Status præsens:* Apex bent just within nipple, a little forcible. Apex systolic bruit heard along anterior axillary fold and in middle axilla. Second left accentuated.

CASE LII.—Annie B., aged eighteen. No rheumatism. In 1882 a loud apex systolic bruit. Has had shortness of breath and palpitation. *Status præsens:* Beat forcible, outside nipple line; dulness increased. Apex systolic murmur, heard also in axilla and at angle of scapula; also as high as second rib. Second left loudly accentuated.

CASE LIII.—Mary J., aged fourteen. Attacks also in 1883, '84, and '85. No rheumatism. Heart normal in 1882. No symptoms. *Status præsens:* Impulse forcible. Soft systolic bruit at apex, heard as high as third space, not propagated to axilla. Remarkable accentuation of second left.

CASE LIV.—Bessie P., aged thirteen. Second attack in 1883. Rheumatism in hands and feet with first attack. Heart said to have been normal. *Status præsens:* Impulse forcible. Apex in sixth space an inch outside nipple line. Slight presystolic rumble at apex. Loud systolic murmur in second and third interspaces, not so marked at apex. Second left loudly accentuated. No symptoms.

CASE LV.—Harriet H., aged eight. No rheumatism. Died of heart disease with dropsy, November 8, 1883.

CASE LVII.—Sadie C., aged twelve. Second attack in 1885. In 1886 ankles swollen and sore; never had rheumatism with the attacks of chorea. No note of heart in 1882. In 1885 "hypertrophied and loud apex systolic murmur." *Status præsens:* Apex an inch outside nipple line. Impulse forcible. Dulness increased. No thrill. High-pitched systolic bruit at apex, loud also in axilla and at angle of scapula. Very accentuated second left. Has much throbbing of heart on exertion, and has vomited after skipping.

CASE LIX.—Maggie W., aged fifteen. Second attack in 1885. No rheumatism. Heart normal in 1882. *Status præsens:* A soft murmur at apex, not transmitted; increased on holding breath. Second left very accentuated.

CASE LX.—Fannie S., aged eleven. Second attack in 1883, third in 1884, and fourth in 1885. Rheumatism in 1883; severe attack. In November, 1882, a basic systolic murmur, which persisted in 1884. In June, 1885, there were hypertrophy and evidence of aortic and mitral disease. Died of cardiac dropsy, July 11, 1886.

CASE LXI.—Catherine B., aged thirteen. A second slight attack in spring of this year. No rheumatism. No note of heart in 1882. *Status præsens:* Impulse forcible, at and a little outside nipple line. Dulness

increased. Feeble presystolic thrill. Loud apex systolic murmur, propagated to axilla. In fourth space just within nipple, a rumbling presystolic murmur. Second left very accentuated. Has had at times severe pain in heart; no shortness of breath.

1883 (four years). Fifteen cases; eight affected.

Case LXII.—James G., aged thirteen. Second attack in 1885, third in 1886. No acute rheumatism; pains in shoulder. In 1886 a systolic apex murmur. *Status præsens:* Apex outside nipple line; large area of forcible impulse in fourth and fifth spaces. Transverse dulness increased. No thrill. High-pitched apex systolic murmur transmitted to axilla and angle of scapula. In fourth space a faint rumble before first sound; second left accentuated and reduplicated. Has no heart symptoms.

Case LXIII.—Tinnie B., aged twelve. Second attack in 1884, third in 1886. No rheumatism. In 1886 well-marked cardiac lesions. *Status præsens:* Apex beat forcible, outside nipple line. Dulness increased. Loud, rough apex systolic bruit, transmitted to scapula; second left accentuated and reduplicated. Has pain, and at times palpitation.

Case LXIV.—Henrietta K., aged twenty-one. Second attack in 1884. No rheumatism. In 1883 heart's action intermittent. *Status præsens:* Beat forcible. No thrill. Loud, rough apex systolic bruit heard at angle of scapula. Second left much accentuated. Has great shortness of breath on exertion.

Case LXV.—Lorenzo D'A., aged eleven. Two slight returns. No rheumatism. No note of heart in 1883. *Status præsens:* Impulse slow, forcible; apex in fifth space, in nipple line. Soft apex systolic murmur, louder on exertion; not heard at mid axilla. Second left much accentuated and reduplicated. Has distress at heart on exertion.

Case LXVI.—Nellie H., aged nine. Second attack in 1884, third in 1885. No rheumatism. No note of previous heart-condition. *Status præsens:* Apex beat diffuse, maximum in sixth space, one inch outside nipple line. Dulness increased. No thrill. Loud apex systolic murmur transmitted to angle of scapula. Just below and inside the nipple a *soft* presystolic bruit. Second left much accentuated. In December, 1886, the child had a sharp attack of cardiac dyspnœa.

Case LXVII.—Edward R., aged twelve. Second attack in 1885. No clear history of rheumatism; has had pains. No note of heart. *Status præsens:* Beat in fifth, just outside nipple line. Dulness increased. Just above apex, in localized region, a presystolic murmur; louder in recumbent posture. When breath is held, soft apex systolic murmur. Second left much accentuated.

Case LXXI.—Annie C., aged eleven. Bad attack for a month; no recurrence. No rheumatism. No note of heart in 1883. *Status præsens:* Beat at nipple, in fourth space. Transverse dulness increased. Feeble thrill above apex. Rough presystolic murmur in third and fourth spaces; heard also along pectoral fold. Just outside apex a soft systolic. Loudly accentuated second left. Is short of breath on exertion.

Case LXXIV.—William H., aged fifteen. Still has twitches at times. No rheumatism. No note of heart. *Status præsens:* Apex beat in nipple line. Dulness increased. Feeble presystolic thrill at apex. In second left interspace a loud, *rough*, systolic murmur. In third and fourth spaces a softer bruit. Distinct presystolic rumble above apex beat. First sound reduplicated at apex. Second left much

accentuated. Has what his mother calls "asthma spells," particularly on exertion.

1884 (three years). Thirteen cases; ten affected.

CASE LXXVII.—Harry B., aged thirteen. Second attack in 1885, third in 1886. Rheumatism with attack in 1884. Apex murmur in 1886. *Status præsens:* Impulse feeble, just inside nipple line. No thrill. Dulness not increased. Soft apex systolic bruit; heard well to [illegible]-axilla. Rough presystolic murmur, maximum intensity *at apex*. B [illegible] intensified after exertion. Loudly accentuated and reduplicated second left. No palpitation; no shortness of breath. Cheeks are flushed, and he has a *cardiac* look.

CASE LXXVIII.—Ida M., aged fourteen. No other attack. No rheumatism. No note of heart. *Status præsens:* No enlargement. Soft apex systolic bruit propagated along anterior axillary fold. Systolic murmur at second left space. Loudly accentuated left. Has no symptoms.

CASE LXXIX.—George G., aged thirteen. No other attack. Had pain in left hip in 1884. Heart normal. *Status præsens:* No enlargement. Soft apex systolic bruit; not heard in axilla, but well-marked in third left apex. Second left very accentuated, and the diastolic shock here loud.

CASE LXXX.—Nellie M., aged eleven. Right knee was swollen. No note of heart. *Status præsens:* Forcible apex beat in fifth space, one inch outside nipple line. Dulness increased. At apex first sound booming and echoing. In third and fourth left spaces loud systolic bruit; feeble at second left cartilage; not audible in axilla; faintly heard in mid-sternum. Much accentuated second left. Has no symptoms.

CASE LXXXII.—John D., aged eighteen. Second slight attack in 1886. In 1887 slight rheumatism. In 1884 soft murmur at base. *Status præsens:* Impulse just within nipple. Dulness increased. No thrill. At apex a rumbling presystolic murmur. No systolic bruit audible at apex. At fourth left and up and down the sternum is a long-drawn diastolic murmur, of maximum intensity on sternum, opposite fourth cartilage. Heard at aortic cartilage and at xiphoid. No aortic systolic bruit. Second left very accentuated. Posture did not alter the murmurs. He had no heart symptoms.

CASE LXXXIII.—Kate H., aged fifteen. Rheumatism very badly at the time. Heart said to be normal. *Status præsens:* Apex beat forcible, outside nipple line. Cardiac shock over a large area. No thrill. Loud apex systolic murmur propagated along anterior axillary fold. Second left much accentuated. Has no heart symptoms.

CASE LXXXIV.—Henry M., aged fifteen. No rheumatism. Heart normal in 1884. *Status præsens:* Impulse diffuse in fourth and sixth spaces, one inch outside nipple line. First sound at apex booming. When recumbent a soft systolic murmur in second and third left spaces near sternum. Second left much accentuated.

CASE LXXXVI.—Lillie D., aged twelve. No rheumatism. Heart normal in 1884. *Status præsens:* No enlargement. When recumbent a soft, long, apex systolic murmur, not heard in axilla or in second or third spaces. Disappears when erect. Second dull and loud, not sharp and ringing, like second right.

CASE LXXXVII.—Fannie P., aged ten. Second attack in 1885. Pains in wrists, but no swelling. In 1885 apex murmur, presystolic; soft basic murmur; hypertrophy. *Status præsens:* Forcible apex beat in fifth space, outside nipple. Feeble thrill. Loud, high-pitched apex systolic bruit, transmitted to scapula; and, in fact, all over left chest. Presystolic bruit. At aortic cartilage a rough, systolic murmur. Second left accentuated. Has palpitation at times.

CASE LXXXIX.—Annie T., aged thirteen. Several slight returns since 1884. Rheumatism three months after the chorea. No note of heart in 1884. *Status præsens:* Action rapid, apex a little out from nipple line. Dulness increased. Loud, rough systolic bruit at apex, transmitted to scapula. Second sound very accentuated at third left cartilage. Has "spells" with her heart; has fainted. Is short of breath on exertion.

1885 (two years). Eighteen cases; five affected.

CASE XCI.—Lizzie B., aged fifteen. No attack since. No rheumatism. No note of heart. *Status præsens:* Impulse strong. Thrill at apex. Localized systolic murmur at apex, not heard in axilla or [illegible] third or second spaces. Loudly accentuated second left.

CASE XCII.—Alice N., aged ten. No rheumatism. In 1885 loud mitral systolic. *Status præsens:* Apex beat diffuse in fourth and fifth spaces in nipple line. Transverse dulness increased. Apex systolic murmur, heard beyond mid-axilla; intensified in recumbent posture. Marked accentuation of second left.

CASE XCVII.—William R., aged nine. No rheumatism. Heart in 1885 said to be normal. *Status præsens:* No enlargement. First sound not clear, and on exertion a soft systolic murmur at apex; heard also two inches beyond nipple, and as high as third rib. Loudly accentuated second left. Has no symptoms.

CASE C.—Georgie G., aged thirteen. No rheumatism. In 1885 a basic systolic murmur. *Status præsens:* Impulse diffuse, forcible; apex just outside nipple line. Dulness increased. Thrill. At apex loud systolic bruit, propagated to posterior axillary fold. Second left dull, thudding, and accentuated. Heart's action irregular. Has palpitation and shortness of breath.

CASE CI.—Jennie N., aged nine. Second attack in 1886, in which she had rheumatism. Heart in 1885 normal. In 1886 loud apex systolic murmur. *Status præsens:* Impulse forcible, apex in nipple line. Dulness increased. Apex systolic transmitted to axilla and angle of scapula; heard also as high as second rib. Second left loudly accentuated. Has, at times, throbbing, palpitation, and pain.

Of the 43 cases in which the heart was found normal, 12 had had three or more attacks, 8 had had two, and 23 a single attack. There was a history of rheumatism in 8—*i. e.*, 18.6 per cent. In 6 of these cases the rheumatism was acute. In only 2 cases had there been a murmur noted at the time of the original attack.

From the cases presenting abnormal physical signs, 13 may be separated as examples of functional trouble. They are cases without signs of enlargement of the heart and with localized or variable murmurs. Ten presented soft apex systolic bruits not propagated, in 3

variable with position. In most of these there was accentuation of the second left pulmonary sound, but I do not think much stress is to be placed upon this sign in young persons, as it is by no means uncommon in normal hearts. Particular attention was paid to this point in the examination of all the cases and comparison made between the sounds in the second right and second left spaces. There were 10 normal cases in which the pulmonary sound was distinctly louder than the aortic, and in some instances reduplicated. No note was taken of the murmurs, so often developed in the region of the pulmonary artery during respiration and which are extremely common in thin-chested children. In 2 cases the sounds in this region were clear in the erect posture, but in the recumbent position systolic bruits developed; in both the second sound was accentuated, and in one the area of pulsation somewhat increased. In a third case there was a soft systolic murmur in the second and third spaces in the recumbent position only, with accentuation of the pulmonary sound and the apex beat outside the nipple line. In some of these there may have been organic changes in the valves, but I deemed it best to exclude all doubtful cases.

There remain for consideration 54 cases with signs of valve disease. In 21 cases there had been three or more attacks of chorea.

The facts regarding rheumatism are interesting. In 22 cases, 40.7 per cent., there was a distinct history of articular trouble, sometimes with the chorea, but in 6 cases from one to five years after the attacks. Comparing the frequency of rheumatic affection in this group, 40.7 per cent., with that in the total number of cases, 15 per cent., or with the group of 43 normal cases, 18.6 per cent., we see the influence this disease exercises in producing the heart lesions. We have, however, the larger proportion, 59.3 per cent., of the cases without any history of rheumatic trouble. Of the 21 cases which had had three or more attacks of chorea, only 7 had rheumatism.

In this group there are rather more than 3 females to 1 male, a proportion considerably greater than in the total number of cases.

With reference to the nature and seat of the lesion, there were 44 cases of uncomplicated mitral affection and 4 instances of combined aortic and mitral disease. In 25 cases there was a mitral systolic murmur; in 17 a distinct presystolic murmur, with or without a thrill, and usually with a systolic bruit. Of the aortic lesions Case XII. presented a soft aortic direct murmur and a mitral systolic; Case XXIV. a double aortic murmur as well as a mitral systolic; Case LX. died of combined aortic and mitral disease; Case LXXXII. presented the unusual combination of an aortic diastolic and a mitral presystolic murmur. The overwhelming proportion of cases, with mitral lesions, is what we might expect from the constancy with which the acute endocarditis of rheumatism and chorea attacks these valves

There are many points of interest in physical diagnosis which these cases illustrate, but I am only concerned now with the clinical problem of the frequency with which organic heart disease follows chorea.

Not many of the cases had subjective symptoms of cardiac disease. In 14 instances there was complaint of shortness of breath; 16 cases had attacks of palpitation, and in 6 cases there was cardiac pain. Two cases had died of heart disease, 1 was in bed with cardiac dropsy, and in several others there were premonitions of heart failure. The majority illustrated the important clinical law in valvular disease, that the symptoms do not result from the lesion, but from failure in the compensatory action which for years may equalize the circulation and obviate completely the most serious mechanical defect.

A study of these cases justifies, I think, the following conclusions:

1. That in a considerable proportion of cases of chorea—much larger than has hitherto been supposed—the complicating endocarditis lays the foundation of organic heart disease.

2. In a majority of the cases the cardiac affection is independent of rheumatism, and cannot be regarded as in any way associated with it; unless, indeed, we hold with Bouillaud, that in the disease "chez les jeunes sujets le cœur se comporte comme une articulation."

3. As the presence of an apex systolic murmur in chorea is usually an indication of the existence of mitral valvulitis, as much care should be exercised in this condition as in the acute endocarditis of rheumatism. Rest, avoidance of excitement, and care in convalescence, may do much to limit a valvulitis, and obviate, possibly, the liability to those chronic nutritional changes in the valves wherein lies, after all, the main danger.

HEREDITARY TREMOR,

A HITHERTO UNDESCRIBED FORM OF MOTOR NEUROSIS.[1]

By C. L. Dana, A.M., M.D.,

PRESIDENT OF THE NEW YORK NEUROLOGICAL SOCIETY, VISITING PHYSICIAN TO BELLEVUE HOSPITAL, PROFESSOR OF NERVOUS AND MENTAL DISEASES, NEW YORK POST-GRADUATE MEDICAL SCHOOL.

The object of this paper is to call attention to a peculiar hereditary motor disorder which has heretofore never to my knowledge been systematically described by medical writers.

Definition.—The affection in question consists of a fine tremor, con-

[1] I am under great obligations to Dr. Henry Boynton and Dr. Fred. T. Kidder, of Woodstock, Vt., and to Dr. Coulard, of Brattleboro, Vt., for assistance in securing data for my histories.

CASE OF

CHOLESTEATOMA

OF FLOOR OF

THIRD VENTRICLE AND OF THE INFUNDIBULUM.

BY

WILLIAM OSLER, M.D.,

PROFESSOR CLIN. MED. UNIVERSITY OF PENNSYLVANIA; PHYSICIAN TO THE UNIVERSITY HOSPITAL, TO THE PHILADELPHIA HOSPITAL, AND TO THE INFIRMARY FOR NERVOUS DISEASES.

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CASE OF CHOLESTEATOMA OF FLOOR OF THIRD VENTRICLE AND OF THE INFUNDIBULUM.

CLINICAL SUMMARY.—W. A. L., æt. 29. As a lad, had violent headaches which became more frequent about the eighteenth year. About this time several attacks of transient blindness. In 1876, '77 and '78, when a student, had trouble with his eyes, had headaches and would frequently fall asleep during the day. He graduated in 1879, and began practice. In June, sudden loss of power and sensation in left arm and leg, which returned in an hour. Shortly after, violent headache with vomiting. After an attack of somnolence, he had a brief maniacal outbreak. From July to October much headache, vomiting, and great drowsiness. Would sleep many hours. Pulse often as low as twenty-eight or thirty. Intervals of several days between the attacks. In October was at times incoherent, and lost all recollection of his wife and family. Sight much disturbed, and there was diplopia; one slight epileptiform convulsion. Throughout November and December great improvement, and rapid gain in flesh. For the first six months of 1880 he was able to be about, though the headaches recurred at inter-

vals, and the constant tendency to sleep persisted. Gait staggering. In March, double optic neuritis was determined by Dr. Buller. In beginning of July, another severe attack of headache and vomiting lasting three days, followed by a severe convulsion and prolonged sleep, from which he awoke quite blind. From this time rapid recovery of health, and for five years was able, though blind, to manage a drug business. On June 3d, 1885, return of attacks of headache, vomiting, and prolonged somnolence. Remained unconscious until August 27th, when he awoke at 4 A.M. quite suddenly. From this time pain in the head was the prominent symptom; no further loss of consciousness. Death suddenly, April 25th, 1886.

ANATOMICAL SUMMARY.—Cyst at base of brain in position of optic chiasm. Infundibulum greatly thickened. Small solid tumor in anterior and lower part of third ventricle. Dilatation of the lateral ventricles. Atrophy of optic nerves and tracts. Numerous pearly bodies scattered in the lining membrane of the cyst, and throughout the solid parts of the tumor.

The full account of this remarkable case is thus given by Dr. Buller of Montreal, and by the patient's brother, Dr. J. L.

The early history of the case, as related to me in a letter from the patient's brother, Dr. J. L., dated March 22d, 1880, is as follows: "My brother began to complain of his eyes about the beginning of the year 1877, and all the following summer he complained of more or less pain and uneasiness, but they did not give out until near the close of next winter. He was then in his primary year as a student of medicine, and found great difficulty in writing for his examination. His visual troubles continued to increase until about the month of May, when he went to Toronto to consult an ophthalmic surgeon, who pronounced his condition retinitis albuminurica. This diagnosis I never accepted, for it seemed unreasonable to me that he should have such advanced symptoms from a constitutional disease without having any of the physical or other symptoms of that affection.

"Notwithstanding his imperfect vision he continued his course of studies, never missing a lecture up to the time he was first seen by Dr. Buller at Christmas time, 1878. His vision had then so far improved that he was able to read without difficulty. He completed his medical studies in the spring of 1879, having enjoyed excellent health the whole winter. Immediately after obtaining his degree, he commenced the practice of his profession in a country village, and all went well until about July 20th of the same year, when he was attacked with violent frontal headache and nausea with occasional vomiting; this continued for about a fortnight, accompanied by great lassitude and inability to make any exertion. It seemed an effort for him to exist. He had made up his mind to go to Ottawa for medical advice, and while waiting for the conveyance that was to have taken him there he fell asleep for a short time, and awoke in a violent attack of delirium, with complete suppression of urine, which lasted for about twenty-four hours. A brisk purge set him right, and the next day he left for Pembroke, where he arrived at my house the same night. It should here be mentioned that he had been vomiting his food for several days before his arrival here. This was about August 22d last (1879). The second night after his arrival, the pain became very severe, accompanied by uninterrupted vomiting for about eighteen hours. For several days he had repeated attacks of pain and vomiting, now always aggravated after a long and profound sleep. During the attacks of pain, the pulse would fall in frequency to about forty or forty-five, and even to twenty-eight and thirty; the temperature was not increased. (Probably any subnormal temperature would have been noticed by the writer of this letter if it had existed, but he does not speak of it.—F. B.)

"In the intervals between the attacks of pain, his appetite would return, he would eat freely and apparently be improving. The first treatment he got some time during the first week here while suffering dreadfully. I applied six leeches and a blister, which gave immediate relief; in fact, the leeches had hardly taken when his pulse began

to rise, and in less than twelve hours he was perfectly easy.

"This condition continued with very little variation for about three weeks, when the attacks became milder and the intervals longer, but with a steady decrease of weight. I applied blisters repeatedly, always with marked benefit. I also applied a seton at the nape about the fourth week. On one occasion, about the fourth week, on attempting to stand up to pass water he was seized with a slight spasm, and I think if he had been kept in the upright position it would have developed into a convulsion, but immediately on his assuming the reclining position it passed off, which made me think it was from deranged circulation on account of his having suddenly assumed that position. About this time he complained of a loss of feeling passing all over his body; it used to alarm him very much, and he used to say, 'I cannot feel anything but my poor head.' It seemed to be a numbness lasting only for a little while; it occurred several times, sometimes all over the body, and sometimes only on one side. He never suffered from paralysis of any part or any organ with the exception of his sight. The special senses were all perfect the last time I saw him, about four weeks ago.

"About September 28th he began to show signs of mental failing, evidenced by slight loss of memory, and at times it was difficult to arouse him to perfect consciousness; he would mutter on being shaken, but you could not bring him to himself. This would continue for some hours, when he would wake up quite bright. This was his condition at intervals for the last week before I started to New York with him. The pain during this time was not very bad, and there was not much vomiting.

"He complained continually of feeling a sensation, in different parts of his body at different times, of the touch of what he called a pebble. He would describe the size of it as that of a pigeon's egg, with a rough surface. Of course he knew it was only an illusion, that it did not exist, but he had the sensation, and used to say he had a lump in his brain and that it was the size and shape of the pebble,

but the fact of his knowing the diagnosis was tumor would be a sufficient reason for him to connect the two and give rise to the idea.

"The morning of Oct. 3d, on preparing to dress him for the journey to New York, he was very poorly and could hardly realize that we were starting; indeed, before we left the house it was impossible to make him understand anything, and after we had started I decided to take the Perth train at Smith's Falls and return home, but before we arrived at Smith's Falls he wakened up quite bright and remained so until we arrived in New York on Saturday morning. He kept nicely all day Saturday and also on Sunday, which was the day we saw Dr. Janeway. He was then well enough to give the doctor a history of his case, but on Sunday night he began to suffer pain again, and for the next four or five days he vomited constantly and was at times more or less unconscious, still never so profoundly so as before leaving home, but he showed a dulness of perception of what was going on around him and partial loss of facts as to days, etc. I started for home Oct. 10th, and on moving him from one train to another I had to elevate his head and shake him. Once, in doing this, he had a distinct spasm; in fact, I think it might safely be called a convulsion. He remained more or less unconscious until we arrived at his own home in Perth on Oct. 11th. From this time until the 26th he was perfectly helpless in bed and quite unable to assist himself in any way. I was not sure if he was conscious when relieving himself; he apparently would recognize any person passing before his sight, but could not connect any ideas or think; took very little nourishment and was reduced to about eighty pounds—a perfect skeleton. Exactly a fortnight from the day we left New York, he opened his eyes on Sunday morning as bright as a dollar, and began from this time to eat, sleep, and gain strength. For eight weeks he gained flesh at the rate of one pound per diem until he weighed about 150 pounds. This change took place without treatment of any kind. After he began going about, he commenced taking iodide potass. up to

almost twenty grains twice daily, but not regularly, and another seton was put in the neck.

"From this time until Christmas he remained to all appearances perfectly well, without headache, nausea, or vomiting, and in the full enjoyment of all his faculties. About Christmas time he paid me another visit in Pembroke. After he had been here a few days, the headache and vomiting returned. He remained here a short time and then returned to Perth, where he remained until he visited Montreal."

I (Dr. Buller) saw W. L. for the first time about the end of December, 1878; he then appeared to be in good health and quite capable of carrying on his studies as a medical student. I was asked to examine his eyes in order to ascertain whether there remained any evidences of the retinitis albuminurica thought to have been discovered in the previous month of June. I could find no trace of disease of either retina or optic nerves. Vision was normal, refraction, H. $\frac{1}{30}$. I also examined the urine and found neither casts, albumin, nor sugar. The specimens examined under the microscope, however, contained numerous crystals of triple phosphates and large numbers of small octahedral crystals of oxalate of lime. At that time, he was not suffering from headache or any inconvenience from using the eyes for close work many hours daily. There was nothing in his manner or appearance to indicate a defective state of health. He next came under my notice on the 20th of March, 1880. His history during the intervening period has been given in detail in the foregoing communication from his brother. He came unattended to Montreal. The following day I noted his condition as follows:

The patient has a somewhat slow and hesitating manner of speaking; occasionally he forgets words that he should be familiar with, walks slowly, as if feeble and languid, and has a certain unsteadiness of gait which at times is almost staggering, especially on getting up after resting in a recumbent posture; at such times he feels a sort of giddiness. There is no evidence of weakness in executing

any ordinary muscular movements. The tendon reflex, however (knee jerk), is slow and weak. Complexion is rather fresh; the face has a puffy look and appears somewhat too fleshy for the body, and may best be described as a stolid heavy countenance entirely destitute of expression or animation; even when he smiles there is the same want of animation. At the same time, there is no defect in the voluntary movements of the facial muscles and no defect in cutaneous sensation. He still suffers a good deal from frontal headache, especially in the morning, and always carries the head somewhat thrown backwards. Vomited a little the morning he left home, but not since.

Four days later (March 25th) he was found to sleep most of the time, and when awake yawned very frequently. He is also much troubled with hiccough. The attendants in the hospital notice that he seems to forget to take his meals, and at times acts somewhat like a drunken man in his walk, and once or twice has almost fallen backwards when going up-stairs. In walking rather swings the legs. He attributes the uncertainty of gait to weakness—an idea that is perhaps not altogether without foundation, as the muscular power of hands tested with dynamometer only amounts to sixty pounds.

The appetite is fairly good, tongue a little furred, bowels inclined to be costive. Urine thirty-six ounces in twenty four hours, slightly acid, of a pale yellow color, deposits a little flocculent mucus, contains neither casts, albumin, nor sugar. There is no anomaly of sensation discoverable in any part of the body, and now he never feels "the lump" spoken of by his brother in the early stage of his complaint; is able to give a clear description of his past life; close questioning does not discover more than a possible venereal origin of the disease; it was, however, thought best to try the effect of iodide of potassium in full doses, commencing with twenty grains and increasing as rapidly as the stomach would bear the drug well diluted; this was commenced the second day after his arrival in Montreal. On March 26th he was examined by Dr. R. P. Howard, who gave me the following notes:

"Heart sound, normal; pulse, 65; presents no peculiarities; lungs healthy, but respiratory sounds weak; right side of chest flatter than left, and lower respiratory movements on this side markedly less excursive than on left side; shows an annoying restlessness under examination; has a papular (? iodide) rash on body and slight coryza; body emits a peculiar musty odor, which, however, is probably due to external circumstances. Is now taking iodide gr. xxx. thrice daily, preceded by a small dose of hydrocyanic acid a few moments before the iodide is administered. Still has hiccough and morning headache." The condition of the eyes was not placed on record until March 27th, but had not in any way changed since the 21st. It was as follows:

Pupils equal, in ordinary daylight about 2½ mm. wide, act sluggishly both to light and acc., V=$\frac{20}{30}$ and Hm $\frac{1}{28}$ each. The ophthalmoscope shows well-marked double optic neuritis—choked discs—not neuroretinitis, the swelling being little wider than the normal disc and quite steep. With hyperopia = $\frac{1}{28}$ at macula, the surface of the nerves is best seen with + 10. Veins dark and tortuous, but of normal size; arteries a little smaller than normal; vessels only here and there hidden or obscured by the swelling of papilla; no hemorrhages, and only a moderate degree of white striation, and the papilla appears rather reddened; macula regions entirely normal. There is no contraction of the visual fields, no defect in perception of colors, and the muscular system of the eyes presents no abnormality.

He remained in Montreal until April 3d without any material change in his condition; some days feeling a little better and others suffering more from headache (always frontal), occasionally vomiting, was taking pot. iod. gr. lx. three times daily, when he returned to his home in Perth.

Oct. 21st. Came to Montreal again for the day in order to have another examination of the eyes, having now become entirely blind. Continued taking the iodide in about the same doses all summer, but for the last three weeks has omitted it. Vision failed steadily from the time he

left Montreal, but could still see fairly well about the beginning of July, when he had another severe attack of headache and vomiting which lasted some three days, and culminated in a convulsion. This was followed by a profound sleep from which he awoke entirely blind, which has continued up to the present time. Since this last severe attack his general health has steadily improved. Has had no headache to speak of since the end of August, only a little occasionally just on the top of the head; feels strong and well; walks without staggering; his countenance has gained in expression; is well nourished, and in the matter of appetite and sleep there is nothing amiss; also avers that sexual power is unimpaired. The appearance of the optic nerves has undergone a great change: both are alike extremely pale, scarcely if at all swollen, a little irregular at the margin. The veins tortuous, but both veins and arteries much diminished in size. Was next seen by me on June 24th, 1882; came on account of an acute catarrhal otitis media of the left ear, which has caused him a considerable degree of pain for the past ten days, otherwise his health has been very good since his last visit. The completely atrophic optic nerves have never afforded him a glimmer of light since the day he became blind. The ear trouble yielded readily to the usual treatment, and he returned home on June 24th.

The remainder of the history is thus given by his brother, Dr. J. L. "He recovered perfectly from the ear trouble and remained well, enjoying good health until June, 1885—making five years of relief from his trouble—when the pain reappeared, and up to the 27th of August, he suffered much as in the first illness, with severe attacks of pain, vomiting, and long spells of somnolence. During some of these attacks the pulse was very weak and fluttering, and in one it was thought that he was going to die, and I was telegraphed for. He was more or less unconscious all this time, and it is said that when the attack passed off on the 27th, the first word which he spoke was to take up the sentence he left off in June, three months before, when seized with the headache. On the 28th of August he sat

up and took his dinner at the table, and remained well, with the exception of slight attacks of pain until Nov. 15th, when he was seized with a terrible stabbing, piercing, unendurable pain in the head and his face flushed crimson. This gradually passed off, and he was able to walk to the post-office. From this time he was up and down, one day well and several days in pain, but there was very little vomiting and no disturbance of the pulse. He slept well when not suffering.

"During the last month the intervals of relief were very short, a day or two at most, and the attacks of pain longer, and for the last fortnight the pain was nearly constant; he has to have some person sitting beside him to keep him from falling asleep; if he happened to fall asleep, in a few minutes he would wake up *frantic* with the increased suffering. The Thursday before he died he was down-stairs enjoyed his meals, and he looked quite well, and likely to be so; he was always so cheerful and bright when free of pain and suffering. He passed away without any struggling or any particular warning of the approach of his death. He had peculiar attacks, the last three weeks before his death. I was at his bedside one morning, and he called me in distress and complained of a strange feeling in his head. He said his head was all drawn up, and that his face was also all drawn up, although showing no indication or appearance of any change in expression. His hands and feet were extended and rigid, but could be flexed by force. He appeared greatly alarmed and distressed, and his appeals of distress and alarm were pitiful. During the attack, which lasted half an hour, his pulse never varied or changed; it was perfectly normal. The attack lasted about half an hour; it returned again several times during the day. Another expression he used, 'My inside is all drawn up.' He used the word *drawn* to describe the sensation in his inside, face, and head. He had several attacks of this character the last two weeks before his death, and it was fearing an attack like this, and feeling it coming on, that he called his mother the night of his death: he said,

"*Mother, mother,* I am going to have one of those attacks; raise me up!' He then said, 'I feel like fainting, get me a glass of water!' He tried to drink it, but it came back, his head fell forward and he passed away, and never moved again."

Dr. Fraser, of Perth, Ont., has also written an interesting account of the patient's last illness which practically corresponds with the above description.

I happened to be in Montreal the day on which Dr. L. received word of his brother's death, and as I had seen the case on several occasions with Dr. Buller, I gladly consented to go to Perth with Drs. Buller and Wyatt Johnston to make an examination.

Autopsy, twenty hours after death. Body well nourished. Face and general surface blanched, rigor mortis present, *calvaria* of normal thickness. *Dura mater* not very adherent. Sinuses contain fluid blood. Surface of brain as examined *in situ*, symmetrical, but rather wide in parietal regions. A large quantity of clear fluid escaped in removal of the organ. A few adhesions of the pia mater and brain substance to the dura covering the middle fossæ so that the brain substance here tore in lifting out the temporo-sphenoidal lobes. No adhesions at the base, but the infundibulum was greatly thickened, and cut with resistance at its point of junction with the pituitary body.

Parts of the base present the following appearance: Olfactory bulbs look small and the nerves seem a little flattened, particularly the posterior third. A cystic tumor, the size of a walnut, occupies the space between the corpora albicantia and the commencement of the longitudinal fissure. It measured about three by three centimetres, and consisted of two parts, an anterior cyst, somewhat translucent, and a posterior firmer, cone-shaped portion which represents the infundibulum and was attached to the pituitary body by a stalk five millimetres in thickness. The mass occupies the position of the chiasma, no trace of which can be seen. The optic nerves are atrophied, only two millimetres in diameter, gray in color, and were at-

tached to the antero-external angles of the cystic tumor. The optic tracts pass off from the postero-external portion and as far as the anterior fibres of the crura are distinct, but from this point they are represented by a thin, pale, gray bands, scarcely discernible. In front the tumor presents a rounded smooth surface, which rests upon the longitudinal fissure, and the hinder part of the first frontal convolutions. Laterally it does not extend upon the anterior perforated spaces. Posteriorly it reaches the corpora albicantia, but does not involve them. The crura form part of its posterior boundary, and they look as if slightly spread by it. The pia mater covers the mass, but is not specially adherent or thickened. The vessels of the circle are a little displaced, but are otherwise normal. The nerves at the base appear healthy; the left third nerve looks a little translucent at one spot.

The convolutions are slightly flattened, and the vessels of the pia not unusually full. On section the substance cut with firmness. Centrum ovale looks natural, puncta vasculosa numerous. Corpus callosum normal. Lateral ventricles are considerably dilated, and contain an excess of fluid. The posterior cornua seem particularly large. The veins along the surface are full. Fornix and septum are flattened, but can be lifted readily. Velum interpositum very vascular, and the venæ Galeni full. The third ventricle presents the following condition: Pineal gland, with its peduncles, and the posterior commissure look normal. The middle commissure is large and distinct. A firm mass occupies the anterior and lower part of the ventricle between the pillars of the fornix. It is about 2.5 centimetres in length by 1.5 in breadth. Behind it is in contact with the [illegible]alami, and on the right side with the smooth surface of the caudate nucleus. The right pillar of the fornix is distinct, the left appears to be involved, and the mass is of greater extent towards this side where it is firmly connected with the caudate nucleus. It is solid in the greater part of its extent, but centrally there is a cyst with clear fluid. Whether this

originally communicated directly with the third ventricle could not be determined, but at the upper part the wall is very thin and translucent. The cyst is directly continuous with the one at the base of the brain.

The corpora striata and optic thalami appear normal.

The tumor then occupied the anterior extremity of the third ventricle, partially involving the left pilar of the fornix, but not extending laterally into the ganglia. At the base, it involved the parts known as the tuber cinereum, the lamina cinerea, and the infundibulum, destroying completely the chiasma and producing wasting of the optic nerves and tracts.

The infundibulum forms a firm conical mass attached to the hinder part of the tumor, and tapers to a diameter of five millimetres at its insertion into the pituitary body.

The tumor consists of a cyst with solid walls of variable thickness and clear contents. Whether it communicated with the third ventricle was unfortunately not accurately ·'ed, probably it did not. The lining membrane of the cyst is smooth and glistening like that of a ventricle, and here and there in the surface are small yellow granules.

At the base, anterior to the thickened infundibulum, the walls are very thin and translucent, but laterally and behind they form a firm, solid mass of a grayish color and present a rough, uneven surface. The portion in the third ventricle has thicker walls in proportion to the cyst, and the tissue has a grayish translucent aspect. Through the wall in places, particularly where thin, a yellow color is noticeable, not uniform, but in small areas. The tissue of the infundibulum is solid, gray externally, but yellowish-brown in the inside and on section it cuts with a gritty sensation.

Pons normal. Fourth ventricle and corpora quadrigemina present nothing special. The *iter* not much dilated. The posterior aspect of the cord, about twelve millimetres below the calamus scriptorius, presents a very remarkable depression, as if a fine tight cord had been

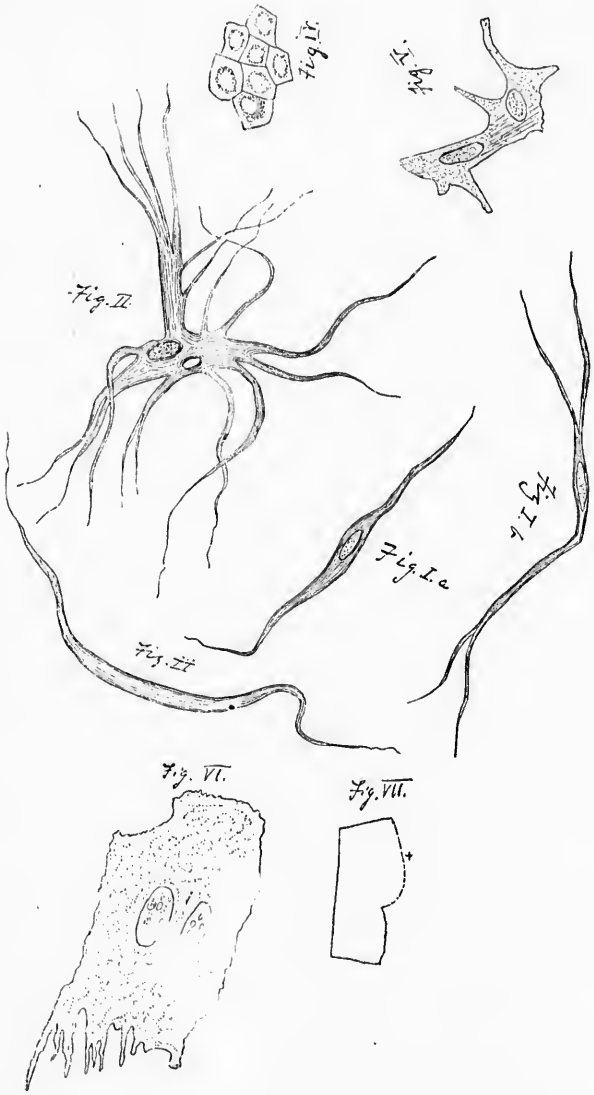
Fig. IV.
Fig. V.
Fig. II.
Fig. I.a
Fig. III
Fig. VI.
Fig. VII.

passed round in an oblique direction, extending from a point just above the line of emergence of the anterior roots of the first cervical nerve. The part above the constriction projects seven millimetres beyond the level of the rest of the cervical cord. The pia mater dips into the depression, and the outlines of the funiculi graciles and restiform bodies are quite distinct to its margins. There is no softening, no hyperæmia, no alteration in color, and it looks like an anomaly rather than a pathological condition. Fig. 7 shows a facsimile outline sketch after section in the groove between the restiform bodies and the posterior column on the right side.

Histological examination.—The tumor consisted chiefly of: (1) a matrix of densely interwoven fine fibres without definite arrangement. In the infundibulum and on the wall of the cyst they were more closely set than in the softer mass within the third ventricle.

(2) Spindle and branched cells which were found in all parts, but more particularly in the softer portions by the base of the cyst and in the ventricle. From the latter situation, teased bits showed very remarkable forms; many were fusiform, greatly elongated and with the extremities prolonged into delicate filaments (Fig. 1, *a* and *b*). Some of the branched forms were the largest and most beautiful structures of the kind which I have ever met with in either normal or pathological growths. Fig. 2 represents one of these large "spider" cells outlined with the camera. Many of the processes were prolonged far beyond the margins of the field. The protoplasm was as a rule delicate, with but few granules. Here and there were noted curious elongated non-nucleated cells with a hyaline, homogeneous stroma (Fig. 3). I have described these as occurring in a case of medullary neuroma of the brain,[1] and have since met with them in several gliomas.[2] They probably result from the transformation of the ordinary spindle cell, many of which are identical in form.

[1] Journal of Anatomy and Physiology, London, vol. xv.
[2] Medical News, Phila., 1886.

(3) A beautiful pavement epithelium (Fig. 4) lined the cyst; the cells were not extremely flattened, and in many places were filled with granules.

(4) Pearly bodies which were attached on the inner wall of the cyst, and were also very abundant in the thickened infundibulum. These consisted of nests of epithelial cells, and as many of them were calcified, section with the knife gave a gritty sensation. The concentric arrangement was well seen in the smaller nests, but not in the larger ones, which were too deeply impregnated with lime salts. The epithelial elements were very numerous in the thickened infundibulum, and all shapes and sizes occurred in teased preparations. Many were much flattened and curved; others of irregular and bizarre form (Fig. 5). Some of these were of comparatively enormous size and very flat (Fig. 6). It was difficult at first to believe that we were dealing with epithelial cells. It is interesting to note that there were no cholesterin crystals. The remarkable indentation in the posterior aspect of the upper part of the cord, an outline of which is given at Fig. 7, showed in section a normal white matter at the base of the groove without a trace of induration or increase in the fibrous elements.

Remarks.—Indications of brain trouble existed in this case for at least ten years, and possibly the headaches which occurred when a lad may have been due to the growth in the third ventricle either beginning or assuming a more active condition. During the year 1879 and the first six months of 1880, the growth extended to the base of the brain, and produced at first neuritis and finally atrophy of the optic nerves. This was due to the gradual formation of the cyst which occupied the position of the chiasma. At this time, too, the headache was most intense, the signs of irritation (convulsions, paræsthesia, vomiting, staggering gait) most marked. Recurring attacks of somnolence occur with great frequency in brain tumor—particularly in syphiloma, but I do not think we have yet reached a satisfactory explanation of their variability. We may reasonably assume that from July, 1880,

to June, 1885, the brain accommodated itself to the increased pressure, and that during this time the growth remained stationary. The return of the symptoms in 1885 may have been connected with the development of the hydrocephalus due to pressure of the tumor on the veins. A portion of the mass in the third ventricle looked recent, and certainly contained less of the dense fibrillar connective tissue than in other parts, indicating possibly a more recent formation. I thought at first that the constricted furrow on the upper portion of the cervical cord might be due to pressure, and in this way might perhaps explain some of the symptoms of tingling, etc., of which he complained; but the situation and character of the groove and the absence of the slightest induration are very much opposed to such a view.

The tumeur perlée of Cruveilhier, or cholesteatoma of Johannes Müller, is a very rare growth, most often met with at the base of the brain. It is in reality an endothelioma, and in this instance probably began in the cellular lining of the third ventricle, and its extension in the infundibulum.

EXPLANATION OF THE FIGURES.

FIG. 1, *a* and *b*.—Spindle cells from the mass in third ventricle.

FIG. 2.—Enormous "spider" cell from the same situation. Nos. 7 and 3.

FIG. 3.—Non-nucleated, translucent fibre cell.

FIG. 4.—Endothelial lining of the cyst wall.

FIG. 5.—Irregular form of endothelium obtained by teasing a small piece of the central part of infundibulum.

FIG. 6.—Enormous flat endothelial scale. Nos. 9 and 3.

FIG. 7.—Outline of medulla and cord showing the furrow in the posterior surface; + indicates the calamus scriptorius.

Extracted from the American Journal of the Medical Sciences for April, 1888.

HEREDITARY ANGIO-NEUROTIC ŒDEMA.[1]

By William Osler, M.D.,

Professor of Clinical Medicine in the University of Pennsylvania, Physician to the University Hospital, to the Philadelphia Hospital, and to the Infirmary for Nervous Diseases.

Under the terms *acute local, acute circumscribed* or *angio-neurotic* œdema, a disease has been described, characterized by the sudden onset in various regions of œdematous swellings, more or less limited in extent, and of transient duration. Although not referred to at any length in text-books or cyclopedias, the affection is evidently not very uncommon, as Dinkelaker,[2] a pupil of Quincke, has collected a number of cases from the literature. Quincke has himself referred to the subject in *Monatshefte für practische Dermatologie*, 1882. Jamieson,[3] of Edinburgh, has written on the subject and Graham[4] has given a good account of the disease. Riehl[5], Falcone,[6] Strübing,[7] Matas,[8] have recently reported cases.

In three instances the disease appeared in succeeding generations, and it is this hereditary aspect which gives special interest to the following report:

Briefly summarized, the affection in the family which I have studied has the following characteristics:

1. The occurrence of local swellings in various parts of the body, face, hands, arms, legs, genitals, buttocks, and throat. In one instance, possibly in two, death resulted from a sudden *œdema glottidis*.

2. Associated with the œdema, there is almost invariably gastro-intestinal disturbance: colic, nausea, vomiting, and sometimes diarrhœa.

3. A strongly marked hereditary disposition, the disease having affected members of the family in five generations.

A member of the family, Mrs., H., aged twenty-four years, was admitted to the Infirmary for Nervous Diseases, September 20, 1887, and the following notes were taken by Dr. Burr, the house physician:

Medium sized, well-nourished brunette, admitted with neurasthenic symptoms. Has been married two years, no children. Has had good deal of back pain and menstruation is irregular and painful; was healthy as a child, and as a young woman. As long as she can remember, she has been subject to attacks of transient swelling in various parts—

[1] Read before the Philadelphia Neurological Society.

[2] Dinkelaker: Ueber acutes Œdem. Inaug. Dissertation. Kiel, 1882.

[3] Edinburgh Medical Journal, June, 1833.

[4] Canadian Practitioner, 1885.

[5] Riehl: Abstract in London Med. Record, Dec. 1887.

[6] Falcone: Gazzetta degli Ospitali, Feb. 24, 1886.

[7] Strübing, quoted by Matas.

[8] Matas: New Orleans Medical Journal, Oct. 1887.

hands or fingers, knee caps, elbows, buttocks, arm or thigh in fleshy parts, face, or more often the lips alone. The fingers have been so swollen that it was impossible to move them, and once the ring-finger was so greatly enlarged that the ring had to be filed off to prevent gangrene. The underlip has been swollen to such a degree that the mouth could not be opened, and milk had to be poured in from above. A slight redness and itching of the part is first noticed, or a sensation of heat; the redness is not always present. The effusion may take place with great rapidity. She often has red spots on various parts of the skin, or irregular lines of redness without any swelling. The duration varies from one to four days. There is not much itching, particularly when the swelling is great, but a sense of distention and stiffness. When fully *out* it does not pit, but does so when going down. The attacks may come on when she is feeling quite well or there may be slight indisposition. In all the severer ones there is abdominal pain, described as colic, with nausea, and often vomiting. There is sometimes headache; no fever. The attacks have no relation to the menstrual flow. She rarely passes two weeks without an attack. She does not think that food has any influence on her case. She remained in the hospital three weeks, during which time there was no severe attack, but she had numerous wheal-like eruptions on the chest and sides of the thighs, with very slight swelling, and the day before she left there was a large spot of local œdema on the inner aspect of the left thigh. Dr. Morton dilated a very narrow cervix, and she went home much improved. She had not passed three weeks without a severe attack for a long time. I saw her again on January 16th. She had four or five bad attacks on the hands, feet, and thighs, since leaving the hospital.

From Mr. T., my patient's grandfather, a venerable old patriarch of ninety-two, with unimpaired vigor of mind and body, I was able to obtain a tolerably clear history of the affection as it has existed in his family.

First Generation.—The disease first appeared in his mother, *Margaret A., b.* 1762, *d.* 1834. He thinks it began with her, and feels sure that had it been in her father's or mother's family she would have known of the fact and mentioned it. She was twice married and had two children by the first husband, and three by the second. She had the attacks from an early age in the hands, feet, face, and neck. He had frequently seen her in them, and on one occasion she nearly died in an attack of shortness of breath. She had colic with them. After the age of forty-five or fifty years she was not so much troubled, but her constitution was much weakened by the strong medicines which she had taken. She had evidently, from the account, been badly salivated. She sought advice everywhere, but in vain, and, according to my patient's mother, was brought to Philadelphia, to the Pennsylvania Hospital, to see Dr. Rush or Dr. Physick. She died at the age of seventy-two.

Second Generation.—Of the children, all boys, four grew up; Samuel, Stacy, John M., and Allan.

Samuel was not affected, but his children have the attacks, and one of them, John, died of the disease in Salem, Mass. Particulars could not be obtained.

Stacy was never attacked.

John M. suffered from his youth, and had frequent attacks on the

hands and privates. He has four children living, of whom only one is affected.

Allan, aged ninety-two years, a hale, vigorous man, with perfect faculties, and still able to walk five or six miles a day. He was healthy as a child. Remembers that the attacks began while he was an apprentice, at the age of eighteen or nineteen. They have recurred at intervals of a month or six weeks. A few years ago they became less frequent. The last attack was two weeks ago. The swelling is usually the first symptom, and in his case the hands and privates are the parts commonly affected, less often the trunk, and never the face. Sometimes itching precedes the onset. The œdema comes on rapidly, and the fingers in an attack are so thick and stiff that it is impossible to move them, the condition lasting some hours, or an entire day. Colicky pains are felt in the abdomen and become so intense that vomiting follows, usually with relief. The ejecta are yellowish, and, as he expressed it, "the bile had to come up before the pain got better." The swelling generally goes down before the sickness. Vomiting is not a constant feature of an attack. The entire duration is from one to three days. He never has headache, and very exceptionally diarrhœa. Very hard work, exposure to cold, and indiscretion in diet were the only circumstances which he thinks determine the attacks, but they as often come on without any apparent cause.

He has been married twice and has had fourteen children, of whom only three, one son by the first marriage and two daughters by the second wife, are affected.

THIRD GENERATION.—*George* began to "swell," as they term it, about the age of twenty and had very many bad attacks. He died, aged sixty, of Bright's disease. Of his nine children all with one exception are affected.

Sallie, married, no children, has very severe attacks in which Dr. Shipps has repeatedly attended her and given hypodermatics of morphia for the colic.

Emma began at the age of ten or twelve. Has attacks every few weeks. Face, hands, and sometimes the feet swell; less often on the body. Has to be very careful in her diet, cannot eat apples and certain vegetables.

FOURTH GENERATION.—George, the son of Allan, had nine children, of whom eight have been attacked. I am indebted to his widow for the following facts about the affection in this family.

1. *Hamilton*. Always suffered with attacks of cramps in the stomach and of late has very often swollen.

2. *Rebecca* began to "swell" when she was four or five years old, and the attacks became much more frequent after she was married. She had three children, one at seventh month, dead; a second at seventh month and now living (is seventeen and has recently had her first attack); a third at eighth month, living. In each instance the labor was prematurely brought on by the complaint. She died in an attack at 5 A.M., evidently a sudden œdema of the larynx. The late Dr. Van Dyke, of New Brunswick, was called, and before her regular physician, Dr. Williamson, arrived, she was dead.

3. *Almira*, who has never had it.

4. *Mary* has always had the cramps but "swelled" for the first time this winter.

5. *Julia*, "who always has swollen ever since she was a small child."

6. *Kate* has it, but "swells" less frequently than the others.
7. *Edwin* within the past few years has had bad spells of both cramps and swelling.
8. *Maggie* (case of Mrs. H. who came to Infirmary).
9. *George* has always had bad spells of the cramps, and last summer "swelled" for the first time.

The mother writes that none of her children has ever had chilblains, but all suffer with cold feet.

FIFTH GENERATION.—*Lizzie*, daughter of Hamilton, has had some very bad attacks. She was married in February, 1887, and has had six bad spells since. Once her face "swelled out of all shape."

A son of H., also has bad attacks.

A daughter of Rebecca, now seventeen years of age, "swelled" for the first time this winter.

GENEALOGICAL TABLE SHOWING ANGIO-NEUROTIC ŒDEMA IN THE FAMILY OF T.

I.	II.	III.	IV.	V.
Margaret,[1] b. 1762, d. 1834.	Samuel,	3 children all affected; 1 (John) died of it.	One girl affected.	
			Hamilton,	*Thomas*, *Lizzie*.
	Stacy,			
			Rebecca, died of it.	2 children, aged 17 and 11, one of whom has recently had her first attack.
		George,		
			Almira,* *Mary*, *Julia*, *Katie*, *Edward*, *Maggie*, *George*.	
	Allan, 10 children, 3 affected,			
		Emma, single.		
		Sallie, married; no children.		
	John M.	4 children; 1 (Angey) affected.		

The general characters of the œdema may be gathered from the description given of the cases of Mrs. H. and her grandfather. A review of the literature shows that all of the cases in this respect are

[1] Those in italics have suffered with the disease.

very similar. In some, the swelling is more constant in one locality, as eyelid or lip; but, as a rule, various parts are affected. The hands, face, and genitals, are most frequently attacked. Itching, heat, and redness, often precede the outbreak. In many cases the patient also had urticaria.

A special interest pertains to the occurrence of œdema about the throat and larynx, as sudden and extreme involvement of these parts may prove fatal. In Case I. of Quincke[1] and Dinkelaker,[2] the patient, a man aged twenty-two, had repeated attacks of suffocation, often with cyanosis, in association with local œdema about the joints, and colicky pains. The mucous membrane of the larynx was greatly swollen, and scarification had to be performed. There was no difficulty in swallowing.

In a case of Goltz,[3] male, aged thirty, there was œdema of the uvula and pharynx, in association with swelling of sides of arms and scrotum. Laudon[4] had in his own case swelling of the pharynx. Cuntz[5] describes a case in which the patient awoke one night with great dyspnœa and a sense of suffocation, which passed off in a few hours.

In one of Riehl's cases the patient had three attacks of angina, with difficulty of swallowing, and great breathlessness. In his second case also, the man is said to have had inflammation of the vocal cords, which had produced symptoms of suffocation.

In several of the cases there was a remarkable regularity in the sequence of the attacks which recurred on the seventh, fourteenth, or twelfth day. In Matas's case, this periodicity was very striking, the attack coming on every day at 11 or 12 A.M.

The hereditary aspect of the disease, which is so well illustrated in the family which I have studied, has been noticed by three observers. In Quincke's[6] first case the man had two children, one of whom, the son, aged one year, had had, from the age of three months, attacks of local œdema, often preceded by a red and marbled condition of the skin of the breast.

One of Strübing's[7] cases, a man aged seventy, had a son who suffered with the attacks of œdema.

In Falcone's case,[8] a lad of seven years, with well-marked attacks, the father had not been affected, but the grandfather had been afflicted in the same way.

The intestinal trouble, which forms so striking a feature of the attack, is of the nature of colic, and is really the most distressing symptom, usually requiring morphia for its relief. It is interesting to note that

[1] Loc. cit.
[2] Loc. cit.
[3] Deutsche med. Wochenschrift, 1880, No. 17.
[4] Laudon: Berliner klin. Wochenschrift, 1880.
[5] Archiv der Heilkunde, Bd. xv.
[6] Loc. cit.
[7] Loc. cit.
[8] Loc. cit.

there is a disease in children characterized by painful œdomatous swellings about the joints, a purpuric or urticarial eruption, and most intense colic. There may be hemorrhage from the bowels, but the skin affection and the colic are the prominent features. The attacks may be repeated at intervals for many months. Couty[1] has given the only full account of the disease. Henoch[2] has also reported four cases. I have recently had an opportunity of seeing a typical case of the kind with Dr. Dunton, of Germantown. A boy aged six, has had, during the past ten weeks, three attacks, each one extending over many days, of purpura, with urticuria, swellings about the ankles, and intolerable colic. He has also passed blood in the stools, and the urine contains blood, albumen, and tube casts.

So far as I can gather, none of the members of the T. family has had purpura, nor have there been *painful* swelling of the joints. Some of them have had urticaria, and Mrs. H., while in the Infirmary, had very characteristic wheals on the chest and thighs.

The colic is, in all probability, due to œdema of local regions of the intestinal wall interfering with the regular and uniform progress of peristalsis. The colic of horses is, in most cases, the result of hemorrhagic œdema—infarction—of a limited portion of the intestine, due to embolism in association with the common verminous aneurisms of the mesenteric arteries.

Quincke has termed this condition *angio-neurotic œdema*, and regards it as a vasomotor neurosis, under the influence of which the permeability of the vessels is suddenly increased. That it has close relationship with urticaria, a skin disease of unquestioned neurotic origin, is shown by the frequency with which in the reported cases we find mention of the affection preceding or accompanying the local œdema. The condition resembles in some points urticaria tuberosa, and Juler,[3] in a very able article, describes a case of u. porcellana which evidently belongs to the affection under discussion. In our present state of ignorance of the factors which regulate transudation, it seems useless to enter upon a theoretical discussion on the subject of nervous œdema, and we may conclude with Cohnheim,[4] "that we have to do here with clinical facts and observations which urgently call for scientific solution, and that we possess at present but extremely scanty material for an adequate explanation regarding neurotic œdema."

[1] Gazette Hebdomadaire, 1876.
[2] Henoch: Berliner klin. Wochenschrift, 1874.
[3] Cincinnati Lancet and Observer, 1878.
[4] Allgemeine Pathologie, Bd. I, p. 500.

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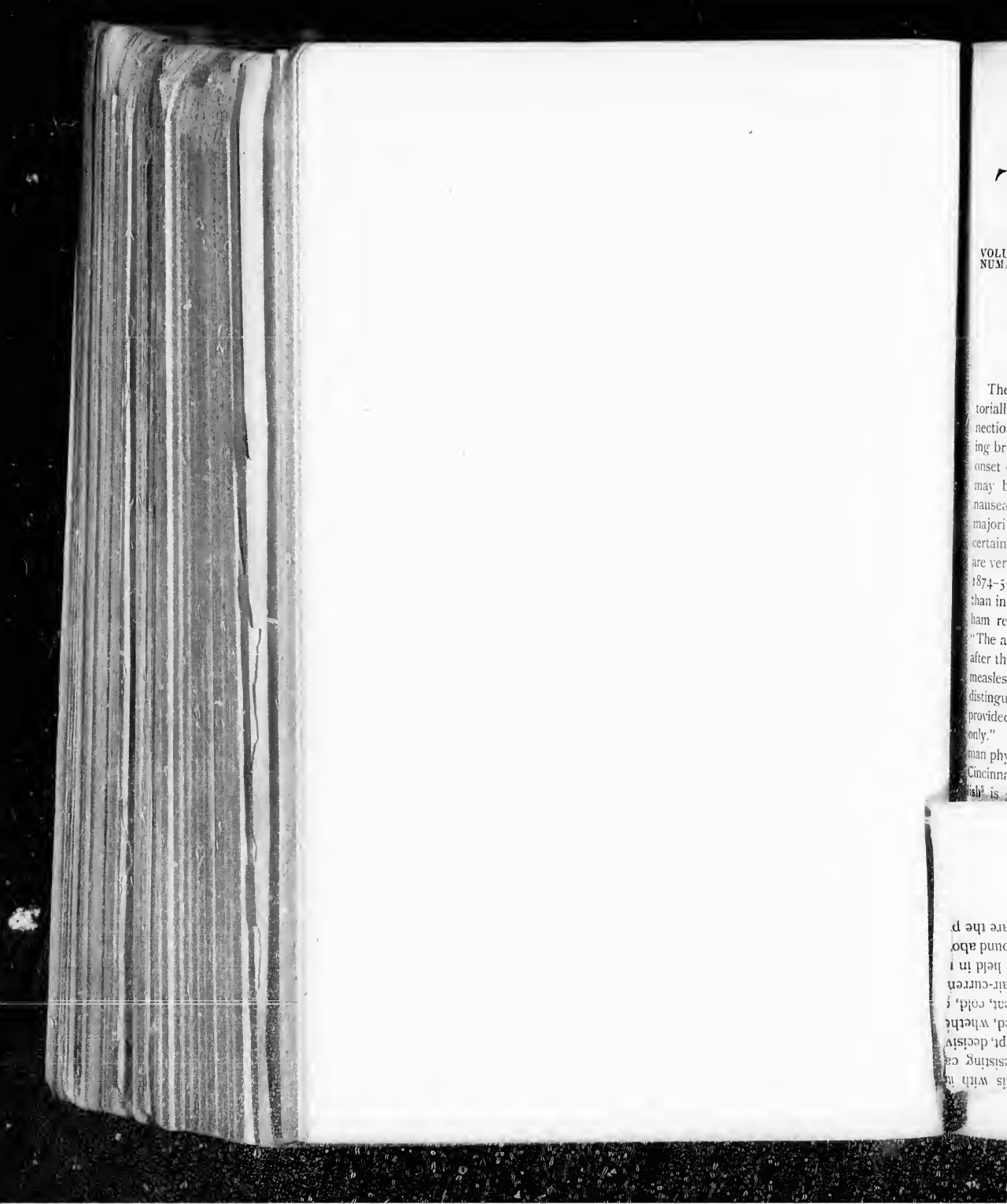

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THE DIAGN

BY WILLIAM OS

PROFESSOR OF CLINICAL MED

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THE MEDICAL STANDARD.

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THE DIAGNOSIS OF SMALL POX.[1]

BY WILLIAM OSLER, M. D., PHILADELPHIA.

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

The MEDICAL STANDARD (March) has editorially outlined the present subject, and in connection with this editorial discussion the following brief notes may prove of interest. In the onset of the disease the difficulty of diagnosis may be very great, even with well-developed nausea and backache. Mistakes arise in the majority of instances from the occurrence of certain initial rashes which in some epidemics are very common. In the Montreal epidemic of 1874-5-6, they were more frequently met with than in the recent outbreak of 1885-6. Sydenham refers to them in the following words[2]: "The aforesaid smallpox breaks out sometimes after the fashion of erysipelas; sometimes like measles. From these they are difficult to be distinguished, even by the practiced physician, provided that he goes by external appearance only." They have been well studied by German physicians. Bartholow observed them in Cincinnati. The fullest description in English[3] is given in an article which appeared in 1875, and was based on observations made in the Montreal General Hospital, and in an article by Dr. Seymour Sharkey.[4]

There are three principal forms in the initial rash. First: The hæmorrhagic, which consists of minute petechiæ, usually seen in the lower abdominal region and the groins; sometimes along the sides of the throat or in the axillæ. An erysipelas may precede or accompany the outbreak of the petechiæ. This form of rash constitutes an important diagnostic sign, as it may occur as early as the second day. Owing to its presence I have known the necessary precautions to be taken even before the pustules had appeared, and the diagnosis positively determined. On the whole, I think the purpuric rashes in the crural or axillary triangles, appearing from the second to the fifth day, are of favorable import, as they more often precede the severe forms of the disease.

Second.—The erythematous rash, which may be diffuse and scarlatina form or limited to the crural and lateral thoracic regions, in which case it is usually associated with petechiæ. I have heard, but not known, of cases in which this variety of rash occurring early, led to the diagnosis of scarlet fever. The cases of combined scarlet fever and smallpox, described by the older writers, were probably of this nature.

Third.—The maculous or measly rash is not so common. I have seen only one good example of it. In two instances a mottled rash, with papules, led to serious error. I found one morning in the ward a young man who had been sent in the previous evening supposed to have smallpox. He had a fading rubeolous rash, with distinct small papules which, however, had not the shot-like harshness of variola. In the evening, as the rash was less marked, I felt sure that a mistake had been made, and sent him to his home. During my absence a child was also admitted with measles. Neither of these cases took smallpox. A third case, which I saw at the City Hospital in consultation with Dr. Laroeque, was less fortunate. The mottled and papular rash was mistaken for smallpox and the young man removed to the hospital. I saw him the day after admission, when there was no question that the rash was measles and not variola. He was vaccinated and sent home, but to be returned in ten days with severe smallpox.

In cases of hæmorrhagic smallpox the diagnosis may present serious difficulties, particularly in the form known as purpura variolosa, in which the cutaneous hæmorrhage occurs early. Death may occur before the papules appear, and the symptoms do not differ essentially from those of hæmorrhagic scarlet fever or malignant purpura—the morbus maculous Werlhoffii. It is rare, however, for cases to die before the fourth day, and even when the skin is uniformly purpuric, the papules may be felt, particularly about the wrists. In only one[1] of twenty-seven cases of hæmorrhagic small pox occurring in the

[1] Provisional communication.
[2] Works, Sydenham Society, Vol. I, p. 127.
[3] Canada Medical and Surgical Journal, 1875.
[4] St. Thomas Hospital Reports, 1882.

[1] Canada Medical and Surgical Journal, 1875.

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small pox department of the General Hospital did death occur on the third day. The most careful inspection failed to detect any papules. In three cases in which death took place on the fourth day, the characteristic rash was beginning to appear. When an epidemic is prevailing, there is rarely any difficulty in diagnosing this so-called black small pox, but in isolated cases it may be impossible, if a papular rash do not develop before death.

The prodromata of small pox are very characteristic and of great service in diagnosis in the early stage. I saw only one case of mistaken diagnosis in purpuric small pox. A four-year-old child was taken ill suddenly with fever, great pains in the back and head, and on the second or third day petechiæ appeared on the skin. The nervous symptoms were marked; there was retraction of the head and rigidity of the limbs. The cutaneous hæmorrhage became more abundant and the case was regarded as one of cerebro-spinal meningitis. Hæmatemesis occurred and death followed on the sixth day. The child had not been vaccinated. At the autopsy, the papules could readily be detected in the deeply hæmorrhagic skin, and this fact, with the absence of the lesions of cerebro-spinal meningitis, led to the postmortem diagnosis of small pox, which was confirmed by the mother taking the disease, of which she unfortunately died.

In the pustular stage it would scarcely seem possible to make a mistake, but I had one case sent to me in which diagnosis of small pox had been made. The history, the distribution (chiefly on trunk and covered portions of limbs, sparing the face and hands), left no doubt that it was an unusually well developed pustular syphilide.

The diagnosis of small pox from varicella is not always easy. In 1885, the Chicago case which conveyed the disease to Montreal, was regarded as varicella and not isolated; an error which was directly responsible for one of the most fatal of modern epidemics.

"CHOLERAIC DIARRHŒA."

BY G. WHEELER JONES, M. D., DANVILLE, ILL.

The term "Winter Cholera" is a misnomer—a relic of the time when "Break-bone Fever," "Black Measles," "Winter Fever," "Spine-in-the-Back" and similar nosological terms were invented; terms as vague in meaning, very often, as are the theories of the fathers in medicine and theology. Whether this term originated with some newly-fledged graduate of a moss-backed Chicago or Eastern medical school, or with the cut-and-dried remnant of other days in Egypt or Kentucky, cannot be determined. At any rate, it is not a proper designation for a disease whose pathology is so comparatively well-known. "Choleraic Diarrhœa" perhaps comes nearest to filling the demands of nomenclature; the qualifying phrase, "of winter," "of summer," "of the Chicago River," "of the Mississippi" would clearly designate the disease.

The large majority of cases depend on imprudence in diet and malaria. The processes of food fermentation, the ptomaines and the germs of zymotic diseases have to answer for most of these diseases in summer and winter. The only differences are such as would necessarily arise from seasonal influences. Dirty surroundings, filthy homes, debased and uncleanly habits, each and all, predispose to the disease in winter as in summer. In this extremely variable climate where a variation of 60° F. may occur in 24 hours, I have often noticed that a few days' extremely cold weather would be accompanied or followed by numerous cases of diarrhœa, assuming all the phases and types of the summer disorder, from the simple "biliousness" of a slight "ague" to the collapsing cases and rice water discharges of true serous flux.

The predisposing causes are similar in both seasons; the vitality is reduced below the point of successful resistance, which reduction is accomplished as readily by extreme cold when properly applied, as by excessive heat. The resisting powers of the constitution being thus enfeebled from whatever cause, improper food and congestive disorders easily induce intestinal fluxes in all grades and forms of action.

One very common source of malarial disturbance in the country and in country towns, which is generally overlooked, although it produces much diarrhœa of special types, is the presence of those former reservoirs called cellars. From these arises a steady influence which produces a toxæmia in the inhabitants above, infested by many odd forms of disease of applicable on the hypothesis of a paresis with accompanying loss of function and resisting capacity. These demand certain, prompt, decisive treatment if a fatal issue is to be averted, whether the loss of nerve force be due to heat, cold, or blood poison. The underground air-current laden with gases and disease germs held in constraint by the snow, ice and frozen ground above find outlets into cellars where they are the p

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occurred and death followed on the sixth day. The child had not been vaccinated. At the autopsy, the papules could readily be detected in the deeply hæmorrhagic skin, and this fact, with the absence of the lesions of cerebro-spinal meningitis, led to the postmortem diagnosis of small pox, which was confirmed by the mother taking the disease, of which she unfortunately died.

In the pustular stage it would scarcely seem possible to make a mistake, but I had one case sent to me in which diagnosis of small pox had been made. The history, the distribution (chiefly on trunk and covered portions of limbs, sparing the face and hands), left no doubt that it was an unusually well developed pustular syphilide.

The diagnosis of small pox from varicella is not always easy. In 1885, the Chicago case which conveyed the disease to Montreal, was regarded as varicella and not isolated; an error which was directly responsible for one of the most fatal of modern epidemics.

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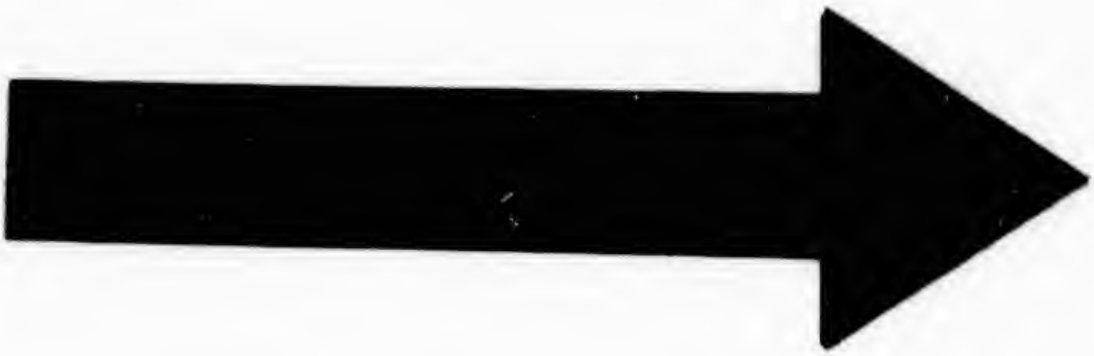
GLIOMA OF THE MEDULLA OBLONGATA.

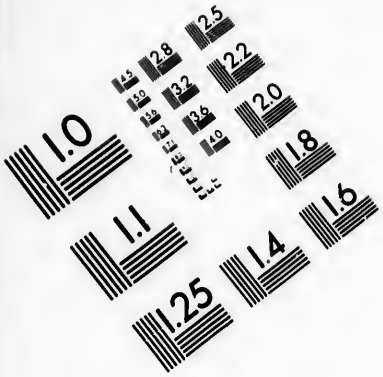
BY WILLIAM OSLER, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; PHYSICIAN TO THE UNIVERSITY HOSPITAL, TO THE PHILADELPHIA HOSPITAL, AND TO THE INFIRMARY FOR DISEASES OF THE NERVOUS SYSTEM.

ROBERT B——, aged 32, laborer, colored, was admitted to the Philadelphia Hospital on the 4th of March, 1887. He was a well-nourished, muscular man, and gave a very good account of his condition and history. He knew little or nothing of his family; had lost his mother and all his brothers and sisters. He had a chancre two years ago, with secondary symptoms. With the exception of a very severe attack of headache with dizziness in 1885 he has been well until six or eight weeks ago, when he began to have fits, for which he was admitted to the Pennsylvania Hospital, where he remained a week. At first he had only one or two attacks a week; now they recur more frequently, and he has had three in the past six days; he begins also to feel a little uncertain on his feet.

Condition on the 6th, when first seen, was as follows: Is intelligent and answers questions promptly. Complains of headache, unsteadiness in walking, odd sensations over his body, and fits. There is no wasting, no paralysis. The grasp of the hands is fairly strong; muscular power of legs unimpaired. He complains of great stiffness and pain in the muscles of the back of the neck, and on getting up he carries the head and back stiffly, but turns the head easily from side to side. He walks without assistance, but says he feels "drunk," and he tends to sway. He paced the ward alone, and with the aid of an assistant's arm went to the ophthalmoscope room, fully 100 feet off. The co-ordination in hands





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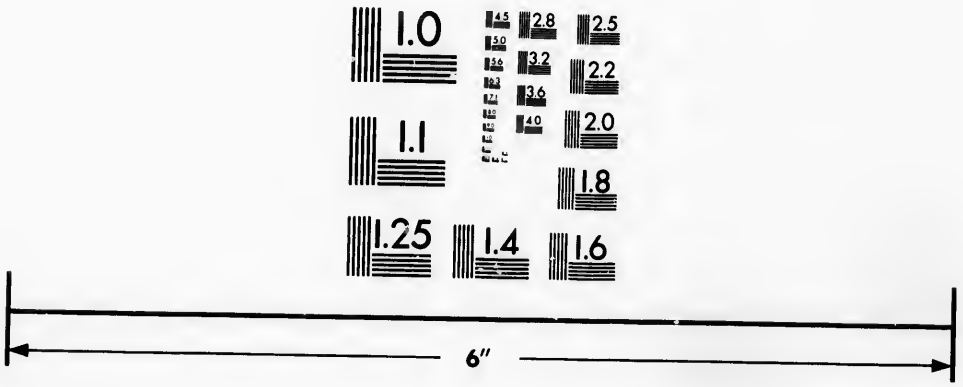

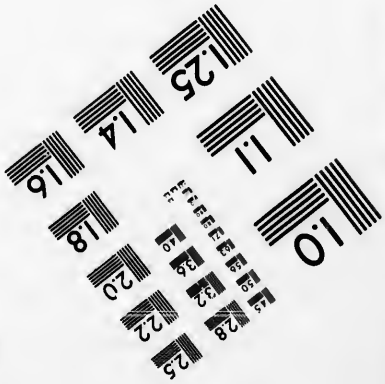

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is impaired, he does not grasp objects quickly, nor can he rapidly touch the tip of his nose. He gets out of, and returns to bed with great deliberation, like a man with lumbago. Sensation is everywhere retained; feels a pin-prick rapidly. Complains of numbness, tingling, and creeping feelings in the hands and feet. Says his legs "feel as if something had laid upon them and put them to sleep." Has also sensations of cold in hands and feet, and, to use his own words, "they are warm, but they feel so cold." This was a very frequent complaint. Sensation in region of fifth nerve normal. Special senses unimpaired; he hears the watch well at either ear; no affection of taste or smell. Vision good. The eye-grounds were examined twice; no neuritis; veins looked full, but there were no special changes. The headache was not constant, was chiefly occipital, and he did not seem clearly to be able to separate it from the painful feelings of stiffness in the nape of the neck.

Reflexes are present; patellar somewhat exaggerated. In the fits the movements are bilateral; he froths at the mouth; says he does not lose consciousness. This is probably a mistake. He fell out of bed last night in one and knocked his head. They last from five to fifteen minutes, and he comes out of them, as a rule, with the mind clear.

The appetite is good; he vomits sometimes; bowels regular. There is a loud apex systolic murmur, transmitted to axilla, and the pulmonary second sound is accentuated. Pulse fair in volume, 90 per minute. Urine clear; no albumen.

Taking into consideration the fact that he had had a chancre two years ago, the lesion was thought to be syphilitic, and he was given large doses of potassium iodide.

On the 7th and 8th he was better, but the pain in the back of the neck was severe. On the 9th the tingling and numbness of hands and feet were not so distressing, and he had less headache. Had a severe convulsion last night. There is increasing difficulty in getting in and out of bed. Pupils are dilated to-day. He talks clearly and says he is improving.

On the 10th, at 12 o'clock, he was given a dose of the iodide and immediately had a sort of fit, but he did not move

the hands. At 12.45 I came into the ward and found him in the following condition: Is unconscious. Respirations very slow, three, four, and five in the minute. Inspiration is prolonged and quiet; expiration short and noisy. Pulse, 100–108, fair in volume. At 12.55 the respirations had fallen to two in the minute, and pulse stopped somewhat suddenly. No heart-beat or heart-sound could be detected after 12.55. Last inspiration at 1 o'clock.

AUTOPSY.—Twenty-four hours *post mortem*. Old scars on forehead and arms. Calvaria normal, perhaps a little thick in the frontal region. Much blood escaped on removal of brain. Dura is adherent, sinus very full—on either side there is a line of fresh-looking pachymeningitis. Arachnoid is clear at base. Veins of pia dilated and full. Parts at base present following condition: Olfactory and optic nerves small, but have normal color. No effusion in interpeduncular space. Anterior margin of pons is very close to optic commissure. Vessels of circle of Willis contain blood; they are not atheromatous. The third, fourth, and fifth nerves look normal, and those emerging from the lateral part of medulla have a natural appearance. The crura were cut, and cerebrum removed separately. Vessels on the cortex very full; gray matter of pink-red color. White matter, in section, looks moist and glistening; no foci of disease. The ventricles contain a slight excess of fluid; lining membrane normal. Crura show no change. Pons normal. The fourth ventricle is dilated, particularly in the lateral recesses. The Fallopian aqueduct not enlarged. The floor of the ventricle looks normal above the level of the acoustic striæ, the right of which are not so distinct as the left. A large vein curls over the left margin of the medulla at the level of the left striæ.

The lower part of medulla and beginning of the cord are occupied by a large growth extending from below the calamus, projecting more on the left than on the right side. It is everywhere covered by pia. On the left side it has a reddish-brown vascular appearance; on the right side the white substance of the medulla is apparent. No trace to be seen of restiform bodies or of posterior pyramids. The olivary bodies are visible, but wider apart than normal, and the lower parts

absorbed. The growth reaches to within 7 or 8 millimetres of the fissure separating the medulla and pons.

The cerebellum is a little compressed just above the tumor.

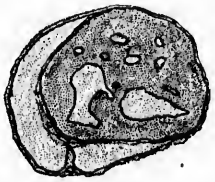


FIG. 1.—Section through the Tumor below level of Calamus. Natural size.

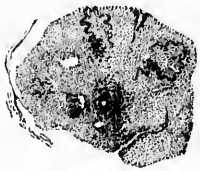


FIG. 2.—Section through the Olivary Bodies and uppermost portion of the Tumor.

No other changes. The upper part of cervical cord is soft and the postero-lateral columns have a very translucent aspect. The central canal is somewhat dilated. A cross-section just

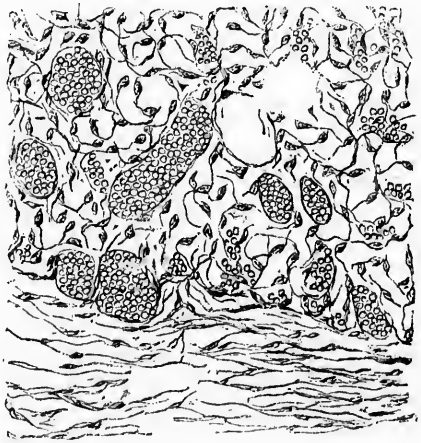


FIG. 3.—Section at the edge of the Growth, showing the gliomatous tissue and distended Blood-vessels Nos. 7 and 3.

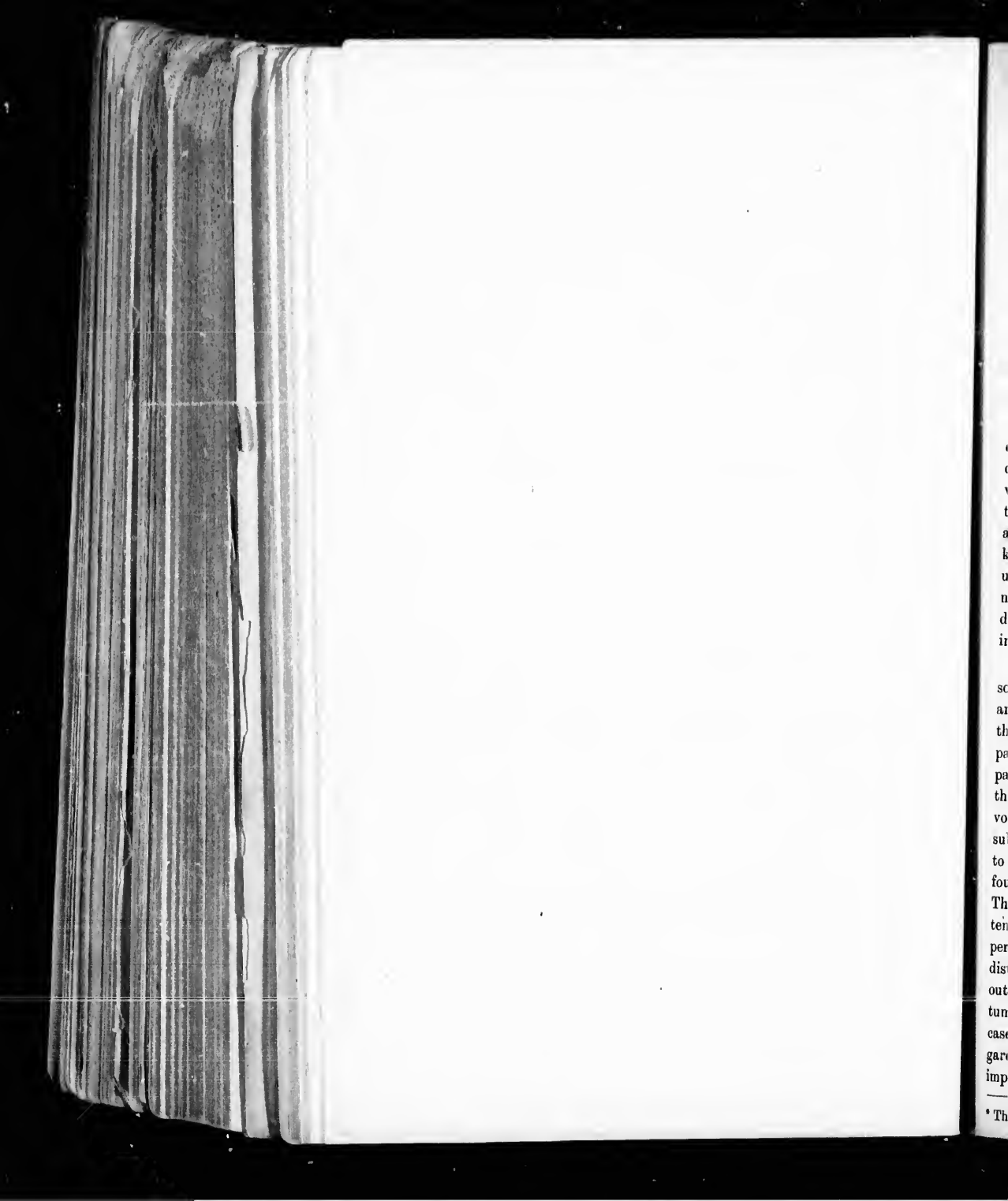
below the calamus has the appearance represented in Fig. 1 (actual size). The tumor is an inch in breadth by three-fourths of an inch in antero-posterior diameter. In fully one-half of the circumference it is in contact with the pia mater

of the left side; in the rest of the extent, with the compressed and flattened columns of the cord. In the medulla it does not reach above the middle of the olivary bodies; Fig. 2 represents the section at this level. The tumor was firm, of a red-brown color, with recent hemorrhages into its substance. The large lacunæ represented in Fig. 1 were filled with clots. Histologically, as shown in Fig. 3, the tumor is composed of a stroma of nucleated fibre-cells supporting blood-vessels which in places are so closely set that the appearance is that of an angioma. In other regions the gliomatous tissue is more dense and the blood-spaces less numerous.

The situation of the tumor, pushing aside and compressing chiefly the posterior columns, explains the disturbances of sensation and the inco-ordination which were the prominent features of the case. It is probable that the central hemorrhages, which looked recent, caused death by increasing the pressure and disturbing the respiratory and cardiac centres which lay just above the growth.

Gliomata of the medulla are rare. Sokoloff has recently described a case,* and has collected seven instances from the literature.

* Deutsches Archiv. f. klin. Medicin, B. xli., H. 5, 1887.



TYPHLITIS AND AP

By WILLIAM OSLER, M.D., F.

Professor of Clinical Medicine in the Univ

(*Reprinted from* The Canada

Cæcal and peri-cæcal inflammations are described under the various terms typhlitis, peri-typhlitis, para-typhlitis, peri-cæcal abscess, and appendicitis. I think we may clinically, and for practical purposes, distinguish two groups of cases, to the first of which the name *typhlitis* may be restricted, and to the second *appendicitis*, or, perhaps, better, as Dr. Fitz suggests, *perforative appendicitis*.

Typhlitis.—By this we understand inflammation of the cæcum. The term has also been used to designate inflammation of the contiguous parts as well; but it may be limited to the cases in which the caput cæci and the adjacent portion of the ascending colon are involved. Unfortunately, we know nothing of the anatomical condition described under this term. I have myself never seen a post-mortem, nor do I know of a report in which the disease was confined strictly to the walls of the intestine in these regions.

The cases are commonly met with in young persons, particularly in young males. The attacks are very often associated with errors in diet. In the majority of cases there is a history of constipation. The symptoms are very distinctive. The patient complains of pain in the right iliac fossa; there is constipation and often nausea—sometimes vomiting. At first there may be no fever, but subsequently the temperature rises from 100° to 102°. On examination, the patient is usually found with the right thigh flexed on the abdomen. There is slight fullness in the right iliac fossa; tenderness on pressure, and, often, dullness on percussion. In the majority of instances there is distinct induration, which may have a rounded outline, so that the expression "sausage-shaped tumor" has been applied to the condition. Such cases are extremely common, and are usually regarded (no doubt properly) as the result of fæcal impaction — typhlitis stercoralis. With proper treatme
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* The substance of remarks made at the Toronto Medical Society, December 26, 1888.

TYPHLITIS AND APPENDICITIS.*

By WILLIAM OSLER, M.D., F.R.C.P., Lond.,

Professor of Clinical Medicine in the University of Pennsylvania.

(*Reprinted from* The Canada Lancet.)

Cæcal and peri-cæcal inflammations are described under the various terms typhlitis, peri-typhlitis, para-typhlitis, peri-cæcal abscess, and appendicitis. I think we may clinically, and for practical purposes, distinguish two groups of cases, to the first of which the name *typhlitis* may be restricted, and to the second *appendicitis*, or, perhaps, better, as Dr. Fitz suggests, *perforative appendicitis*.

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Attacks of this kind may repeatedly occur in the same patient; I have known of four or five recurrences within four years. There can be very little doubt that this local inflammation is due to fæcal impaction. The inflammation is confined to the intestinal wall, and rarely extends to the tissues in the neighborhood. It is true, that occasionally there may be more serious disease of the cæcal coats. I have put on record two instances of round ulcer of the cæcum, in both of which perforation occurred, with the production of peri-cæcal abscess. It is quite possible, of course, that inflammation may extend to the loose connective tissue behind the cæcum—when that organ is attached—and even go on to suppuration. But, with the exception of the cases of ulceration, I have no personal knowledge of instances in which there has been peri-cæcal abscess apart from disease of the appendix.

The opinion has been expressed, and is I believe widely held, that the cases such as I have here described are also in reality due to appendix disease; that typhlitis and peri typhlitis mean in all cases tubal affection. I confess there is often great doubt as to the true nature of a case, but, clinically, I believe we can recognize a stercoral typhlitis. There is at present in my wards at the Philadelphia Hospital a case in illustration. Lad, æt. 22, admitted 22nd, with temperature of 102°, a furred tongue, constipation and abdominal pain. On examination, there was tenderness in the right iliac fossa, the thigh was drawn up and everted; the right iliac region was dull, tender to the touch, and presented a distinct induration, without definite outlines. He had nausea and vomiting on admission. Stupes and poultices were applied,

* The substance of remarks made at the Toronto Medical Society, December 26, 1888.

and large enemata were given; no opium, as the pain was not excessive. The injections brought away a number of hard fæcal masses. The temperature on the third day was normal, the induration and tenderness gradually disappeared, and on the sixth day the sense of resistance in the two sides was equal, and the patient said that he felt quite well. He had had a similar attack six weeks before. Such cases we have all seen, and whatever the morbid condition may be, I think they possess features which separate them from the next group.

Appendicitis.—In the second group of cases the lesion proceeds from the appendix vermiformis, which is liable to various affections—catarrhal inflammation, catarrhal ulceration, obliteration, obliteration of the proximal end, dilatation of the tube, and perforation. Foreign bodies may also lodge in it, and fæces moulded to the tube may become hardened and calcified so as to form small enteroliths.

In a recent report (*Med. and Surg. Rep.*, Oct. 6th, 1888) I gave notes of eleven cases in which I had met with ulcers in the appendix, usually in connection with phthisis or typhoid fever. I have never met with foreign bodies in the appendix. On one occasion five apple pips were brought to me as having been found in, and removed from the tube, in a dissecting-room subject; and in one of the cases in the post-mortem books of the Montreal General Hospital, Dr. Sutherland (who was acting as Pathologist in my absence) records the presence of six or eight snipe shot in the appendix of a man dead from Bright's disease. The resemblance of the small enteroliths to date-stones, frequently leads to error.

Inflammation and ulceration of the appendix vermiformis (so long as it is confined to this tube) may produce no definite symptoms. There may be the most extensive ulceration, the lumen may be completely obliterated, there may be extreme distention, without the patient manifesting any signs of abdominal disorder.

If the appendix is quite free, it is possible that ulceration may go on to perforation, without the tube forming attachments. This, however, is very exceptional. More commonly adhesions form and the perforation leads to localized abscess, the situation of which will depend upon the position of this extremely variable structure. It is most commonly situated in the right iliac fossa, and is either within the peritoneum, when the appendix is entirely surrounded by this membrane, or it is behind the peritoneum, when the appendix (which is rarely the case) has only a partial serous covering. I have seen perforation occur with the formation of localized abscess, within the pelvis in the neighborhood of the broad ligament; in another instance immediately upon the sacrum, the tip of the appendix lying to the left of the middle line; and, in a third instance, the abscess was high up behind the mesentery upon the psoas muscle.

I do not think that sufficient stress has been laid upon the fact, that this local inflammatory process almost invariably precedes the graver manifestations. That healing may take place at this stage, is shown by the occurrence of an obliterated tube closely adherent with fibroid thickening and much pigmentation of the surrounding tissue. Once perforation has occurred with abscess formation, the course is extremely variable. It is within the experience of almost every physician to have seen the pus appear anteriorly in the neighborhood of the groin, where it may open spontaneously. The presence of gas, or even small fragments of fæces, may show that there is open communication with the bowel. Two such cases I saw with my preceptor, Dr. Holford Walker, of Dundas, in 1868 and 1869. One of these cases made a good recovery; the other, with much more extensive abscess formation and perforation in several places (through which gas discharged), succumbed to septic fever. That the tube of the appendix is not always obliterated at its cæcal end before perforation occurs, as is claimed by some writers, is shown by such cases. The pus may burrow and appear in the lumbar region, or it may pass down and appear in the peritoneum and form a peri-rectal abscess. A more favorable event is, when the abscess perforates into a neighboring viscus—the colon, the cæcum, the rectum or the bladder. In a recent report of a case in a French Journal, in which the abscess perforated into the bowel, the characteristic oval enterolith was found with the discharged pus and fæces. Perforation into the bladder is less common. At the Montreal General Hospital, in the Summer session of 1882, I lectured upon two cases in which this event occurred with

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s quite free, it is possible that n to perforation, without the nents. This, however, is very commonly adhesions form and to localized abscess, the situ- depend upon the position of this extremely variable structure. It is most commonly situated in the right iliac fossa, and is either within the peritoneum, when the appendix is entirely surrounded by this membrane, or it is behind the peritoneum, when the appendix (which is rarely the case) has only a partial serous covering. I have seen perforation occur with the formation of localized abscess, within the pelvis in the neighborhood of the broad ligament; in another instance immediately upon the sacrum, the tip of the appendix lying to the left of the middle line; and, in a third instance, the abscess was high up behind the mesentery upon the psoas muscle.

I do not think that sufficient stress has been laid upon the fact, that this local inflammatory process almost invariably precedes the graver manifestations. That healing may take place at this stage, is shown by the occurrence of an obliterated tube closely adherent with fibroid thickening and much pigmentation of the surrounding tissue. Once perforation has occurred with abscess formation, the course is extremely variable. It is within the experience of almost every physician to have seen the pus appear anteriorly in the neighborhood of the groin, where it may open spontaneously. The presence of gas, or even small fragments of fæces, may show that there is open communication with the bowel. Two such cases I saw with my preceptor, Dr. Holford Walker, of Dundas, in 1868 and 1869. One of these cases made a good recovery; the other, with much more extensive abscess formation and perforation in several places (through which gas discharged), succumbed to septic fever. That the tube of the appendix is not always obliterated at its cæcal end before perforation occurs, as is claimed by some writers, is shown by such cases. The pus may burrow and appear in the lumbar region, or it may pass down and appear in the peritoneum and form a peri-rectal abscess. A more favorable event is, when the abscess perforates into a neighboring viscus—the colon, the cæcum, the rectum or the bladder. In a recent report of a case in a French Journal, in which the abscess perforated into the bowel, the characteristic oval enterolith was found with the discharged pus and fæces. Perforation into the bladder is less common. At the Montreal General Hospital, in the Summer session of 1882, I lectured upon two cases in which this event occurred with

recovery. I met with a curious sequel in a case of peri-cæcal abscess which perforated into the bowels. The patient had for some years after, and may still have for aught I know, persistent enlargement of the right leg, due, undoubtedly, to chronic venous stasis consequent upon the narrowing of, or perhaps the obliteration, of some of the large veins in the pelvis. A third and almost necessarily fatal mode of termination, is when the local circumscribed abscess perforates the peritoneum, setting up a diffuse, virulent and septic inflammation.

I have never yet seen instances of perforative appendicitis in which there were not attempts made to limit the inflammation. Even when the appendix has been free in the peritoneum, walls circumscribing the abscess are formed by the adherent mesentery, retro-peritoneum and intestinal wall. Symptoms of perforative appendicitis are fairly well defined. A number of cases begin with intestinal trouble, constipation or pain in the ilio-cæcal region, lasting for a variable time. A more characteristic mode of onset is a sudden, sharp pain in the right iliac fossa. This may be followed by collapse symptoms, or more usually by an aggravation of the intestinal disturbance. It is worth noting, that strain, such as sudden lifting or jumping, may be followed by an acute pain, and may, apparently, be the starting-point of appendicitis. The local symptoms are rarely as well marked as in typhlitis Tenderness is usually present; there may be fullness, or even induration, but in my experience, these signs are more frequently absent. The leg is usually drawn up, thereby relaxing the psoas muscle. Irritability of the bladder, as shown by frequent micturition, not infrequently occurs. The fever is moderate; the tongue is furred, but constipation is not so constant a feature as in stercoral typhlitis. Abdominal distention (tympanites) comes on early, and may interfere with proper examination. A rectal examination may indicate fullness towards the roof of the pelvis, but unless the whole hand is used, the ordinary digital exploration is practically worthless. Practice on the cadaver, with the pelvis exposed, shows how futile is the attempt to reach, even with the longest finger, those higher portions of the pelvis which the peri-cæcal inflammation usually affects. Increasing tympanites,

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In a considerable majority of cases, I think the sudden onset with sharp intense pain, indicates, not the perforation of the appendix, but the extension of an already existing inflammatory process. As I have stated, extensive ulceration, distention, adhesion and obliteration of the tube, may occur in persons in whose history there is no account of localized abdominal inflammation. It is not impossible that ulceration, leading to perforation and local abscess, may occur without exciting severe symptoms. I have so often seen, about the perforated appendix, signs of chronic inflammatory misehief indicated by fibrous bands and pigmentation, that the process has certainly ante-dated the onset of the acute fatal illness of only a few days duration. Marked tendency to recurrence finds also its explanation here, in the temporary aggravation of the condition. Surgeons have repeatedly, in these cases of recurring attacks in the peri-cæcal region, cut down and removed an adherent, chronically inflamed and even perforated appendix.

In many instances the diagnosis of perforated appendix presents great difficulties. Perhaps, of all the symptoms, the most important is the sudden agonizing pain occurring either at first, or after gastro-intestinal symptoms have lasted for some days. Its importance may be gathered from the fact, that of 257 cases analyzed by Fitz, it was present in 216. Abdominal pain and distention are more marked, and occur earlier than in ordinary typhlitis. Induration in the iliac fossa is also less common; indeed, a very considerable proportion of the cases present no local tumor. The diagnosis in such cases rests largely upon the mode of onset, the development of symptoms, the previous history of the patient, the absence of signs of hernia or of internal strangulation. The occurrence of frequent micturition and the characteristic

decubitus of the patient, are highly suggestive symptoms. Cases occur in which it seems impossible to accurately determine the condition, and the patient presents the picture of general peritonitis, which has started from some unknown locality.

Treatment of peri cæcal abscess from appendix disease has made great progress within the past few years, and the operation devised by Willard Parker has now become, not only a very frequent, but a most successful one. As I have already stated, there are many instances of spontaneous recovery, even when extensive suppuration has occurred. We all have seen, in the recurring attacks of this disease, the gravest symptoms disappear and the patient rapidly convalesce. The medical treatment is much the same as I have spoken of in typhlitis. Opium, in some form, has almost always to be used to relieve pain. For constipation, large injections may be employed. In the early stage I never use purgatives. I would hesitate to employ even a saline cathartic, which moves the bowels with very little disturbance of the peristalsis. Not that I would hesitate when general peritonitis is established, as I believe this method of treatment to be in a high degree rational. A concentrated saline purge produces local depletion of the intestinal vessels from duodenum to cæcum, and removes in great part the interstitial œdema of the intestinal wall upon which, chiefly, the paralysis depends. But, in the early stages of the affection, our means should be directed towards limiting the inflammatory process, and favoring those conservative barriers which nature invariably sets up against extending inflammation. I have been so much impressed with the fact, that in these cases the dangerous symptoms seem to originate by the extension of the disease from a localized peri-cæcal abscess—the walls of which may be in part mesenteric, or, as I have seen, intestinal—that I dread the disturbing influence of purges. The indications for surgical interference are not always clear; but my experience has taught me that the abdomen is much more frequently left untouched than it should be, and that an operation is too often deferred until practically useless. Local indications may be very positive, particularly when the perforated appendix lies behind the peritoneum, in the iliac fossa spine above Poupart's ligament. But when the abscess is high on the psoas muscle, or lies within the brim of the pelvis, or far over towards the middle line, these symptoms are absent, and in such cases, from the general condition alone, the indications for operation must be gathered. We may say, as a general rule, that in young persons, in whom the attack has set in with severe pain in the right iliac fossa (whether preceded or not by previous digestive disturbance), and in whom the constitutional symptoms, as shown by rapid pulse, fever and coated tongue, indicate a serious lesion—when tympanites and abdominal tenderness exist, it is better in these days of safe laparotomy to give the patient the benefit of any diagnostic doubt, even without the existence of local tumor, and to explore thoroughly the peri-cæcal region. Still more urgent would such indications be, if the patient had had previous, though less severe attacks.

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PUERPERAL ANÆMIA, AND ITS TREATMENT WITH ARSENIC.

BY WILLIAM OSLER, M.D.,

Professor of Clinical Medicine in the University of Pennsylvania.

THE first article on pernicious or essential anæmia contributed to literature was by Dr. Walter Channing, of Harvard, who, in the *New England Quarterly Journal* for 1842, published an article with the title, "Notes on Anhæmia, particularly in connection with the Puerperal State, and with Functional Diseases of the Uterus, with Cases." This was a year before Addison, as stated by Stephen Mackenzie, had first publicly taught the existence of idiopathic anæmia.

In 1853 Lebert described cases of what he called "puerperal chlorosis." In the second volume of *Archiv für Gynekologie* Gusserow described similar cases, and his paper, with that of Bierner's, which appeared about the same time, 1872, aroused a deep interest in this subject.

The importance of this etiological factor in pernicious anæmia is shown by the fact that of ninety-one observations collected by Eichhorst, the symptoms in twenty-nine cases developed in connection with pregnancy; of these, nineteen occurred during the pregnant state and ten after delivery.

Of twenty-one cases of pernicious anæmia of which I have notes, nine were in women, in five of whom the condition developed post-partum. Of

[illegible] First. Sudden intestinal hemorrhage in an apparently healthy person, which tends to recur and produce a pro-

[1] Archives Générales, April, May, and June, 1887.
[2] American Journal of the Medical Sciences, 1888, i.
[3] Canada Medical and Surgical Journal, March, 1887.

these cases, three recovered; of one I am doubtful, as the patient removed to a distance and has not since been heard from; the fifth case I have here given in full, as illustrative of certain important points in connection with the treatment of this condition.

Amelia T., aged thirty-five, domestic, was admitted to the medical wards of Philadelphia Hospital on 25th February, 1888. Nothing of note in family or previous personal history. In October, 1887, she was confined of her fourth child — easy delivery. She was well through her pregnancy, but in last month had suffered with bleeding piles. She was up and about two weeks after delivery, nursed the baby, but was very pale and weak. She was discharged in about six weeks. She never regained color after her confinement and had many spells of fainting, once or twice having fallen in the street. After January 1st this condition grew worse, and diarrhœa set in. When admitted she was in a condition of profound anæmia, and had severe diarrhœa with irregular fever. She was placed on Tr. perchl. Fe, gtt. 20, t.i.d. She remained in bed and had not improved; and when I saw her first on 17th April she was in the following condition: —

Profound anæmia; face and general cutaneous surface has slight subicteroid hue; fat is fairly well retained, though the arms look thin, conjunctivæ pearly, tongue extremely blanched. She is unable to sit up on account of the fainting. Has three or four movements of the bowels daily. Pulse 120°, small, jerky. Peripheral veins not very full. Apex beat of heart at fourth interspace; visible pulsation in subclavians and carotids. There is a rough thrill with first sound. Cardiac dulness from lower border third rib. On auscultation both sounds heard

at apex with much echo; loud systolic murmur, propagated to axilla; also heard very plainly along left sternal border. Distinct systolic murmur at aortic cartilage. Second sound much accentuated.

Lungs normal. No enlargement of spleen or liver. Tenderness on pressure over abdomen. Glands are not enlarged. Fever range of 2 or 3 degrees daily. Blood very watery; red corpuscles per cu.mm. 1,170,000; percentage white to red, 1 : 484; color by Gowers' hæmoglobmometer, about 15–18%; corpuscles extremely irregular in size and shape; considerable proportion of larger ones are oval. There are many microcytes. Several nucleated red blood corpuscles were seen.

She was ordered Fowler's solution, five minims t.i.d. for a week, and then to increase one drop each day until ten minims were reached; opium suppositories for the diarrhœa, and in a few days enemata of dried blood. Blood count on April 26th, 1,480,000; color percentage, 20. She took the arsenic well; began to improve in color, and on May 19th blood count by Dr. Henry was as follows: Red corp., 2,890,000; hæmoglobin, 40%.

Patient improved rapidly through the summer, the diarrhœa stopped and she gained greatly in weight. When I went on duty Sept. 3rd I did not recognize the patient, now a large robust-looking woman with excellent color. The apex systolic murmur persists.

We have in this case a history very similar to that which is met with in the majority of instances of post-partum anæmia. It is interesting to note that the patient, prior to delivery, had suffered with hemorrhoids, and had lost from this source considerable blood. She never regained her color after confinement, but remained very pale, and after discharge from the hospital she had many fainting

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spells. The condition in which I found her was extremely grave. She could not sit up in bed without fainting; and she had constant vomiting, with uncontrollable diarrhœa. I did not expect her to recover. The blood condition was typical as regards the appearance of the corpuscles. The percentage of coloring matter was, however, reduced proportionally to the corpuscles. Indeed, the individual value of the corpuscles in hæmoglobin was rather below par. In the majority of instances of pernicious anæmia the reverse holds good.

The case illustrates an important point in the treatment of profound anæmia. This patient had received twenty drops of the tincture of perchloride of iron three times a day, from Feb. 25th to Apr. 17th. Her diet had been carefully regulated, and every possible means employed to check the diarrhœa and vomiting.

Fowler's solution was begun with five minim doses three times a day, and for a time was well borne. The dose was gradually increased, and the improvement was rapid. On several occasions the sickness of the stomach was aggravated, and the medicine was interrupted for a week.

By the 19th of May she was able to sit up in bed, her appetite began to improve, the corpuscles had more than doubled in number per cubic millimetre, the hæmoglobin had risen from 15 to 40%. Rectal injections of dried blood were, for a time, employed, but had to be stopped on account of the irritation they produced.

I did not see this patient from the end of May until I went on duty Sept. 3rd, at which time I did not recognize her. She had grown stout, her color was excellent, and she looked in robust health. The patient's recovery may be attributed to the arsenic,

and I believe that if the iron had been continued she would have failed progressively, as she did during the six or seven weeks in which it had been administered.

This is by no means a unique history. To Bramwell, of Edinburgh, the profession is indebted for pointing out the almost specific action of this drug in certain cases of pernicious anæmia.

The statistics collected by Padley[1] a few years ago show forty-eight cases treated without arsenic, of which forty-two died. Of twenty-two cases treated with arsenic sixteen recovered, four died, and two improved.

Within the past few years, numerous observations have shown the powerful effect of arsenic in certain cases. Unfortunately, we do not yet fully understand why, in some instances, the drug should be well borne and prove successful, while in others the patient continues in the progressively downward course.

That the cases which we group as pernicious anæmia are very varied is now recognized by all writers on the subject. It is not to be expected that when the gastric tubules are atrophied arsenic can be curative. We need a careful study of those instances in which the drug has proved successful and of those in which it has failed.

To judge from therapeutic test alone there must be a very deep-seated difference between the two classes.

I know of nothing more remarkable in practical therapeutics, nothing so resembling specific action (unless we except iron in chlorosis and quinine in ague) than the rapid recovery of profound anæmia under this drug. As a rule it is well borne; and should

[1] Lancet, 1883, ii.

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be given, as Bramwell advises, in increasing doses, beginning with five minims, and rising gradually to twenty or thirty three times a day.

Puffiness of the eyelids, œdema above the eyebrows, vomiting or diarrhœa, indicate that the drug should be suspended for a time, or the dose reduced. It is interesting to note that the existence of vomiting or diarrhœa does not, however, contraindicate the employment of the medicine, as in the case here reported. These symptoms seemed to improve, for a time at least, when the arsenic was first given.

If the Fowler's solution disagrees, arsenious acid may be tried. I have known it to be well borne when the liquor arsenicalis disturbed the stomach. The drug may be given hypodermically, but in these instances of profound anæmia the tendency to hæmorrhage is so marked that the punctures may become hemorrhagic. I have known considerable subcutaneous extravasation follow an injection. The point of the greatest importance is the fact that the medicine must be given in increasing doses, and for prolonged periods.

I find practitioners express great surprise when they hear of doses of Fowler's solution, of fifteen, twenty, and twenty-five drops three times a day. There is, I think, but one rule in the matter: give the drug cautiously until physiological effects are produced. The tolerance of the system for arsenic is well known. I have never seen serious consequences from its careful administration. Young persons, as a rule, take it better than adults. In an instance of pernicious anæmia which I reported a few years ago, the patient took twenty minims of Fowler's solution three times a day for weeks, with the most satisfactory results.

In post-partum cases recovery is always slow. It may be many months before perfect health is restored. It is well to intermit arsenic for a few weeks, but the drug should be given at intervals for many months, even when the health is apparently re-established, as there is a well-recognized tendency in these cases to relapse.

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ON THE DIAGNOSIS OF DUODENAL ULCER.

By WILLIAM OSLER, M.D.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

Reprinted from THE MEDICAL RECORD, *November* 24, 1888.

IT has recently been suggested by Bucquoy[1] that the duodenal is to be distinguished from the gastric ulcer by certain well-defined clinical characters. Dr. W. W. Johnston, of Washington, has reported[2] an interesting case which seems to bear out this author's statement. I have expressed myself somewhat sceptically on this point, although one of the nine cases which formed the subject of my recent paper[3] was regarded during life, by Dr. Palmer Howard, of Montreal, as probably duodenal, on much the same grounds as Bucquoy lays down.

Physiologically, the portion of the duodenum above the bile papilla belongs to the stomach. Peptic digestion only ceases where the acid chyme is neutralized by the bile. When we consider how limited is this region, and how close to the pyloric ring many gastric ulcers lie, it is not surprising that difficulty should exist in the diagnosis.

The points upon which Bucquoy lays the greatest stress in the diagnosis of the duodenal ulcer, are as follows:

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found anæmia. Hemorrhage from the stomach may precede or accompany the melæna.

Second. Pain in the right hypochondriac region coming on late; two or three hours after eating.

Third. Gastric crises of extreme violence; the hemorrhage being more apt to occur about the time of these attacks.

The following cases are of interest in connection with possible existence of duodenal ulcer.

CASE I.—*Dyspepsia. Hæmatemesis and melæna in* 1870. *Repeated attacks during the past eighteen years, with the exception of the three years,* 1877–1880. *Frequent attacks of hemorrhage from the bowels without vomiting of blood. Severe gastralgia.*

Henry C——, upholsterer, aged forty, was brought to the Philadelphia Hospital by the ambulance, on January 4, 1888, in a condition of profound exhaustion. The next morning he gave the following account: For a month he had had diarrhœa, and on several occasions had passed blood in the stool, without any vomiting. On the night of January 1st, he vomited nearly two quarts of blood. On the 2d he remained in bed very much prostrated, and that night again vomited a large quantity of blood, "half a basinful," he said. On the 3d he had no vomiting, and on the evening of the 4th, when in hospital, he vomited three or four times and brought up clots of dark granular matter. On inspection, the patient was found to be profoundly anæmic and unable to sit up in bed without fainting; his skin was like alabaster; pulse 130, small; respiration 20; blood-count, 950,000 r.c. per c.mm. Hæmoglobin, twenty per cent.

The history which he gave was remarkable. He had been healthy as a young man, with the exception of dyspepsia. In February, 1870, he had a hemorrhage from the stomach and brought up, he says, two bowlfuls of blood, and also passed blood in the stool. During the next two years he had several attacks, and suffered constantly with pains. In 1873 he nearly died of hemorrhage, and during the next four years, three months did not pass without a recurrence. In 1877, he was four weeks in the Pennsylvania Hospital, having had profuse hemorrhage from bowels and stomach. He returned to France after this, and on August 10th had bleeding from the bowels. For the next three years he had no hem-

orrhage, though he was never free from uneasy sensations in stomach, and at times had attacks of severe pain.

In 1881 the hæmatemesis recurred, and since then he has had repeated attacks. In 1883 he was in the hospital sixty-five days; lost sixty-five pounds in weight, and was believed to have cancer of the stomach. From this time he had more or less gastric disturbance, consisting of pain after eating, usually delayed for several hours. At intervals of a few weeks there would occur severe gastric crises, in which the pain would be agonizing in character, shooting from the stomach, back, and sides; he vomited sometimes large quantities and occasionally had attacks of diarrhœa. When in hospital, in 1883, he was taught to wash out the stomach with a tube, and he has done it ever since, at intervals, with great benefit. He remained under observation until March 26th, and the blood condition was carefully studied, with the following results:

January 5th, r.b.c., 950,000 per c.mm.; 6th, 770,400; 7th, 1,053,000; 8th, 1,086,400; 9th, 1,175,000; 10th, 1,179,000; 12th, 816,400 (bleeding the night before); 13th, 1,034,400; 15th, 916,320; 19th, 1,300,000.

From this time the rate of increase was rapid. When he left the hospital the blood-count was over 3,500,000 per c.mm.

On January 14th he had a large movement of the bowels containing blood, but there was no vomiting. From this time on the bleeding ceased. His appetite became ravenous, and it was with the greatest difficulty that he could be confined to proper diet. Examination of the abdomen revealed slight distention; no tenderness; no trace of tumor. The abdominal walls were thick, and it was difficult to outline the stomach, the gastric tympany extending a hand's breath below the costal margin. The organ appeared to be slightly enlarged; liver dulness normal; splenic dulness not increased. There were the usual cardiac and arterial phenomena of profound anæmia. Throughout the month of February the improvement was very rapid. He gained in weight; began to have a little color and had no gastric distress, even after a full meal. He had diarrhœa at times; three or four stools in a day. Early in March he was anxious to go to work, and was with difficulty kept in hospital. He had no vomiting, and stated that he felt perfectly well with the exception of a slight weakness. He had a ravenous

appetite, and I repeatedly had to warn him against eating too much. He returned to work March 26th, and through the spring and summer remained fairly well.

On August 4th the hemorrhage from the stomach recurred and continued four days. He lost much blood and grew rapidly weak. In the course of a week he returned to work, and on September 5th called to see me at my office, having come directly from the workshop. He was profoundly anæmic, extremely short of breath, and could scarcely get up the stairs. For nearly a week he had been passing blood from the bowels, without vomiting. He was admitted to the University Hospital September 5th. He complained of slight gastric distress, but had no bleeding until the 20th, when he vomited nearly a pint of blood, dark in color, mixed with food. The same evening he passed large quantities from the bowels. With the exception of weakness he insisted that he felt well, and was always asking for more to eat. There was no further vomiting during his stay in hospital, and his blood-count, which had been about 1,500,000 on October 8th, rose rapidly to nearly 3,000,000 per c.mm. He gained seven pounds in weight within a month.

On the 8th the examination of the abdomen gave results as follows: Somewhat dilated; uniformly tympanic; no tenderness; no tumor to be felt; obscure sense of increased resistance at a point midway between the navel and right costal margin; liver dulness from the sixth rib to costal margin.

He has periods of freedom from abdominal pain, but not of long duration. After a full meal he is at first comfortable, but in three or four hours there are uneasy sensations in the stomach, often positive pains, which may become severe. When the stomach is empty and the pain becomes intense, taking food, even a biscuit or half a glass of milk, will give relief. As stated, there is no epigastric tenderness, and he always locates the pain along a line from the ensiform cartilage to the spine of the left ilium.

Case II.—*From* 1869 *dyspepsia and occasional attacks of gastralgia. In* 1880 *hæmatemesis and melæna. In* 1882 *slight melæna without vomiting. Since then repeated attacks of gastralgia.*—A. B——, aged forty, good family history; was delicate as a lad, but after the age of fourteen enjoyed the average health with the exception of dyspepsia, to which he was liable, and he would at times

regurgitate food without discomfort or nausea. In 1869 he had gastric distress sufficient to make him at times press hard against the stomach; no nausea; no vomiting. With the exception of attacks of dyspepsia he remained well until September, 1876, when he had fever, and, during convalescence, violent attacks of gastralgia. These occurred sometimes with vomiting. He had more or less gastric distress until 1879, and he was believed at this time to have malarial gastralgia, and was ordered quinine and arsenic in large doses. In September, 1880, after a hard day's work, he returned home at 10 P.M., and had a great deal of gastric trouble, and before he went to bed regurgitated his food and, mixed with it, some black material. He slept well that night, and in the morning had a large bloody stool. That day he vomited a large quantity of blood and became very exsanguine. After this time the pain increased very much, but it was always relieved by a hearty meal.

In November and December he was in the hospital on the strictest diet, and lost in this time about forty pounds in weight. He improved after this, and in July, 1881, went abroad and was away for two years, during which time he had much discomfort but no very severe attacks of pain.

He consulted many of the leading physicians of Europe, and the diagnosis was uniformly gastric ulcer. While in Paris he had slight hemorrhage from the bowels without vomiting blood. He returned to this country in December, 1882, and has been working off and on ever since, but never entirely free from gastric distress, occasionally having severe attacks of pain.

In January, 1887, he had such an attack which lasted fourteen days, and lost twenty-eight pounds in weight. He has repeatedly had to take morphia in large doses to relieve the pain. The patient looks well; weighs one hundred and sixty-five pounds; tongue clean; good appetite; good digestion. Examination of the abdomen, negative; no tenderness; no tumor.

REMARKS.—These two cases have certain points in common. In the first place, the long duration; the symptoms in one instance recurring over a period of eighteen years; in the other at least twelve years. The peptic ulcer, gastric or duodenal, may be an exceedingly chronic malady, lasting ten, fifteen, twenty, or, according to Brinton, even thirty, years. Anatomical observations

show that a large proportion of these ulcers heal, yet there are others which, from their general condition, can scarcely be repaired. The deep excavation, the size of a dollar-piece, with hard fibrous base, thickened peritoneal coating, and indurated edges, which we find so often in fatal cases, is an unlikely ulcer for cicatrization. The time element in these two instances gives no clue whatever to the situation of the ulcer.

The pain in gastric and in duodenal ulcers is very similar, with the exception of the time of onset, which, as a rule, in gastric ulcer more closely follows ingestion of food, while in the duodenal it is deferred two or three, or even four, hours. This is, however, an uncertain symptom.

In Case IX. of my series, close questioning elicited the most positive statement that food had no special influence, one way or the other, in inducing or in aggravating the pain, which was more likely to come on while the stomach was empty than subsequent to a meal.

The late onset of pain in duodenal ulcers has usually been attributed to the action of acid chyme passing out of the pylorus toward the close of gastric digestion. It is to be remembered, however, that the chyme passes continuously from the stomach, commencing, probably, within a half-hour after taking food. The increased acidity of the gastric contents toward the close of digestion may have something to do with it.

While perhaps too much stress has been laid upon this point in the differential diagnosis between gastric and duodenal ulcers, it does hold good in certain instances. A more important criterion, I think, is in the occurrence of gastric crises, agonizing attacks of colic, which seem to be more severe in the duodenal disease. A feature worthy of notice is the occurrence of severe gastralgic attacks at night.

Absolute immunity from all gastric distress in the intervals between taking food is more common in duodenal than in gastric ulcer. It is to be noted, in the cases here reported, that gastric distress has been more or less constant. A feature common to both ulcers is the prolonged interval of freedom. In Case VIII. of my series, a diagnosis of malarial gastralgia was made by an eminent clinician, based largely upon the fact that the patient had repeated periods of complete immunity from all symp-

toms, but followed by attacks of the most aggravating character.

The point upon which the greatest stress has been laid in the diagnosis of duodenal ulcers is the occurrence of melæna without hæmatemesis. Bucquoy and Johnston both hold that it can be recognized by this symptom alone. If so, the diagnosis in the patients whose history is given above is plain. The first case had repeatedly passed blood from the bowels without hemorrhage from the stomach, and the second on, at least, one occasion. As already stated, it was this symptom which, in Case VIII. of the series I have reported, led Dr. Palmer Howard to suggest the existence of duodenal ulcer. In the above-reported cases I should hesitate to give a positive diagnosis on this symptom alone, with the co-existence of such marked gastric disorder. In Johnston's case and in several of Bucquoy's patients, I grant that the conditions for a correct diagnosis were fulfilled, and I accept the importance of melæna alone as a valuable localizing index; but I submit that instances such as I have given illustrate the uncertainty, rather than the certainty, which still pertains to the diagnosis of duodenal ulcer.

[Reprinted from THE MEDICAL NEWS, December 15, 1888.]

ON LESIONS OF THE CONUS MEDULLARIS AND CAUDA EQUINA, AND ON THE SITUATION OF THE ANO-VESICAL CENTRE IN MAN.[1]

BY WILLIAM OSLER, M.D.,
PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

THERE have been published recently several observations which add materially to our knowledge of injuries and lesions of the terminal section of the spinal cord and of its nerve roots, and which also throw considerable light on the exact situation of the ano-vesical centre.

In a suggestive and valuable communication "On the Segmental Distribution of Sensory Disorders," Ross[2] analyzes the distribution of the sensory branches of the lumbo-sacral plexus, and calls attention to the arrangement of the lower sacral and coccygeal nerves, which supply by the small sciatic, derived from the third and fourth sacral roots, the external aspect of the skin on the back of the thigh, and from these same roots, through the in-

[1] Read before the Philadelphia Neurological Society, October 22, 1888.

[2] Brain, January, 1888.

materially enlarged during the past twenty years, has increased with each decade; in 1873—83 as many were admitted as in the previous twenty years. Taking the statistics of four periods we have in 1853, '54, '55 a death rate of 24.3 per cent.; 1863, '64, '65,

[1] Read by title before the Canada Medical Association, September, 1888.

ferior hemorrhoidal, pudendal, and pudic nerves, the anus, perineum, scrotum, and penis.

Cases of injury have been reported in which a sensory paralysis of this distribution has been associated with paralysis of the rectum and bladder, and with little or no involvement of the parts supplied by the first and second sacral and the lumbar nerves. Such instances are, in fact, important and valuable experiments from the study of which much may be gathered. Thorburn[1] reports four cases of injury of the cauda equina in which, with paralytic symptoms of variable extent, there were incontinence of urine and of feces, and anæsthesia in the distribution of the branches of the lower sacral nerves. He quotes also a case of Olivier's of gunshot wound in the lumbar region, which nine years after the accident presented complete anæsthesia of the postero-internal and anterior parts of the thighs and of the penis and scrotum.

Bernhardt[2] records a case of injury, the result of a fall on the buttocks from a height, which was followed by retention of urine and incontinence of feces. There was no paralysis of the legs, but there was absolute anæsthesia of the anus, perineum, scrotum, penis, and the skin of the upper two-thirds of the thighs. There were erections and within a few weeks after the injury coitus was possible, but ejaculation was defective and the semen flowed slowly *post cohabitationem*. Although the scrotum was anæs-

[1] Brain, January, 1888.
[2] Bernhardt: Berliner klin. Wochenschrift, No. 32, 1888.

Reprinted from the New York Medical Journal

thetic, the testes were sensitive to pressure, and the cremasteric reflex was present. These parts are supplied from the genito-crural nerve, a branch of the lumbar plexus, which is, as Thorburn points out, usually unaffected in these cases.

A still more instructive case is reported by Oppenheim in the last number of the *Archiv f. Psychiatrie*, Bd. xx. Heft 1. A workman fell from a height of nineteen feet upon his sacrum. There were numb feelings in the legs, paralysis of the bladder and rectum, and complete anæsthesia of anus, perineum, scrotum, penis, and of the skin on the postero-internal aspects of the thighs. No erections. The reflexes were retained. The movements of the legs were perfect and the numb feelings disappeared. The other symptoms persisted and death took place about three and a half months after the injury. The autopsy showed a fracture of the first lumbar vertebra, and a traumatic myelitis and hæmatomyelitis of the conus medullaris, and a degeneration of the posterior roots of the third and fourth sacral nerves coming from the conus at the seat of injury. We have here the very anatomical facts needed to complete the picture, and they moreover render it very probable that in these cases the terminal portion of the cord—the conus—is itself the seat of the lesion, although it is possible that involvement of the nerves alone would produce the symptoms.

By no means the least interesting aspect of these cases is the light they throw on the situation of the ano-vesical centre in man. Kirchoff[1] had already

[1] Archiv f. Psychiatrie, Bd. xv.

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[1] Read by title before the Canada Medical Association, September, 1888.

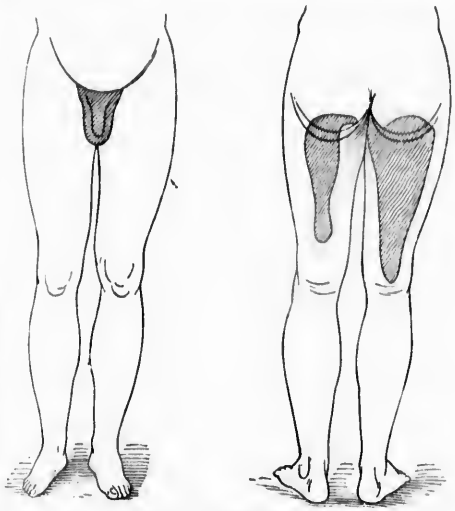
concluded that it was situated in the conus medullaris in the region of exit of the third and fourth sacral nerves. In the case of a man who had fallen on the nates, and whose important symptom was paralysis of the bladder and rectum, the lesion was found in the conus three centimetres above the filum terminale. Oppenheim's case is a still more accurate demonstration.

The following case can be understood with the aid of the preceding remarks:

Joc. C. H., æt. sixty-three, applied at the Infirmary for Nervous Diseases March 7, 1888. Family history good. Has always been healthy and well, though as a young man he had syphilis. Served in the army and on June 8, 1862, sustained a fracture of the spine. In the battle of Cross Keys, as he was crossing a bridge, a bullet struck him on the cartridge-belt, and the shock knocked him off the bridge, and he fell on the rocks in a sitting posture. He was senseless, and on coming to found himself in the ambulance wagon. Was in the military hospitals three and a half years at Winchester and Fort McHenry, for three years of which time he was on a water-bed. The skin of the back was not broken by the fall. He was paralyzed in the legs and lost control of the bladder and rectum. After a time he could move the legs, but he did not walk until December, 1865. Since that time he has been able to be about, but he has never regained control over the bladder and rectum. Uses a catheter three or four times a day. Never knows when he is going to have a stool.

Present Condition.—Well-built, vigorous-looking man for his age; walks well, but favors the left side

Reprinted from the New York Medical Journal



Distribution of the anæsthesia.
Front view. Rear view.

a little. When stripped, it is seen that the left leg is slightly smaller than the right. Measurements gave, right calf fifteen inches, left thirteen and a quarter inches; left thigh also somewhat smaller. He says the leg has been thin ever since the accident, but he is always able to get about quite well. The spine is straight, the lower dorsal vertebræ a little prominent, lumbar normal; no signs of abrasion or of any scars; no pain on pressure.

There is complete anæsthesia of the lower gluteal

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regions, posterior aspects of the thighs, perineum, scrotum, and penis as far as its root. In all other regions sensation is perfect. He does not feel the passage of a catheter. He is impotent. No information asked about seminal emissions.

Gluteal reflex well marked.

Cremasteric reflex present.

K.-J. + +. No ankle clonus.

We have to deal here with a residual paralysis of the bladder and rectum and of the skin supplied by the small sciatic, inferior hemorrhoidal, pudendal nerves arising from the third and fourth sacral roots. Whether the injury involved originally the cord or only the branches of the cauda equina does not seem possible to determine. The fact that slight wasting of one leg remains would indicate a neural rather than a central lesion.

These cases do not all result from injury. Rosenthal[1] reports the case of a woman, aged thirty, who, as the result of exposure to cold, had incontinence of urine and feces, associated with anæsthesia of anus, perineum, vulva, vagina, and lower gluteal regions. The legs were in all relations normal. From a consideration of these cases we may conclude:

1. That the ano-vesical centre in man is situated in the lowest segment of the spinal cord—the conus medullaris—at the region of exit of the third and fourth sacral nerves.

2. The association of paralysis of the rectum and

[1] Ueber das centrum Ano-vesicale, Wiener med. Presse, Nos. [illegible], and 20, 1888.

Reprinted from the New York Medical Journal

bladder with anæsthesia in the distribution of the inferior hemorrhoidal and pudendal nerves points to a lesion of the lower sacral nerves or of the conus medullaris. It is not always possible to determine which is affected.

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1 Read by title before the Canada Medical Association, September, 1888.

Reprinted from the New York Medical Journal for December 22, 1888.

Die "Hemorrhagische Purpura" von Henoch in Nothnagel's Handbuch 1890

ON A FORM OF PURPURA

ASSOCIATED WITH ARTICULAR, GASTRO-INTESTINAL, AND RENAL SYMPTOMS.

By WILLIAM OSLER, M. D.,

PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

The combination of purpura rheumatica with diarrhœa is frequently referred to by the older writers.

The cases which I here report have additional features, and, with others to be found in the literature, belong to a very remarkable group worthy of more careful study. The characters are:

I. Recurring outbreaks of purpura often associated with urticaria or local œdema.

II. Articular pain, sometimes with swelling.

III. Gastro-intestinal disturbance—colic, vomiting, diarrhœa, and occasionally hæmorrhage.

IV. Hæmaturia, albuminuria, and sometimes a fatal nephritis.

Case I.—A. B., boy, aged six, seen January 23, 1888, with Dr. Dunton. No rheumatic history in family; some members gouty. An aunt's child on father's side, aged three weeks, died of purpura hæmorrhagica. The child has been exceptionally well developed and strong. During the past summer he failed somewhat in health. The present trouble began about four weeks ago with pain about the ankles, followed by attacks of colic, with diarrhœa, and a skin eruption, urticaria-

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like in character, which tended to become purpuric. Large areas were black and blue, just like a bruise.

About ten days after the beginning of the illness there was bleeding from the bowels, but not in large amount. There were not in all more than eight or ten stools, containing from a teaspoonful to a teacupful of blood. No bleeding from the gums or from the other mucous surfaces. For the past two weeks he has been up and down, crops of purpuric urticaria coming out with the recurring attacks of colic. There has not been fever at any time.

Present Condition.—The child is not specially anæmic, not much wasted, though he has fallen away greatly from his former plump condition. Temperature, 98°; pulse, 96; tongue is a little furred; abdomen slightly protuberant, not painful on pressure. When asked where the pain is, he always places his hand upon his navel; no enlargement of the spleen or of the liver; joints not painful. On the skin over the elbows there is a fresh crop of reddish-brown urticaria wheals, rather more solid and less œdematous-looking than ordinary hives; there is a patch also on the flexor surface of the right arm. These spots are all hæmorrhagic, and about the raised ones are numerous small extravasations. There is no swelling of the elbows. About the buttocks and thighs there are very many purpuric spots. No swelling of the ankles.

An attack of pain came on during the visit. It had the character of ordinary colic. The stools were brownish-black in color, but contained no blood. The urine was clear; specific gravity 1·018, containing distinct traces of albumin. Microscopical examination showed a few red blood-corpuscles and fine granular tube-casts.

I saw the boy on four other occasions between January 23d and February 7th. About the 25th of January œdema of the ankles was noticed. This increased, the scrotum became swollen, and within ten days there was general anasarca. The urine was highly albuminous, and contained tube-casts and a few red corpuscles.

I did not see the boy again, but learned from Dr. Dunton that the renal symptoms persisted, and these assumed the

character of Bright's disease, of which ultimately he died in about six weeks. No further articular or purpuric symptoms developed

Case II.—Bartholomew H., aged forty-six, machinist, admitted to the Philadelphia Hospital, October 28th, with diarrhœa, an extensive purpuric rash, and polyarthritis. The patient has been a tolerably healthy man; has used spirits moderately; no history of specific disease; he knows of no similar affection in his family. In April, 1887, he had a severe attack of gastro-intestinal disorder, accompanied with "black eruption," as he describes it, on his legs, similar to that from which he now suffers. There were no spots on the arms. He was ill at this time about two or three weeks. Since April of last year he has been failing in health, and has had several sharp attacks of diarrhœa. The present attack began on Saturday, October 20th, with pain in the arms and knees, and a rash came out on the elbows and legs. Throughout the week he had great pain in the joints, and the knees, ankles, and right elbow became swollen.

On the 29th, the day after his admission, the following note was made: The patient is a moderately well-nourished man; looks pale; the tongue is furred, swollen, and indented. Both elbows tender, not swollen; complains of pain on flexing the right arm. On both arms there are numerous purpuric spots from 1 to 3 mm. in diameter, most abundant on the flexor surfaces. Just below the bend of the right elbow there is a large extravasation the size of a quarter-dollar piece, which is a little raised at the center. There are eighteen or twenty spots on the extensor surfaces of the elbows; no extravasations on the skin of thorax or of abdomen. Hip joint not painful to touch or to movement; the right knee is a little swollen, and can not be flexed; the right ankle is not swollen, but is tender. There are numerous fading ecchymoses on the extensor surfaces of the thighs and many on the skin of the popliteal spaces; there are none on the legs. During the examination he had several attacks of colic. The urine was turbid and deposited a flocculent sediment of mucus. On boiling, it cleared slightly. On the addition of acid there was a distinct deposit. Microscopically,

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there were leucocytes, isolated red blood corpuscles, and a few blood-casts. He has had profuse diarrhœa, but no blood in the stools.

October 30th.—Urine not materially reduced in amount. Specific gravity 1·016. Chemical and microscopical characters as before. Has had persistent vomiting to-day.

November 1st.—Passed a restless night; vomiting has been very distressing; complains a good deal of joint pain; the lobes of the ears are very tender to the touch, congested and red; no distinct extravasation; the right elbow is red and swollen; last night a fresh eruption of purpuric spots appeared on the exterior surfaces of both elbows; the spots are raised, and look like those of purpura urticans. There are also two spots on the metacarpal joint of the left index finger. The ecchymoses on the flexor surfaces of arms have faded. The knees and ankles are not swollen. Temperature, 100°; pulse, 88, small. Heart sounds normal. Tongue still coated; gums not spongy.

4th.—For the past three days the albumin in the urine has been much more distinct, and there are many tube-casts. Uric acid deposits if the urine is left standing. The general condition has much improved; the diarrhœa is checked, and he no longer complains of abdominal pain; vomiting is not so distressing.

5th.—Patient much better to-day; no joint pain; the ecchymoses have almost faded, and the vomiting is checked.

From this date the recovery was rapid, and at present date (November 30th) convalescence is established. The urine is still albuminous. The treatment consisted in the administration of naphthalin with Dover's powder for the diarrhœa and colic, and increasing doses of Fowler's solution.

Remarks.—Atkinson, in Pepper's "System," vol. ii, refers to this form of purpura as described by Henoch ("Berliner klin. Wochenschrift," 1874), and by Couty ("Gazette hebdomadaire," 1876). The latter author, in an exhaustive article, has collected a large number of cases, and describes the disease as "*une espèce de purpura d'origine nerveuse.*" Wagner (Archiv der Heilkunde,"

Bd. x) and Zimmermann ("Archiv der Heilkunde," 1876) have also reported cases identical with those above described With the exception of a paper by Binet on "*Purpura hémorrhagique avec œdèmes mobiles et crises intestinales*" ("Revue méd. de la Suisse Rom.," 1886) I find no very recent accounts in the journals.

I think these cases come properly under the designation *purpura rheumatica*, of which they constitute the most aggravated and serious form. The varieties of this condition may be grouped as follows: 1. Cases in which the purpura occurs with slight articular pain, or with diarrhœa alone, or in which the eruption comes without these symptoms in children who have had rheumatic manifestations. 2. Acute arthritis involving many joints and associated with extensive *purpura urticans*—the *peliosis rheumatica* of Schönlein. 3. The variety here described in which, with articular affection and purpura, there are gastro-intestinal crises, hæmorrhages from certain of the mucous surfaces, albuminuria, and in some cases a fatal nephritis.

Are these cases truly rheumatic, or is not the articular affection upon which so much stress is laid analogous to that which we see in hæmophilia and scurvy? It is difficult to escape from the former view in the presence of characteristic cases of *peliosis rheumatica* with endocarditis and pericarditis; and yet the close relationship and even interchangeability of certain of these cases of purpura with urticaria, with erythema nodosum, and with the angio-neurotic œdema, favor the suggestion that the entire group may depend upon some poison—an alkaloid, possibly, the result of faulty chylopoietic metabolism—which, in varying doses in different constitutions, excites in one urticaria, in a second peliosis rheumatica, and in the third a fatal form of purpura.

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FROM THE UNIVERSITY
MEDICAL MAGAZINE.

THE MORTALITY OF PNEUMONIA.[1]

BY WILLIAM OSLER, M. D.,

Professor of Clinical Medicine, University of Pennsylvania; Physician to the University and Philadelphia Hospitals and the Infirmary for Nervous Diseases.

Whether or not the mortality from pneumonia has increased of late years, and, if so, to what cause or causes this is to be attributed are questions of the utmost practical importance,

What are the facts as to the increase in mortality? The last United States Census Report gives a total of 63,053 deaths from this disease; 8,330 in each 100,000 deaths from all causes, against 8,128 in 1870; 6,874 in 1860 and 3,755 in 1850, with the mean age of death at 32. If correct, these figures would indicate an extraordinary increase in the mortality, but Dr. Billings writes "that the conclusion cannot be drawn that the mortality has increased, because in preceeding years the data were very much more imperfect and unreliable."

The statistics of the large hospitals do not show any decided increase. I have taken the figures of three representative institutions; the Montreal General Hospital, in the North; the Pennsylvania Hospital, and the New Orleans Charité, in the South. At Montreal the statistics are available since 1853, and we find in the decade 1853—63 a mortality of 16.2 per cent.; decade 1863—73 a mortality of 20.3 per cent.; a total of 1012 cases with 206 deaths equal to 20.4 per cent. It is interesting to note that the total number of cases admitted to this hospital, which has not been materially enlarged during the past twenty years, has increased with each decade; in 1873—83 as many were admitted as in the previous twenty years. Taking the statistics of four periods we have in 1853, '54, '55 a death rate of 24.3 per cent.; 1863, '64, '65,

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12 per cent.; 1873, '74, '75, 29.1 per cent.; 1883, '84, '85, 16,1 per cent.; figures which do not indicate a regularly progressive increase in the mortality.

By the kindness of Dr. Matas I have been enabled to get the statistics of the Charité Hospital of New Orleans since 1830. In decades the death rate has been as follows:

1830—39	-	298 cases	-	died	133	-	percentage 44.6
1840—40	-	685 "	-	"	242	-	" 35.3
1850—59	-	1172 "	-	"	378	-	" 32.2
1860—69	-	747 "	-	"	327	-	" 43.9
1870—79	-	1067 "	-	"	429	-	" 40.2
Total.	-	- - 3969			1509		38.01

Here too figures do not indicate that there has been a very marked increase. There was a slight reduction in the decades from 1840 to 1860, but the rise in the succeeding periods never reached the maximum attained in 1830 to 1839. The well known great fatality of pneumonia in the South, particularly among the negroes, is born out by thes statistics.

At the Pennsylvania Hospital the following are the returns which were kindly furnished me by Dr. F. Packard, Resident Physician. Dr. Hartshorne, in his paper before the College of Physicians of Philadelphia, quoted the mortality in three years of the 4th, 6th and 8th decades to show a progressive increase in the death rate, which might possibly be attributed to changes in the methods of treatment. There is indeed an increase, as shown in Table 1, but four other periods of three years in successive decades illustrate the beautiful elasticity of figures and show that the mortality has, if anything, been reduced.

I.		II.	
1845–46–47	16 per cent.	1848–49–50	37.9 per cent.
1855–56–57	25.4 " "	1858–59–60	21.2 " "
1865–66–67	24.1 " "	1868–69–70	22.8 " "
1875–76–77	39.2 " "	1878–79–80	32.7 " "
1885–86–87	36.1 " "		

In a total of 704 cases since 1845 the mortality has been 29.1 per cent.

In the Boston City Hospital the death rate for the past thirteen years has been 29.1 per cent., a total of 1443 cases with 421 deaths.

I regret that I have not been able to get the statistics of the Philadelphia Hospital, but I shall allude in a few moments to the

very high rate of mortality in that institution.

It is very generally acknowledged that the death rate prior to 1840, in the days of active antiphlogistic measures, was very much higher than under the rational methods since employed. Certainly, the figures quoted by Wilson Fox in Reynold's System of Medicine support this, and show particularly that the mortality was greater when bleeding was employed. Not to enter into details which are so accessible, it will be sufficient to recall the remarkable records of the Edinburgh Infirmary. Before 1848 the death rate in 567 cases was 36.3 per cent.; from 1848 to 1856 in 611 cases, 21.2 per cent,; and from 1856 in 548 cases the mortality was only 12.7 per cent. In Dickson's able Essay on Pneumonia[1] the statistics of 80,437 were collected with a mortality of 16,915 giving the proportion of deaths 1 in 4.8. This writer alludes to the remarkable equality of the proportional mortality—"in peace and all comfort, in hospitals of wealthy communities, in the field of destructive war, and in the hospitals and barracks, the emphatic seats of destitution privation, exposure and neglect."

The returns of the Montreal Hospital, the Pennsylvania Hospital and the New Orleans Charité certainly do not bear out Dr. Hartshorn's strong statement that the "mortality of pneumonia to-day is under similar circumstances, more than twice as great as it was forty years ago.[2] The truth would seem to be that in our large city hospitals the death rate in pneumonia always has been, and is likely to continue to be very high, usually over 25 per cent. often reaching 40 or 50 per cent. Unfortunately it is upon the statistics of these institutions that we depend for our information and we have not similar large returns in private practice with which to compare them. The Collective Investigation Committee of the British Association recently published a report of cases drawn largely from private practice, with a mortality of 18 per cent., a ratio considerably lower than that in hospital practice. As illustrating the difference between private and hospital practice in the same city, I may state that the death rate among 170 cases treated by Dr. Palmer Howard of Montreal in twenty years was only 6 per cent., a striking contrast to the rate of mortality at the General Hospital during the same period We must remember that the pauper population in the large cities of this country has developed enormously in the past twenty years, causing a very great relative increase in the number of individuals who live under

1 Studies in Pathology and Therapeutics, 1867.
2. Synopsis of Dr. Hartshorn's paper distributed to the Fellows of the College of Physicians of Philadelphia.

conditions which render them more susceptible to and less able to withstand such an acute affection as pneumonia. To this, I think, we may reasonably attribute any slight increase in the death rate which may have occured at certain hospitals.

In a self-limited fever like pneumonia it is highly improbable that any great increase in the death rate has followed a change in the methods of treatment. *There is no acute disease with so few cases in which the issue of life and death lies in the administration of drugs.* In *young, healthy adults* a large majority of the cases do well without any medicine, and every session I treat in this way eight or ten such cases for the purpose of impressing upon students the lesson, so hard to learn, so often never learnt, that dosing is not the Alpha and Omega of practice. But a third or more of the cases demand imperatively active treatment from the outset, and and yet the records we have been discussing tell how unsatisfactory, how futile our present methods in dealing with the severer forms of the disease. Take an illustration: I had in the Philadelphia Hospital, eleven cases under my care during the months of December and January, of which six recovered and five died. A brief account of the latter will give an idea of the nature of the cases which swell the mortality bills at our general hospitals.

James D., æt. 22, healthy young man, worked until January 6th; admitted on the 13th with consolidation of lower lobe of right lung. The fever was not high, he was conscious and for two days did well, but on the 16th there was evidence of involvement of the lower lobe of the left lung. He had profuse diarrhœa. The temperature range was 102° to 103.° On the 18th and 19th the pulse became more rapid and the respiration rose above 55, and there was consolidation of the entire right lung and all of the lower lobe of the left. Death took place on the 20th, The autopsy showed uniform hepatization of the right lung, and the old pleuritic adhesions, (he had had pneumonia some years before). Consolidation of the left lower lobe and of an inch along the lower margin of the upper lobe. There was a large patch of fresh myocarditis in the septum ventriculorum.

In this case the death was due to direct involvement of an unusually large extent of lung substance. The usual routine stimulating and supporting measures were employed in this case, but without any perceptible benefit. The inhalations of compressed air seemed to do more good than anything else. Would a copious bleeding on admission, the 6th day of the disease, have prevented the extension to the other lobes?

This is, however, an exceptional case for the Philadelphia Hospital. Young healthy fellows with pneumonia usually do well. Here are some every-day cases when the disease is prevalent.

Jeff. B., æt. 25, bartender, brought by police patrol on the 21st. Had been drinking heavily for three or four months. Attacked suddenly on the 20th. Violently delirious on the 21st anf 22d; had to be constantly watched and restrained. Temperature 103—104°; signs of pneumonia at right base. On the 23d profoundly unconscious. Death on the morning of the 24th.

I. M. D., æt. 40, painter. Had pneumonia twenty years ago. A hard drinker, was on "spree" and sat up in a bar-room on Friday night the 23d, Had pains in chest and cough next day. On the 26th was admitted to the venereal ward and there had a chill. When transferred to the medical ward the emperatur. as 104°, pulse 120, respiration, 40. Signs of consolidation of right apex, w ch had rapidly extended and by the 1st had involved the entire lung. The tongue was dry and tremulous and he had low delirium. The pulse feeble, 120—130. Respiration not very rapid, rarely above 40 per minute. Death on the morning of the 3d. The autopsy showed pneumonia of right lung and marked interstitial nephritis.

William N., æt. 25, rag picker, very hard drinker. On Saturday, December 10th, drank very heavily; was out all night and much exposed in the cold, On Sunday 11th, had a chill with pain in left side. On 16th was brought by ambulance to the Hospital and admitted to the ward for drunkards. He was delirious, with a dry tongue; pulse 135, respiration 35. at left base. During the first week the temperature range was not high, 100—102°, pulse 112—128 respiration 40 to 50, and the delirium was the most serious symptom. From the 24th to the 27th profuse diarrhœa. Gradual failure and death on the 3d.

Thomas L., æt. 30, a heavy drinker. Fell on Saturday 7th in a pit and cut his head, which was dressed at the Pennsylvania Hospital. Was seen by Dr. Edwards on Monday 9th, at 10 A. M., and then looked like a man in the early stage of delirium tremens. Was sent to the Hospital and admitted to the ward for drunkards. In the evening was conscious. Temperature 104½°, pulse 120, respiration 34. Was very delirious through the night, and in the morning there were signs of pneumonia at the right base and he was transferred to the medical ward. At 1 P. M., he was actively delirious, pulse 120, respiration 40 temperature 104.4–5°. Much tremor; lips a little cyanotic. Soldification of right lower lobe. He gradually became quieter. Temperature rose to 105.4–5°, respiration 70, pulse 120, and he died shortly after mid-night, about thirty-two hours after admission. The autopsy showed red hepatization of the lower and middle lobes of the right lung. Kidneys healthy.

These are fair illustations of the fatal cases, which are so common at the Philadelphia Hospital and similar institutions which admit the pauper sick. Occasionally a tough-fibred drunkard will survive, but as a rule the disease is fatal in those who are attacked while under the influence of alcohol. Often the patients are admitted moribund or extremely cyanosed. Last winter I had three such cases bled with temporary relief to the engorged venous system, but without retarding the downward course of the disease. Could we exclude from our tables the subjects of chronic alchoholism, I am sure that, even at the Philadelphia Hospital, the death rate from pneumonia would not be more than 8 or 10 per cent.

The serious complications of pericarditis, myocarditis, endocarditis, meningitis or colitis cause death in many healthy persons attacked with the disease, but a careful examination of post-mortem records will show that apart from these complications the fatal cases usually show signs of more or less extensive disease in other organs, interstitial nephritis, fatty liver, fatty heart or chronic endarteritis. I was much impressed with this in reviewing the records of 100 autopsies in this disease which I made in Montreal.[1] Excluding the cases with almost necessarily fatal complications, and those with serious alterations in important viscera, but a small number remained in which a simple pneumonia, however extensive, killed a healthy man.

A good many complicated factors combine in an individual to cause death, but studying the fatal cases of pneumonia as so many lessons from which to learn wisdom for the future, we may, I think, divide them into three groups. 1st. Those in which the death has resulted from such complications as gangrene, meningitis, ulcerative endocarditis, conditions at present beyond our art to remedy. 2d. Cases in which death has resulted from mechanical causes, over-distention and paralysis of the right heart. 3d. The large group in which death has been due to failure of the general powers under the influence of the high fever, or of the specific poison, or of both combined.

We are likely to be deceived in our therapeutical conclusions unless we bear in mind the unquestionable fact that a very large proportion of all cases of simple acute pneumonia in healthy adults recover without the use of drugs. Careful nursing, feeding, local applications, keep the bowels open and the skin active, meet the indications. Even cases of great severity with extensive involvement of the lung we see the crisis occur normally under most adverse circumstances. Such a case occurred last session at the Philadelphia Hospital. The patient, admitted on the seventh day of the disease, had been up and about at his lodging and drinking heavily, and had had neither medical nor domestic care. Although delirious on admission, the crisis occurred on the morning of the eighth day and he entered upon a convalescence as satisfactory in every respect as if he had had the most approved antiphlogistic treatment.

I have often puzzled over the cadavers of persons dead of pneumonia and asked why should this man have died? Too

[1] Canada Medical and Surgical Journal. 1885. Trans. of the Philadelphia Pathological Society, vol. xii.

often the answer is the echo of the question. The cause is evident in many cases in the form of serious complications, such as endocarditis and meningitis. Some years ago I was struck in the post-mortem room, with the cases of young vigorous men, who had died with distended right hearts and systemic veins and extensive, though in some instances limited, areas of consolidation. It seemed as if the heart had failed in over-distension—asystole—and I determined, when the opportunity arose, not to let such cases die without a copious venesection. Clinically, I think, we see this condition in two different periods of the affection. There is an early cardiac embarrassment during the first few days of the disease, leading to slight cyanosis; and in a later period, at the 7th—10th day, we see with increasing anxiety, the changing color, a dull suffusion, a deepening hue, then the marked cyanosis. Bleeding may be indicated at both these periods. In hospital practice we more commonly see the patients in the latter. For ten years past I have practiced free bleeding to the amount of from 20 to 25 ounces in adults, and yet I have to confess to disappointment in my results I have seen but one case recover after bleeding, out of twelve or fifteen. The cases of bleeding in the late stages have been uniformally fatal. I know they have often been performed with the patient *in exiremis*, but it seems imperative to attempt to relieve an over-distended circulatory system. I know it does relieve in the cyanosis of cardiac dilatation from other causes, but in pneumonia there are doubtless conditions other than mechanical. In these cases the administration of oxygen or compressed air is often most serviceable. Complications carry off many, and direct cardiac failure not a few, but both together do not number the cases, which we see gradually fail under the continued influence of the fever, the disturbed cardiac-respiratory mechanism and the poison. Here we are are often baffled, but in this group we see repeatedly the beneficial effects of the timely use of cardiac and respiratory stimulants.

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ON PHAGOCYTES.

An Address
before the Alumni Association of Bellevue Hospital, New York, delivered April 3, 1889.

BY WILLIAM OSLER, M.D.,
PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA.

THERE are in the body groups of tissues possessing cells, which either normally display amœboid changes, or are capable, under certain conditions, of assuming them. By amœboid properties we mean not only the capability of free movement, but the possession of a power which enables a cell to take foreign particles into its interior. Tissues containing such cells are derived from the mesoderm, the type of which, phylogenetically, is a free wandering cell. (Minot.) In the development of this layer epithelial and non-epithelial portions may be distinguished. For the former Minot has suggested the term mesothelium, and the latter His calls mesenchym. The distinction between the two is, however, largely artificial, as the epithelium may be, and in places is, in development changed into connective tissue. And, thirdly, there are in the mesoderm, at all stages of its development, certain cells which are free and independent—mesamœboids (Minot), and which persist subsequently as leucocytes.

These mesodermic cells in the adult body, which are capable either of free amœboid movements, or of taking up into their protoplasm solid particles of various sorts, are met with:

tenderness on palpation.

I saw the patient for the first time on March 5th, and was struck with his distressed appearance. He lay propped up in bed, had slight dyspnœa, dry tongue, pulse 100, temperature 100°. He complained of

[1] Read by title at the meeting of the Association of American Physicians, Washington, 1888.

(1) As the colorless corpuscles of blood and mucus.

(2) The connective-tissue cells, free and fixed, within the connective tissue proper, or forming the supporting framework of the solid organs.

(3) Cells of the spleen, bone, marrow, and lymph glands.

(4) The vascular and lymphatic endothelium.

(5) The alveolar epithelium of the lungs.

All of these cells possess, in a greater or less degree, the power of taking solid particles into their interior, virtually, as we say, of eating them.

On account of the possession of this property, Metschnikoff has suggested for these groups of cells the term *phagocytes*, as expressive of their most distinctive feature, and for the process in general the term phagocytosis.

He regards this function as a property handed down from the primitive unicellular organism, and traces in an interesting manner the evolution of cells possessing it throughout the animal kingdom; attempting to show a genetic relation, physiologically at least, between the free living rhizopods and the cells of the middle germinal layer of the higher animals. Not a little of the attractiveness of Metschnikoff's views is derived from the glamor of evolution thrown over them by thus attributing the retention in certain cells of an atavic property in the highest degree useful to the organism.

I shall consider first the action of these phagocytes as normal physiological factors in the work of the body; and, secondly, take up the theory that these bodies play an essential *rôle* in the protection of the organism from the invasion of specific germs.

And, first, two illustrations from comparative physiology to indicate the important part assigned to phagocytes in certain transformations which animals undergo. In the development of the frog, the removal of the tail of the tadpole, and of the gills, by gradual atrophy, is effected, according to Metschnikoff, by the activity of

the amœboid cells. At a time when the hind legs begin to bud, the leucocytes migrate into the tail, and by their phagocytic action remove the tissue, fragments of which, as muscle, bits of nerve fibres, etc., may be seen in the interior of their protoplasm. The gills are absorbed by an identical process. In the transformation of the larva into the fly, Kowalewsky[1] has shown that the large masses of muscle tissues, so abundant in the larva, and other parts unnecessary in the matured condition, are removed by the activity of the phagocytes.

It has long been known that foreign bodies, such as ligatures, portions of dead bone, and other substances, may be completely removed by leucocytes. Interesting as is this, and bearing directly upon the question, I propose to limit myself entirely to the consideration of the two aspects above referred to.

Nowhere in the body do we have such a facility for studying the action of phagocytes as in the organs of respiration, in which, with the cilia of the bronchial mucosa, they share in the work of cleansing the air-passages; and of these two important agencies it is hard to say which plays the more important part in the expulsion of those particles of foreign matter which, in cities at least, we constantly inhale. There are several groups of cells engaged in this work: The ordinary mucus corpuscles; the alveolar epithelium; the connective tissue elements of the pulmonary stroma, and the leucocytes of the lymph tissue in the bronchial, tracheal, mediastinal glands.

The mucus corpuscles, which in health are derived largely from the muciparous glands, and in inflammatory states from the general bronchial mucosa, are actively concerned in attacking the dust which reaches, in ordinary inspiration, as far at least as the medium-sized tubes.

The examination of the morning sputa of a cigarette-

[1] Zeitschrift für wissenschaftliche Zoölogie, Bd. 45.

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smoker, or of a person who has been exposed to a dusty atmosphere, shows very clearly that no small proportion of the carbon grains is included within protoplasm. The free granules are abundant, but almost every leucocyte has its little load which it has picked up on its road from the finer tubes to the trachea. I have always thought this represented a neat bit of economy of labor, as there can be no question that it is easier for the cilia to sweep half a dozen angular particles, when enclosed in a cell, than to work at the same when free. In all probability, the finer particles which fall upon the tracheal or the bronchial membranes are gotten rid of almost entirely by cells and cilia. There does not appear to be, to any great extent, penetration of pigment granules between the ciliated epithelium. It is unusual to see beneath the tracheal mucosa any collection of carbon grains. We do meet with it in the submucous bronchial tissue, but the active vibratile lining seems to afford a tolerably sure protection. The lymph vessels open on the surface in the pseudo-stomata, and in the experimental work of Arnold[1] and others, leucocytes carrying black grains have been seen in the submucous lymph vessels; yet the process does not seem to go on to any great degree.

The particles which reach the air cells find no active current to sweep them from the spots on which they fall. It is possible to conceive, under certain conditions, of the air cells gradually filling, were it not for the activity of phagocytes, derived largely from the alveolar epithelium, which stands, as it were, at the gateway of the lymphatic circulation.

The cells lining the air cells, seen, for instance by scraping gently the cut surface of an œdematous lung, look as flattened, desiccated, and lifeless as do the scales of the scarf skin. But appearances are deceptive in this

[1] Untersuchungen über Staubinhalation und Staubmetastase. Leipzig, 1885.

case, and the protoplasm of these cells is not only active but probably varies much in shape with the distention or contraction of the alveoli. When in contact with liquids and in pathological conditions, they change so much in form that I find it often a difficult lesson to teach students familiar with normal histology only, to recognize in the large, swollen ovoid cells so common in sputa, alveolar epithelium. Moreover, from the rapid way in which they may be desquamated, there must be ample provision for their rapid restitution. How far in a normal state these cells take part in the work of cleansing the lungs, is not yet definitely settled. In the young, they do not often appear in the sputa, except when there are indications of catarrhal changes, but, in the adult, their presence is very common. It is rare to see one in the sputa of a hospital patient, which has not brought with it a load of carbon, all of which may not have been derived from the air cells, as these bodies can undergo amœboid changes, and, like the leucocytes, are probably not above picking up a grain or two in their course toward the larynx. In cases of bronchial catarrh, and in phthisis, these pigmented cells of the alveoli may be very abundant, producing the blackish streaks which may be seen with the naked eye. When these cells have undergone the myelin degeneration they seem no longer capable of performing scavenger work.

In coal-miners, or even in stokers and coal-heavers, these pigment-laden cells may be extraordinarily abundant. It is not only when the patient comes direct from the mines, or from the coal-yards, but the old *poitrinaires* which haunt in such numbers our city hospitals, expectorate for months, or even longer, sputa containing the pigment-laden alveolar cells, staining the entire expectoration. So persistent may this be that the process may be regarded, not simply as an extrusion of the daily dole of carbon, but as a definite excretion, if we may so use the term, of particles which have been stored up in pulmonary parenchyma.

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A certain proportion of the inhaled dust particles escapes the mucus cells and the alveolar epithelium and penetrates the substance of the lung, entering at the *kitt-substanz* between the cells, or through the pseudo-stomata existing in the alveolar wall. The particles of coal-dust have such sharp angles that we may suppose them capable of mechanically lacerating the delicate alveolar cells.

In dwellers in the country, as well as in wild animals, breathing an air comparatively pure, the cilia and the phagocytes in the air-passages appear quite able to prevent access of the carbon grains to the lung tissue; whereas in the dwellers in the cities, and in animals kept in confinement, the impurities in the air are so abundant that these agents are insufficient, and sooner or later the grains penetrate the air cells, aided, no doubt by the movements of inspiration and expiration; and we have the well-known marbled or carbonized organs which we see every day upon the post-mortem table.

When the particles reach the lymph spaces, the fixed and free connective tissue cells of the stroma join actively in the work. On section we see in the alveolar septa large numbers of round protoplasmic bodies, two or three times the size of colorless blood-corpuscles, which are usually packed full of dark grains. A certain proportion is seen within the ordinary connective tissue corpuscles, and, in addition, there are, in variable numbers, ordinary leucocytes. But even these forces are insufficient to meet the constantly advancing stream of dust particles. The destiny of those which escape the phagocytes in the alveolar stroma has been accurately followed in the investigations of Arnold and others.[1] Entering the lymph stream they are carried first into the lymph nodules, which, in the lungs surround the bronchi and bloodvessels, and a large number becomes fixed in the cells of the follicular cords or are permanently embedded in the stroma.

[1] Vide recent work of Fleiner. Virchow's Archiv, Bd. cxii.

As they pass along the lymph channels into the interlobular septa beneath the pleura, a still further number lodge, and become permanently enclosed in the stroma cells, and, finally, the remnant pass into the larger lymph channels and ultimately lodge in the bronchial and tracheal glands. Here the lymph and stroma cells of the follicular cords dispose of them permanently. That this is effected in great part by the phagocytes is, I think, unquestioned. A scraping from any moderately pigmented lymph gland shows that the chief part of its carbon load is warehoused (so to speak) in protoplasm, the granules lie for the most part imbedded free in a connective tissue matrix. Here the struggle is practically over, and though not a victory, yet the compromise which has been made is the best which could possibly be effected. The sharp irritating particles have been placed in position in which they could do the least harm, and, though not expelled, have been safely imprisoned.

Once in the lymph glands of the bronchi, it is thought they never reach the general circulation, but it has been shown of late years, that under certain circumstances the carbon particles may pass the bronchial filters and spread far and wide throughout the system. Soyka's remarkable case in which undoubted coal particles were found in the tissue of the spleen and of the liver illustrates what really may occur. Weigert[1] in particular has called attention to the frequency with which in the spleen and in the liver carbonization of the connective tissue occurs. He states that it results whenever densely pigmented bronchial glands form close adhesion to the pulmonary veins, through the walls of which the carbon particles pass and so reach the general circulation. I would not call the condition common, but I have seen at least three instances at the Philadelphia Hospital in which the ir-

[1] Fortschritte der Medicin, Bd. i.

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regularly distributed pigment in the spleen and in the liver (in the latter chiefly along the portal canals) was undoubtedly of extraneous, not of hæmic origin.

The steps in this process described may be followed in the lungs of any town dweller, but to see in perfection the remarkable activity of the pulmonary phagocytes, one must study the early stages of anthracosis, particularly in those exceptional cases which we see occasionally when a miner has been killed by accident or dies of acute disease. It is not, I think, too much to say that the larger part of the pigment contained in lungs almost, if not quite, black, is enclosed in protoplasmic cells. Here too the invading particles are more formidable and not so readily dealt with; yet one frequently finds long irregular bits completely encircled by a film of protoplasm, which the phagocyte has stretched to the utmost, just as we may see an amœba extend along the whole length of one of the short rod-like diatoms.

I know of nothing which illustrates better the remarkable amœboid properties of human protoplasm than a slide prepared from the scraping of such a lung, or of the black juice pressed therefrom. Scarcely a leucocyte can be seen which has not been at work, and many of the larger cells have the protoplasm stuffed to the full with carbon grains. Only in the work of the pond amœbæ preying amongst desmids, diatoms, and algæ can we see such better illustrations of active work. There is, of course, this difference, that the amœba eats to live, and so far as I know never loads its protoplasm with useless stuff. The body phagocytes take anything, never exercising selective powers. The particles which gain entrance to the lungs may be far too large for a single phagocyte to attack successfully. I have sketches showing rod-like particles, the ends of which appear enclosed in protoplasm of a dumb-bell shape; while in one instance not only were the ends enclosed, but the

central portion was completely enveloped by the third leucocyte.

A physiological process in which phagocytes play a leading *rôle*, is the removal and digintegration of the red blood-corpuscles which have lived their life and are no longer fit for work. The cells containing the red blood-corpuscles, which are found in the bone marrow and in the spleen, however much opinion may differ as to their mode of origin, cannot, I think, be regarded in any other light than as phagocytic elements with this definite function. They exist normally in the red marrow, and in the spleen and we may recognize (1) cells which appear to be, from their size and shape, elements of the pulp and (2) cells which belong to, or are derived from the endothelium of the capillaries, and (3) the cells of the stroma. The gradual production of the pigment in this way has been so often described, and is so well known that I need not now dwell upon it. In certain morbid conditions we see this process widely extended, and we find cells containing red blood-corpuscles in the liver, in the lymph-glands, even in the blood itself; and particularly is this the case in those states associated with rapid blood deterioration and destruction, as in acute fevers, when these bodies may be enormously increased. In certain forms of anæmia so abundant are they in the bone marrow and in the spleen that they have been regarded as directly concerned in the widespread hæmophthisis.

The observations of Quincke[1] and his pupils have shown that the liver is the chief seat of blood destruction in pernicious anæmia, but the totally different appearance presented by this organ, even in long-standing cases, to that met with in malaria, shows a radical difference in the nature, possibly in the seat of the hæmolytic action. In the former case, the pigment is chiefly in the liver

[1] Deutsches Archiv f. klin. Med., Bds. xxv., xxvii., xxxii., xxxiii.

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cells; in the latter, in the stroma and about the blood-vessels. We cannot from this regard pernicious anæmia as an hepatic disorder. The liver, probably, makes the best disposal it can of an abnormally large amount of coloring matter, which is, I should suppose, not brought to it in the same form as in malaria, but rather in a form similar to the raw material of the bile pigment, which would account for the active participation of the liver cells. The deep beefy-red color of the muscles in pernicious anæmia also tells of an abnormally large quantity of coloring matter at the disposal of the tissues.

In chronic emphysema, in mitral obstruction, and in all affections in which the circulation within the lungs is permanently embarrassed, the condition of brown induration which ensues affords a very beautiful illustration of the same process. The blood corpuscles by diapedesis reach the stroma of the air cells, where they are seized upon, just as are coal particles, by the connective-tissue cells, and are gradually converted into a pigment which retains for a long time its brownish tint, but which may ultimately become black.

Neumann, in a recent paper,[1] doubts whether the brown induration of the lungs is really the result of the ingestion of the red blood-corpuscles by the stroma cells. He holds that in many instances, at least, structures within the corpuscles, which resemble so closely the red blood-disks, are in reality only pigment forms having the size and color of the red blood-cells. We certainly see structures within the cells which cannot possibly be mistaken for anything but red blood-corpuscles, and, I think, the expert eye can usually discriminate between such and the round aggregations of pigment, however deceptive may be their form and color.

Phagocytosis has been studied in the process associated with absorption of extravasated blood. Langhans

[1] Virchow's Archiv, Bd. 110.

was the first to show that blood effused into the tissue did not simply disintegrate and disappear, but that the connective tissue elements were actively at work, and that no small proportion of the colored corpuscles was ultimately taken into the interior of their protoplasm. This has been amply confirmed, and I think there can be no question as to the fact; but observers are by no means unanimous, however, whether the phagocytes are essential in the process. Probably in large extravasations only the peripheral parts are dealt with in this way. The fixed connective-tissue cells with migrated leucocytes all share, I believe, in the process. It must not be forgotten, as Neumann has pointed out, that pigment granules in the interior of the cells may resemble blood corpuscles very closely. However this may be, there can be no doubt that the cells are concerned in the transformation of the hæmoglobin, whether they take it up with the corpuscles or after it is diffused from them.

Remarkable differences exist in the final transformation of the hæmoglobin, resulting in the formation of two pigments, hæmatoidin, which develops chiefly in the central parts of the extravasation, and an albuminate of iron, hæmosiderin (Neumann), which is formed at the boundaries of the clot and wherever the coloring matter comes in contact with the tissues. That this difference is related in some way to the influence of the cells, is in the highest degree probable, though Neumann is not inclined, from his observations, to attribute an important action in this respect to either the fixed or wandering connective tissue elements. The question is one to which a few years ago I gave some study in connection with development of cells containing red blood-corpuscles, and I was much impressed with the truth of Langhans' statement as to the frequency and numbers of these structures in the vicinity of extravasations of all kinds.

In the intestinal canal the leucocytes assist, to some

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tenderness on palpation.

I saw the patient for the first time on March 5th, and was struck with his distressed appearance. He lay propped up in bed, had slight dyspnœa, dry tongue, pulse 100, temperature 100°. He complained of

[1] Read by title at the meeting of the Association of American Physicians, Washington, 1888.

extent at least, in the absorption of fat. Schaefer's observations upon this point[1] show very clearly that during digestion the amœboid cells of the mucous coat become filled with fat globules. How these are obtained we do not as yet know clearly. Whether the fat penetrates between the epithelial cells, or whether the leucocytes pass up between the cells reaching to the surface and here secure the fat, has not been definitely determined; though from the presence of an occasional cell, or even a nest of cells between the cylinders, the latter view is probably the correct one. The leucocytes pass to the central lymph vessels, where they disintegrate, and discharge their load of fat granules which has, meanwhile, in the protoplasm of the cell, been broken up into finer particles, which form the so-called molecular base of the chyle. Possibly, too, the leucocytes may take up other ingredients. It is interesting to note that in many of the lower animals the amœboid cells of the endoderm possess an active digestive function. The observations of Parker and Lankester appear to confirm fully the researches of Metschnikoff on the phenomena of intercellular digestion in invertebrates.

So far, we have been dealing exclusively with the action of phagocytes under normal conditions. And it is clear that these mesodermic cells have important functions throughout the life-history of the organism. Not only in the early steps in the development of the blastoderm do we see them actively at work, but in various stages of development, particularly in that of the bone, their action is of the first importance. In the mature body we have seen that in the lungs, in the intestines, and in the blood-making organs, the phagocytes have most essential functions; but the question of chief interest to-day relates, not so much to this normal process about

[1] Monthly International Journal of Anatomy and Physiology, 1885.

which there has never been much doubt, as to the supposed part which these cells take in protecting the body against the invasion of parasites.

The theory elaborated by Metschnikoff had been hinted at by many previous observers, but to him is undoubtedly due the credit of bringing it into prominence, and of doing in connection with it a very large amount of interesting work. It must be allowed that he came to his task well prepared. Many of us can look back with pleasure to his brilliant investigations upon the intracellular digestion in the Planariæ and in Sponges, carried on largely at the Naples Marine Station; investigations the truth of which, so far as I know, has not been controverted. Following these studies, directly in the same line, was his interesting research into the method of the absorption of the tail of the tadpole, already referred to, in which he appears to have demonstrated that the atrophy of this organ results in reality from the active removal of the fragments of the tissue by leucocytes.

So far the work was biological, and had no direct bearing upon the phenomena of disease further than that, in the latter illustration, it bore out the well-known fact of the absorption by leucocytes of foreign bodies placed within the tissues. In 1884, in the 96th vol. of Virchow's *Archiv*, he published a paper[1] which arrested the immediate attention of students in parasitology. It is now too old a story to narrate at length; it will be sufficient to remark that in the daphnia, the common water-flea of the aquarium, he had studied the relation of the leucocytes to a fungus with which these insects are prone to be infected. The phagocytes attack the fungi which enter the body cavity from the intestines, and practically eat them, enclosing them in protoplasm. Where one cell is insufficient, several combine to enclose the spores in

[1] Ueber eine Sprosspilzkrankheit der Daphnien.

tenderness on palpation.

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large plasmodia-like aggregations—giant-cells. If the invasion was in such large numbers, and the activity of the fungus so great that conidia were formed, the resisting forces were insufficient, victory remained with the enemy, which meant the death of the daphnia. Of 100 insects studied, 73 became infected, of which 59 recovered and 14 died.

Following this line, Metschnikoff proceeded to study the relation of leucocytes to anthrax bacilli, to the micro-organisms of erysipelas, and to various other affections. He likened specific inflammation to a warfare in which the invading army is represented by microörganisms, and the resisting forces by the leucocytes. Even in details the analogy was maintained. Notice of the arrival of the invaders was telegraphed, so to speak, by the vaso-motor nerves; the line of communication, the avenues of mobilization, were represented by the bloodvessels. The aim of the invader is to secure the territory, to multiply rapidly, to live at the expense of his host, and to manufacture and circulate substances injurious to him. The aim of the resisting forces is to encircle the enemy, inclose him, digest him, and render him inert in battle. Many phagocytes die in the process and, if in large numbers, the heaps of the slain represent pus; an abscess is a battleground densely packed with dead bodies. If victory remains with the invaders the organisms pervade the affected part, multiply, and induce conditions incompatible with the life of the part, or perhaps with the life of the entire organism. If the battle is with the host, the parasites are destroyed, perhaps not without loss, but the normal state is gradually restored. Practically, on this theory each organism is regarded as possessing a standing army composed of mesoblastic cells, capable of rapid reproduction and rapid concentration, one important function of which is to protect the organism against destructive agencies invading it from without. Certainly a most attractive theory, fully deserving the attention

which it has aroused. On the one hand widely accepted on the other bitterly assailed, the question is as yet far from settled, and to the position in which it stands I propose briefly to refer, and then to offer some results of my own observations upon a disease in which special facilities exist for the study of the problem.

Metschnikoff has studied a number of diseases, erysipelas, anthrax, relapsing fever, and tuberculosis, with a view of finding facts in support of this theory, and his communications within the past four years have been numerous and elaborate.[1] They have been so widely abstracted and so often referred to that I shall not occupy your time by entering into details, but will briefly indicate the chief points upon which he lays special stress in these different affections, and note certain of the observations which have been made by other workers.

In erysipelas the cocci are attacked first by the leucocytes filling the lymph spaces, which rapidly proliferate and actively eat the microörganisms. Not alone do the colorless corpuscles act as phagocytes, but the fixed connective tissue cells assist in an important manner. In cases of recovery he found that behind the advancing cocci the leucocytes were crowded with parasites which showed evidences of digestion and destruction. The connective-tissue [illegible] do not appear to attack the cocci, but are chiefly concerned with the absorption of the inflammatory exudate, even taking up the leucocytes which have died. In fatal cases there was enormous development of micrococci, the majority of which lay free in the tissues not enclosed in the phagocytes. Inoculations with erysipelas cocci in white rats confirm these observations made in man. The leucocytes attack the parasites, which undergo rapid degeneration in the protoplasm. The larger connective tissue cells, macrophages, did not attack the cocci. Metschnikoff recommends ex-

[1] Published chiefly in Virchow's Archiv.

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periments upon these animals with the erysipelas coccus as an especially favorable field in which to study the struggle between the cells and bacteria.

In anthrax Metschnikoff has studied the relation of the phagocytes to bacilli introduced into frogs, which, as is well known, possess immunity at the ordinary temperature, but succumb when the temperature is raised. A graft of a piece of anthrax tissue under the skin of a frog is within from fifteen to twenty hours surrounded by leucocytes, which take up many bacilli. According to Koch, they may grow inside the cells and even burst them, but Metschnikoff holds that the anthrax filaments do not develop within the cell, but are gradually destroyed by them, and that this is the reason why the frog at an ordinary temperature recovers. In the heated frog the bacilli rapidly develop and the efforts of the leucocytes proving insufficient, the animal dies; not, it is asserted, from any inactivity on the part of the leucocytes but because the bacilli secrete a liquid which protects them from attack.

In Baumgarten's criticism[1] he relates some experiments with the anthrax bacilli which directly antagonize these observations. Pigeons do not die when inoculated with anthrax, and he found that the bacilli injected degenerate in precisely the same way in these creatures as when in distilled water; only here and there did the leucocytes contain the rods.

He found that in frogs, though the bacilli are eaten by the leucocytes inversely to the degree of heat to which the animal is exposed, there is never total destruction of the bacilli by the phagocytes.

Hess[2] has performed experiments which bear directly upon these points. Anthrax cultures in Zeigler's glass chamber, inserted beneath the skin in animals not very

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[1] Zeitschrift f. klin. Medicin, Bd. xv. Hft. 1 u. 2.

[2] Virchow, Archiv, Bd. 109.

susceptible to the disease, as dogs and birds, showed active migration of the leucocytes into the chamber which appear to attack the bacilli and to destroy them. These very striking experiments certainly indicate what, of course, is well known, a high degree of activity on the part of the leucocytes, finding their way, as they do, into the chamber closed at all points except one narrow orifice. But, as Hess says, it is a question whether the disintegration in the cells necessarily means destruction by the cells.

In relapsing fever Metschnikoff states that the spirilli are not attacked by the leucocytes in the blood but are destroyed only in the spleen. In the artificially produced disease in monkeys, he finds abundant inclusion of the spirilli in the phagocytes of the spleen during the period of the rise in temperature before the crisis. This, however, may simply mean that the spirilli, most of which gradually disappear from the blood at the crisis, have lived their life and are about to die, and in this state are taken up by the normal splenic phagocytes, just as are the effete red blood-corpuscles. He explains the recurrence of the second, or even of the third, attack of the fever by supposing that certain spirilli remain alive after the crisis and start afresh a new generation, which is not retarded in its growth, as the phagocytes are too busy in digesting the spirilli which they had eaten during the former attack.

An interesting study of phagocycosis has been made by Laehr, a pupil of Ribbert,[1] who has studied the effect of injection into the lungs of rabbits, through the trachea, of staphylococcus pyogenes aureus. Within a few hours the cocci are almost all to be seen within the alveolar epithelium, and in the leucocytes, which latter, in the course of a few days, disappear from the alveoli and pass into the bronchi. Meanwhile, the alveolar epithelium

[1] Abstracted by Bitter; Zeitschrift f. Hygiene, Bd. 4.

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proliferates, causing a catarrhal inflammation. Within the first week the cells contain many cocci, which gradually become less numerous, and in the second week entirely disappear. He looks upon this as a confirmation of Metschnikoff's views.

In a second investigation, Hess[1] has studied, in rabbits and in cats, the relation of the leucocytes to the staphylococcus aureus inoculated in the cornea. At first there is marked increase, which leads to an acute inflammatory process in the neighborhood of the cocci. The leucocytes increase rapidly, and within two or three days almost all of the cocci are within cells. In cases which recover, by the sixth day no cocci are found. When the process does not result in healing, the phagocytosis is slight.

Baumgarten states[2] that experiments made in his laboratory do not confirm these results of Hess.

Ribbert, in his study on the destruction of pathogenic bacteria in the body, supports Metschnikoff's[3] views. He found, after injection of the spores of Aspergillus and Mucor, that they collected in the organs of the experimental animals, particularly in the liver and lungs, and that within a few hours after injection they were surrounded by leucocytes, which either completely prevented or restricted the growth of the germs. Injections in very large quantities might not be sufficient to hinder the growth of the parasites, and the animal died. In the lungs and in the liver the phagocytes are much more active than in the kidneys. Precisely similar occurrences were found where the spores were injected into the anterior chamber, and it is worthy of note that he found on the anterior surface of the iris, in the neighborhood of the pupil, the phagocytes much more active and the dis-

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[1] Virchow's Archiv, Bd. 110.

[2] Jahresbericht, Bd. 3.

[3] Abstracted by Bitter; Zeitschrift für Hygiene, Bd. 4.

integration of the spores much more marked than in the posterior part of the iris in contact with the lens. Ribbert holds that the destructive influence of the leucocytes is exercised chiefly by their preventing access of nourishment to the spores (particularly of oxygen), and in favoring, also, an accumulation about them of destructive metabolic products. He regards the fixed connective-tissue cells of the liver, and the giant cells which develop in the liver and in the lungs, as the most important agents in the final destruction of the spores.

As we might suppose, the views of Metschnikoff have met with sharp criticism in many quarters, and from no one more ably and at greater length than from Baumgarten.[1] While not denying that the leucocytes eat the bacteria, he claims that the process is by no means universal, and is carried on so unequally, that we can scarcely speak of an active warfare waged against the parasites.

As a specially weak point, he alludes to the powerlessness of the phagocytes in the Daphnia disease so soon as the conidia are formed from the spores.

In relapsing fever, the freedom from attack which the spirilli enjoy in the blood is urged strongly against the phagocytic theory. The fact that spirilli are found in a number of cells of the spleen toward the crisis simply means that the phagocytes of this organ behave to them as to other foreign bodies. Probably, too, the spirilli begin at this time to lose their vitality, as is shown by their less active movements, and are then readily taken up by the splenic leucocytes in a manner precisely similar to effete blood corpuscles.

In erysipelas, Baumgarten criticises the position in which Metschnikoff finds the parasites, namely, in the second zone, behind the advancing cocci, as conclusively showing that they are not fighters of the battle—not, as

[1] Loc. cit.

tenderness on palpation.

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[1] Read by title at the meeting of the Association of American Physicians, Washington, 1888.

he expresses it, "the heroes of the day, but the hyenas of the field."

The observations of Christmas-Derkinck-Holmfeld[1] are also directly opposed to the theory of phagocytosis. He finds in anthrax experiments that very few of the bacilli are taken up by the leucocytes. In rats they degenerate within two or three days after inoculation, and for the most part outside of the cells. He holds that pus formation is a conservative reaction against the penetration of the bacterial germs, but that the neutralization of the action of microörganisms depends much more on the chemico-biological relations of the tissues than on any property of the cells to destroy them by inclusion. His view, in fact, approaches that of Ribbert already referred to, in ascribing the limitation of bacterial growth to nutritive changes particularly to the restriction of oxygen, rather than to any phagocytic action of the cells.

In Flügge's laboratory, observations have been made by Bitter and by Nuttall,[2] of San Francisco, which directly contradict those of Metschnikoff. Nuttall's elaborate experiments appear to show conclusively that the destruction of the bacilli in the living body is not effected by the phagocytic action alone.

And, lastly, in tuberculosis, the question of the relation of the cells to the bacilli is being carefully studied. In his recent paper on the subject,[3] Metschnikoff claims that the degeneration of the bacilli, which has long been known to occur within the giant cells, results directly from their phagocytic action, and is not a natural decay. Baumgarten, on the other hand, regards the relation of the giant cells to the bacilli as one of the strongest evidences against the theory of phagocytosis.

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[1] Fortschritte der Medicin, 1887.

[2] Archiv für Hygiene, Bd. iv. I would particularly recommend the summary of Bitter's to those wishing further details, and for a striking series of experiments, the paper of Nuttall's.

[3] Virchow's Archiv, Bd. 113.

With the relations of phagocytes to bacteria, I have had so little practical experience that I hesitate to express any positive conviction on the question, but I have, for nearly three years, been working at a problem identical in all its relations, but in which the parasitic bodies belong to a higher class of organisms. I refer to malaria, and to the hæmatozoa which occur in the blood of this disease. A sceptical attitude in these days of hasty observation and of still hastier conclusions is peculiarly appropriate. I complain of no one who, without ample opportunities for personal study, claims the right to question the full significance of Laveran's important discoveries. Perhaps better than any one else, I am in a position to extend sympathy to the sceptic, as, until ample material came to hand in 1886, I was among those who looked upon the work of Laveran with extreme incredulity. The corroboration in almost every detail which his studies have received during the past three years is in all respects remarkable. Working as he did, alone in Algiers, under circumstances the reverse of favorable, without proper laboratory equipment, without the stimulus to be found in the association of men in large cities, it is not only in the highest degree creditable, but most encouraging, that an army surgeon, actively engaged in the duties pertaining to his battalion, could accomplish so thorough a piece of work, requiring but little subsequent correction, and receiving at all hands ample confirmation.

Richard, in France; Marchiafava and Celli, Golgi and his pupils, in Italy; Sternberg, Councilman, James, Shattuck, and myself, in this country; and Vandyke Carter, in India, working far apart, have all practically confirmed, with minor modifications and amplifications, Laveran's observations.

While the invariable association of these parasites with malaria would appear to be settled, their precise morphological relations are still a matter of discussion. I

tenderness on palpation.

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have urged, from their resemblance to other hæmatozoa, that they should be classed with the genus of Hæmatomonas (Metrophanow), which includes all forms of monads parasitic in the blood, of which a considerable number is known among the lower animals. Briefly, to refresh your memory, I may refer to the forms which occur in ordinary malaria. In the acute cases there exist in the red blood-corpuscles hyaline and pigmented bodies which undergo amœboid changes, and which gradually destroy the corpuscles, converting the hæmoglobin into a black pigment. Under certain circumstances, more particularly during the paroxysms, these bodies increase in size, and undergo segmentation, breaking up into a number of small free spherical bodies. In smaller numbers in the blood, but more constantly in the spleen, are the remarkable flagellate organisms. Lastly, in more chronic cases there are the still more extraordinary crescentic forms. Practically, the unanimity which exists in the statements of the observers above named regarding these bodies, places the question of their existence in malaria (and I may say, based upon the number of negative observations, in malaria only) beyond any reasonable doubt.

That they truly constitute the actual germ of the disease is, however, a point upon which opinions may differ. The constancy of their presence, their absence in other individuals in malarial regions, their abundance in the graver forms of disease, the destructive influence they exert upon the blood-corpuscles, are urged by Lavaran in evidence of their pathogenic nature.

However this may be, the question which here concerns us relates to the relation between the phagocytes and these bodies. Surely one might suppose that here, if anywhere, the theory of phagocytosis might receive confirmation or rebuttal. What but phagocytes are the amœboid forms of these parasites which exist in the red blood-corpuscles, gradually destroying the stroma and

the hæmoglobin until nothing but a shell remains? Here, indeed, are foemen worthy of the steel, or, rather, of the plasma, of the leucocytes. What, then, are the facts? How far can we say that in the blood in malaria, the seat most assuredly of the chief pathological changes, in acute cases, that there are evidences of a struggle between the phagocytes and the hæmatozoa. It has long been known that the leucocytes in this disease (particularly in chronic cases) contain pigment granules. There is no other affection in which melanæmia is so constant a feature, though it is now and then met with in other conditions. The leucocytes obtain the pigment either in the blood itself, or in the liver, spleen, or marrow, where the red corpuscles undergo their final destructive changes. In an examination of nearly one hundred and fifty cases of all forms of malarial affections, I have looked carefully at this point with a view of determining the exact mode in which the leucocytes obtain their pigment, and in my observations of the past two years the question of their relation to the various forms of the hæmatozoa has engaged my special attention. It may be remarked, in the first place, that there is certainly an increase in the number of white blood-corpuscles, an increase not associated, so far as I know, with any special change in the character of these bodies.

The result of my work in this direction may be stated in a few words. In the blood, at least, there is very slight evidence of the existence of phagocytosis. Here and there, it is true, we meet with leucocytes which have included the amœboid forms of the parasite, either free or still surrounded with the shell of a red blood-corpuscle. I have but three or four sketches in a whole series illustrating this fact. Occasionally a crescent may be seen within the white blood-corpuscle, more frequently the smaller free bodies which result from the segmentation. I have in my paper on this subject, given a sketch of a leucocyte which was watched for an hour

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and one-half and had included one pigment body, and was about to take a second, behaving identically though more deliberately than its great prototype, the pond amœboid. I confess myself disappointed in this respect. It may be urged that in a blood drop after withdrawal, the conditions are not favorable for study. But the absence of any great number of leucocytes containing parasites in a comparatively unaltered state, shows that certainly in the circulating blood the leucocytes do not actively attack and eat the parasites. More probably, I think, they pick up the pigment granule after the disintegration of the parasite, or in such regions of the circulation as the spleen or the bone marrow where the conditions are more favorable to phagocytic action. Even on the warm stage with the leucocytes displaying for hours amœboid movements, and in specimens which contained "foes" innumerable, it was exceptional to see evidence of active warfare.

It is, of course, more difficult to obtain evidence of the relation of the supposed contestants in the spleen, liver, and marrow, the organs in which regressive and progressive blood changes are constantly going on. I have not myself practised puncture of the spleen in these cases, as has been done extensively by Councilman. Fatal cases of malaria are not now very common. I have only had opportunities of examining two, both of chronic paludal cachexia, the result of prolonged exposure in Panama. One, an old man, admitted under my colleague, Dr. Musser, whose blood presented many of the characteristic forms; the other, a profoundly anæmic man, with a greatly enlarged spleen, but in whose blood very few of the parasites were found. In both instances the liver, spleen, and bone marrow showed charrcteristic melanotic changes. In the spleen the pigment in various shades, from brown to deep black, was chiefly in the thickened trabecular tissues and about the vessels. Teased portions showed:

(1) Large numbers of leucocytes containing brownish-black pigment grains. A few of the leucocytes contained the small amœboid forms which had been noticed to be very abundant during life.

(2) Larger cells, containing red blood-corpuscles in all stages of degeneration. These cells were of various sizes, and contained a variable number of corpuscles, from eight to ten, or even more. Some of the red corpuscles contained amœboid parasites, but by far the larger portion of them presented the usual appearance met with in cells of this character in the spleen.

(3) Large, irregular, flattened cells, probably derived from the epithelium of the spleen capillaries, which contained granular black pigment, and occasionally red blood-corpuscles.

(4) Spindle or branch cells of the reticular tissue enclosing brownish or black pigment grains.

(5) Free pigment.

Practically the condition was similar, though more extensive in degree, to that met with in this organ and in other febrile states associated with extensive blood destruction. I really could not say that the splenic phagocytes exercised any selective power in picking out for attack those corpuscles which contained parasites or crescentic forms, which in one of these cases existed in considerable numbers. The bone marrow in both cases presented microscopic changes characteristic of the lymphoid tissue, and had a grayish-brown color, due to excess of pigment. There were in it in large numbers marrow cells and ordinary leucocytes containing irregular pigment, and occasionally free amœboid forms of the parasites. The cells containing red blood-corpuscles were very abundant, but here, as in the spleen, it was particularly noted that the red corpuscles not containing the parasites were as frequently, or even more frequently, enclosed in the cells. In the liver the pigment existed in three elements.

tenderness on palpation.

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(1) In leucocytes, which seemed numerous in the lobular capillaries, particularly at the periphery.

(2) In the walls of the capillaries, in all probability in the endothelial cells.

(3) In the stroma cells, particularly of the interlobular tissue about the portal canals, where in places it was sufficiently abundant to cause ordinary diffuse pigmentation, a part of which was due to grains lying free in the interstices of the tissue.

Metschnikoff states that in malaria the parasites are attacked chiefly in the spleen and the liver by the larger phagocytes existing in these organs, and to a much less extent by the leucocytes in the circulating blood.

We see, then, in malaria very little evidence in the blood favoring a theory of phagocytosis; certainly no such campaigning on the part of the leucocytes as might be expected from the presence, in such numbers, of foes so destructive to the red corpuscles. In the spleen, bone marrow, and liver, the organs in which the dead or dying blood-disks are normally cremated, to use Weigert's expression, we have, as might be expected, an activity proportionate to the increased amount of material to be consumed, but scarcely such heightened phagocytic action as would indicate, on the part of the leucocytes, an aggressive warfare.

Into the interesting theory that to the action of phagocytes is due the immunity against certain diseases or against a second attack, I cannot now enter. In the present unsettled state of our knowledge it would be premature.

To conclude: While phagocytosis is a widespread and important physiological process throughout the animal kingdom, and while it undoubtedly plays a most important part in many pathological conditions, the question of an active destructive warfare waged by the body cells against the microörganisms of disease must still be considered an open one.

tenderness on palpation.

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XCV

Extracted from the
American Journal of the Medical Sciences for January, 1889.

PULSATING PLEURISY.[1]

By William Osler, M.D.,
Professor of Clinical Medicine in the University of Pennsylvania.

Pulsating pleurisy is such a rare condition that the following case is worth placing upon record:

Strain in lifting: pain in left side; rapid effusion, at first serous, necessitating two aspirations; pyo-pneumothorax; pulsation of side; free drainage; recovery.—James F., aged twenty-three years, laborer, was admitted to the University Hospital March 3, 1888. Family history good; none of his relatives have had phthisis; with the exception of an attack of rhumatism in 1885, he has enjoyed uniformly good health.

On February the 23d, eight days before admission, he sprained his back by lifting a piece of timber twenty feet in length and ten inches in diameter. Three men were lifting it, but one of them let go his hold so that the patient had to exert his utmost strength to support his end of the piece. At the time he did not feel any discomfort, but that evening he became sore and stiff. He slept well, and the next day, a public holiday, he went about with his comrades, but complained on several occasions that he had sprained his back with heavy lifting. During the evening the pain grew worse and he passed a restless night. The following morning he did not feel well enough to get up and the pain had become almost unbearable. There was no cough or shortness of breath; he does not know whether he had any fever.

From the 26th to the 3d, the date of his admission, he was "up and down;" in bed part of the time, and part of the time by the kitchen fire. The pain in the back was his only complaint. He is positive he had no cough, but he was short of breath.

On admission, the patient looked very ill; face flushed, tongue dry and coated; respirations 36, temperature 100⅘°. He was able to lie down in bed. The importance attached to the lifting on February 23d may be gathered from the fact that he was admitted to the surgical ward as a case of injury to the back, and subsequently transferred. The day after admission he had much pain, of a cutting nature, in the left side, in the axillary region outside the nipple. There was also extreme tenderness on palpation.

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[1] Read by title at the meeting of the Association of American Physicians, Washington, 1888.

severe pain in the left back, just below the scapula. On examination the existence of a large effusion in the left pleura was readily determined. The cardiac impulse was in the third right interspace in the para-sternal line. I noticed one or two special features in the case: the sudden onset after the strain, the remarkable rapidity with which the effusion had taken place, and the unusual amount of pain on palpation.

March 6th, a more thorough examination was made: expansion was almost negative on the left side; the intercostal spaces indistinguishable. The only cardiac impulse visible was in the third right interspace. Tactile fremitus was diminished. There was uniform dulness on the left side reaching to the clavicle and extending a little beyond the right margin of the sternum in the second interspace. By a hypodermic puncture the fluid was shown to be serous. On the principle that a full pleura demands immediate aspiration this operation was performed by Dr. Daland before the ward class, and fifty ounces of clear serum removed.

On the 5th and 6th, the patient seemed much relieved. By the 9th the fluid had reaccumulated and the heart beat was again visible to the right of the sternum, the dulness reaching to the level of the clavicle. Aspiration was again performed and two quarts of slightly turbid serum removed. He seemed to improve very much after this. The temperature kept below 99°, the dyspnœa was relieved, the appetite improved, and with the exception of pain in the left side he felt very comfortable. The signs of effusion persisted and the heart beat could be seen in the third left and the third right interspaces.

16th. The following note was made: Condition of patient has improved, pulse 84, respiration 28, temperature 98°; dyspnœa seems quite relieved, sleeps with his head low, complains only of chest pain; left side scarcely moves, and looks somewhat bulged. Cardiac impulse seen in the second and third spaces on both sides close to the sternum. The left interspaces not specially prominent. Tactile fremitus felt at the extreme apex, but nowhere else on the left side; percussion note clear to the second rib, dull below this. On the right side normal.

Auscultation: Inspiration is loud and breezy in the subclavicular and supra-scapular regions. Below these points the respiratory murmur has a distinctly amphoric character, contrasting remarkably with the breath sounds over the upper part of the lung. The voice sounds in the lower regions are very articulate; no metallic tinkling on coughing. No bell sound, nor could succussion be obtained.

19th. To-day for the first time it was observed that the percussion note in the left subclavicular region was distinctly tympanitic. Dulness extended from the upper border of the third rib, and was distinctly movable. This was very marked when he lay on his right side, in which position the percussion note in the axilla became hyper-resonant without tympanitic quality. Posteriorly in erect position at outer angle of the scapula the percussion note was distinctly tympanitic. To-day, for the first time, the bell sound was obtained with the coins.

26th. Since the 20th he has had irregular fever reaching 102° in the evening. He has, however, felt much better. The physical signs persist; in the recumbent posture the note is hyper-resonant to the lower border of the third rib. Just below the nipple it is distinctly tympanitic, from this point into the axilla there is dulness. When he turns on his right side the entire left axilla is resonant. There is amphoric breathing from the third rib, best marked in the lower axilla, where the percussion

note is dull. There was noticed to-day in the fourth, fifth, and sixth interspaces in the mid-axillary line a remarkable pulsation. The whole side received a very positive shock, systolic in time and synchronous with the cardiac impulse in the third right interspace just above the nipple; the hand placed on the left side is distinctly lifted with each impulse. When he lies toward the right side the pulsation in the left axilla is a little more marked than when he is flat on his back.

27th. The common decubitus is on the left side and in this position the heart impulse is well seen just above the right nipple. The pulsation in the left mammary and axillary regions is very marked. The maximum intensity is outside the left nipple. When he turns on the right side the pulsation is most marked in the fifth and sixth interspaces in the mid-axillary line. Palpation gives a very decided heave and a distinct shock is felt. In the erect posture, the pulsation is not so forcible, though still very evident. The coin sounds are now unusually distinct. Succussion is not obtainable.

29th. The left chest looks larger and fuller than the right; it is completely immobile. The intercostal spaces are obliterated with the exception of the sixth, which is still visible. The systolic impulse on the left side is very marked, and can readily be seen by the students in the distant seats of the amphitheatre. Measurement on the right side gives sixteen and one-eighth inches, expansion one-half inch; on the left side, seventeen and one-quarter inches, practically no expansion.

Palpation.—Tactile fremitus is absent on the left side. Heaving impulse in the mammary and axillary regions well felt with the hand.

Percussion.—Clear, hyper-resonant note to upper border of the third rib. From the third to the fifth it is distinctly tympanitic. Below this, in the axillary region there is dulness. When he turns on his right side the pulsation in the mammary and axillary regions is more marked. Where the percussion note was dull, it is now tympanitic.

Auscultation.—In the left infra-clavicular region the breath sounds are loud and distinct, not amphoric. In the third and fourth interspaces the respiratory murmur is scarcely audible. In the axillary regions there is distant but distinct amphoric breathing, very clearly heard when a deep breath is taken. No special amphoric echo about the voice, the vibrations of which are not communicated to the ear; posteriorly there is distant amphoric breathing.

31st. The irregular fever has persisted and the presence of pus was demonstrated with a hypodermic needle. It was decided to open the pleura, which was done by Dr. Ashhurst; fully three pints of pus escaped. A large drainage tube was inserted in the eighth interspace below the angle of the scapula. After the operation, the heart did not return to its normal position, though it beat to the left of the sternum. Patient stood the operation very well, the evening temperature was only 98.2°.

April 3. Pulse 92, respiration 24, temperature 98°. Inspection showed a remarkable change on the left side of the chest; it already looks smaller than the right, and there is flattening in the second, third, fourth, and fifth intercostal spaces; there is very marked pulmonary resonance to fourth rib. Tympanitic in the fifth, sixth, and seventh interspaces.

With the exception of the fifth, when the temperature rose in the evening to 102°, the patient's condition was most satisfactory. He slept

well, appetite good, temperature did not rise above 99°; there was free drainage through tube.

14th. Chest measured to-day: right side, fifteen and a half inches; left, fifteen and one-eighth. Discharge very light. From this time the patient improved very rapidly; temperature has not risen above 100°.

May 9. The discharge is now slight. A smaller drainage tube was introduced; the discharge gradually diminished, and he improved rapidly in strength and weight. Early in June the tube was removed.

June 10. The note is that the sinus has entirely healed. He left the hospital on the 15th, weighing 140 pounds, a gain of twenty-two pounds since April 14th.

The condition of his chest on discharge was as follows: There was marked flattening of the left side, particularly in the axillary and mammary regions. The circumference was: right, fifteen and three-quarters; left, fifteen and one-quarter inches. The percussion note was clear to the fifth rib and the spine of the scapula behind, below these points there was dulness. Loud breath sounds in the clavicular and mammary regions, feeble and distant in lower axillary, and at base.

I believe that this was an instance of pneumothorax from the outset, one of those interesting cases to which Dr. Samuel West[1] and Dr. de Havilland Hall[2] have called attention, in which the condition has followed strain in a person previously healthy. It is very improbable that on the eighth day of an acute pleurisy there would be a serous exudation of such extent as to reach the clavicle and encroach on the pleura of the other side. On the other hand, the percussion note, as is well known, may be dull in pneumothorax when the tension of the thoracic wall is very great, and I think that in this way the mistake arose. The mode of onset in a healthy man, the course of the disease, and the rapid and complete recovery favor the view that the strain had induced a pneumothorax which excited the pleurisy.

The chief interest of the case lies, however, in the curious phenomenon which developed in the fifth week after the attack.

Instances of tumors of the thoracic wall, which pulsated synchronously with the heart, are mentioned by several of the older writers—Baillon (1640), Le Roy (1776), and Pelletan (1810)—but the first cases of pulsating empyema, recognized as such, were reported by the late Dr. R. L. Macdonnell,[3] Professor of Clinical Medicine in McGill University, Montreal, who, at the time, was clinical assistant to Drs. Graves and Stokes, at the Meath Hospital, Dublin.

In the first of these cases a large tumor appeared in the cardiac region, which, after pulsating for some time, became red, tense, and shining, and then burst, giving exit to a large quantity of pus.

In the second case two tumors appeared in the lower part of the left

[1] Clin. Soc. Transactions, vol. xvii.
[2] Ibid., vol. xx.
[3] Dublin Journ. Med. Science, March, 1844.

side, presenting fluctuation and pulsation. When opened purulent matter escaped in large quantities.

In the third case two large tumors appeared in the lower portion of the left side of the chest, presenting fluctuation and pulsation. They were opened and discharged a large quantity of pus. Death followed in all these cases.

Dr. Macdonnell remarked that this condition was new in the history of empyema.

Several careful studies of pulsating pleurisy have recently been made. One by Comby,[1] who collected 27 cases; and a second by Kepler,[2] who has collected 38 cases, only 2 of which are reported by American authors—Drs. Flint[3] and Dillingham,[4] from the wards of Dr. J. H. Ripley at St. Francis Hospital, New York.

I am able to add the reports of a few additional cases from this side of the Atlantic, but from inquiries which I have made from the hospital physicians of this country the condition appears to be extremely rare. Dr. George Ross, Professor of Clinical Medicine in McGill University, Montreal, has given an account of an extremely interesting case,[5] which closely simulated aneurism:

A man, aged thirty-seven years, was admitted to the General Hospital suffering from pain in the side, cough, and fever, which lasted about five days, and which followed a severe wetting. There was deficient expansion on the left side with dulness to the angle of the scapula and diminished fremitus. Within ten days the expansive movement of the left side became more impaired. The second and third intercostal spaces in front became prominent, presenting perceptible pulsation synchronous with systole of the heart. About five days after the onset of the illness he had a severe fit of coughing, in which he brought up, at least, a pint of pure pus, thick, creamy, and odorless. The cough continued for a few days, with expectoration of pus. The percussion note on the left side became clearer and the pulsating tumor entirely disappeared. The temperature fell to normal and the man's strength returned. Ten weeks from the onset the man left the hospital strong and well.

Dr. F. P. Henry, of Philadelphia,[6] reports a case from the Episcopal Hospital:

Woman, aged thirty years, admitted in the spring of 1880. On the left side of the thorax there were three strongly pulsating tumors—one about the size of half a large orange, in the left mammary region, directly over the central portion of the heart; a second, much smaller and acuminated—*i. e.*, with apex much smaller than the base—was situated on the left antero-inferior portion of the thorax; and a third, the largest of the three, on the left postero-inferior portion, its long diameter, about four inches, corresponding with that of the vertebral column. All these tumors possessed a strong expansile, systolic pulsation. The day after admission pus was withdrawn hypodermically from the smaller tumor. The tumor over the heart contained air, which

[1] Archives Générales, 1883.
[2] Deutsches Archiv für klin. Medicin, Bd. xl. 1887.
[3] Clinical Report on Chronic Pleuritis, p. 47; and On the Respiratory Organs, p. 581, 1856.
[4] New York Medical Record, 1884.
[5] Canada Med. and Surg. Journ., May, 1885.
[6] Proceedings of the Phila. Co. Med. Society, vol. iii. p. 85.

was very evident on manipulation. Aspiration was performed, and, some time after, a drainage tube was inserted by Dr. Ashhurst. The woman was removed by her friends, but was alive a year after the operation.

Dr. Janeway, of New York, writes that he has met with one case of empyema of the left side, in which the tumor was situated in the left second interspace, which pulsated when the patient stood erect, but when the patient was lying down air filled the sac.

These cases, with the thirty-eight collected from literature by Comby and Kepler, make a total of forty-two cases. The condition is almost invariably met with on the left side. In only three instances, those of Kepler, Heyfelder,[3] and Geigel,[1] was the empyema in the right side. Kepler thinks there may have been a doubt in Heyfelder's case, but the report seems perfectly clear. The tumor appeared between the second and third ribs on the right side, and pulsated distinctly. It may possibly have been a mediastinal abscess, as it was close to the pleural margin. Only eight ounces of pus flowed out when punctured.

In the case of Geigel, a man, æt. fifty-seven, had in the right mammary region a prominent projection which pulsated synchronously with the heart. The case terminated fatally. Between six and seven pounds of pus were found in the pleura.

Empyema existed in all the cases, with the exception of one reported by Kepler, from Eichhorst's clinic, in which the fluid was serous. It occurred in a boy æt. fourteen, who, fourteen days before his admission, had been seized with a severe pain on the right side, and shortly afterward great tenderness at the seventh rib. There was dulness at the right base, which rapidly increased until it reached the angle of the scapula, and within a few days there were signs of effusion in the right thorax. On first examination the right side was enlarged, intercostal spaces prominent. There was active pulsation over the antero-lateral region of the right side of the chest reaching as high as the third rib, and synchronous with the movements of the heart. The apex-beat of the heart was 1.5 cm. above the nipple in the left mammary line. On account of suffocative symptoms aspiration was performed and 800 c. cm. of pure serous fluid removed. At a second puncture 200 c. cm. more were removed. Pulsation ceased after the withdrawal of the fluid. In fourteen days the fluid reaccumulated. An exploratory puncture showed it to be pus, and the operation for empyema was made. The seventh rib was resected and 300 c. cm. of pus removed.

In only two instances of Kepler's series was pyopneumothorax present. One reported by Féréol,[2] a man æt. twenty-two, had, in July, 1882, left-sided serous effusion, which was tapped, and he recovered. On October 27th there was again a large left side effusion with air. The beat was at the right nipple, and about the end of November pulsation of

[1] Abstract by Kepler, l. c.

[2] Quoted by Kepler.

the whole left side was noticed, synchronous with the heart. It was most marked behind and in the axilla. The aspiration of 2½ litres of pus abolished the pulsation. In Dillingham's case the man had pneumothorax.

To these cases must be added the one which I here report, and the cases of Henry and Janeway, in both of which there was evidently air in the pleura.

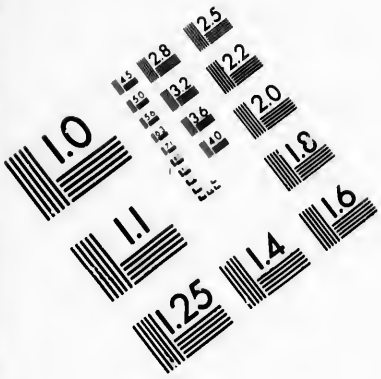
Two groups of cases may be recognized: 1, the intra-pleural pulsating pleurisy; 2, the pulsating empyema necessitatis, in which there is an external pulsating tumor. The latter condition, the most common, occurred in twenty-five of the forty-two cases, probably also in a larger proportion, as there are several reports with very scanty details. The external tumor is usually single, but in five cases there were two tumors, and in one, Dr. Henry's case, three. The perforation of the pleura usually occurs in the anterior aspect of the chest, from the second to the sixth rib, sometimes close to the sternum. In three cases the tumor appeared posteriorly—at the spine, at the angle of the scapula, and in the lumbar region. In the intra-pleural cases the pulsation is usually in the antero-lateral region of the affected side, and may be evident on palpation only, or, as in the case here reported, it may be visible even at a distance.

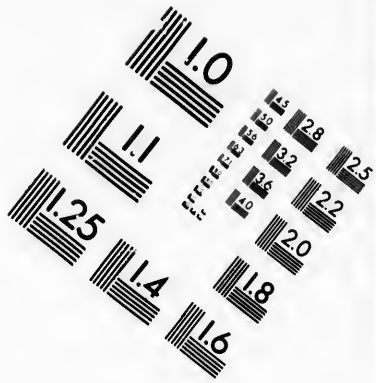
Pulsating pleurisy usually occurs in cases in which the fluid has existed for some time, but that it may occur in acute cases, even with a serous exudation, is illustrated by Kepler's patient. In Ross's case and in mine the condition was also acute.

Various explanations of the phenomenon have been offered. Dr. Broadbent[1] suggests that it occurs when adhesions exist between the layers of the pericardium and between the pericardium and the chest wall. But that this cannot hold good in all cases is shown by reports of post-mortems in which such adhesions were not present. Traube regarded destruction of the costal pleura, and marked paresis of the intercostal muscles as the conditions which rendered pleurisy possible. In the case which I have reported, there was persistent tenderness of the thoracic walls, suggestive, to say the least, of involvement in an unusual degree of the parietal structures, but there was no œdema or special protuberance of the spaces, and the condition came on too early to have been due to destructive changes in the pleura. It was probably due to extreme distention of the side. Bouveret, in his recent monograph on empyema,[2] holds that the pulsation is met with whenever the resistance of the thoracic wall is greatly reduced, as in the way Traube suggests, or when the resistance on the part of the diaphragm is heightened, as by the deposition of a thick layer of fibrin. The fact that the abstraction of a very small quantity of fluid will at once abolish the pulsation, indicates

[1] Lancet, 1884.

[2] Traité de l'empyeme, par L. Bouveret, Paris, 1888.





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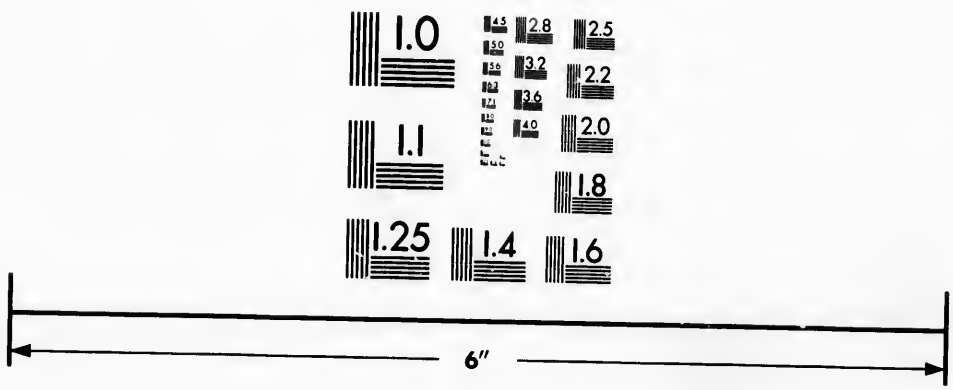

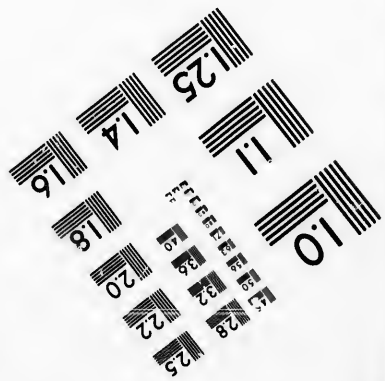

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that a certain degree of pressure is a necessary condition. Comby thinks that the pulsation only occurs when the lung is compressed and adherent to the pericardium, so that the heart movements are communicated through it to the pleural fluid, and so to the chest wall. Féréol makes a somewhat similar suggestion, holding that in every instance the condition is one of pneumothorax, in which air forms an elastic cushion between the pericardium and the fluid through which the pulsations of the heart are directly transmitted to the chest wall.

The cases have been mistaken for aneurism, and the situation in which the pulsating empyema necessitatis usually develops renders the error very pardonable. The doubt can readily be solved with a fine hypodermic needle.

The prognosis in pulsating pleurisy is not very favorable. Of the thirty-eight cases in Kepler's series, seventeen died. But we must remember that most of these cases occurred before the days of safe and frequent operations upon the chest wall.

Complete evacuation of the fluid with free and permanent drainage meets the indications for treatment.

[*Reprint from "Transactions of the Medical and Chirurgical Faculty of Maryland" for 1889.*]

ANNUAL ADDRESS.

THE LICENSE TO PRACTISE.

By WILLIAM OSLER, M. D.
Professor of Medicine, Johns Hopkins University, Baltimore.

Mr. President and Gentlemen:—I shall not offer any apology for making the "License to Practise" the subject of my address, as it is one in which all, high and low, rich and poor, lay and professional, are deeply interested. I am fully aware that it is a subject thought to require the delicate handling which we are accustomed to give to topics arousing heated discussion, and upon which diametrically opposite views are held. Still as the question agitating the profession to-day, it requires to be persistently and thoroughly ventilated, and those who have opinions on the subject should speak out in no uncertain tones. I have not had an opportunity of ascertaining the feelings of the members of this ancient and honorable Faculty on the question, one which touches closely, I believe, certain vested rights of this body; but I have learned that three years ago a Bill for a State Board was rejected, so I presume the matter has often been before you. I am the more emboldened, therefore, to speak freely, knowing full well that I address men who have given time and thought to the problem, who know its difficulties, and who appreciate its importance.

In this country a man can follow the vocation he pleases, subject only to such restrictions as may be necessary for the public welfare. The right to regulate the practice of medicine rests with the State, and I believe it is acknowledged that this right comes within that general police power which extends protection to the life and limbs of the citizens. At present, this power is very variously exercised in different States. In

many, no regulations whatever exist. Any one who wishes, irrespective of qualifications, can practise. In a majority, however, there are restrictions which demand evidence on the part of the practitioner that he has studied, for a longer or a shorter period, at an incorporated school. Practically, the rule prevails that with a diploma from a chartered school he can begin at once, without any hindrance other than that relating to registration. The educational duties of the State do not here extend beyond the system of common and normal schools, though, in a few higher university work is also undertaken. Special education does not receive support from the public revenues. Schools of law, medicine, engineering, theology, all the special branches of study, are private enterprises, chartered by the State and maintained by fees from pupils, or by the munificence of private friends. Certain privileges are granted to these Institutions by the State, the most important of which, in the medical school, is the recognition of the diploma as a qualification for practise. So unsatisfactory, however, has this system proved, that there is on the part of the public, and of the profession, a growing sense of the necessity for radical changes, as shown by the number of cases in which bills have either been already passed, or have been before the legislatures dealing with the problem.

It is universally conceded that the basis of legislation is the necessity of protecting the people against the depredations of ignorant graduates and of quacks. The aim is to provide a minimum standard of qualification to be exacted of all persons who desire to follow the calling of physician and surgeon.

Whilst we find Legislatures everywhere willing to support enactments necessary for the safety of the public, they will not (and it is right that they should not) support class legislation: and herein lies one of the chief difficulties.

If we look around upon those engaged in the practice of medicine, we find that an overwhelming proportion belongs to the regular, or so-called, old school. A second small division professes to follow the precepts of Hahnemann; while a third, still smaller, neither one thing nor the other, but a little of both, professes a judicious eclecticism. These three bodies have schools, medical journals, and in each State a more or less complete organization. In the eyes of the law (which

rightly disregards medical theories), all are equal. This unhappy division of the body medical is not limited to professional matters, but is complicated with ethical questions of the highest moment. The outcome of it all has been that there are hostile camps and bitter war.

The homœopathists and the eclectics, will, I think, concur in the necessity of a full and proper curriculum of study in the great branches of medicine. Anatomy, physiology, chemistry, histology, embryology, medicine, surgery, obstetrics, gynæcology, and medical jurisprudence know no "isms." The differences only become glaring when we touch the subject of Therapeutics, a subject in which amongst members of each of the so-called schools the greatest individual differences of opinion exist. So strong, however, is the feeling (largely an ethical one), that the divergence of opinion on this one branch separates absolutely the different classes of practitioners from each other; and I do not say that this should not be so, while antiquated dogmas are professed in opposition to a rational and a free science.

We cannot, however, escape from the important fact that in the eyes of the law we all stand equal, and if we wish legislation for the protection of the public, we have got to ask for it together, not singly. I know that this is gall and wormwood to many—at the bitterness of it the gorge rises; but it is a question which has to be met fairly and squarely. When we think of the nine or ten subjects which we have in common, we may surely, in the interest of the public, bury animosities and agree to differ on the question of Therapeutics.

In connection with the license to practise, there are, it seems to me, three courses open: 1. A continuance in the plan at present, widely prevailing, which makes the college the judge of the fitness of the candidate; and State supervision is only so far exercised that the diplomas are *visé*, and registered, if from legally incorporated schools. 2. The appointment by the State or by parties so deputed of a board of examiners, which shall, irrespective of diplomas, examine all candidates for the license. 3. The organization of the entire profession in each State into an electorate, which shall send representatives to a central parliament, having full control of all questions relating to medical education, examination and registration.

These various places are at present in operation in different parts of the Continent; let us see how they work.

And first of the colleges, which have practically had a monopoly for years, as the diploma has carried with it the privilege of registration.

To all intents and purposes the medical schools of the country are private organizations, managed in the interest of the professors, who, with scarcely an exception, have direct pecuniary interests in the size of the classes. The greater the number of students and graduates, the larger the fees, and the higher the income of the teachers. The running expenses and the interest on the moneys expended for the teaching-plant are the first call, after which the balance is divided. These chartered corporations are wholly irresponsible, without supervision by the State, the profession or the public. It would not be difficult, without fear of just rebuke, to bring a railing accusation against them for persistently acting in their own, and not in the interests of the public. But the time has passed for this. Yet, it is surprising to think that so many men, distinguished in every way in their profession, cultured and liberal, still cling to, and even advocate, the advantages of an irresponsibility, which has made the American *system* of medical education a by-word amongst the nations.

Let me not be misunderstood. These very men are, in many instances, those whom we delight to honor, with names which will last as long as American medicine. Yet, to an unbiased mind, there can be no hesitation in affirming that the system which has been permitted to develop in our midst has done, nay, is doing, irreparable wrong. But, it may be urged, on the part of the schools, that they are what the profession wishes. The stream does not rise higher than its source. I do not think that this holds good at present. It does not require a very wide professional acquaintance to gather, that there is now developing, throughout the length and breadth of the land, an earnest desire to support a higher medical education, and this is borne out by the success which has attended the tentative efforts in the direction of the larger schools, which have made a three years' college course compulsory.

Here, let me remind those doctors who talk loudly of medical reform, of the selfishness of schoolmen, of the difficulty in

getting colleges to advance, that very much rests with the degree of support given by them to those schools which really make sacrifices for the elevation of the standard. If, for instance, the University of Pennsylvania or Harvard, or the College of Physicians and Surgeons in New York, or the University of Maryland, were to extend to four full years the course of study, there would be at each of these schools, without the slightest doubt, a falling off in income, from the reduction in the number of students; so much so, that it would be impossible to run these large establishments at their present full equipment. Manifestly, it would be suicidal, without the guarantee of outside aid, to imperil corporate interests of such magnitude. But if, on the other hand, those physicians throughout the country, who strongly favor a four years' course as the minimum in which a man can obtain a reasonable knowledge of the science and art of medicine, if these men were to direct their students to such institutions (and in this matter we all know how much influence the physician has), the problem would be at once solved.

Too often college faculties seem stricken with timidity in the presence of suggestions to lengthen the curriculum and to raise the standard. Yet, a superficial study of the history of the movement since 1871 and 1872, when Harvard so nobly took the lead, should be convincing to all that even from the lowest considerations the advance should be successful. You have but to look to the condition of the schools which have been in the van, to see that the bread cast upon the waters has already been found. I do not say that these schools are in all instances the most prosperous numerically. Heaven forbid; that is not a standard of merit. But, take the laboratory equipment, the measure in which they fulfill medical requirements, the practical teaching and the development of clinical instruction, and I say, without fear of contradiction, that these schools have met with an ample and a just reward. And yet, these are the very schools which clamor loudest for further advance, showing how dangerous it is to arouse the slumbering conscience, and to abandon the conviction that a two session course is sufficient for the average American student. But in spite of all that has been done, in spite of the agitation which has been so active during the past ten years, the sad truth must be told, that a

large percentage of doctors are graduated annually after only two sessions of study.

On paper, the two session schools almost universally demand three years; one of which, it is stated, may be with a physician. Now, it is notorious in these schools that a large majority of the men receive the degree at the end of the second college year, and it is just as notorious that not 5 per cent. of the cases in which a preliminary year of study has been passed with a physician is a *bona-fide* period of medical instruction. It practically amounts to this, that a man enters without any fair preliminary test as to elementary education, say on the first of October of the present year; and eighteen months from date, or rather seventeen months, sometime in March, 1891, he will be let loose upon the commonwealth. Eighteen months in which to master one of the highest, as it certainly is one of the most difficult of the professions which man is called upon to practice! That, gentlemen, these are facts, sad facts, each one of you knows. Yet so blind do men seem in this matter, so wedded to this pernicious system, that I have known physicians in large practice, able, cultivated men, contributors to medical literature, standing high in the esteem of their brethren, permit their sons to follow out this curriculum. Picture, if you can, the mental condition of such a graduate; an incoherent jumble of theories, a chaotic assortment of what he would call practical tips. But this question has its tragic side, which completely overshadows everything else. It makes one's blood boil to think that there are sent out year by year scores of men, called doctors, who have never attended a case of labor, and who are utterly ignorant of the ordinary every day diseases which they may be called upon to treat, men who may never have seen the inside of a hospital ward, and who would not know Scarpa's space from the sole of the foot. Yet, gentlemen, this is the disgraceful condition which some school men have the audacity to ask you to perpetuate; to continue to intrust interests so sacred to hands so unworthy. Is it to be wondered, considering this shocking laxity, that there is a wide-spread distrust in the public of professional education, and that quacks, charlatans and impostors possess the land?

But the handwriting is on the wall, the interpretation has been read, and the propheey indeed is in course of fulfillment. It needs not the vision of a son of Beor to advertise that within ten years in searcely a State of the Union will the degree carry with it the privilege of registration; and with this removal of the kingdom from the schools will dawn a new era for the profession in this country. This will happen when unrestricted competition between the colleges and the total absence of professional and State restraint are things of the past.

Under the second plan the entire question of registration is placed in the hands of examiners, appointed by the Governor, or by the State societies. Such a board, to be effective, must constitute the only portal to practice. The practical working, as shown in North Carolina, Virginia and Minnesota, presents no difficulty, and it constitutes an effective barrier against the inroads of poorly qualified graduates. Within a few years this measure will be widely adopted. It has certain advantages in a simple mechanism, and in clearly defined duties. But the powers are too limited, and there is no control of education, preliminary and special, such as comes strictly within the power of the profession in each State.

The record of the Virginia Examining Board for the four years ending October, 1888, is an excellent illustration of the good which may be done. Of 240 candidates examined, 54, or 22 per cent., were rejected, a percentage which might be increased considerably if practical examinations were instituted in the practical branches.

Ultimately I believe a more elaborate plan will prevail, more difficult to organize, but practical, and possessing the great advantage of giving the control of the profession into the hands of the practitioners, and of doing away forever with the minority rule of the college.

Theoretically, there can be no question (particularly in democratic communities) that a State board should be elective, not appointed by the Governor or the societies. An elective board is in reality a medical parliament, which should take cognizance of all matters relating to medical education, and perhaps, though of this I am not so sure, of questions of public health within the State. The assembly districts, or other territorial divisions which might be made, would send one, or

perhaps two, representatives to the board (depending upon the professional population in each district). The electors would be constituted by all practitioners irrespective of schools, which had registered at a certain date. A man who had practiced, even without a diploma, for a certain time would, under these circumstances, have to be recognized and permitted to register. The Governor of the State would issue the first warrant for the election, which would subsequently be the prerogative of the executive of the board. It might be necessary, at first, to have, from each district, members returned from at least three of the divisions which at present constitute practitioners. The representation should be per capita, the number of constituents in each electorate to be previously arranged. The term of the board should be, at least, four or five years, and members should be eligible for re-election. Conducted by ballot, there should not be the slightest difficulty in carrying out such an election. There would be, of course, active canvassing, and perhaps, many nominated from one district. Though there would be opportunities for political trickery and gerrymandering, I think, on the whole, it would be found that an election could be conducted with tolerable purity. The universities and schools would have full representation on the board. To such an organization, I believe, might be intrusted the control of all matters relating to medical education in the State. It would correspond to the law societies, and to the synods and conferences of the various religious denominations. The powers of such a board would be accurately defined by legislation, and should relate first to preliminary education; secondly, to the examination and registration of candidates for the license to practice; and thirdly, the control of all matters relating to discipline with the profession. The necessary expense would be met—first, by the fees paid by the candidates for examination; secondly, by a small annual tax levied upon all registered practitioners. Such a body could look forward hopefully to a permanent establishment in each State, with buildings suitably equipped for examination, and with every possible provision for conducting, in an orderly and systematic manner, the business of the profession.

The first important function of the board would be the regulation of the minimum standard of education required on

entering the profession. It is perfectly legitimate that the profession should say, through its representatives, what should be the qualifications of a candidate who desires to enter upon the study of medicine. In law this holds good; why should it not be so with us? A guarantee of uniformity would thus be given which cannot be expected in the schools. The examiners at the preliminary test should be independent teachers, not professional men, and the examinations could be arranged in different parts of the State. The period of study would date from the passing of this preliminary examination. Such a measure would effectually prevent the entrance of men whose education was such that they could not subsequently grapple with the subjects of professional study.

The examination and registration of candidates would constitute the most important function of the board.

Upon no question will there be a greater diversity of opinion than upon the selection of examiners. The opposition to State Boards on the part of school men is very largely based on the doubt which they have as to the selection of thoroughly equipped men for this work. On the part of the profession such a feeling exists that would prevent the appointment by the board as examiner on his own subject a teacher in any school. The difficulties, however, are not insuperable. With the proper system of numbers for written examinations, and with two examiners at every oral, there could not be the slightest objection, so far as I can see, to the selection of school men as examiners in certain of the branches. In anatomy, chemistry, physiology and pathology, that is to say in all the scientific branches, it would be almost impossible to secure from the general profession examiners with the necessary training. It certainly would be most unjust to well-equipped students from the laboratories of our first-class schools to subject them to examination on these branches by men who had crammed on purpose from two or three of the most recent text books. On the other hand, in the more practical subjects, there are certainly in each State to be found men fully capable of conducting the necessary test work. I have the honor to know personally, in many States of the Union, men to whom I would entrust with the utmost confidence the examination of my students in the theory and practice of medicine, and I

doubt not that in surgery, midwifery, gynæcology, and in the polyglot subject of therapeutics men equally able in these departments would be forthcoming.

There need not be any difficulty in the existing differences between the various schools of practice. All students would be examined in the great primary divisions, anatomy, physiology and chemistry, and so also in pathology and morbid anatomy, obstetrics, and in operative gynæcology and in medical jurisprudence.

The examinations in these branches would be uniform. In therapeutics only would there be separate tests for regulars, homœopathists and eclectics. On application, the student would have to indicate for which of the three he wished to apply, and, if successful, would be placed in one of the three divisions of the State Register. I am free to confess that this scheme may, to some, seem Utopian, but I am firmly convinced that the majority of those that hear me to-day will live to see State Boards organized on this, or upon a modified plan.

With the third function of the Board, viz., that relating to discipline, I need not detain you further than to say that in any effective act there should be penal clauses giving authority to prosecute irregular and unlicensed practitioners; to remove for cause a name from the register; and to exercise such additional powers as might, in the opinion of the framers of the bill, be thought justifiable.

Now the entire feasibility of such a scheme is illustrated by the professional history of the Province of Ontario. Up to 1865-6 there was a Licensing Board appointed by the State, which dealt, however, in examinations only in the case of candidates without diplomas, but to all intents and purposes it was simply a Board of Registration to which holders of degrees presented themselves, paid a small fee and obtained the license. The schools practically controlled it.

In the session of 1865-6 the profession of the Province sought incorporation, and the Act was framed which, with certain important modifications, at present remains in force. It practically hands over to the profession, through the elected representatives, the management of their own affairs so far as they relate to preliminary and professional examinations and certain disciplinary enactments. In spite of the strenuous oppo

sition on the part of many who felt that it was a most degrading thing thus to lop the important privilege hitherto held by the Universities which enabled graduates to obtain the license without further examination; in spite of dissensions and dissatisfaction, such as are almost inevitable in connection with a new organization, the Board has persisted in its good work, and to-day, after 23 years of existence, it has a record of which the entire profession of the Province is most justly proud. On no point was opposition more bitter or more prolonged than on the admission to representation of members of the homœopathic and eclectic bodies. My very first introduction to the profession was a visit with my preceptor to the committee room of the House, in which certain amendments to the Act were being pushed by the colleges. I can recall with vividness the heated dispute with reference to this very question of admission of the homœopathists and eclectics to proportionate representation. It was thought to be a defilement even to come near unto the unclean thing. But wise counsels prevailed, and representation remained general, as it was, though it is true, I believe, that the eclectic body no longer has practitioners enough in the Provinces to send a representative.

The influence which this organization has exerted has been in the highest degree beneficial, and the schools now accept the inevitable with a perfectly good grace. The Board possesses a magnificent central building in which to conduct the examinations, with offices for registration and rooms for a Provincial Library. The fees from the examinations and a small annual tax levied on each registered practitioner have proved sources of ample income.

The same condition, with modifications, exists in the other British Provinces.

To those who look upon such a scheme as I speak of as Utopian, and urge difficulties on account of the deeply-seated prejudices and wide dissensions existing between the schools, I might say that the condition here is practically the same in kind, though perhaps greater in degree, to that which existed in the British Provinces prior to 1866. What has been done there so successfully can be equally well accomplished in every State of the Union.

The great gain is the public guarantee that when a man has received the license to practise, he has, at any rate, the elements of a solid education; that he knows the structure and functions of the human body; and that he is capable of meeting the ordinary emergencies of professional life. Such a plan removes the irresponsibility of the schools, establishes a uniform curriculum of studies in each, and exacts a minimum time for theoretical and practical work.

The difference is simply this, that under our present system independent and irresponsible schools have the upper hand and dictate terms to the profession and to the public, and do whatever they please. With an organized profession, through its representatives in session, the schools take the second place —they exist for the profession and the public. There can be no question as to the great superiority of this method. It is essentially democratic, and should commend itself in every particular to the profession of this country. It is infinitely superior to the second method carried on at present in many of the States, although the Examining Boards nominated by the Governor or the societies are better than unrestricted registration. While the interests of corporations are fully represented in this system, they have not the overshadowing power such as was granted in Great Britain by the recent Act in which it seems almost ridiculous to think that only six representatives from the profession at large found a place in a Board, and this number grudgingly granted as a privilege, not as a right.

It does not do, however, to underestimate the difficulties which have to be encountered in any attempt to organize these Boards. It may be premature in many States. The profession, I have frequently heard it stated, is not ready for it. This, from my own observation, I should doubt. I believe the general body of the profession, when it fully understands the question, cannot but agree that the method is in reality a safe one. I am sure that the public, through the press, will heartily concur in any plan which will guarantee that the practitioners to whom they entrust life and limb shall be educated men.

Opposition will be strongest on the one hand from the schools, which look askance at any measure likely to interfere with their prerogatives, and on the other hand, the members of the homœopathic and eclectic fraternity, not unnaturally dread

lest in any such arrangement a full measure of justice should not be meted them.

The antagonism of the schools is not, I believe, serious. To be effectual they would have to be united. It is notorious that many of the Faculties, or perhaps, more truly, many of the prominent members in each Faculty, urgently support State Boards, and a return to the old and normal condition in which a university degree partook somewhat of the nature of an honor, and had no relation to the license to practise. The opposition from the homœopathists and eclecties need not be serious. They profess to seek for better things and to look for a higher standard of examination. If we are truly anxious to deal fairly with them in a matter, not relating so much to our own as to the interests of the public, I am quite sure that we shall find them ready and willing to join hands in such a laudable work. Nor must we talk to them of concessions, but acknowledge plainly their rights, which before the law are the same as our own.

To move surely we must move slowly, but firmly and fearlessly, confident of the justness of our claims on behalf of the profession and of the public, and animated solely with a desire to secure to the humblest citizen of this great country in the day of his tribulation and in the hour of his need, a skill worthy of the enlightened humanity which we profess, and of the noble calling in which we have the honor to serve.

ÆQUANIMITAS:

VALEDICTORY REMARKS

TO THE GRADUATES IN MEDICINE OF THE UNIVERSITY OF PENNSYLVANIA, MAY 1ST, 1889.

BY

WILLIAM OSLER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE.

PHILADELPHIA:
PRESS OF WM. F. FELL & CO.,
NOS. 1220-24 SANSOM STREET.
1889.

ÆQUANIMITAS.

Gentlemen.—Custom, which lies upon us with a weight, heavy as frost, has made even stale to many these imposing annual ceremonies. To you at least of those present they should have the solemnity of an ordinance—called as you are this day to a high dignity and to so weighty an office and charge. You have chosen your Genius and have passed beneath the Throne of Necessity, and with the voices of the fatal sisters still ringing in your ears, will soon enter the plain of Forgetfulness and drink of the waters of its river; but ere you are driven all manner of ways, like the souls in the tale of Er the Pamphylian,* it is my duty to say a few words of encouragement and to bid you, in the name of the Faculty, God-speed on your journey.

I could have the heart to spare you, poor careworn survivors of a hard struggle, so "lean and pale and leaden-eyed with study;" and my tender mercy, which has been ever towards you, even now extends so far as to permit me to consider but two of the score of elements which will make or mar your lives, two which may contribute to your success, or, more important to many, help you in the days of failure.

In the first place, of all qualities in the physician or surgeon no one takes rank with imperturbability, and I purpose for a few minutes to direct your attention to this most essential bodily virtue. Haply those of you in whom it has not developed during the critical scenes of the past month may catch a hint or two of its importance, perhaps a prescription for its preparation. It means coolness and presence of mind under all circumstances, calmness amid the storm, clearness of judgment in moments of grave peril, immobility, impassiveness or, to use an old English and most expressive word, phlegm. It is the

* The Republic, Book X.

quality of all others which is appreciated by the laity though often misunderstood by them; and the physician who has the misfortune to grow up without some share of it, who betrays indecision and worry and who shows that he is flustered and flurried in ordinary emergencies loses rapidly the confidence of his patients.

In full development as we see it in some of our older colleagues it has the nature of a divine gift, a blessing to the possessor, a comfort to all who come in contact with him. You should know it well, as for years there have been before you several striking illustrations, the example of which has, I trust, scored deeply. Largely a bodily endowment, there are those amongst you, I regret to say, who may never, owing to congenital defects, be able to acquire it. Education will do much, and with practice and experience the majority of you may expect to attain to a fair measure. The first essential in the development of imperturbability is to have your nerves well in hand. The physician or surgeon who under any circumstances, no matter how serious, allows "his outward action to demonstrate the native act and figure of his heart in complement extern," in other words, who shows in his face the slightest alteration, expressive of anxiety or fear, has not his medullary centres under the highest control and is liable at any moment to disaster.

I have spoken of this to you on many occasions, and have urged you so to educate your nerves centres that not the slightest dilator or contractor influence shall pass to the vessels of your face under any professional trial. Far be it from me to urge you, ere Time has carved with his Hours those fair brows, to quench on all occasions the blushes of ingenuous shame, but in dealing with your patients emergencies demanding such should certainly not arise, and an inscrutable face may prove a fortune. In its perfect and true form imperturbability is indissolubly associated with a wide and ever increasing experience and an intimate knowledge of the most varied aspects of disease. Nothing that can happen disturbs the mental equilibrium as the conditions are familiar, the possibili-

ties manifest, the course of action clear. This precious quality is liable from its very nature to be misinterpreted, and the general accusation of hardness so often brought against the profession has here its foundation. Now a certain measure of insensibility is not only an advantage but a positive necessity in the exercise of a calm judgment, and in carrying out delicate operations. A keen sensibility is doubtless a virtue of high order, but if it interferes with steadiness of hand or coolness of nerve, a callousness which thinks only of the good to be effected and goes ahead regardless of minor considerations is preferable wisdom in the working-day-world of the doctor.

Cultivate then, gentlemen, that judicious measure of obtuseness which while it enables you to meet the exigences of practice with firmness and courage, does not at the same time harden "the human heart by which we live."

In the second place, there is a mental equivalent to this bodily endowment, which is to a man on his pilgrimage as important as imperturbability to the surgeon. Let me recall to your minds the incident related of that best of men and wisest of rulers, Antoninus Pius, who, as he lay dying, in his home amidst the Apennine hills, summed up the philosophy of life in the watchword Æquanimitas. As for him, about to pass *flamantia mœnia mundi*, the flaming rampart of the world, so for you fresh from Clotho's spindle a calm equanimity is the desirable attitude. How difficult to attain, yet how necessary in success as in failure! Natural temperament has much to do with its development, but a clear knowledge of our relation to our fellow creatures and to the work of life is an indispensable factor. One of the first essentials in securing a good-natured equanimity is not to expect too much of the people amongst whom you dwell. "Knowledge ~~grows~~ but wisdom lingers," and the average citizen of to-day has not, in matters medical one whit more sense than the old Romans, whom Lucian scourged for a credulity which made them fall easy victims to the quacks of the time; such as the notorious Alexander, whose exploits make one wish that his advent had been

delayed some eighteen centuries. Deal gently then with this deliciously credulous old human nature in which we work, and restrain your indignation, when you find your pet parson has triturates of the 1000th potentiality in his waistcoat pocket, or you discover accidentally a case of Warner's Safe Cure in the bedroom cupboard of your best patient. It must needs be that offences of this kind come; expect them, and do not be vexed.

They are curious, odd compounds these fellow creatures, at whose mercy you will be; full of fads and eccentricities, of whims and of fancies. I do not mind telling you, Gentlemen of the graduating class, a secret which I would not for my cap and gown mention in public. It is this: the more closely we study their little foibles of one sort and another in the inner life which we see, the more deeply is the conviction borne in upon us of the similarity of their weaknesses to our own, until we weary of a uniformity which would be intolerable did not a happy egotism render us oblivious. Hence the need of an infinite patience and of an ever tender charity toward them; have they not to exercise the same to us?

A distressing feature in the life which you are about to enter, a feature which will press hardly upon the finer spirits among you and ruffle the equanimity, is the uncertainty which pertains not alone to our science and art, but to the very hopes and fears which make us men. We aim at the unattainable in seeking absolute truth and must be content with broken portions. You remember in the story how the Egyptian Typhon with his conspirators dealt with good Osiris; how they took the virgin Truth, hewed her lovely form into a thousand pieces, and scattered them to the four winds; and as Milton says "from that time ever since, the sad friends of truth, such as dost appear, imitating the careful search that Isis made for the mangled body of Osiris, went up and down gathering up limb by limb as they could find them. We have not yet found them all," but each one of us may pick up a fragment, perhaps two, and in moments when mortality weighs less heavily upon the spirit, we can, as in a vision,

see the form divine, just as a great Naturalist, an Owen or a Leidy, can reconstruct an ideal creature from a fossil fragment.

It has been said that in prosperity our equanimity is chiefly exercised in enabling us to bear with composure the misfortunes of our neighbors. Now, while nothing disturbs our mental placidity more sadly than straitened means, and the absence of all those things after which the Gentiles seek, I would warn you against the trials of the day soon to come to some of you, of large and successful practice. Engrossed late and soon in professional cares, getting and spending, you may so lay waste your powers that you may find too late, with hearts given away, that there is no place in your habit-stricken souls for those gentler influences which make life worth living.

It is sad to think that for some of you there is in store disappointment, perhaps failure. You cannot hope, of course, to escape from the cares and anxieties incident to professional life. Stand up bravely even against the worst. Your very hopes may have passed on out of sight, as did all that was near and dear to the Patriarch at the Jabbok ford, and, like him, you may be left to struggle in the night alone. Well for you if you wrestle on, as in persistency lies the victory, and with the morning may come the wished for blessing. But not always, for there is a struggle with defeat, and this some of you will have to bear. Well for you in that day if you shall have cultivated a cheerful equanimity; remember, too, that sometimes "from our desolation only does the better life begin." But even with disaster ahead and ruin imminent, face it with a smile and with the head erect rather than crouch beneath the blow. And if the fight has been for principle, for justice, even when failure seems certain where many have failed before, cling to your ideal, and, like Childe Roland before the Dark Tower, set the slug-horn to your lips, blow the challenge, and calmly await the result.

It has been said that "In *patience* ye shall win your souls," and what is this but an equanimity which enables you to bear troubles and to rise superior to the trials of

life. Sowing as you shall do beside all waters, I can but wish that you may reap the promised blessing of quietness and of assurance forever, until

"Within this life,
Though lifted o'er its strife,"

you may in the growing winters glean a little of that wisdom which is pure, peaceable, gentle, full of mercy and good fruits, without partiality and without hypocrisy.

Gentlemen—The past is always with us, never to be escaped; it alone is enduring; but amidst the changes and chances which succeed one another so rapidly in this life we are apt to live too much for the present and too much in the future. On such an occasion, when the *Alma Mater* is in festal array, when we joy in her growing prosperity, it is good to hark back to the olden days and gratefully to recall the men whose labors in the past made the present possible.

The great possession of any University is its great names. It is not the "pride, pomp and circumstance" of an institution, not its wealth, nor the number of its schools, not the students who throng its halls, but the *men* who have trodden in its service the thorny road through toil, even through hate, to the serene abode of Fame, climbing "like stars to their appointed height." These bring glory; such bring honor: and it should thrill the heart of every alumnus of this school, of every teacher in its faculty, as it does mine this day, reverently and thankfully to recall such names amongst its founders as Morgan, Shippen and Rush, and such men amongst their successors as Wistar, Physick, Barton and Wood.

Gentlemen of the Faculty,—*Noblesse oblige.*

And the mortality of the past touches us to-day in the freshness of sorrow at the loss of friends and colleagues, "hid in death's dateless night." We miss from our midst one of your best-known instructors, by whose lessons you have profited, and whose example has stimulated many. An earnest teacher, a faithful worker, a loyal son of this University, a good and kindly friend, Edward Bruen has

left behind him, amid regrets at a career untimely closed, the memory of a well-spent life.

We mourn to-day, also, with our sister college, in the grievous loss which she has sustained in the death of one of her most distinguished teachers, a man who bore with honor an honored name, and who added lustre in his own to the profession of this city. Such men as Samuel W. Gross can ill be spared. Let us be thankful for the example of a courage which could fight and win; and let us emulate the zeal, energy and industry which characterized his career.

Personally I mourn the loss of a preceptor, dear to me as a father, the man from whom more than any other I received inspiration, and to whose example and precept I owe the position which enables me to address you to-day. There are those present who will feel it no exaggeration when I say that to have known Palmer Howard was, in the deepest and truest sense of the phrase, a liberal education :—

> "Whatever way my days decline
> I felt and feel, tho' left alone,
> His being working in mine own,
> The footsteps of his life in mine."

While preaching to you a doctrine of equanimity, I am, myself, a castaway. Reeking not my own rede, I illustrate the inconsistency which so readily besets us. One might have thought that in the premier school of America, in this Civitas Hippocratica, with associations so dear to a lover of his profession, with colleagues so distinguished, and with students so considerate, one might have thought, I say, that the Hercules Pillars of a man's ambition had here been reached. But it has not been so ordained, and to-day I sever my connection with this University. More than once, gentlemen, in a life rich in the priceless blessing of friends, I have been placed in positions in which no words could express the feelings of my heart, and so it is with me now. The keenest sentiments of gratitude well up from my innermost being at the thought of the kindliness and goodness which have followed me

at every step during the past five years. A stranger, I cannot say an alien among you, I have been made to feel at home—more you could not have done. Could I say more? Whatever the future may have in store of successes or of trials, nothing can blot the memory of the happy days I have spent in this city, and nothing can quench the pride I shall always feel at having been associated, even for a time, with a Faculty so notable in the past, so distinguished in the present, as that from which I now part.

Gentlemen,—Farewell, and take with you into the struggle the watchword of the good old Roman—***Æquanimitas.***

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Extracted from the
American Journal of the Medical Sciences for September, 1889.

LAR ATROPHY,
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[Reprinted from THE MEDICAL NEWS, September 7, 1889.]

TIMORE.

NOTE ON INTRA-THORACIC GROWTHS DEVELOPING FROM THE THYROID GLAND.

BY WILLIAM OSLER, M.D.,
PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE.

IT has been shown that portions of thyroidal tissue may be met with anywhere from the base of the tongue to the heart, and in regions lying between these points the so-called struma tumors may be found, or even in rare instances within the trachea. Thyroidal growths also occur within the thorax, most commonly sub-sternal in position, and connected directly with the gland. Of these a number have been described (Virchow, *Geschwülste*, Bd. 3). More rarely tumors develop from the deeper portions or aberrant bits of a lateral lobe and extend into the chest, forming large intra-thoracic growths.

A most remarkable case is reported by Dettrich (*Prager med. Wochenschrift*, No. 31, 1887). In a woman, aged sixty, who had suffered for some time with cough and hæmoptysis there was found, filling the greater part of the right side, a cystic tumor the size of a man's head. It was covered by the parietal pleura and naturally caused great compression of the lung. Above, it was connected with the right lateral

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lobe of the thyroid. The cyst had yellowish-brown contents and contained cholesterin. Kretschy (*Wiener med. Wochenschrift*, 1877) describes a sarcoma of the thyroid, four and three-quarters inches in length, which formed an extensive mediastinal tumor passing to the level of the ninth dorsal vertebræ.

In the following case, No. 702, Post-mortem Records, Montreal General Hospital, there was a tumor similar in situation to Dettrich's, though not so large:

The patient, a woman, had died with symptoms of purulent bronchitis. There was no special emaciation. Occupying the top of the left thoracic cavity, outside the pleura, was a mass the size of a large orange, closely attached to the œsophagus. The arch of the aorta lay on the right side, the left subclavian passed directly over it and the left carotid passed just beside it. There was no special connection with any thoracic organ, though filling completely the top of the left thorax. There was a large bronchocele, the left lobe of which was in contact with the tumor and could not be isolated from it.

On section, it consisted of a series of imperfectly separated cysts containing a yellow-brown fluid in which were plates of cholesterin. The upper part of the tumor was firm and hard; some of the septa had calcified, others had a fibro-cartilaginous consistence.

The relations of this mass, its anatomical character, and the nature of the contents of the cysts, identical with that which is found in so many cases of old

Extracted from the
American Journal of the Medical Sciences for September, 1889.

bronchocele, leave no question that it had developed from an outlying lobule of the left thyroid.

In connection with the case of Kretschy, above referred to, a somewhat similar instance was reported by me a few years ago (*Montreal General Hospital Reports*, Vol. I., 1880):

A girl, aged sixteen, had been under treatment for what appeared to be ordinary bronchocele. It had grown with great rapidity. There was marked difficulty in breathing and the question of tracheotomy was considered, but, as the dyspnœa became easier, the operation was deferred. Death occurred suddenly. Post-mortem, a tumor was found which involved exclusively the left lobe of the thyroid and formed a large round mass eight inches in circumference; above it extended to the level of the thyro-hyoid ligament, while below it passed down beside the trachea to the bifurcation. From behind, the mass had an elongated, somewhat oval shape; the lower end rested upon the left bronchus. Along this surface it measured one and three-quarters inches in length. At the upper right angle of the mass in front was a small thin remnant of the left lobe capping the tumor, the tissues of the two blending, not separated by a capsule. The right lobe of the thyroid was of normal size and appearance. Histologically the growth consisted of small lymphoid corpuscles.

I reported this case as one of lympho-sarcoma of the deep cervical glands involving the thyroid and simulating goitre, but I have no doubt now that it was a case similar to Kretschy's, in which the growth developed from a thyroidal lobe with extensions down the trachea.

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ON A CASE OF SIMPLE IDIOPATHIC MUSCULAR ATROPHY, INVOLVING THE FACE AND THE SCAPULO-HUMERAL MUSCLES.

By William Osler, M.D.,
Professor of Medicine, Johns Hopkins University, Baltimore.

In the classification of primary myopathies, the difficulties have been greatly increased by the description of forms depending upon the situation of the atrophy. Varieties of the same disease have been described as separate maladies, and from the inevitable confusion we have scarcely escaped.

Erb has simplified matters very much by grouping all the forms under one designation—dystrophia muscularis progressiva—of which two chief types are recognized:

(1) With primary hypertrophy, the pseudo-hypertrophic muscular paralysis.

(2) With primary atrophy.

As cases of pseudo-hypertrophic paralysis occur in which atrophy and hypertrophy exist in the same muscle, or wasting occurs in one group and enlargement in another, or atrophy in one group precedes for months the development of hypertrophy in another, it is not surprising that these two forms are regarded by many as identical. Gowers, however, calls attention to the fact that, when cases of atrophy occur in families, they never present the features of pseudo-hypertrophic disease.

It is in the cases with primary muscular atrophy that the greatest confusion exists in classification, and the following forms have been recognized and described:

(1) Erb's juvenile form.

(2) The facio-scapulo-humeral form of Duchenne, and of Landouzy and Déjérine.

(3) The hereditary form of Leyden.

(4) The peroneal type of Charcot, Marie, and Tooth.

Gowers has, it seems to me, followed the sensible plan in disregarding all of these subdivisions, and describing the cases under the designation "simple idiopathic muscular atrophy."[1]

Case.—Sebastian B., aged fifteen, sent to the University Hospital

[1] A full discussion of the relation of these forms to each other has recently been published by Dr. B. Sachs. New York Med. Journal, Dec. 15, 1888.

November, 1888. Good family history, both parents living; mother lame, cause unknown. Has one brother, aged twenty, and a second aged thirteen. Has three sisters, aged seventeen, eight, and three, respectively, all well. Two brothers are dead, cause unknown.

Personal history.—He has had measles, smallpox, and possibly scarlet fever. For several years he has had attacks of abdominal pain. He has also had earache. Until five years ago he was well and strong, and played about like other boys. From this time he had gradually been getting weak in the arms, and for between three and four years he has not been able to whistle. All of this time he has been in fair health, but has had increasing difficulty in dressing himself, and in getting from the recumbent to the erect posture.

Present condition.—Station erect, back not curved, gait normal.

Face smooth, immobile, and expressionless—the so-called facies myopathique; naso-labial fold absent; lips project, but the prominence is in

Fig. 1.

Appearance of face.

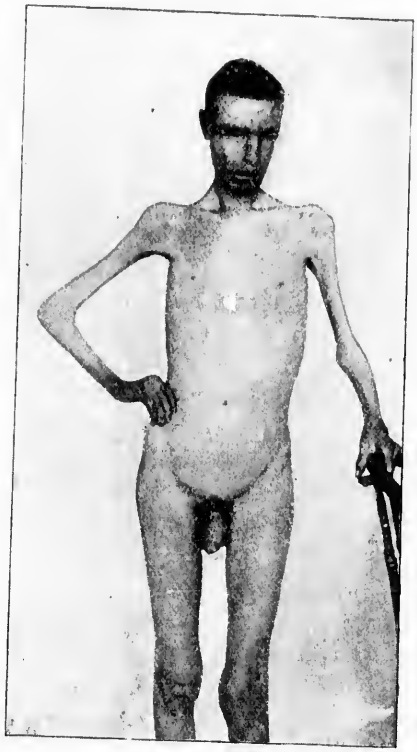
part owing to the teeth. The eyes are large, no exophthalmos; movement of the eyeballs normal. On attempting to close the eyes the palpebral slit remains open about two mm. in breadth. Most forcible contraction of the orbicular muscles fails completely to cover the eyes. (See Fig. 1.) He is unable to frown or to pucker his eyebrows. The forehead can be wrinkled. He has fair power of movement of lips, and he can pucker them in the movements to whistle, but cannot make the sound. When he laughs he opens the lips vertically, but the angles of the mouth are not drawn out. The zygomatics do not appear to act. The dilators of the nose move slightly on deep inspiration.

Neck. Thyroid is a little enlarged. The clavicular portion of the sterno-cleido muscle is wasted, the upper part is better marked than at the lower. The scaleni seem well developed,

Thorax. Long, and depressed in antero-lateral regions. The pectorals are extremely wasted, scarcely a portion of the muscle can be felt.

The subclavicular regions are much flattened. The scapulæ are winged and stand out prominently. Trapezius is wasted in its lower portion. The superior fold on either side is still well marked. The neck does not look so thin from behind. The latissimi dorsi and serrati muscles are much wasted. The interscapular regions are flattened as if the rhomboids were involved. The supra- and infra-spinati are thin, and the scapular fossæ show with great distinctness.

Fig. 2.



Showing muscular atrophy.

The *upper extremities* are extremely wasted, contrasting strongly with the legs. The movements are considerably impaired. The right arm can be lifted above the head; the left only to the level of the ear. At the most prominent part of the biceps the circumference is only five inches. The bony prominences of the shoulder-joints stand out almost free from muscular covering. The acromion and coracoid processes and the greater and lesser tuberosities can be plainly seen. The deltoids are extremely wasted. When the arm is everted there is a small

portion of the muscle, just above its insertion, which stands out with great prominence. The biceps, triceps, and brachialis anticus on both sides are much wasted. In making strong flexion of the arm there is still a slight belly on the biceps. At the outer margin of the upper part of the right biceps there is an oval, firm portion. Proportionally more muscle remains on the triceps. The forearm mensures at the middle five and a quarter inches. The supinators have lost their prominence. The flexors remain in considerable bulk. There is a fair volume of muscle in the extensor surface. Pronation and supination are perfect. The hands are thin; no special wasting of the thenar or hypo-thenar eminences, or of the interosseus spaces. He cannot make a fist satisfactorily with either hand. Movements of the fingers are slow but perfect. There are little warts on the hands, several on the palmar surfaces and terminal phalanges.

Fig. 2 gives a fair representation of the distribution of the atrophy.

Lower extremities. The glutei do not appear wasted. The thighs at the middle measure eleven and a half inches. The region of the internal vasti seem somewhat wasted. The calves measure nine and a half inches No wasting of the leg muscles. Moves the feet and toes perfectly.

There are no fibrillary tremors. Sensation everywhere perfect. Knee-jerk extremely feeble.

Dr. Willets reported that there was no reaction of degeneration in any of the wasted muscles.

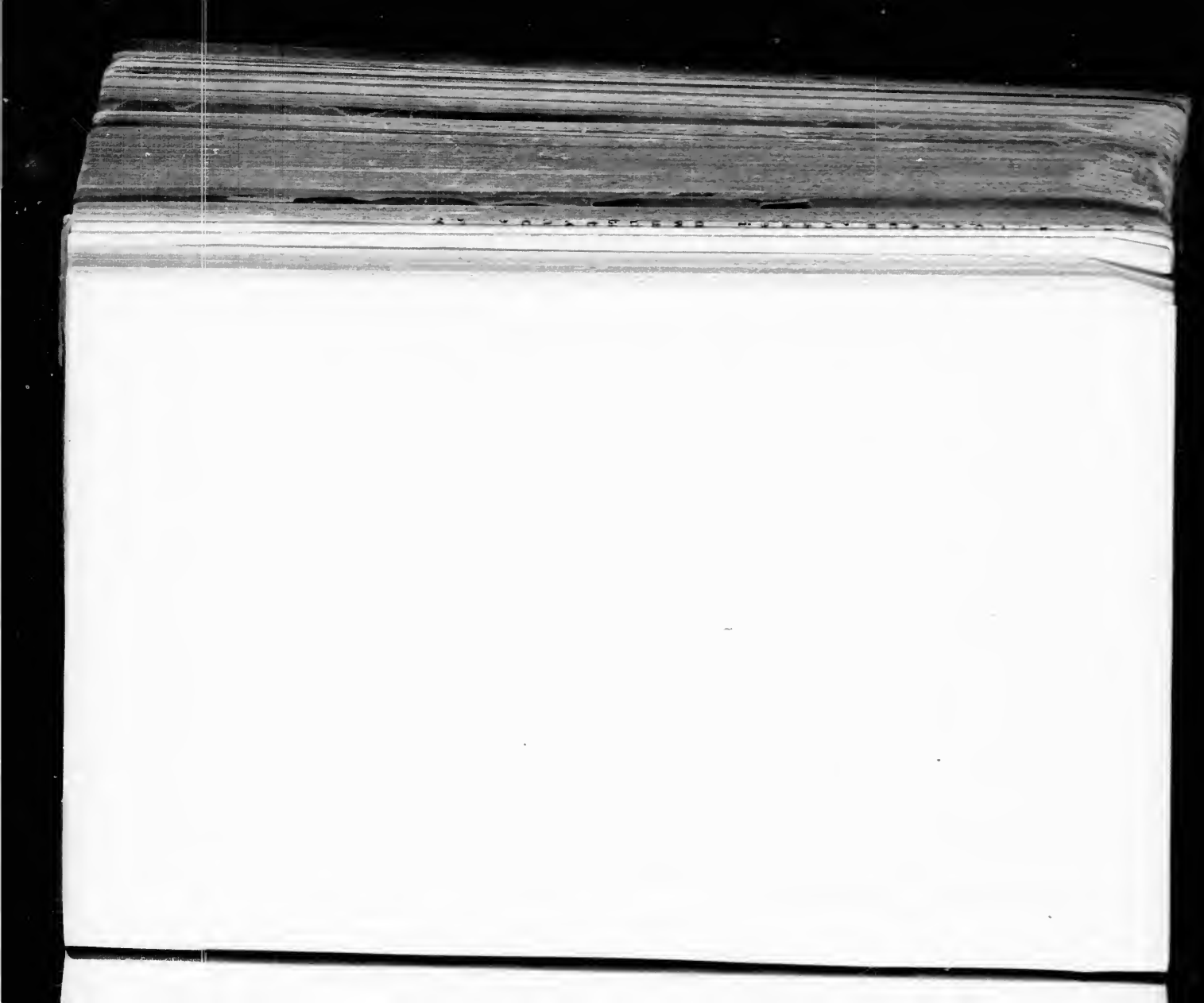
The patient can still dress himself, but with difficulty. When recumbent, he cannot raise himself upright. He gets out of bed by rolling the feet and legs out first, then turning on his face and sliding out.

Duchenne first described a form of muscular atrophy beginning in infancy and attacking the muscles of the face. Landouzy and Déjérine (*Revue de Médecine*, 1885) have studied this form with great care, and regard it as different from the other forms of juvenile hereditary myopathies. In their first communication they described two families, and reported a post-mortem which showed the spinal cord to be normal. In a second communication (*Revue de Médecine*, December, 1886) they described six cases, and again expressed doubts as to the identity of this with Erb's juvenile form, and also denied that it has any connection with pseudo-hypertrophic muscular paralysis. Marie and Guinon (*Revue de Médecine*, 1885) describe four cases in two families, in one instance beginning at the age of thirty. They hold that this form is not essentially different from the other varieties of the primary myopathies. Remak (*Neurologisches Centralblatt*, 1884) describes the case of a man, aged thirty-two, in whom the affection began in childhood; there were other members of the family also affected. He, too, seems to regard it as a variety of the juvenile form of progressive muscular atrophy. Kreske (*Neurologisches Centralblatt*, 1886) reports the case of a boy of ten, affected since his fourth year. There were no other members of the family affected. Singer (*Zeitschrift für Heilkunde*, Bd. 8; *Neurologisches Centralblatt*, 1887) reports the case of a man, aged thirty-

four, who for two years had difficulty in whistling; the muscles of the shoulder and of the face were also affected. He, also, regards this form as only a variety, not a separate affection. Spillman and Haushalter (*Revue de Médecine*, 1888), and Sperling (*Neurologisches Centralblatt*, 1889) also report cases.

Altogether, there are recorded about twenty-five of this variety of idiopathic muscular atrophy. In the great majority of cases, the disease has begun in childhood or in youth. One case of Landouzy and Déjérine began at the fortieth year in the shoulder and arm; four years later it affected the face. This, with the case of Singer's, which began at thirty-two years, and the case of Marie and Guinon, which began at thirty years, shows that the onset of the affection may be delayed until adult life. The cases all seem to conform to the characteristics of simple idiopathic muscular atrophy, and I see no reason why we should classify this variety as a separate disorder.

The cases of this kind, and of Erb's juvenile form, do not appear to be nearly so frequent in this country as the pseudo-hypertrophic variety, which is not at all an uncommon disease. With the exception of the case of James Stewart's report (*Canada Lancet*, September, 1884) no cases of Erb's juvenile form have been reported, and none, so far as I know, of the so-called Landouzy-Déjérine type.



Reprinted from THE JOURNAL OF NERVOUS AND MENTAL DISEASE, August, 1889.

CASE OF SYPHILOMA OF THE CORD OF THE CAUDA EQUINA—DEATH FROM DIFFUSE CENTRAL MYELITIS.

By WILLIAM OSLER, M. D.
Professor of Medicine, Johns Hopkins University, Baltimore.

THE following case which was under the care of Dr. S. Weir Mitchell, at the Infirmary for Nervous Diseases, Philadelphia, presents many points of clinical and anatomical interest.

Clinical Summary.—Chronic alcholism, history of syphilis. For nine months pains in the legs, particularly in the left, which wasted rapidly, and presented vaso-motor changes. Pains in the arms, especially the right; no wasting, and, on admission arms of equal strength. About two months before death loss of control of bladder and rectum. Within the last month of life loss of power in the right arm, with pains; partial loss of power in the left arm with marked inco-ordination, complete paralysis of the left leg, gradual loss of power in the right. Development of bed sores. Arthritis in knees and ankles. Towards the close of life, high fever with delirium.

Anatomical Summary.—Gumma in antero-lateral columns of cervical cord opposite the right fourth anterior nerve root. Gummata involving the third, fourth and fifth anterior sacral nerve roots, and the second and third posterior sacral roots on the left side. Ascending degeneration of the left posterior median column. Central myelitis. Partial atrophy of the sciatic nerves.

A. B., æt. 42, lawyer, admitted February 5, 1888. Family history good. Had been a hard drinker for years and had smoked and chewed to excess. He had gonorrhœa four times, and a soft chancre but no history of secondaries could be obtained.

In 1876 he had delirium tremens.

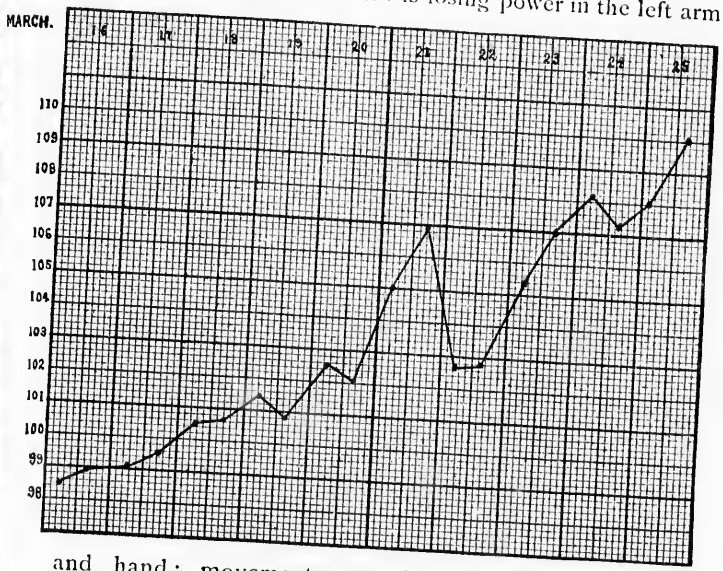
About April, 1887, he began to have sharp, shooting pains in the arms and legs. They came on suddenly, were stab-like in character, lasting only a moment and then passing off. No definite regions in the arms and legs were involved. He also had dull pains in the back of the head and neck. These troubled him more or less throughout the summer, but he could get about fairly well. Towards the second week in October the pains began to be more severe in the left leg; they were thought to be rheumatic in character. About the twenty-fourth of October, his suffering was so great that he was confined to bed. By November 5th he could scarcely walk. The pain began in the right arm and shoulder, the right leg also was painful and weak. There was no redness or swelling of the knees, but the left foot and ankle would get red and swollen, almost purple. The left leg wasted rapidly and for a time he lost sensation in the legs completely. The left arm remained unaffected. About a month before his admission he lost control of his bowels and had a constant desire to urinate. He had to use the catheter for several weeks.

The following notes of his condition were taken on admission by Dr. Burr, Resident Physician.

"He can stand a little with the aid of a chair and he can flex and extend the right knee and hip. He cannot move the left leg, the knee of which is swollen. He has very little pain, none in the right leg. The wasting of the left leg is marked. The knee-jerk is present on the right side but on the left side it is obtained with difficulty. On the right side cremasteric reflex is present, absent on the left. Abdominal reflex present on both sides. No tender spots over spine; bed sores on the coccyx and on the left buttock; has pain in the shin bones and in the groin at night. The arms show almost equal strength. The dynamometer registers 115 for the right hand and 120 for the left.

For two weeks he seemed to be in much the same state though in rather less pain. Towards the end of the month the ankles and knees became more swollen; the bed sores had healed.

On March 16th, the note is as follows: "Has been unable to move the right knee or thigh since yesterday; the swelling has subsided in the knee but the ankle remains swollen; the fingers of the left hand have been numb since yesterday; pain along the inner side of both arms and at the points of the elbow; pain in the left shoulder for several days; right hand is powerless; fingers held flexed in palm; can move the right shoulder; is losing power in the left arm



and hand; movements are distinctly ataxic; there is pain on spine over the seventh cervical vertebræ, worse on pressure."

From the 17th to the 20th the temperature rose gradually, reaching 102°, and at this date he lost sensation in the ulnar distribution of both hands.

21st.—Delirious, but can be easily roused, when he will talk rationally for a few minutes; tongue red, dry and coated; pupils contracted; pulse rapid and feeble; gangrenous bullæ on the outer side of heel; temperature rose this morning to 105° and remained high all the morning. At 2 P. M. it reached 106.8°. Cold sponging and antipyrin reduced it to 102° by evening.

22d.—The delirium persists and bed sores have again appeared on the sacrum; the scrotum is œdematous; he has difficulty in swallowing; the breathing is diaphragmatic; does not complain of pain; temperature, to-day remained below 104°.

23d.—General condition unchanged; is unconscious and is roused with difficulty; morning temperature was 102° rising gradually during the afternoon till it reached 105.6° at 7 P. M.; at 10 P. M., it was 106.8°

24th.—Low, delirious fever continues, reaching at 12 M. 107° and continued elevated during the afternoon. At 10 P. M., the rectal temperature was 108°; at 12:30 A. M., 108.4°; at 2 A. M., 108.8°; at 3 A. M., 109.4°. See chart.

Death occurred at 4 A. M.

Post-mortem, five hours after death.

Body emaciated, left leg smaller than the right; scrotum œdematous; superficial gangrenous bullæ on each heel; recent bed sores on sacrum.

The skull cap was removed with difficulty, as there were strong adhesions to dura.

Logitudinal sinus contains blood. Parts at the base of skull normal; cortical arachnoid, opaque. Pachiionian granulations abundant and large; pia mater turbid, strips off readily from hemisphere, but is somewhat œdematous. Convolutions look healthy, and the gray matter is of a rosy pink color; white substance moist, with very few bleeding points; lateral ventricles look dry; third and fourth ventricles present no changes; in the latter, the vessels just above the acoustic striæ are a little congested.

Section of the ganglia at the base show no foci of disease; pons and medulla symmetrical; no descending lesions.

Cerebellum normal.

Spinal Cord.—Dura mater natural looking, nowhere adherent except at the anterior part of cervical enlargement; no sub-dural exudation; arachnoid thin and clear. On the right half of the cervical enlargement the dura is attached to the arachnoid and to the pia over an area the size of a split pea. There is here a firm solid mass in the cord, not producing any special deformity, but appearing extern-

ally as a grayish region, situated between the anterior roots of the third, fourth, and fifth cervical nerves. The fourth is involved in the adhesion of the dura. The anterior roots are not involved, nor does the adhesion of the dura extend laterally beneath the dentated ligament. The grayish translucent appearance of the mass extends for about a line beyond the posterior median fissure. Vertically it is about one-third of an inch in length.

Fresh sections were made at the following points:

Second Cervical.—Interior soft, but outlines of gray matter distinct. The left column of Goll has a grayish-white translucency.

Sixth Cervical.—Gray matter has lost its firm appearance, and is very soft and reddish in color.

Seventh Cervical.—Central softening still apparent. Cornua not distinguishable.

Second Dorsal.—Gray matter more natural looking.

Eleventh Dorsal.—Outline of gray matter quite distinct. There is a marked degeneration of the left postero-median fasciculus.

The cauda equina presents the following alterations: The three last anterior nerve roots leaving the conus medullaris are involved in a gummous growth the size of a bean, into which pass also the posterior roots of the second and third sacral nerves of the left side. They are involved about two inches from the cord. Lower in the canal there are two or three small fibres, which present slight tuberous enlargements.

The tumor of the cord varies in transverse diameter from three-eighths to one-quarter of an inch in diameter; it is completely within the cord, the symmetry of which is not materially altered (Fig. 1). In shape, above and below, it is rounded; in the middle, more ovoid. The vertical extent is not quite half an inch. At a limited region the dura is adherent to the pia, which membrane, at this point, is distinctly thickened. With a low power it is seen that the growth occupies the right antero-lateral region, destroying and pushing aside the anterior cornu, displacing the antero-median fissure and pushing back the posterior

cornu. In the upper part of the growth, the outlines of the gray matter of the left side and of the right posterior horn are well seen. In the middle portion they are much less distinct; and here the growth reaches so far over that it is only one-eighth of an inch from the left lateral margin of the cord. The growth is firm, not encapsulated, and sections in carmine stain of a deep red color. The greater portion of the mass is made up of a dense fibro-caseous tissue, devoid of cell-elements, and through which passes a

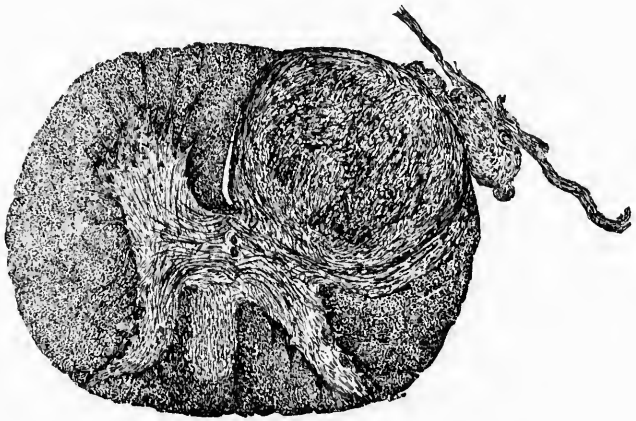


Fig. 1.—Gumma of cervical cord opposite fourth nerve root.

number of blood-vessels, some of which are obliterated, some free. At the periphery, there is marked cell proliferation, particularly towards the gray matter. This is also very distinct in the anterior median fissure. The anterior spinal artery is involved at the edge of the growth, and the adventitia encircled in three-fourths of its extent. The intima is greatly thickened, and the cell elements look much swollen. In the adherent dura, which is not thickened, there are amyloid bodies. The gray matter looks swollen; at the upper portion of the tumor area, the large cells are distinct, but the nuclei do not stain well in carmine. In the middle and lower portions of the affected

regions, the nerve cells are much less distinct, and there is extensive infiltration with leucocytes, particularly in the neighborhood of the vessels.

In the white matter the axis cylinders everywhere stain in the carmine, but the neuroglia looks swollen, and has very indistinct outlines.

The cervical cord, above the gumma, stains well in both carmine and by Wiegert method. The gray matter is distinct, and the nerve cells look somewhat swollen; their nuclei stain well.

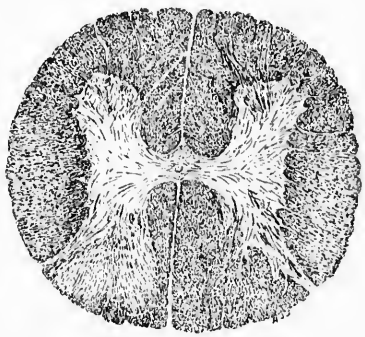


Fig. 2.—Lumbar cord, showing degeneration of the left posterior column.

The tumor of the cauda has matted the nerve roots together, and sections in hæmatoxylin and eosin show large areas of indifferent tissue stained red, surrounded by zones of actively poliferating connective tissue, the cells of which stain deeply in the hæmatoxylin. In the central caseo-fibrous regions the outlines of the nerve bundles can be seen, and, in places, numerous irregular areas, lighter in color, closely set together, which represent the degenerating nerve fibre with their medullary sheaths pale, and many of the axis cylinders stained.

The degeneration of the left posterior column is interesting. In the lumbar cord it involves a wide area, chiefly in the root zone, not reaching the median surface or the posterior, except close to the nerve root (Fig. 2). In the dorsal cord (Fig. 3) the root zone is not involved, and the whole column of Goll is affected except a narrow wedge.

In the region of the tumor the degeneration does not reach so close to the posterior margin (Fig. 1).

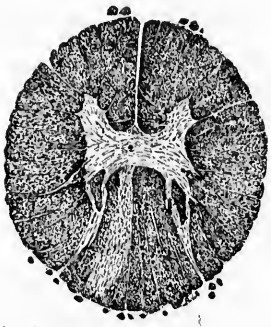


Fig. 3.—Dorsal cord. Descending degeneration of left columns of Goll.

The left sciatic is extensively degenerated. In the right there are two or three bundles in which atrophy is apparent. By Weigert's method the contrast is very striking, as shown in Figs. 4 and 5.

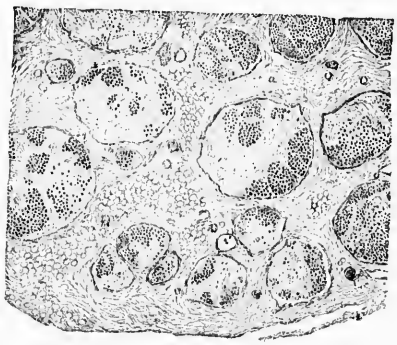


Fig. 4.—Left sciatic nerve. Cross section.

The early pains, at first in the arms and legs, then chiefly in the right arm; the wasting, weakness, and gradually total paralysis of the left leg; the slow onset of the paralysis of the right arm with paresis of the left, find their explanation in the progressive growth of the tumor in the cervical cord. The involvement of the anterior sacral roots was responsible in part for the loss of power in the legs,

but the early affection of the left with rapid wasting was undoubtedly the result of the cord lesion.

The accurate localization of the lesions in the cauda equina makes a consideration of the symptoms produced by them of some importance. Unfortunately, there is no note upon sensation in the perineal and gluteal regions, but for two months previous to death there was loss of control of the bladder and rectum. We can, I think, look upon this case as confirming the view that the ano-vesical centres are in the

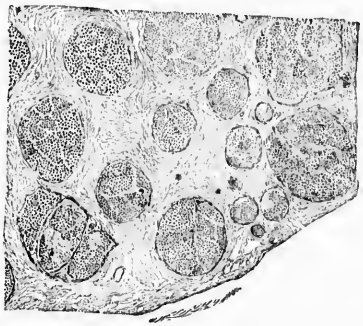


Fig. 5.—Portion of cross section of right sciatic nerve.

sacral, not in the lumbar segments of the cord. The disturbance in the reflex arc was here chiefly in the efferent branches involved in the third, fourth and fifth cords. It will be remembered that of the afferent branches only the second and third sacral roots were involved.

A third point of interest is the ascending degeneration in the left column of Goll due to the lesion in the second and third posterior sacral roots, and, in part also, undoubtedly, to extensive disease of the left sciatic nerve. As is shown in the figures, the distribution of the sclerosis presented the well-known variations in passing from the lumbar to the cervical cord.

Lastly, the case offers an excellent illustration of the chief symptoms of acute cental myelitis, particularly in the high temperature, the arthritic disturbances and the marked trophic changes, as shown in the rapid development of bed sores.

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[From *The Johns Hopkins Hospital Bulletin*, No. 1, December, 1889.]

ON THE VALUE OF LAVERAN'S ORGANISMS IN THE DIAGNOSIS OF MALARIA.

By Professor William Osler, M. D.

The attitude of the profession on the question of micro-organisms of malaria is one of judicious skepticism. Between the bacillus malariæ of Klebs and Tomassi-Crudelli, and the protozoa described by Laveran, the average doctor cannot be expected to decide; but even among workers and teachers, there is by no means unanimity. So far as I know, there has been no confirmation of the observations of the first named authors on a specific bacillus in the disease. It is far otherwise with the organisms described by Laveran, whose work has now been confirmed by competent observers in Italy, America and India. I do not know of a single clinician or pathologist, living in a suitable region, who has really worked at the subject, who has not been convinced of the truth of Laveran's statements. Doubtless many have had my experience. In 1886, at the meeting of the "Association of American Physicians," when Dr. Councilman presented a summary of Laveran's views, I (speaking out of the fulness of my ignorance) was extremely skeptical. When I had the opportunity of giving to the question, the study which its importance demanded, I was soon convinced, and I had the satisfaction of confirming, in almost every particular, the observations which Laveran had made, and discussed the whole subject in a paper, published in the *British Medical Journal*, March 12, 1887. For the past two years, at the Philadelphia and University Hospitals, I have had abundant opportunities of studying cases of malaria, with an ever-deepening conviction that the organisms of Laveran are peculiar to the disease.

The experience of Dr. Vandyke Carter, Principal of the Grant Medical College, Bombay, one of the most distinguished pathologists in India, appears to have been very similar to my own. He, too, had been rather repelled by the apparently extraordinary statements of Laveran, and had not given careful study to the subject, until the appearance of my paper in the *British Medical Journal*. His elaborate contribution to the subject, one of the most important which has been made, confirms in almost every detail the statements of the French observer. To the impartial student, this remarkable unanimity in observations made by Laveran in Algiers, by Marchiafava and Celli and Golgi in Italy, by Councilman, James and myself in this country, and by Vandyke Carter in India, should, to say the least, carry conviction as to the importance and constancy of these bodies in malaria. While it may be a little early to ask acceptance of the view that

these organisms constitute the specific germ of the disease, the work already done warrants positively the statement that they are peculiar to and diagnostic of the presence of the malarial poison. It is not surprising that certain observers, who have perhaps seen but few cases, have been inclined to regard the changes in the red corpuscles as degenerative rather than as the manifestations of an intracellular parasite; but the study of the remarkable serial development of the segmenting forms described by Golgi cannot possibly be explained by any other view, than that we are dealing here with an independent organism. The crescentic bodies, too, are so peculiar, so characteristic, so unlike anything which we meet with in the blood in other conditions, that I have usually found it an easy matter to convert the most hardened unbeliever by a demonstration of their presence in a few cases. Still more remarkable are the flagellate organisms.

Putting aside, for the time, until the complete life history of these organisms shall be worked out, the question of their ætiological relation to the disease, I would briefly refer to their diagnostic importance. In my former paper, I gave in this connection several interesting illustrations. Since that date, I have, in an increased experience, become even more convinced of the really great value in doubtful cases of these blood examinations. In ordinary intermittent fever, of recent origin, there is hardly ever any question in the diagnosis, and any doubts which may exist, quinine readily clears up. The value of the blood examination lies particularly in the chronic cases and in anomalous forms. Here one has to be constantly on guard and it may be impossible for days to determine definitely the nature of the affection. We have since the opening of the hospital, admitted twenty-four cases of malaria to the wards, of which, in seven instances, the diagnosis was definitely determined by blood examination, and could have been determined in no other manner. So important do we consider it, that we now, as a matter of routine, examine the blood of all cases of fever, and indeed all cases of low temperature, which seem so peculiar in certain forms of chronic malarial poison. We had a salutary lesson in the early part of the summer, in the case of an old man, aged 81, admitted July 25th, with a temperature of 104°. He had on the 9th, a heat stroke, while picking berries, was better the next day and kept about until his admission. There were signs of bronchitis at the bases of the lungs, and in the right inter-scapular region, the note was higher pitched and the breathing tubular. The temperature rose to 105°, and throughout the 26th, 27th and 28th, kept between 101° and 103°; on the 28th, between the hours of 6 and 12 a. m., the temperature was subnormal, but he had no chills. He was extremely feeble, not cachectic or sallow; the pulse was very irregular. Neither I nor Dr. Atkinson, who saw the case for me during an absence of three days, had any other idea than that the case was one of low pneumonia in an elderly man. The patient died on the 8th day of his admission, and to my surprise and chagrin the post-mortem examination of the blood and spleen showed the case to have been one of malarial fever. Had a thorough blood examination been made and full doses of quinine administered, the man's life might have been saved. In five or six cases of irregular fever, the presence of the organisms in the blood has determined the nature of the disease.

The routine examination is really not tedious, and we have adopted it now in the dispensary, as well as in the wards. Unfortunately for the general practitioner, the determination of the intra-cellular forms requires a tolerably high power with good illumination. We use the one-twelfth immersion, but with care a good eighth is sufficient, and in the chronic cases, with the crescents in the blood, a sixth suffices. It is important to have the finger tip, from which the blood is drawn, thoroughly cleansed, and it is best to take a very small drop of blood, so as to have the layer uniformly and thinly spread out with the corpuscles isolated not in rouleaux.

Briefly to summarize for the information of those who may not have access to monographs on the subject, the following are the important facts relating to these organisms:

First; In the acute forms of malaria there exists, within certain of the red corpuscles, amoeboid bodies, usually pigmented, which undergo a definite evolution, increasing in size, gradually filling the entire corpuscles, and which prior to and during the chill, undergo a remarkable segmentation. There are also, in some cases, free pigmented bodies. To the form within the corpuscles, which undergoes changes, the term *plasmodium* has been applied. Occasionally in acute forms, flagellate bodies are seen free in the blood, presenting from three to eight long, actively moving cilia. According to Councilman, these are much more common in blood withdrawn from the spleen.

Second; In more chronic cases, particularly in the forms of remittent fever, which are so apt to be taken for typhoid, the corpuscles do not so often present the intercellular forms, but there are remarkable ovoid, rounded and crescentic bodies deeply pigmented. These are, in all probability, related to and developed from intercellular forms. From certain of these, particularly the ovoid and rounded forms, the flagellate bodies may be seen to develop. Dr. Ghriskey has recently been studying the evolution of these forms in the Clinical Laboratory, and has been able to demonstrate on many occasions the development of the flagellate bodies from ovoid-rounded forms.

I hope, in an early number of the forthcoming Hospital Reports, to review fully the present status of the malaria question and to report our experience, particularly in the anomalous forms of fever in which the blood examination is so important. It is particularly to be desired that those who have ample opportunities for the study, shall approach the problem with unbiassed minds. It requires a little patience in order to become thoroughly familiar with the various phases of development of the organism. Additional workers are needed. We have yet to determine fully the relation of the forms to each other and the complete life history of the parasite in the body; and, what is much more important, to ascertain its existence outside and to learn the conditions of its development and the way in which it gains access to the body.

A ready method of separating malarial from other forms of fever will prove a great boon to southern physicians. Dr. Carter's paper contains many illustrations of the value of Laveran's observations in this respect, and workers in sub-tropical and tropical regions cannot longer afford to neglect so valuable an aid in diagnosis.

ON FEVER OF HEPATIC ORIGIN, PARTICULARLY THE INTERMITTENT PYREXIA ASSOCIATED WITH GALLSTONES.

By WILLIAM OSLER, M. D.

Apart from suppuration, we meet with fever as a prominent symptom in the following diseases of the liver: (1) cancer and sarcoma; (2) certain forms of cirrhosis; and (3) chronic obstruction of the bile passages by calculi, tumors, etc.

Cancer.—In all rapidly growing large neoplasms of the liver, there is more or less fever, usually continuous and not often reaching a high grade. Thus of four cases of tolerably extensive cancer of the organ, in which there was fever, in only one did the temperature rise above 102°. In a remarkable case, recently in the Hospital, of cirrhosis with diffuse cancer, the temperature ranged for the first week from 98° to 100°, once reaching 101°, and subsequently remained normal. In the large secondary growths of the organ, the existence of fever when combined with jaundice may be of service, helping to differentiate between this condition and other forms of enlargement of the liver. I have only once seen a marked intermittent fever with severe rigors, in a case of cancer of the liver, and the question of abscess was raised. The post-mortem showed that in addition to extensive secondary cancer, there were several abscesses, caused by the compression of larger gall ducts by the tumors. It is not impossible that a form of intermittent pyrexia might be associated with a rapidly

growing cancer of this organ, such as Hampeln[1] has described in cases of cancer of the stomach and such as are met with occasionally in rapidly growing lymphatic growths, as noted by Pel of Amsterdam.

Since writing this paragraph, there has been in the Hospital a case of primary cancer of the left lobe of the liver in a young man, who gave a history of several rigors of so pronounced a nature, that among other possibilities that of abscess was discussed.

Cirrhosis.—It is not usually recognized that in cirrhosis there may be fever. The systematic authors on affections of the liver, such as Frerichs and Murchison, speak of slight pyrexia in the early stages, particularly when the organ is enlarged. Carrington[2] has made an interesting study of this question, and states that of forty-four cases in which temperature observations were made, in thirteen fever was a more or less marked symptom. In certain cases, such for example as the one which he described in full, serious difficulties in diagnosis might readily arise and it would be quite pardonable to suspect, from the irregularity of the temperature curve and the existence of slight jaundice, that suppuration was going on. My experience with fever in cirrhosis is small and I have not my clinical records at hand to examine into the point. I have a distinct recollection in one or two instances, particularly in the hypertrophic form, of marked increase in the temperature, but, I should say that in the majority of instances of cirrhosis, fever was not a special symptom.

Obstruction of the Duct by Gallstones.—Since the bile passages have been brought within the sphere of surgery, a renewed interest has been taken in all symptoms which give us more accurate knowledge of the character and situation of lesions in these parts; and I wish particularly in this paper to deal with a form of fever met with chiefly in chronic obstruction of the common duct by gallstones, as it possesses features of the greatest importance for diagnostic purposes. The fever I speak of is intermittent in character and the cases present the following group of symptoms:—

First: Jaundice of varying intensity, deepening after each paroxysm, and which may persist for months or even for years.

Second: Ague-like paroxysms characterized by chill, fever and sweating, after which the jaundice usually becomes more intense.

[1] Zeitschrift f. klin. Medicin, Bd. XIV.

[2] Guy's Hospital Reports, 1884.

Third: At the time of the paroxysms, pains in the region of the liver, with gastric disturbance.

In a majority of cases this combination of symptoms is, I believe, characteristic of the existence of gallstones in the common duct.

We meet with rigors, fever and sweats in three conditions of the bile passages:—

As an acute and transitory process in ordinary hepatic colic associated with the passage of a stone through the duct.

In chronic obstruction of the duct, usually by stone, without lesions of the bile passages other than dilatation and catarrhal cholangitis.

In suppurative cholangitis produced by gallstones or other causes.

With the first of these, I am not specially concerned, except so far as it may help to explain the occurrence of the paroxysms in the second group. The distinction between the cases of suppurative cholangitis and those of the second category shall be considered subsequently, and I shall now proceed to speak of intermittent hepatic fever with its associated symptoms as characteristic of chronic obstruction of the duct by gallstones and without suppuration.

The literature of the subject, though interesting, need not, for the purposes of this paper, be discussed at length. Of the numerous writers on gallstones during the last century, Soemmering[1] appears to be the only one to mention the symptom, using the phrase, in speaking of the fever associated with gallstones, "et ipsa febris intermittens."

We owe to French physicians our knowledge of this valuable symptom. Monneret[2] is usually credited with its recognition, but the thesis of Magnin[3] and the work of Charcot[4] present us with the first satisfactory studies, from which indeed has been derived most of the information on the subject which we find scattered through the text-books and monographs.

Among German writers the work of Frerichs contains many cases, illustrating this symptom of chronic obstruction, but he does not appear to lay special stress upon its importance in diagnosis. In von Schueppel's article upon gallstones, in Ziemssen's Cyclopædia,[5] the remarks are based on the work of the French writers. Wagner[6] has reported interesting cases. References to these symptoms occur in

[1] De Concrementis biliariis, 1795.
[2] Pathologie Interne, Tome I.
[3] Paris, 1869.
[4] Leçons sur les Maladies du Foie, 1877.
[5] Vol. IX.
[6] Deutsches Archiv. f. klin. Med., Bd. XXXIV.

the various German text-books, but the question does not appear to have received the full consideration which its importance demands, and the majority of the writers, as Strümpell, for example, speak of the *fièvre intermittente hepatique* as if it were always associated with suppuration.

Among English writers, Murchison, in his work upon the liver (third edition), notes the occurrence of rigors in chronic obstruction, and in his paper upon conditions causing an intermittent fever,[1] he deals more fully with the general features of the affection. Harley, in his work on the liver, does not mention it. Ord refers to it in his paper on some of the rarer symptoms produced by gallstone.[2] In the English text-books on medicine, it is not often spoken of; even Fagge, whose work is such a store-house of clinical facts, has no reference to the subject.

In this country, the question has been discussed by Bartholow, who gives, in Pepper's System of Medicine, a full summary of the French observations. In Sajous' Annual for 1888, Dr. W. H. Thompson, of New York, refers to intermittent hepatic fever as occurring frequently in this country and as well recognized by authors; but in a private communication he informs me that he had been under a misapprehension, and so far as he knows the subject had not been discussed by any American writer. Musser,[3] of Philadelphia, has reported several interesting cases.

The following cases have been under my observation :—

CASE I.—*Jaundice of three years duration. Repeated attacks of chills and fever; cholæmia, death. Gallstones in common duct.*

J. H. R., aet. 68, admitted to the Johns Hopkins Hospital, May 25th, 1889, complaining of jaundice, chills and fever, which had lasted on and off for three years. With the exception of attacks of eczema, he had been a healthy man until three years ago, when his present trouble began with dyspepsia and pain in the pit of the stomach. In the first attack there was sharp pain in the epigastrium, followed by a chill and vomiting. These recurred very frequently, and with them he invariably became deeply jaundiced and the stools

[1] Lancet, 1879. [2] British Medical Journal, 1887, I.

[3] On Paroxysmal Fever, not Malarial. Proceedings of the Phila. Co. Med. Society, 1884.

were putty colored. He had been subject to catarrh of the stomach and had always been constipated. The attacks of chills and fever had, at times, been very severe, and he would sweat heavily after them. On the occasion of his first visit to Hospital a violent attack came on while he was in the waiting-room; he shook as in an ague paroxysm. His wife stated that he had rarely passed three weeks without a chill of great severity.

Present condition.—Much emaciation; skin dry and harsh and of an intensely bronze color. It presented many small scabs, the result of scratching. The muscles were very flabby. The conjunctivæ and mucous membrane of the mouth were stained, as were also the nails of the fingers and toes. The expression of the face was dull and the speech slow. Articulation was impaired from dryness of the mouth. Examination of the thoracic organs negative. Pulse 68, small and regular. Abdomen was a little distended, somewhat tympanitic, everywhere painless.

The edge of the liver could not be felt. Dullness in mammary line began at the 6th rib and extended 2½ inches (6+ cm.) vertically. The most careful palpation could not discover the gall bladder. The splenic dullness was slightly increased, but the edge was not palpable. The urine was of a deep brownish-red color, acid in reaction, specific gravity 1008. It contained a small amount of albumen and a few tube casts. Temperature on admission was 98°. His chief complaints were of intense itching of skin and of occasional pains in the abdomen.

On the morning of the 26th he had a chill, in which the temperature rose to 101° and he became delirious, would not answer questions, and wanted constantly to get out of bed. The temperature sank to about 96° and remained at that point until eleven o'clock when it rose to 97°. Gradually coma supervened; the pulse rate increased to 160 and the respiration became very irregular, 30 per minute. He was given an active purge and sweated. The coma gradually deepened; the temperature rose, reaching towards evening 101°. He died early on the morning of the 27th.

From his history and the repeated attacks of hepatic intermittent fever extending over a period of three years (a period of sufficient length to exclude suppurative cholangitis, abscess, or cancer), I made a diagnosis of obstruction of the common duct by gallstones, and suggested to him the propriety of an operation. To this he had

given his consent, and entered the Hospital with a view of remaining a week to gain strength before submitting to it.

Post-Mortem, by Dr. Welch. Peritoneum contained 30 cc. of yellow serum.

In thorax the pleural membranes were normal. The pericardium contained an excess of fluid. The heart was a little enlarged, weighing 11½ oz. (326+ gms.) The segments of the aortic valve were indurated along free and attached margins. On the aortic aspect of one segment was a fresh, reddish-grey, partially detached, vegetation. The remaining two segments had coalesced in consequence of ulceration and nearly total disappearance of the septum, in the situation of which was an irregularly indurated, ulcerated, slightly elevated ridge, partially covered with red-grey fresh vegetations. On the ventricular aspect of this fused segment was a vegetation 15x10 mm. The mitral and other valves were normal. The heart muscle was flabby and brownish in color; on microscopical examination not fatty.

The lungs were normal.

The spleen was 15 cm. long and 10 cm. in breadth. Its contents were soft and dark red in color.

The combined weight of the kidneys was about 12 oz. (340+ gms.) Cortex of average thickness. The striæ obscured; organs not firm.

Bile duct. The orifice of the common duct was dilated and contained a plug of thin, pale yellowish mucus, easily displaced. Upon passing a probe into the duct it entered a sac 1½ cm. from the orifice, which corresponded to the dilated ductus communis choledochus. A round ulcerated opening 3 mm. in diameter communicated between the lumen of the duodenum and the common duct in its course in the intestinal wall. A sac resulting from the dilatation of the common duct measuring 2½ cm. in diameter was completely filled with gallstones of varying sizes, the largest being 2 cm. long by 1½ thick; the smallest not larger than a pea. All were provided with facets. The walls of the dilated common duct were thickened and the surrounding connective tissue very dense and intimately adherent to the adjacent parts. The gall bladder was shrunken to a small sac 2 cm. in length by 2 cm. in breadth. The walls were thickened and it contained a number of gallstones around which it had contracted. The cystic and hepatic ducts were greatly dilated and contained gall-

stones; altogether not less than twenty could be felt in the duct. Externally they were deep black in color.

The liver weighed 3 lbs. 11½ oz. (1686.8 gms.); the surface was smooth, mottled greenish and pale yellow in color. Outlines of the lobules were indistinct.

On section the bile ducts appeared moderately dilated. The walls were thickened and the contents yellowish, viscid, and not purulent.

The aorta presented several small atheromatous ulcers.

CASE II.—*History of previous attacks of gallstone colic. For eight months recurring attacks of pain with ague-like paroxysms and intensification of the jaundice. Passage of the gallstone. Recovery.*

N. K., act. 30, a dark, slightly built woman, was admitted to the Montreal General Hospital November 17, 1879. She had been healthy with the exception of occasional attacks of indigestion. Four years before she had several attacks of cramps in the abdomen. In the middle of September, 1879, they recurred after a wetting. At this time she had vomiting, and the attacks were of such severity that morphia was given hypodermically. Two days after the onset she became deeply jaundiced, the attacks of pain recurred, and the vomiting became very troublesome, but in about two weeks she was able to go to her home, where she remained until November 17th. When admitted she was deeply jaundiced, the tongue was furred, she had nausea and looked feeble. She remained in hospital during the winter, and I found her in Ward 23 when I went on duty. During a residence of five and one-half months in hospital her chief symptoms had been: first, jaundice, varying greatly in intensity, sometimes almost disappearing, but recurring again in a few days; second, ague-like paroxysms—chills, fever and sweating—accompanied by severe abdominal pains, coming on at intervals of from three to ten days; third, great impairment of appetite, dyspepsia, frequent vomiting, especially about the time of the paroxysms; fourth, great tenderness in the epigastrium, most marked over the right costal border.

After an interval of a week or ten days—during which the jaundice would diminish, the bile almost entirely disappear from the urine, the fæces become slightly bile-tinged, the appetite improve, and the patient would sit up—the paroxysm would come on, either with a slight chill, not more perhaps than a transitory feeling of cold; at

others it would be a severe rigor, in which she would shake as if in an ague-fit. This cold stage lasted from fifteen minutes to three or four hours and was followed by great heat of the skin and burning fever, which after continuing for an hour or two would be followed by a profuse perspiration. The temperature, which was usually normal, or even sub-normal, would rise in the attacks, reaching 102°–104°, subsiding quickly after the paroxysm, and sometimes sinking to 97°. The fever rarely persisted for an entire day. Among the concomitant symptoms of these attacks, vomiting with severe gastric pain were the most common. The pain which usually gave indication of the onset resembled that of hepatic colic, being epigastric, and radiating to a point beneath the right shoulder blade. It was scarcely ever as agonizing as the pain of ordinary biliary colic, but was often severe enough to require morphia. Before and after the attacks the epigastrium was very tender, so much so that she would even complain of the weight of the bed clothes. Vomiting was a marked feature, and usually accompanied the paroxysm. The bowels were moved every day, sometimes two or three motions. The color of the feces depended on the intensity of the jaundice—light color when the skin was deeply tinted; brownish when the color of the skin was less intense.

For a long time the motions were filtered in the hopes of finding gallstones. Invariably after an attack the jaundice deepened, and we could generally tell by her appearance alone whether she had had one. The urine also at this time became deeply bile-tinged. In the intervals the pain subsided, and the nausea and vomiting became less troublesome, but for days she could not take anything but a little biscuit and milk. She usually remained in bed, but during a long interval she would get up and go about the ward. Itching of the skin was occasionally a distressing symptom.

In April I made the following notes:

"Moderate jaundice; nothing special to be seen on inspection of the abdomen; on palpation decided tenderness in the epigastric region, most marked towards the right costal border; no fullness or increased resistance; limit of dullness extends in nipple line from upper border of 6th rib to within half inch (1.3 cm.) of the margin of tl. rib; splenic dullness 2½ inches (6.3 cm.); heart and lungs normal; urine bile-tinged, specific gravity 1020, no albumen; enormous dark,

granular, bile-stained casts, some containing epithelial cells; fæces clay-colored, soft and a little offensive; no fever."

Towards the end of April she left the hospital and went to her home at St. Johns, where she was attended by Dr. Robert Howard, who treated her for gallstones, giving large doses of bi-carbonate of potash. She had several paroxysms of pain with fever, and the jaundice continued. On June 3rd she passed per anum a large round gallstone, which Dr. Howard kindly sent to me. It weighed 60 grains (3.9 gms.), and measured a little over one cm. in diameter. She improved very rapidly after this, the jaundice disappeared, and she recovered her usual health and strength.

CASE III.—*From July, 1879, until August, 1882, jaundice of varying intensity, with recurring attacks of pain and intermittent fever. Recovery.*

November 9, 1880, I was asked to see Mrs. S., act. 55, a well-nourished woman, wife of a florist. She had always been healthy and had borne five children. Had been accustomed to work in the garden and in the greenhouses. Her illness began July, 1879, and her physician, Dr. Simpson, gave me the following particulars of the onset and development of the disease.

"In July, 1879, Mrs. S. consulted me at her house for a mild attack of jaundice, which she ascribed to having seen a disgusting object which emitted a most offensive odor, causing her to feel sick at her stomach. When a young girl she had an attack of jaundice following a fright. On August 4th, I saw her again; the jaundice had deepened and she complained of a dull pain in the region of the liver and general distress. She remained in this state until the morning of the 6th, when she was seized with a severe chill and intense pain below the ribs on the right side, extending into the epigastrium and to the right shoulder. It was increased by pressure and motion, the breathing was hurried and the anxiety of the patient most distressing. A chill of about two hours was followed by high fever, then copious sweating, which stained the sheets a deep yellow color. The liver was distinctly enlarged. The pain gradually abated but the tenderness persisted for several days. All the essential phenomena of jaundice were present. She remained under my care until January, and during this time she had a paroxysm every two or three weeks, varying somewhat in in-

tensity and duration. The pain gradually became less and less. The chill, fever and sweating were invariably present after each attack, and the jaundice deepened. Itching of the skin was a most distressing symptom, preventing sleep and rendering life almost unendurable. For days at a time the stools were strained, but without finding gall-stones. The enlargement of the liver disappeared."

During the early part of the year the attacks continued, but during the summer, under homœopathic treatment, the jaundice almost disappeared, and for many weeks she had not a paroxysm. When first I saw her she was intensely jaundiced and suffered with the most terrible itching of the skin which I have ever witnessed. Warm alkaline baths were ordered with great benefit. One night after a bath she became quite incoherent. On examination, her condition was as follows: well-nourished, somewhat stout woman; thick layer of panniculus over the abdomen. She says, however, that she has lost flesh during the past year. The skin has a deep greenish-yellow tint, and is covered with scratches; edge of the liver could not be felt; no tumor evident below the right costal border; she winces when firm pressure is made between the navel and costal margin; area of liver dullness somewhat diminished and the organ is not tender to firm pressure; the splenic dullness is increased, 7 inches in vertical diameter (17.8 cm.); heart and lungs normal; tongue red and indented with the teeth; bowels irregular; stools clay-colored and offensive; urine very dark-colored and contained much bile pigment; temperature 98.4°; appetite poor, can only take soft food. Within a few days the itching disappeared, excepting on the palms of the hands and the soles of the feet. These parts had always been the most troublesome, and the pads at the bases of the fingers were much swollen and tender. By the 15th she was very much better. The jaundice had begun to disappear, but at noon on the 16th she had a very severe paroxysm, the chill lasting nearly two hours, and there was no vomiting with this attack and no special abdominal pain; no change noticed in the hepatic region.

From this time until Christmas day she had seven severe attacks, varying in intensity, five of which followed each other on Fridays. The rigors were most intense in violence, shaking the bed and causing the room to vibrate. Temperature reached from 103° to 104°. The jaundice intensified after each attack.

After Christmas she improved very much; jaundice almost entirely disappeared and she was able to get up and go about the house. On two occasions she had severe headache and great depression, followed by copious sweating. The palms of the hand continued very tender. A troublesome symptom was the profuse sweating about the waist, sufficient to saturate the under-linen and render it necessary to wear cloths about her. The urine became clear, the fæces contained bile; the liver showed no special alteration. The tenderness on the right side of the epigastrium persisted. During the spring of 1881 the daily amount of the urea was estimated during a period of three weeks, but there was no special diminution during the paroxysms.

I lost sight of Mrs. S. after the spring of 1881, when she was still considerably jaundiced and had paroxysms at prolonged intervals.

On the 7th of July, 1882, she came to see me and stated that her condition had remained unchanged; the paroxysms still recurred at intervals, but she once passed six weeks without one. In May of this year she had them worse than ever, and to use her own expression, "she was dead of them." After August, 1882, the jaundice disappeared and she now looks in perfect health.

Dr. F. G. Finley, of Montreal, recently (Oct. 1888) made inquiries for me about this patient and writes that she continues well and has had no return of the pain or of the jaundice.

CASE IV.—*Repeated attacks of biliary colic. For three months jaundice with repeated paroxysms, chills, fever and sweats. Operation. Death. Gallstone in common duct.*

Mrs. S., aet. 51, patient of Dr. Bolling, of Chestnut Hill. Seen March 2d, 1887.

She had been a healthy woman, but since 1862 had several attacks of biliary colic, on one occasion with jaundice. Since Christmas she she had pain in the upper part of the abdomen, and very severe jaundice, which has gradually deepened. The urine has been intensely bile-tinged and the fæces clay-colored. For two weeks she had been worse and confined to bed. A special feature had been chills, recurring daily, followed by fever rising to 103° and 104°, and then copious sweating. The chills were most severe and the fever most pungent. The stools had been carefully examined for gallstones, but without result. The patient was a well-built, well-nourished woman, with

intense icterus; tongue coated and dry; pulse 120, small and feeble; no fever; abdomen large; fat abundant; liver dullness not increased. On palpation, nothing to be detected along the costal border in the right hypochondrium; towards the epigastrium great tenderness and distinct sense of increased resistance. A most careful examination failed to reveal the presence of enlargement of the gall bladder. The history of the previous attacks, the persistency of the present one, and the recurrence of intermittent fever pointed clearly to obstruction of the ducts, probably by gallstones. The question of surgical interference was raised, and possible obstruction by malignant disease at the head of the pancreas was also debated.

March 3d. The patient was seen at 2 p. m. by Doctors Agnew, J. W. White, and Bolling. The condition was worse. The patient was weaker; tongue very dry; abdomen distended; diffuse tenderness, and in the epigastrium extreme sensitiveness to pressure.

Dr. Agnew made an incision between six and seven inches (16 cm.) in length, the outer edge meeting the rectus muscle. When the peritoneal cavity was opened a bile-tinged, slightly turbid fluid escaped. The liver looked very dark, and a conical, pointed gall-bladder projected beyond the edge not more than one inch (2.5 cm.) from the surface, the liver being slightly atrophied above it. On lifting the liver the bladder was seen to be enormously dilated, and by aspiration 18 oz. (431 gms.) of dark bile were removed. There were no gallstones in it, but a stone was felt low down in the common duct and pushed back into the gall bladder and removed. The head of the pancreas seemed hard and indurated but not enlarged. The patient sank and died twelve hours after the operation. No autopsy was allowed.

CASE V.—*Jaundice of two and a half years duration. Recurring attacks of intermittent fever, with pains. Operation. Death. Gallstone in the common duct.*

A. B., a woman aged 40, was in the Philadelphia Hospital, September, 1887, when I took charge of the wards. She had been under my care previously, in the spring of 1887, when I was on duty for Dr. Tyson. This had been her third or fourth admission within two years with attacks of pain in the region of the liver, and chills, fever and heavy sweats. My colleagues had on two occasions brought her blood to me for examination, the existence of malaria having been

suspected. Once certainly, possibly twice, her liver was aspirated, the recurring chills having aroused a suspicion of abscess.

The patient was a medium-sized, fairly well-nourished woman. She had lived a hard life and had had specific disease. Attacks similar to those from which she at present suffered, came on about two years ago and she had not been entirely free from them for a period of three months, nor does she think that she had in this time ever passed two months without a slight tinge of jaundice. When first seen, she was up and about the ward and showed only the slightest lemon-tint of the skin and of the conjunctivae. The urine was a little high-colored. The stools contained bile. On examination the liver appeared to be enlarged. In the mammary line, the right lobe extended four fingers breadth below the costal margin; in the median line a distinct irregularity in outline could be made out. The gall-bladder could not be felt. Palpation was not painful. Early in October, she had an attack of violent pain with vomiting and a moderately severe rigor, after which the temperature rose to nearly 104°, and she sweated profusely, the entire paroxysms lasting over twelve hours. The next day she was distinctly jaundiced, free from fever, the tongue heavily coated and the stomach extremely irritable. The urine was very dark, containing bile-pigment and the stools were light-colored. The liver did not seem to be larger but it was sensitive to pressure. The gall-bladder could not be felt.

In three or four days, the gastric symptoms passed away and she was able to sit up. The jaundice deepened distinctly for three or four days and then gradually lightened.

The case was made a subject of almost daily demonstration in the ward-class and I confidently predicted a return of the paroxysms. Throughout the winter she had four or five, each similar to the one just described, varying somewhat, however, in intensity.

I had made up my mind from the length of time which the woman had suffered and from the character of the attacks that the case was one of obstruction of the common duct by gallstone; and early in February, I asked Dr. White to see her in consultation. The patient consented to an operation, and Dr. White made a free abdominal incision along the line of the costal cartilages. There was extensive perihepatitis with puckering of the edges of the liver, due to the cicatrization of old gummata. The gall-bladder was not enlarged;

there was a great deal of fibroid matting of the tissues in the gastro-hepatic omentum. No gallstone could be felt in the gall-bladder, nor in the duct. The patient came out well from under the influence of ether; had no shock, and six hours afterwards her temperature and pulse were normal. The following day there was a rise of temperature and she died on the third day after the operation.

I had been so confident, from the history of the case, that it was one of obstruction by gallstones, that I was naturally chagrined at the negative result of the operation. The friends removed the body at once to Jenkintown, but I was fortunately able to secure an autopsy, when the following condition was found.

Perihepatitis with deep puckering, owing to the cicatrization of old gummata. The liver was not enlarged; the apparent increase in size, during life, was due to the tilting forward of the convex surface of the organ. There was recent acute peritonitis, confined to the region above the transverse colon. The liver, stomach and duodenum were removed together for dissection. On slitting open the duodenum, a bile-tinged mucus was seen oozing from the papilla. Projecting into the duodenum and covered by the mucosa only was a gallstone, the size of a marble. It lay entirely within the bowel, quite close to the narrow orifice of the duct, through which it could be seen after the removal of the mucus. The stone could not be moved up or down, though it had slight play in the dilated pouch, at the termination of the duct. The common duct and its main branches were dilated; the former about the size of the index finger. The contents of the duct was a bile-stained mucoid fluid. The cystic duct was wide. The gall-bladder was a little enlarged, but did not contain any stones. The terminal bile-ducts were not dilated. The other organs presented no special change.

CASE VI.—*Jaundice of varying intensity from July, 1887, until August, 1888. Repeated paroxysms of intermittent fever. Death.*

A. B., aet. 70, physician. Family history good; has enjoyed excellent health with the exception of an attack of nervous prostration in 1863. Some years after he got stout and was unable to take proper exercise. He never had a strong digestion and always had to be careful in his diet. He was in his usual health until July, 1887, when he had an attack of jaundice, coming on with severe pain, evi-

dently biliary colic. The jaundice gradually disappeared, but returned in five or six weeks with pains of the same character. The second attack did not last so long, but in December he had a third attack, again associated with pain in the upper portion of the abdomen. Since then he has not been free from the jaundice which has, however, varied greatly in intensity. About Christmas he had a severe chill, followed by fever and sweats. At intervals of about ten days the paroxysms have recurred, and after each one the jaundice deepened. On March 10th, when I saw the patient with Dr. Murray Weston, his condition was as follows: Stout, well-nourished old man; deeply jaundiced; pulse 92, feeble; no fever; skin moist; complained of much itching; tongue coated; abdomen large; panniculus thick; omental fat excessive. On palpation, the edge of the liver not to be felt; dullness diminished, not more than three fingers breadth in the middle line, and two and one-half inches (6.35 cm.) in the nipple line; no tenderness on deepest pressure over the pancreas. The patient was bright mentally. No vomiting had occurred throughout the illness, but there had been attacks of nausea; bowels constipated; stools of the consistency and color of putty. They have not been dark and normal in appearance for months. Urine scanty, deeply bile-tinged.

The night before I saw him he had a very severe chill, lasting one and one-half hours, which was followed by a burning fever and profuse sweating. He was much prostrated by the attack, and in the morning, as was usual after an attack, the jaundice had deepened and intensified. He was not emaciated, though he said that he had lost flesh, particularly in the limbs, during the past three months. I saw him at intervals of a few weeks for several months. Throughout April he had no chills and was comparatively comfortable, and the jaundice began to lighten. In May he had several very severe paroxysms, in which the temperature reached 103°–104°. After each one the color became more intensified, and the urine became darker. With some of the chills he had severe abdominal pains, but with others he complained only of a sensation of epigastric distress. Throughout the summer the chills and fever persisted at irregular intervals. In August the jaundice deepened and he died comatose. No autopsy.

CASE VII.—*Jaundice, with attacks of colic, of ten* (?) *years' duration. Under observation for three years, with repeated attacks of intermittent fever, always associated with an increase in the jaundice.*

A. B., aged 46, single, domestic by occupation, was admitted to the Philadelphia Hospital with fever and jaundice.

There was nothing special in the family history. Ten years ago she had the first attack of jaundice, which came on with pain in the abdomen, particularly on the right side. She was in bed for two weeks. From that date until the present the skin has never been of the normal color, though for weeks the jaundice would be extremely light. During this period she has had repeated attacks of pain in the region of the liver, usually accompanied with vomiting and diarrhœa. In one of these "spells," as she calls them, she was admitted to Hospital. She states that for the past ten years she has had on an average three or four of these attacks a year, always associated with chills and fever and with sweats. She has had also what she terms "burning spells," in which she would get very hot but would not sweat.

Inspection. Patient not emaciated. There is a thick layer of fat over the abdomen; the face is fairly plump; she is deeply jaundiced, color of dark, olive-yellow, not the light soft tint of recent icterus. The conjunctivæ are deeply stained. The skin is dry and harsh. There is no eruption, only a few scratches on the back. She complains of intolerable itching. Temperature was 103° on admission, but fell to the normal; pulse 100. The abdomen is symmetrical, the upper zone not especially enlarged. On palpation it was soft, non-resistent and painless until the epigastric and right hypochondriac regions were reached, which on pressure were extremely tender. The edge of the liver can be felt just below the costal margin. The gall-bladder is not palpable.

Percussion in mid-sternal line shows not more than two inches (5 cm.) of liver dullness; in nipple line about three inches (7.6 cm.).

The spleen is not palpable. There are three inches of vertical dullness in the axillary line.

She has had several movements of the bowels since admission; the fæces are soft and of a grayish-brown color. The urine is high-colored and contains bile-pigment, no albumen.

This patient was under my care on three separate occasions during three years. Each time she was admitted with fever and great pain in the epigastric region, with vomiting and diarrhœa. These attacks usually set in with a heavy chill. The jaundice would gradually get a little lighter, but never completely disappeared. The stools were never quite clay-colored. I urged her repeatedly to submit to an operation, but she would never consent. Twice she was made the subject of a clinic illustrating a form of hepatic intermittent fever, due in all probability to chronic obstruction by gallstones.

CASE VIII.—*Jaundice of ten months duration, with recurring chills and fever. Recovery.*

Agnes S., aged 23, was admitted to the maternity wards of the Philadelphia Hospital in January, 1886. Her labor was normal and the convalescence uninterrupted. Two months after confinement, she fell across a chair and injured herself severely, causing a profuse hemorrhage, said to have been uterine. Three days after the accident she had nausea and vomiting, and in the course of a week jaundice developed. When admitted to the medical ward, she was slightly yellow and complained of pain in the epigastrium and of back-ache. The bowels were constipated and the stools of a clay color; they were frequently examined for gallstones, but none were found. A few weeks after the onset of the jaundice—the exact date is not stated in the notes—she began to have febrile attacks, preceded by a chill and followed by profuse sweating. These attacks recurred at irregular intervals. I saw her first in August, in the obstetrical department, and it was then thought that she had either malaria or abscess of the liver. She was repeatedly made the subject of ward-class demonstration as an instance of true hepatic intermittent fever, probably depending upon gallstones obstructing the common duct. Examination of the liver was negative; the edge could be distinctly felt. The gall-bladder did not seem to be enlarged. There were three inches (7.6 cm.) of vertical liver dullness in the nipple line and the same in the mid-sternal line. The spleen was not palpable. Throughout August, she had four severe chills; after each one the jaundice deepened and each was accompanied by nausea, vomiting and a good deal of pain. In September the paroxysms were less frequent, but she had two distinct rigors, on the 3d and on the 13th. On the 25th, the temperature rose to nearly

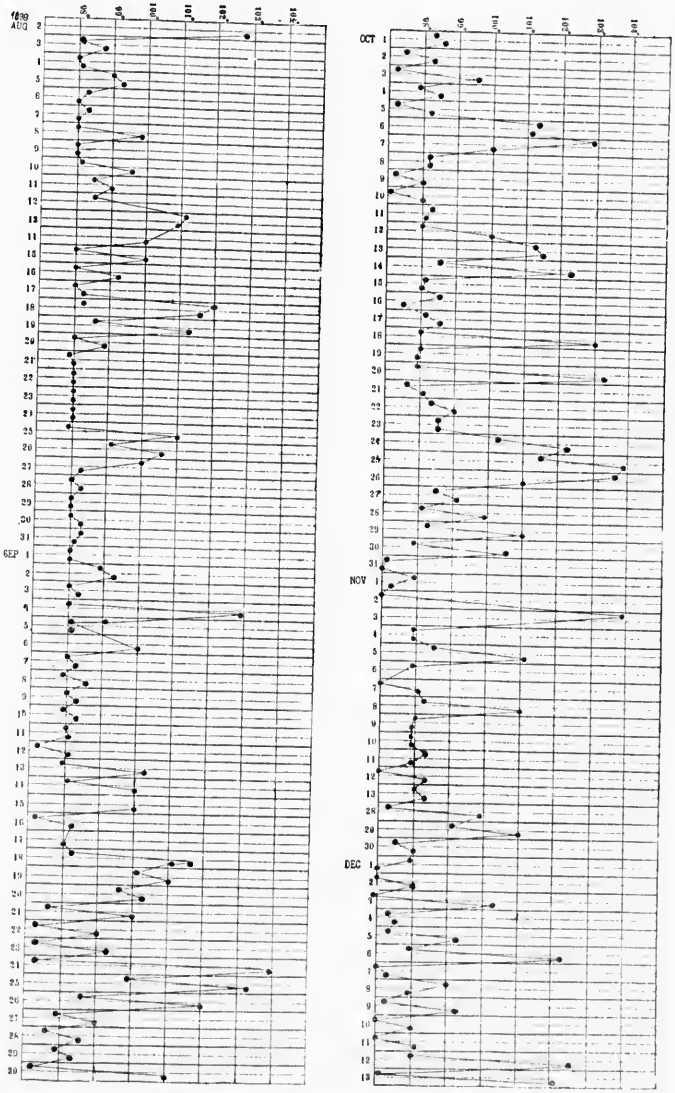
102°, and she had, for ten days, an irregular intermittent fever. On the 2d, 3d and 4th, there were chills, and she had become at this time more intensely jaundiced than at any period since her admission. She improved between the 5th and the 15th, and the jaundice got lighter. On the latter date she had a heavy chill. Chills recurred on the 22d, 26th and the 28th. In the first twelve days of November she had six rigors; the jaundice again became deeper. After this date she improved very much and through the latter part of November and the early part of December, she was remarkably well and presented only a light-lemon tint. She had two or three slight chills, each followed by an increase in the jaundice. On the 27th and 28th, the paroxysms recurred and she again became jaundiced. After January 1st, the color became lighter, and by the 18th, when she went out, the jaundice had almost disappeared. I saw her again more than three months afterwards and the jaundice had completely disappeared and she had had no recurrence of the attacks.

The accompanying temperature record of Case VIII (*see p. 21*) illustrates very well the type of fever met with in these cases.

Of these eight cases, six were women. Two died after operation; two died from the effects of the long continued jaundice; three recovered after the persistence of the condition for from eight months to three years, and one passed from observation.

In analysing the symptoms associated with these paroxysms, we have—

First: *Jaundice.* This was present in every instance and may be said to have been constant, though varying very greatly in its intensity. It will have been noticed that in every one of the cases the statement occurs that after the paroxysm the jaundice invariably deepened. I do not remember ever to have seen a well-marked paroxysm, with intense rigor and high fever, in which this peculiarity did not occur. The patients soon learned to recognize it and to expect, as a matter of course, an intensification of the jaundice. With this, the amount of bile-pigment increased in the urine and the stools became more clay-colored. After persisting for a week or ten days, the tint would become lighter, until as in Cases II and VIII, the skin would become, in the intervals, almost normal. The urine, too, would be lighter in color and the stools contain bile. In certain



TEMPERATURE RECORD. (*See p. 19*)

of the cases, I, III and VII, the jaundice for months together was of the most intense grade.

It is possible that cases of intermittent pyrexia may occur without jaundice, owing to chronic obstruction of a main duct in the liver. I have not met with such a case, but Magnin[1] refers to one under Charcot's care.

Second: *Fever.* This, in well-developed paroxysms, begins with a sharp rigor. I have rarely seen in intermittent fever chills of greater severity. In Case III, in particular, the large, stout woman would, during the rigor, shake the entire room and cause the small, wooden house in which she lived to vibrate. It may be represented, however, only by a sensation of cold, a creeping chill, in contra-distinction to a shaking one. The fever rises suddenly, and, as shown in the chart, may reach from 103° to 105°. At first dry and pungent, the skin gradually becomes moist, and usually within from two to five hours of the commencement of the rigor the patient is bathed in perspiration. The entire duration of the fever is from six to twelve hours; rarely does it persist for an entire day. Defervescence takes place rapidly when the sweating begins. Although the rule is for the paroxysms to present the usual stages, as here described, there were in each of the cases lesser attacks, often of fever alone or of fever with sweating. Slight rises of temperature without chills are indicated in the temperature chart. Sweating was occasionally seen without the fever. In Case III, in particular, local and general sweating was much complained of. The paroxysms occur at irregular intervals, but I have seen them recur daily for a week or ten days. They may present a tertian or a quartan type, and in such cases the diagnosis of ordinary ague may be made. In Case III, the paroxysms recurred for weeks on Friday.

Third: *Pain* of some sort is as a rule present. It may, but certainly does not always, precede the rigor. In some cases it is not at all a striking feature, and the most intense paroxysms may be quite painless or only accompanied by a sense of gastric distress. It may have all the characteristics of genuine hepatic colic, agonizing, griping pain in the liver-region, with the associated symptoms, feeble pulse and clammy skin. In several of the cases the pain was not at all a distressing symptom.

[1] Loc. cit.

Fourth: *Gastric disturbances.* Vomiting often precedes or accompanies the attacks, and frequently before its onset the patient complains of loss of appetite or nausea; the tongue becomes furred, and it seemed very often as if a gastric catarrh really initiated the paroxysm.

The condition of the patients in the intervals between the attacks is a point of considerable importance. They are often well enough to resume their work, or in the case of women, to do light household duties. There is not progressive deterioration of health and strength, such as we meet with in malignant disease. With the exception of Case I, who had been ill three years, the patients were all well nourished, some of them fat; even Case VII, who had been jaundiced, she said, for ten years, and who to my knowledge had been so for three years, had a very fair layer of panniculus.

Regnard[1] found in one case that the excretion of urea was diminished during the attack. Only in Case III was a careful study of the urea made during the attacks, but no special diminution was found.

Diagnosis.—The significance of hepatic intermittent fever cannot be appreciated without taking into account the associated group of symptoms, and when these are present it points clearly to obstruction of the common duct by calculus. The condition of the bile-passages in these cases is one of catarrhal, not suppurative, cholangitis.

Chronic obstruction of the bile-duct, either by stenosis or by gallstones, may persist for months without inducing this intermittent pyrexia, as illustrated by the following cases:

Gallstones in the common duct. Chronic jaundice. No fever.

A man, aged 77, was admitted to Dr. Curtin's ward in the Philadelphia Hospital suffering with jaundice. He was a weaver by trade and a moderate drinker. He had had jaundice on two previous occasions, and had been in the out-ward for several months, having been jaundiced for nearly a year. Careful inquiry from the attendants, and from the man who occupied the next bed, failed to elicit any history of chills or sweating. When admitted to the hospital he had profuse diarrhœa; the abdomen was distended, and evidently there was fluid in the peritoneum; he was extremely feeble; the stools were grey

[1] Quoted by Charcot, loc. cit.

and the urine high-colored and contained bile-pigment. He died on the fifth day after his admission.

I made a dissection with Dr. Atlee, and the following conditions were found: Deeply jaundiced; moderate ascites; liver small, surface granular; gall-bladder slightly distended, projecting one inch (2.5 cm.) beyond the liver margin; the common, hepatic and cystic ducts were greatly dilated. When the duodenum was opened, a nodular body projected beneath the mucous membrane above the bile papilla. This could be felt as a hard body within the head of the pancreas, and was at first thought to be a cancerous mass. A probe was passed through into the orifice of the duct, and on squeezing above the pancreas a bile-stained mucus flowed from the orifice. The nodular mass proved to be a gallstone the size of a cherry firmly impacted into the ampulla of Vater. It could neither be pushed into the common duct nor into the duodenum. A second stone the size of an olive was free in the duct, in which it could be moved up and down. The common duct admitted the index finger, and its main branches in the liver admitted the little finger. The gall-bladder was moderately dilated; contained no stones; the cystic duct was free. The bladder and ducts contained a bile-stained mucus. The liver presented the appearance of ordinary cirrhosis. The kidneys were swollen and bile-stained.

That stenosis of the common duct may persist for months, or years, without inducing chills and fever, is illustrated by the following case:

Stenosis of the common duct. Jaundice of fourteen months duration. No fever.

Hannah C., aged 35, admitted to the Montreal General Hospital, September 25th, 1880, with obstructive jaundice of two months duration. The attack had followed diarrhœa, and had come on without any pain. She remained under observation for nearly a year. The skin was of olive-green color; the stools clay-colored; the urine dark greenish-brown; the liver appeared greatly enlarged, the dullness in the middle line extending four inches (10.2 cm.) from the xiphoid cartilage, four and one-half (11.5 cm.) inches from the sixth interspace, and four inches (10.2 cm.) from the seventh interspace in axillary line. She had frequent severe headaches and occasional attacks of pain, associated usually with vomiting.

The temperature record, which extended over the entire period of her stay, occasionally showed an elevation of two or three degrees, but she never had chills. The liver increased in size, and on May 21st the note was as follows:

"The liver has gradually enlarged until it now fills a large part of the abdomen, extending in the middle line below the navel and in the flank nearly to the crest of the ilium." She died in August, 1881, of gradual asthenia.

Autopsy.—There was moderate emaciation. The liver was enlarged but not so much as was expected, owing to its vertical position. The surface was smooth and of a deep olive-green color. The common bile-duct was pervious to a small probe, but the first inch and one-half from the orifice it was extremely narrow, the wall darkly pigmented and the lining membrane rough. Above this part the duct was greatly dilated and the walls thickened. The gall-bladder was moderately distended; the walls were hypertrophied, and the lining membrane rough and shaggy. It contained three small stones. The hepatic duct and the branches in the liver of the first, second and third dimensions were enormously distended, forming elongated sacculi. The duct passing to the right lobe admitted three fingers with the thumb between them. The lining membrane of the dilated passages was smooth, not ulcerated, not thickened. The dilatation was confined entirely to the branches above named, the terminal branches being little, if at all, affected. There were no dilated ducts to be seen beneath the capsule. The contents of the duct and of the gall bladder consisted of clear mucoid fluid. The tissue of the liver was smooth and the acini well marked. There were no cirrhotic changes.

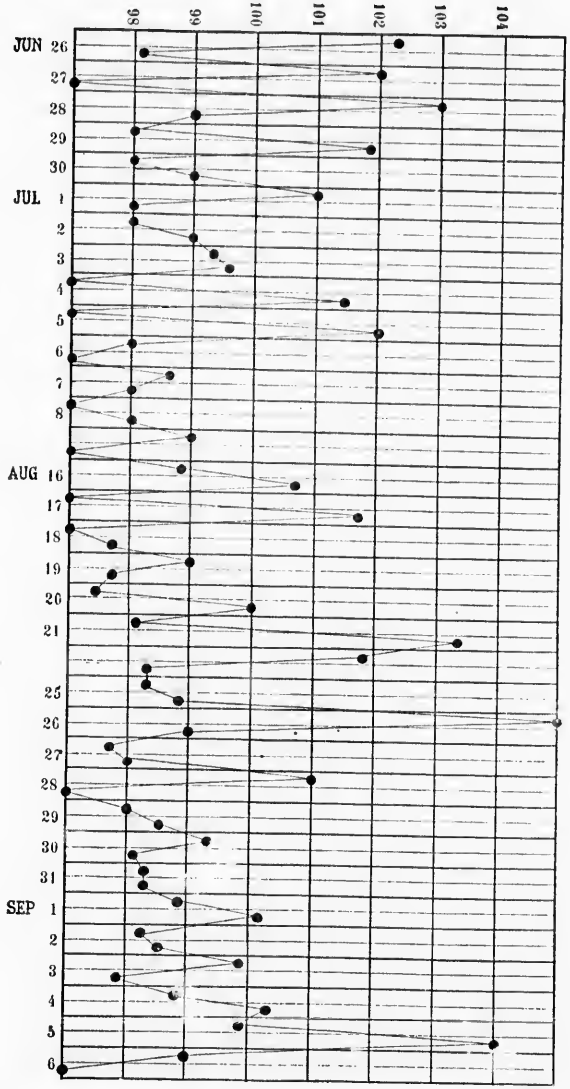
These instances show that it is not the obstruction alone which induces the intermittent fever; there must be something superadded, probably the ferment-producing agents, the micro-organisms, which, as we shall see, have been found in two cases.

From a practical standpoint suppurative cholangitis is the only affection from which gallstones with hepatic intermittent fever is to be differentiated. The post-mortem examination in cases I and V, and numerous observations which I have found in the literature, show conclusively that the intermittent pyrexia in these long-standing cases is not necessarily associated with suppuration in the ducts. But, unfortunately, suppurative cholangitis is most frequently caused by

blocking of the common duct with a stone; and it is important to determine in a given case the onset of suppuration. In deciding this, stress may be laid upon the following points:—(1) increased tenderness in the hepatic region with possibly enlargement of the gall-bladder, as this is a more common event in suppurative cholangitis than in simple obstruction of the duct; (2) the more frequent return of the paroxysms, and in some instances the irregularly remittent character of the fever; (3) the jaundice is not so intense in suppurative cholangitis, and we do not see the remarkable deepening in color after the paroxysms; and (4) the general condition of the patient in the intervals is very different in the two conditions. When suppuration exists there are rarely the prolonged periods of apyrexia, the freedom from distress and the general betterment which we see in cases of simple gallstone obstruction.

There may be, however, the greatest difficulty in deciding, and, after all, in the question of treatment it does not make much difference. I recently dissected a specimen of cholangitis brought to me by my friend Dr. Lainé, of Media, Pa., which was removed from a woman, aged 76, who had had from June until September, chills, fever and sweating, recurring at irregular intervals, either daily, or every third, fourth or seventh day. The liver was tender; no tumor could be felt; the symptoms were evidently pyæmic, and there was inflammation of the right parotid gland. The temperature record, a copy of which Dr. Lainé gave me and has kindly allowed me to reproduce (*see p. 27*), may be compared with the one previously given. The chills recurred more frequently, and the temperature is altogether more irregular than in any case of ordinary hepatic intermittent fever which I have seen. The autopsy showed an abscess of the gall bladder with sinuses. The cystic duct was blocked firmly with a calculus, and another the size of a cherry lay loose in the common duct, not interrupting the passage of the bile. There were two septic abscesses in the lower lobe of the left lung, and there was fresh endocarditis of the aortic valves.

In the chronic obstruction which results from the compression of a cancerous mass either in the head of the pancreas or secondary in the lymph glands, there are occasionally rigors, due to catarrhal or suppurative cholangitis, but the sequence of the symptoms would, I think, enable one to decide between this condition and gallstones.



TEMPERATURE RECORD OF DR. LAINÉ'S CASE. (See p. 24)

The varying intensity of the jaundice and the comparatively easy state of the patient in the intervals between the paroxysms are features which I have not met with, nor seen referred to, in the obstruction by malignant growths.

When the fact is recognized that the lodgment of a gallstone in the common duct may be associated with pyrexia of intermittent type, a confusion of these cases with malaria is not likely to occur. The mistake is, however, very commonly made, and in at least five of the cases here reported the patients were supposed to have chronic paludism, for which they had taken quinine in large doses. The error is a pardonable one when the patient is seen in the interval between two paroxysms, with very slight jaundice and perhaps not more than the lemon-tint of skin seen in chronic malaria. The history of repeated chills is very likely to mislead, and it may require a careful study before the diagnosis can be established. The negative condition of the blood in these cases may be very suggestive, as in cases V and VII, in which the absence of Laveran's organisms led to a revision of the diagnosis.

I have no knowledge of the cases referred to by certain writers, in which a calculus in the duct arouses latent malarial influences, and the paroxysm thus results from the combination of the two factors.

Pathology.—The pathology of hepatic intermittent fever is obscure. Two views have been advanced. Charcot believes that it is due to the production of a ferment in the bile passages, the absorption of which into the blood excites the febrile paroxysms. A certain measure of support is lent to this view by the discovery in the ducts in a case of cholangitis, by Netter and Martha,[1] of a bacillus similar to one of the intestinal organisms.

It is not only in suppurative cholangitis that organisms occur, since in case I, in which the bile-ducts, as stated, contained a yellowish viscid, non-purulent material, Dr. Abbott discovered a short pointed bacillus which did not, in cultures or general characters, appear to correspond with the one described by Netter and Martha.

The occurrence of endocarditis, as noted by these authors, is also extremely suggestive of the action of micro-organisms, and the identity of the organisms in the ducts and those on the heart valves was estab-

[1] Archives de Physiologie, 1886.

lished by Netter and Martha. Altogether the view of Charcot is one which commends itself most strongly to my mind.

On the other hand, Murchison inclines to the belief that the febrile paroxysms are due to the simple irritation of the stone, not to a septicæmia. To this view, Ord subscribes,[1] stating that the paroxysm of fever is "due to local irritation of the mucous membrane propagated to the central nervous system and resulting in pyrexia, mostly in persons apt to take on febrility, and particularly in persons who have previously had intermittent fever."

It was Budd, I think, who drew the analogy between hepatic and urethral fever, but the analogy to which he referred is rather between the rigor in recent cases of renal and hepatic colic and in the so-called catheter fever. There is, however, a renal intermittent fever, closely analogous to the hepatic form. It may occur, first, in tubercular pyelitis; second, in calculous pyelitis; and third, in rare instances of stone in the pelvis, without chronic suppurative pyelitis. The cases in the last category present a curious analogy to hepatic intermittent fever, due to gallstones and without suppurative cholangitis. There are intense rigors, the temperature rising to 104° and 105°, with great pain in the renal region and distinct changes in the character of the urine. In a case of the kind which I had an opportunity of studying for several months, the paroxysms recurred at intervals of a few weeks; in each one the urine became somewhat turbid but not purulent. No enlargement of the kidney could be detected, but there was decided sensitiveness in the left renal region. In the intervals of the attacks, the patient was perfectly well and the urine became clear.

In all of these cases the obstruction is not complete, as shown by the presence of bile in the stools for long periods at a time. The association of the chills and fever with intensification of the jaundice must be more than accidental. The two must be correlated in some way, in all probability through a transient impaction of the stone in the duct. Such a condition might induce the chill, either through reflex irritation as held by Murchison, or by preventing the escape from the bile passages of toxic ingredients—ferments produced by the action of micro-organisms—which are absorbed into the blood instead of

[1] Loc. cit.

escaping freely into the bowel. The impaction is probably overcome by a gradual increase in the *vis a tergo* until the duct is stretched to a point which permits the calculus to fall back into a wider portion. The pressure may reach such a grade that the stone is forced out, as happened in case II, and very likely in the other cases in which recovery followed.

I have emphasized sufficiently the important diagnostic indications afforded by the hepatic intermittent fever, and a careful attention to the group of symptoms presented should enable us to determine whether, in a given case, gallstones alone are present, or whether suppuration has supervened, and the important question remains as to the prognosis and the treatment in these cases.

Prognosis.—I have been fortunate in the cases which I have seen, as three of them recovered; one after a persistence of the symptoms for three years. Judging from the rarity with which recovery is mentioned in the literature, such cases must be deemed exceptional. The great majority of them follow the course which is sketched in the history of cases I and VI, death resulting from exhaustion or cholæmia.

Treatment.—The remarkable success which has recently been obtained by surgeons, indicate clearly the line of treatment which should be followed, and although the results of opening the common duct have not been so favorable as in cholecystotomy, yet they are sufficiently hopeful to warrant the attempt in every case, either to push the stone into the duodenum, to crush or to extract it.

Of medicinal agents I have not found any of the slightest value, either in preventing the onset of the paroxysm or causing the solution or propulsion of the stone. Certain of the cases were drenched with olive oil, and most of them had taken soda salts and mineral waters. Many, perhaps all, of them had taken quinine in large doses, but it is quite ineffectual, either to control or to prevent the paroxysms.

I have dealt thus at length with this special symptom, or rather symptom-group, so characteristic of obstruction of the common duct by gallstones, as I believe a wider recognition of its importance may be the means of saving valuable lives by timely surgical interference.

Conclusions.—1. In cancer and in cirhosis a certain number of cases present fever of moderate grade, but scarcely distinctive enough to be of value in diagnosis.

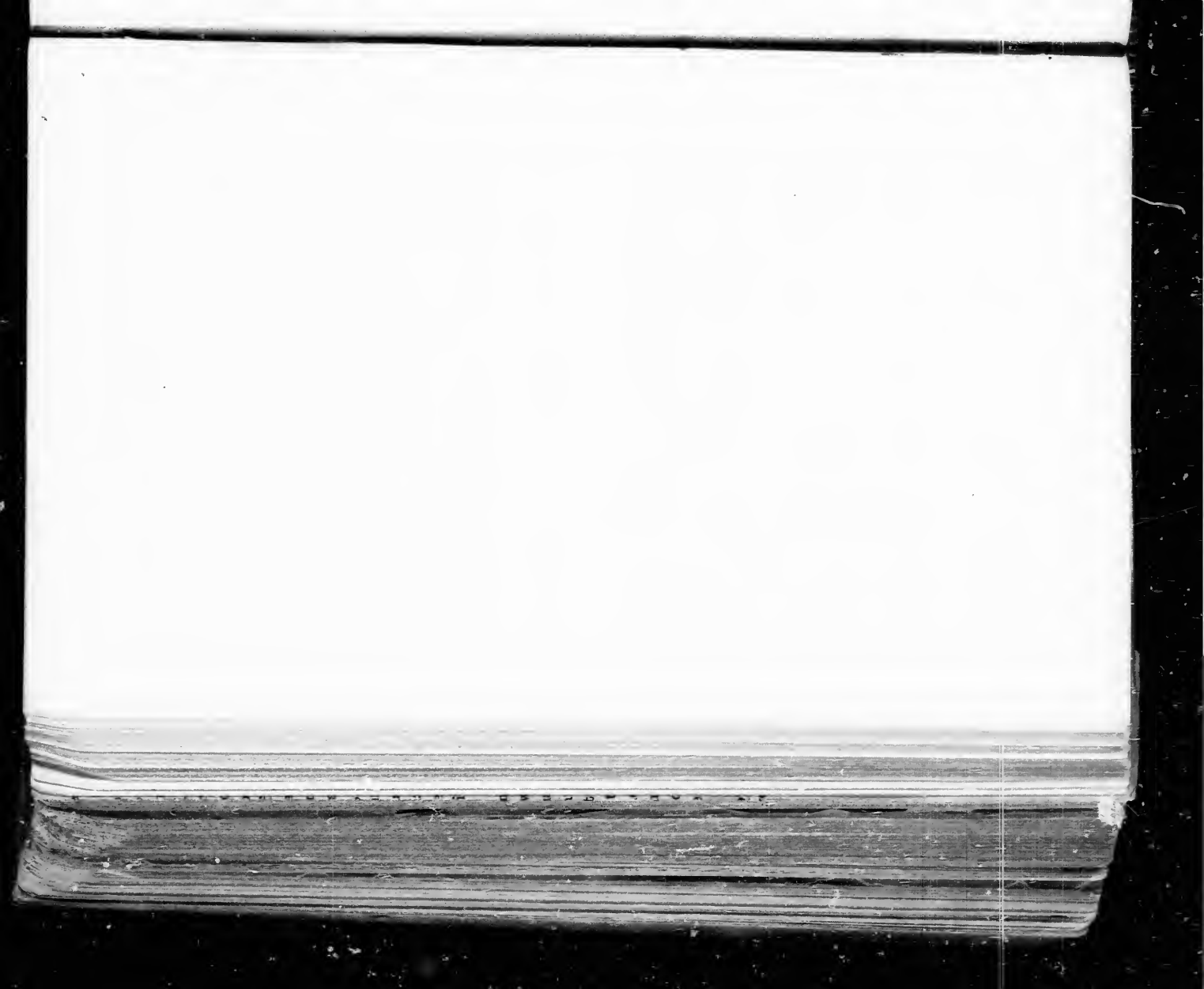
2. Chronic obstruction of the common bile-duct is often accompanied by an intermittent pyrexia, associated with a symptom-group of the greatest diagnostic importance.

3. This pyrexia is not usually the result of suppuration, as has been supposed, but occurs with a catarrhal cholangitis.

4. That it arises from the absorption of a ferment, produced in the ducts, is rendered highly probable by the discovery of micro-organisms, both in the catarrhal (Case I) and in the suppurative cholangitis (Netter and Martha).

5. While recovery may follow, even after months (Cases II and VIII), or even years (Case III), a fatal event is only too common.

6. A recognition of the importance of this intermittent pyrexia and its associated symptom-group, as diagnostic of obstruction of the common duct by gallstones, should, in the present condition of hepatic surgery, lead to more frequent operative interference in these cases.



[From The Johns Hopkins Hospital Reports, Vol. II, No. 1, January, 1890.]

CASES OF POST-FEBRILE INSANITY.

By WILLIAM OSLER, M. D.

One of the most distressing accidents which can follow an acute disease is the development of mental symptoms, which may take the form of excitement, depression, loss of mental power, delusions, or hallucinations. In medical practice these cases form the counterpart of the insanity seen by surgeons after operations, and of the puerperal insanity described by obstetricians. It is a somewhat rare condition, and in a tolerably large hospital experience, I had seen, to January, 1888, but two instances: one after pneumonia, and one after typhoid fever.

At the November meeting of the College of Physicians, of Philadelphia, Dr. H. C. Wood[1] discussed the relation of these forms to each other, and proposed to consider them as instances of "Confusional Insanity," with one common fundamental brain condition, viz: impaired nutrition with consequent exhaustion of the nerve centres. Of the cases which he reports, three followed operations and one typhoid fever. The subject of insanity in surgical practice has recently been brought to the notice of the profession by Shepherd,[2] of Montreal, and by T. Gaillard Thomas,[3] of New York. A report of the following post-febrile cases, five in number, which have been under observation within the past eighteen months may be of interest, as they illustrate the important points in the clinical history of this condition.

Case I.—*Pneumonia. Slow convalescence with development of hallucinations and delusions.*

A. B., aged 42, farmer, applied at the Johns Hopkins Hospital June 20th, 1889. Family history is good; no insanity or any nervous trouble. Patient has been a healthy man and a hard worker; was a staff officer in the war. In March he had a severe attack of pneumonia, the convalescence from which was slow, but at the end of

[1] University Medical Magazine, December, 1889.
[2] American Journal of the Medical Sciences, December, 1888.
[3] Medical News, 1889

six weeks he was able to be up and about. The mind at this time was perfectly clear, and had been so throughout the illness. About two weeks after convalescence he was noticed to be a little odd and peculiar; was low-spirited and depressed, and began to imagine all sorts of troubles; thought that he was in serious financial difficulties. He was never violent, simply melancholic.

When seen the patient was pale, with a sad, depressed expression of face. He would respond to questions, but not promptly, and speech seemed slow and hesitating. It was only with difficulty that any account could be obtained from him, of his feelings. His chief worry seems to be that he has lost the respect of his friends, and that people are plotting against him. His friends were advised to keep him at home carefully guarded.

September 21st. Patient seen to-day by Dr. Toulmin. He is looking, and has been, much better, has gained in weight, complexion is good and expression is cheerful. He still has hallucinations, and thinks that he has done something which he should not. Twice he has been violent, but was restrained without much difficulty. He seems to be progressively improving.

Case II.—*Typhoid fever; severe attack with much delirium. Mania during convalescence. Gradual recovery after four months.*

Mary J., aged 28, seen with Dr. Fussell on February 19th, 1888. Family history bad; a sister died of phthisis. No mental troubles.

The patient in January had an attack of mild typhoid fever, in which the mind was clear, the pulse not above 100, temperature not above 103°; the rose spots were well marked.

On January 29th, with the temperature 101°, the pulse 120, she was delirious for the first time. On the 30th and 31st she was constantly talking, chiefly on religious subjects. She tried to get out of bed, and was full of delusions. Throughout the first week of February, her temperature was not above 101°, but the condition of delirium was most intense, at times becoming quite maniacal.

I saw her on February 16th, in the following condition:

The temperature had been normal for at least a week. She was emaciated, and had a wild, anxious expression. She sat up in bed, and could not be induced to lie down. She talked incessantly, chiefly upon religious subjects. It was with difficulty that she could be kept

in bed. She had taken a violent aversion to her husband. She had both hallucinations and delusions. Unless under the influence of hyoscin she rarely slept. It was found necessary to remove her to the Pennsylvania Hospital for the Insane on February 22d, where she remained three months, when she returned home sound in mind but very weak.

In September she died of what was stated to be ulceration of the bowels.

CASE III.—*Typhoid fever of moderate severity. During convalescence development of delusions. Recovery after six weeks.*

Richard F., aged 30, seen with Dr. Gibb, November 20th, 1888. He had been ill since about the fourth of October, with a perfectly well characterized typhoid fever. The temperature was never very high, but the fever persisted for between three and four weeks. During the fever he had delirium, which set in early in the first week; it was, however, of a quiet character. When I saw him, he had had no fever for nearly two weeks. He was pale, but not much emaciated. The pulse was under 100, and the temperature normal. The tongue was a little furred. He was subject to distinct delusions. He did not know where he was; did not always recognize his wife, and constantly talked about events which had never happened. He was never maniacal. Dr. Gibb thinks that the delusions of the febrile state and of his present condition presented no distinct break. The symptoms persisted for a month subsequent to my visit. Convalescence was very slow, but with the recovery of his strength, the delirium and mental weakness disappeared.

CASE IV.—*Typhoid fever, mild attack. Gradual development of delusions. Slow, halting speech. Recovery.*

Henry C. P., aged 14, applied at my clinic, at the Infirmary for Nervous Disease, on March 6th.

As a child he was always healthy. He is of fair intelligence, and has made good progress in his studies. There are no nervous disorders in the family.

On December 22, 1888, he was taken ill with typhoid fever, apparently a mild attack. Temperature never rose above 103°. From the outset the head symptoms were well marked. He cried and

whined a great deal. He did not know his mother; he had a delusion that she was dead. The fever only lasted for two weeks; the rash was well marked and there was diarrhœa. The mental symptoms persisted for nearly four weeks after the temperature had fallen to normal.

In the early part of February he seemed to have recovered—at any rate to have gotten rid of his delusions; but his parents sought advice as he was, they said, a little queer.

Patient is a bright, well-nourished lad, answers questions rationally remembers all about his illness, and in conversation nothing peculiar would be noticed except that he hesitates and is slow in his speech. His mother says he is very restless, never remaining quiet for more than a few minutes. He is most anxious minded, and constantly thinks something is going to happen to his parents. He frequently wakens at night and behaves strangely. He does not seem to know his father. His slow, halting speech is quite marked, and is a feature which has developed since his illness.

Physical examination, negative. Heart normal. He eats well, and has gained rapidly in weight and in strength. A favorable prognosis was given, and I heard in May that he had recovered.

Case V.—*Typhoid fever, severe attack. During convalescence development of delusions. Persistence of mental symptoms for ten weeks. Recovery.*

Thomas D., aged 39, mechanic, admitted to the Philadelphia Hospital December 29th, 1888.

He had been off work for nearly six weeks, and for nearly a month of this time had been drinking heavily. For two weeks prior to his admission he had had fever and had been in bed a great part of the time, during which he continued to take much alcohol.

On admission he was rational. Temperature 101.6°, pulse 80. The only noticeable feature was the excessive tremor, which was attributed to alcohol, as his general condition was good. During the first week in hospital his temperature remained about 102°. There were distinct rose spots. He had rambling delusions at night, and would constantly attempt to get out of bed. On the 6th and 7th the temperature registered very low, 96.8°, but did not remain depressed for many hours. There was marked tympanitis on the 9th and 10th.

From the 12th to the 20th he improved rapidly. The temperature fell to normal, and he seemed to be convalescing rapidly. From this time on he showed marked mental disturbances. He did not recognize his mother, and constantly attempted to get out of bed. He became suspicious and presented many delusions.

Through February this condition persisted. He was very disturbed at night. He was very feeble and looked depressed. Hyoscin, morphia, paraldehyde, bromide of potassium, and chloral hydrate, were all tried in turn without satisfactory results. At one time he was quite violent, and had to be watched day and night. His delusions were chiefly of an unpleasant character. He thought that the persons in the ward were trying to kill him, and that he was being treated badly, and being kept away from his friends.

During the first and second weeks of March, his condition improved; he took food better and seemed to gain in weight. He was more readily interested, and at times seemed quite rational. The recovery was slow but progressive, and I saw him in June, when he seemed quite well.

Two points of practical interest may be mentioned. The prognosis in these cases is usually good. Of the seven cases in all, which I have seen, five after typhoid fever and two after pneumonia, six have recovered, and case I, reported in this paper, will, in time, probably get well. This should be remembered in considering the treatment of these post-febrile insanities, and renders it advisable, if at all possible, to care for the patient, at home. When actively maniacal, as in case II, this may not be practicable, but in general practice among the better classes, with a hopeful outlook and the prospects of recovery within a period of three months, home treatment should at first be tried. Seclusion, incessant watchfulness, absolute rest in bed, with massage and careful feeding constitute the essentials in treatment. It is interesting to note, as in case III, how, with the recovery of strength and improvement in general nutrition, the mind becomes stronger.

[From The Johns Hopkins Hospital Reports, Vol. II, No. 1, January, 1890.]

RARE FORMS OF CARDIAC THROMBI.

By WILLIAM OSLER, M. D.

We meet in the heart chambers thrombi of the following forms:

First: globular thrombi, with sub-trabecular ramifications, which are common in the auricular apendices and in the apices of the ventricles in cases of extreme dilatation.

Second: mural thrombi, usually laminated, which occur in the dilated auricles, particularly their apendices, in the ventricles in cases of fibrous myocarditis, and in aneurism of the heart.

Third: pedunculated polyp-like thrombi—a very rare form—met with usually in the auricles.

Fourth: ball-thrombi, free in the auricles, which constitute the rarest form of cardiac thrombus.

The first form, the *végétations globuleuses* of Lænnec, occurs not infrequently, and is well known. The polyp-like thrombi are very rare. Hertz[1] has collected nine cases in the literature. I have never met with an instance.

The second variety, mural, laminated thrombi, are not very uncommon, and the case here reported is of interest chiefly on account of the enormous size of the thrombus.

Ball-thrombi, free in the chambers, are excessively rare, only five cases having been recorded.

Case I.—*Large ball-thrombus, free in left auricle; mitral stenosis.*

M. S., aged 35, admitted to Montreal General Hospital, February 8th.

For twenty years she had been subject to attacks of shortness of breath, which within the past three years had become much worse. Two years ago she had an attack of acute rheumatism and during the past eight years she had occasionally spat blood.

In 1878 she had an attack of right hemiplegia, with aphasia. Speech returned in a few days, but the hemiplegia persisted for some

[1] Deutsches Archiv. für klin. Medicin, Bd. xxxvii.

months. Within a year she had a second attack, since which time the paralysis has persisted. When admitted there was orthopnoea; face suffused; no dropsy; complete right hemiplegia; the heart's action was very irregular; pulse 112, rapid and feeble; the cardiac dullness was increased; the apex beat was normal in situation. There was a blowing systolic murmur in mitral region. Temperature 101°. The urine contained 50 per cent. of albumen. The patient became rapidly worse; cyanosis increased, and death took place on the 13th.

Autopsy.—Small, well nourished woman; ecchymoses on face and extremities. Heart large, distended with blood clots, those in the right chamber dark in color and pulpy. The left auricle was greatly enlarged, and contained fluid blood and clots. Among these was a ball-thrombus, ovoid in shape, the size of a small pullet-egg, measuring 3.5 x 2.5 cms. It was quite unattached, and lay free above the mitral orifice. It was firm and elastic to the touch, and on the surface greyish brown in color, and presented little linear fibrinous elevations, but no roughened spot as if it had been adherent to the wall. It gave an indistinct sense of fluctuation as if central softening had occurred.[1] There were no mural thrombi in the chamber. The endocardium was opaque, and the walls thickened. The right chambers were greatly dilated; the tricuspid orifice measured 12 cms. in circumference. The auricular face of the valve presented fresh vegetations, many of them pedunculated. The walls of the ventricle were greatly thickened. The mitral orifice was very narrow, just admitting the tip of the little finger; from the auricle it looked like a small button-hole. At the bottom there was a funnel-shaped depression. The edges of the orifice were thick, of cartilaginous consistence, and were fringed with small vegetations. The chordae tendineae were short, particularly those from the anterior muscle which was attached almost directly upon the flap. The left ventricle was small, the walls over 12 mm. in thickness. The aortic valves were opaque, and presented a row of vegetations.

The lungs were crepitant throughout. They were tough and brownish-red in color; they did not contain an excessive amount of fluid.

[1] The specimen is preserved in the Museum of the Medical Faculty, McGill University.

The spleen weighed 150 gms., and was very firm—no infarcts. The right kidney presented several old cicatrices. In the left internal capsule were spots of old softening.

Of this remarkable form of thrombus, Hertz[1] has reported two cases, and refers to a third. In both of his cases there was mitral valve disease, and the ball-thrombus was found in the left auricle. One measured 2½ cms. in diameter, the other 4 cms. Both were rounded, and had a firm, elastic consistence. They were made up of fibrin externally, with a yellowish, granular, central portion, evidently the result of the softening, which so commonly takes place in cardiac thrombi.

The third case, which he abstracts, is reported by Macleod, in the Edinburgh Medical Journal, 1882–83. In this case a young man, aged 27, had symptoms of cholera, and on the fifth day was seized with convulsions, cyanosis and intense dyspnœa. Death occurred in about 48 hours. There was found in the right auricle a dense grayish-yellow, freely movable clot, half the size of a walnut, which lay above the tricuspid orifice.

In the same volume of the Deutsches Archiv. für klin. Medicin, Prof. von Recklinghausen states that he had first described[2] these ball-thrombi, of which he had seen two instances, both in connection with mitral stenosis. The thrombi were round, about the size of small walnuts, and lay free in the left auricle.

These remarkable structures are, as Recklinghausen suggests, globular thrombi detached from the auricular appendix, and, being too large to pass through the narrowed mitral orifice, are kept rotating in the auricle, growing constantly by the accretion of fresh layers of fibrin. It is not likely that they produce any special symptoms.

CASE II.—*Mitral stenosis of extreme grade. Enormous dilatation of left auricle by large laminated thrombus.*

Mary J. E., white, aged 48, admitted to the Johns Hopkins Hospital, on the evening of June 20th, 1889, with dropsy and extreme dyspnœa. Married and has had five children, all of whom died when young.

[1] Loc. cit.

[2] Algemeine Pathologie des Kreislaufs, Deutsche Chirurgie, Lief, 2 and 3.

IMAGE EVALUATION TEST TARGET (MT-3)

6″

Family history negative.

She does not think that she has had scarlet fever. Has never had acute rheumatism. She has never been a very strong woman; has had shortness of breath at times for ten or twelve years. For six weeks the shortness of breath has been worse. A week ago she began to have a cough for the first time. She has been in bed for eight days, and her feet have become swollen. She has had a good deal of vomiting.

21st. Present condition. Small, spare woman; color ashy-grey; finger tips and lips blue. There is marked orthopnœa. The feet and legs are swollen. When admitted the pulse was scarcely to be felt at the wrist, and she was given two hypodermics of ether and digitalis. This morning the pulse can just be felt, but cannot be counted. Respiration 44.

Heart. Very slight visible impulse. To the hand, marked shock, especially in epigastrium. There is an indistinct thrill. Dullness extends from the upper border of third rib, and to the right is two finger's breadth beyond the margin of sternum.

On auscultation, below the nipple there is a continuous rapidly succeeding series of sounds, the first and second not distinguishable from each other, and the long pause is absent. *There is no murmur.* At lower sternum the first sound is distinguishable. It has a ringing, echoing character. At the base the second sound can be distinguished from the first, and is loudest at left margin of sternum. Most careful auscultation fails to detect a murmur at any of the cardiac areas.

She was ordered hypodermics of ether and tincture of digitalis every three hours. In the evening she seemed somewhat better, the distress of breathing was not so extreme. There was dullness at the left base, as high as the angle of scapula, with feeble breathing.

22nd. The pulse can scarcely be felt. In the mitral area the first sound can be distinguished from the second, and the diastolic pause is more marked. *There is no murmur.* The second left at base is ringing. On palpation the shock in lower sternum is very marked. The discrepancy between the loud, clear ringing sounds, with the moderately forcible impulse of the heart, and the extremely shabby, scarcely detectable pulse is very marked. The urine is scanty and difficult to obtain; it contains a trace of albumen.

The cyanosis became more intense. She got much worse during the night and died on the morning of the 23rd.

A diagnosis of mitral stenosis was made. The absence of murmur was thought to be due to the condition of enormous dilatation of the left auricle.

Autopsy, by Dr. Welch. Multiform ecchymoses on the skin; œdema of the legs; face cyanosed.

In peritoneum, about 150 cc., of clear yellowish serum.

Thorax. The right pleura was everywhere adherent; the left pleura contained 1,500 cc. of serum.

Lungs. The right main pulmonary artery entering the lower lobe was occluded by a firm, greyish-red thrombus which extended only a short distance into the branches of the artery. There was well marked brown induration of the organ, with desquamative heart-pneumonia. The substance was dry. In the left lung the left upper branch of the pulmonary artery was completely occluded by a greyish-red, laminated thrombus. The pulmonary artery and its branches in both lungs were extensively atheromatous. The substance of the left lung was much compressed; it was also in a state of brown induration. There were no infarcts.

Heart weighed 16 oz. (453.6 gms.) (due largely to enormous thrombus in the left auricle). The left ventricle was not hypertrophied or dilated. It appeared to be normal in size, and measured 9 cms. in length. The walls were 1 cm. in thickness. The aortic valves were slightly thickened along the lines of closure; otherwise they were normal. The mitral orifice was extremely stenosed. The segments were completely and firmly united to each other everywhere, except at the aortic extremity of the orifice, where there was an opening measuring about 5 mm. in diameter, which scarcely admitted a small lead pencil. The united segments were thickened and calcified, but the surface was not rough, saving to a little extent on the auricular face. There were no vegetations. The chordæ tendineæ were thickened, and the tips of the papillary muscles fibroid. The left auricle was greatly enlarged, measuring 10 cms. transversely and 7 cms. vertically. The muscle wall was greatly hypertrophied, measuring 6 mm. in thickness. The endocardium was thickened and opaque. The chamber was nearly filled with an ante-mortem thrombus, laminated, partly grey and partly red. Over a greater part of its extent it was firmly

adherent to the wall of the auricle; in other places it was loosely adherent. The thrombus partly occluded the mouths of the pulmonary veins, but there were channels through which the blood could flow. The thrombus had undergone softening in various parts. The pericardial surface of the left auricle was thickened and opaque. The right ventricle was markedly hypertrophied and dilated. It was 9 cms. in length; the walls averaged 7 mm. in thickness. The muscular trabeculae were thickened, and the tricuspid orifice admitted readily four fingers. The segments of the valve were normal, saving a little diffuse fibroid thickening. The right auricle was also much hypertrophied and dilated; its walls measured in places 4–5 m.m. in thickness. The hypertrophy was especially well marked in the trabeculae. The cavity of this chamber was much dilated, measuring at the longest about 8 cms. The coronary sinus was greatly dilated. The pulmonary valves were normal. The pulmonary artery presented several opaque yellow atheromatous patches. At its bifurcation there was a parietal thrombus, which became an occluding thrombus in the vessels going to the left lower and to the right upper lobes, as already described.

The spleen weighed $3\frac{1}{4}$ oz., (92.14 gms.) dark-red in

The kidneys presented patches of atrophy on the surface. The striae of the cortex were distinct. The consistence of the organs was increased. The renal arteries were atheromatous. The liver weighed 33 oz., (935.5 gms.) and was in a condition of red atrophy.

Mural thrombi are quite common, particularly in the auricular appendices, but they are usually small. Massive coagula, with extension into the vessels, such as existed in this case, are extremely rare, and occur chiefly with mitral stenosis. Cases are on record in which the thrombus has passed through the narrowed mitral orifice.

Clinically the case is interesting as illustrating the disappearance of the murmurs in the last stage of mitral stenosis, not an uncommon event when the left auricle becomes over distended. There were no symptoms which could be directly referred to the blocking of the auricle with thrombi, none which we do not meet with in extreme grades of dilatation of this chamber.

[From The Johns Hopkins Hospital Reports, Vol. II, No. 1, January, 1890.]

NOTE ON ENDOCARDITIS IN PHTHISIS.

By WILLIAM OSLER, M. D.

Within the past few years several writers have called attention to the frequent occurrence of vegetations on the heart valves in phthisis. The appearance of Dr. Percy Kidd's paper in the St. Bartholomew's Hospital Reports,[1] and the dissection of a recent case suggested a review of my post-mortems, as I had the impression that the condition was by no means so common as he had found it. The following case presents points of special clinical interest.

Stella D., aged 19, admitted to the Johns Hopkins Hospital, November 1st, with cough, loss of flesh and high fever. Temperature on admission 105°.

Her mother died of consumption. She had always been well until her present illness which began about six months ago with cough and fever. Through the summer she lost flesh and had night sweats. She gave up work in May. On admission the temperature was high, and she was emaciated and anæmic. There were cavernous signs at both apices, most extensive at the left; fine crepitant râles and moist sounds at bases.

Heart. Cardiac pulsation visible in third, fourth, fifth and sixth interspaces. In the third, fourth and fifth, the impulse was wavy. At apex the heart sounds were clear. At the pulmonary cartilage there was a short systolic murmur, quite localized, not transmitted to the left and not heard below fourth rib. At the aortic cartilage the sounds were clear. The patient had persistent high temperature, reaching twice to 105°. She rapidly failed and died on the 22d.

The autopsy showed cavities at both apices. The left upper lobe was small and did not cover the heart to the usual extent. There were numerous groups of tubercles throughout all the lobes and many areas of gelatinous infiltration.

[1] Vol. XXIII.

The heart was large. The cavities contained fresh coagula and a little fluid blood. The valves on the right side were normal. The mitral orifice was of medium size. The edges of the auricular surface were uniformly studded with large, recent vegetations, grayish-white in color, soft and readily removable. The majority of them were pedunculated. The aortic valves were free.

There were no infarctions.

Fresh frozen sections showed:—(1) marked proliferation at the attached edge of the vegetation; (2) A finely granular substance, composing the great part of the granulations,—the granules were uniform in size; (3) Scattered about among them were numerous large compound granular corpuscles, some of which were rounded, others irregular spindles.

Bacilli were not found in the stained sections.

Clinically this case illustrates the well-known fact that a murmur of maximum intensity in the 2d and 3d left interspaces may indicate mitral insufficiency, but I do not remember ever to have heard one so localized in these regions, and inaudible at the apex. I regarded it as an instance of the murmur so common at the left sternal margin in cases of phthisis and thought to originate in the pulmonary artery, but the condition of the valves would indicate that it was produced at the mitral orifice.

In 216 autopsies on phthisis there were 12 instances with fresh endocardial vegetations—mitral valves, 8; aortic valves, 3; aortic and mitral, 1. With one exception the disease was of the verrucose or warty variety, and did not produce any destruction of the segments. The case of the ulcerative form was in a woman aged 28, who was admitted January 8, 1883, to the Montreal General Hospital, under Dr. Molson, with well-marked chronic phthisis and delusional insanity. There was involvement of the greater part of the right lung, with cough, night-sweats, and rapid emaciation. There was nothing in her history to call attention to cardiac trouble, and the condition found at the autopsy was unexpected. There were extensive ulcerative changes on the mitral valves.

In Kidd's series there were twenty-seven cases of endocarditis in five hundred phthisical subjects; in thirteen of the simple warty variety, in nine associated with sclerotic changes, and in four there were chronic endocardial changes alone. In one instance the recent

affection was ulcerative. About the same percentage was affected in his series as in mine.

The tubercle bacillus has been found in these vegetations by several observers (Cornil. Heller, Centralbl. f. Baeteriologie, 1887, 1), but it may be doubted, in the absence of the characteristic changes associated with the organism whether this is anything more than an accidental contamination. In the cases which I have examined they were not present, and Dr. Councilman tells me that he has not been more fortunate. Dr. Kidd, also, has not found them in his cases.

TUBERCULAR PERITONITIS.

GENERAL CONSIDERATIONS—TUBERCULAR ABDOMINAL TUMORS—CURABILITY.

By WILLIAM OSLER, M. D.

The progress of abdominal surgery during the past few years has contributed to our knowledge of tubercular peritonitis in two directions—first, in teaching us with what frequency the condition may simulate or be associated with abdominal tumor; and, second, in demonstrating the curability of a certain proportion of the cases. To a consideration of these two aspects of the subject I propose to devote the following paper, introducing their discussion by a brief summary of certain of the anatomical and clinical features of the disease.

I.—General Considerations.

Anatomically the classifications which have been made of tubercular peritonitis are not altogether satisfactory.

It is customary, and correct, to exclude the cases of scattered miliary tubercles in the diffuse infective disease and also those cases in which the peritoneal surface of tubercular ulcers is alone involved. Practically, the great differences which we see, post-mortem, in this condition result from the situation, the rate of growth of, and the degree of inflammation accompanying the tubercles, and whether there is much or little exudation—serous, purulent or hemorrhagic. The anatomi-

cal basis in all cases is essentially the same, and the variations which we meet, though distinct and marked, are scarcely sufficient to warrant the elaborate subdivisions of this disease made by certain writers. Thus, Spillman,[1] in his excellent recent article on the subject, makes the following five divisions: *tuberculose miliâire aiguë; tuberculose ulcereuse; tuberculose fibreuse; pelvi-péritonite tuberculose; tuberculose péritonéo-pleurale.* I see no reason for the fourth and fifth groups, if we bear in mind the frequency with which the peritoneal mischief is excited by tubal disease and the liability of the pleural membranes to be involved in the process. A large proportion of the cases in the first three divisions would at some period of their evolution come in the fourth or fifth group.

In reviewing a number of post-mortems in this disease we find that they fall naturally into the first-named categories:

(1) *Acute miliary tuberculosis*, characterized by a sudden onset, a rapid development, and a serous or sero-sanguineous exudation.

(2) *Chronic caseous and ulcerating tuberculosis*, characterized by larger tuberculous growths, which tend to caseate and ulcerate, leading often to perforations between the intestinal coils, and a purulent or sero-purulent exudate, often saeculated.

(3) *Chronic fibro-tuberculosis*, in which the process may from the outset be sub-acute, or may represent the final result of the miliary form. There is little or no exudation and the tubercles are hard and pigmented.

There exists the closest analogy between tubercle as we see it on the peritoneum and as it occurs in the lung—the fresh miliary eruption, the caseous, ulcerating masses and the chronic, fibroid, pigmented nodules may be studied with equal facility in either structure.

A few practical points in the morbid anatomy may be mentioned. In many cases the process is entirely local. Thus in five of seventeen cases of which I have post-mortem notes the condition was confined to the peritoneum. Case VIII (given in another section) is an excellent illustration of this, and it will be noted also that the mesenteric glands were not affected. This local character of the disease, upon which scarcely sufficient stress has been laid, is an extremely important feature, particularly in discussing the propriety of operation, as

[1] Dictionaire Encyclopédique, Art. Péritonites.

the outlook is much more favorable in the absence of intestinal, pulmonary or tubal complications.

The Fallopian tubes are often affected, but the proportion given by various writers differs very much. Of my series in one only of four post-mortems in women were the tubes diseased. In seven of sixteen cases from Immermann's clinic[1] these parts were involved. It is safe to say, I think that in from 30 to 40 per cent. of the cases in woman the tubes are found affected. The process is commonly confined to the distal ends and may be primary—which is usual—or is secondary to the peritoneal involvement. Gynecologists now diagnose and remove dilated tubes with such facility that we have numerous opportunities of studying primary tuberculosis of these organs. I have frequently been impressed with the wisdom of this procedure as a protective measure, on seeing large caseous tubes with miliary nodules on the peritoneal surface, since the danger of general extension in such cases is very great. Hegar's monograph[2] is a storehouse of interesting information on this subject.

A third point, worthy of attention on account of its importance as an aid in diagnosis, is the frequent involvement of the pleura. Several of the French writers on the subject have dealt very fully with this, notably Fernet[3] and Boulland,[4] and Spillman, as remarked above, makes a special sub-division to include these cases. In Boulland's list of eighty-two cases there were thirty-eight with tuberculosis of the pleura, with or without effusion.

In only three of the seventeen post-mortems, of which I have notes, was there tuberculous pleurisy,—a comparatively small proportion. In the twenty autopsies in Häne's list there were nine with pleural involvement. In twenty-five of Bristowe's[5] forty-eight cases, the pleura was affected. It is often only a dry pleurisy, occurring most frequently without pulmonary affection, and due to a direct extension through the diaphragm. The pericardium is also liable in these cases to be the seat of an adhesive tubercular inflammation.

Age.—Tubercular peritonitis occurs at all periods of life. It is common in children, in whom it is often associated with intestinal

[1] Ueber Peritonealtuberculose, Häne. Rorschach, 1889.
[2] Genitaltuberculose des Weibes. Stuttgart, 1886. [3] Quoted by Boulland.
[4] Paris Thesis, 1885. [5] Reynold's System of Medicine.

and mesenteric disease. Full statistics dealing with its prevalence in infancy and childhood, are not available; I am sure the figures which follow, do not represent the true proportion of cases at this period of life. It is most common between the ages of twenty and forty. In old age it is rare, but it may occur even in advanced life, as in Case XXI of my series, in which extensive disease existed in a man of eighty-two. In my own cases the distribution has been as follows; Under ten, 2 cases; from ten to twenty, 1; from twenty to thirty, 4; from thirty to forty, 5; from forty to fifty, 7; from fifty to sixty, 1; and above eighty, 1. Adding to these, 69 cases of Boulland,[1] 48 cases of Häne,[2] 39 cases of Maurange,[3] (in which the age was given), and 45 cases of Fenwick,[4] makes 222 in all; and joining these figures to those of Bristowe, Hilton Fagge and Lebert,[5] 135 cases, we have a total of 357. These analyzed according to ages give, under ten, 27; between ten and twenty, 75; from twenty to thirty, 87; between thirty and forty, 71; from forty to fifty, 61; from fifty to sixty, 19; from sixty to seventy, 4; above seventy, 2.

Sex.—The disease is certainly more prevalent among females. The statistics of general hospitals and of average medical practice may perhaps show a preponderance of cases among males. This was the case in Bristowe's figures at St. Thomas' Hospital, in Fagge's at Guy's Hospital, and Fenwick's from the London Hospital, while in my series of twenty-one cases, fifteen were males. But when we go over the recent literature of the laparotomies which have been performed in this disease, we find the number of females to be largely in excess. Thus, if we take the figures of Boulland, Häne, Maurange and my own, there are 60 cases in males and 131 in females.

Race.—It is stated that the disease is more common in the negro than in the white race. Several of the leading physicians of this city have expressed themselves strongly on this subject, particularly Dr. I. E. Atkinson and Dr. W. T. Howard. Three of the four cases which have occurred at the Hospital have been in colored people, but

[1] Loc. cit. [2] Loc. cit.

[3] Paris Thesis, 1889. De l'Intervention Chirurgicale dans la Péritonite Tuberculeuse.

[4] Lectures on some Obscure Diseases of the Abdomen. London, 1889.

[5] Quoted by Spillman, loc. cit.

there are, so far as I know, no figures which could enable us to arrive at a definite opinion as to the relatively greater frequency of the disease among them.

Clinically it is extremely difficult to make a satisfactory classification of the cases of tubercular peritonitis, and I shall here only refer to certain special features in the mode of onset and to peculiar symptoms not, as a rule, very fully discussed.

The process may be completely *latent* and the eruption take place so slowly and so painlessly that the patient may not have presented a single symptom of abdominal disease. The condition has thus been met with in the operation for hernia, and more frequently still in association with ovarian tumor. In three of my cases it was found accidentally, and, so far as could be ascertained, there had not been special symptoms pointing to abdominal disease. Thus in Case X,[1] a man aged 40, well nourished and believed to be in good health, was admitted to the Montreal General Hospital with strangulated omental hernia. He died eighteen hours after the operation, and extensive tubercular peritonitis of the fibrous variety was found. The left pleura was also involved. In Case XI,[1] a girl, aged 18, was admitted to hospital with severe typhoid fever, of which she died. The abdominal symptoms were those ordinarily met with and there was no history of previous trouble. The post-mortem showed, in addition to characteristic typhoid lesions, an extensive tubercular peritonitis, which had taken its start from the Fallopian tubes. The lungs were not affected. Case XII,[1] a healthy looking, well-nourished child of five, died of malignant diphtheria after an illness of a few days. An acute miliary tuberculosis existed over the entire peritoneum, which contained a slight amount of serous and much fibrinous exudation. There were tubercles in the spleen but none in the lungs. A case at present in the Hospital, in Dr. Kelly's ward, illustrates this latency in the disease. The patient had a large ovarian tumor which was removed October 18th. The peritoneum was found universally covered with recent tubercles of various sizes which also existed over the surface of the tumor.

The literature contains very many cases of this kind, so that it is a fair conclusion to regard the disease in many instances as latent in its

[1] Of the series of 21 cases.

course, and it is possible for the process to go on to healing without having induced serious symptoms.

The onset of symptoms may be *sudden* so that the diagnosis of enteritis or hernia may be made. A remarkable instance in which it was mistaken for the last-named disease is reported by Thoman.[1] A well-nourished woman, aged 30, was suddenly seized with pain in the abdomen, vomiting and fever. The physician who saw her believed the symptoms due to a hernia, which he thought he found and reduced. The condition continued and in the evening Thoman was called in. No hernia was found externally but as the abdomen was distended and painful it was decided to operate. The inguinal ring was found closed. In the further course of the disease, the peritonitis became more marked, the ascites increased and death occurred on the fourteenth day. The post-mortem showed extensive tuberculosis, both layers of the peritoneum being covered with a recent eruption. There were no tubercles in the lungs or pleuræ. This case is not unique, as Spillman[2] quotes another instance in which the symptoms were so urgent and deceptive that internal strangulation was suspected.

This suddenness of onset is very deceptive and usually leads to the diagnosis of a simple acute peritonitis. The following case which I saw on several occasions with Ross of Montreal illustrates this point as well as the importance of the pleural symptoms so liable to supervene in the course of the disease:

CASE I.—*Acute peritonitis; tympanites; abdominal tenderness, with loss of flesh and irregular fever. Pleurisy with effusion. Tubercles on peritoneum, pleura and parietal pericardium.*

G. C., aged 17, colored, was admitted to the Montreal General Hospital, January 23rd, 1884, with an attack of acute peritonitis which had begun suddenly three days before. For a year he had had irregularity of the bowels, with occasional pains, and had lost flesh. On admission, temperature was 104°, pulse 92. The abdomen was tympanitic and there was pain on pressure. Under appropriate treatment the pain became less and he improved. The temperature fell and became subfebrile, until February 1st, after which it was very irregular, rising to 102°, 103° or 104° at night, becoming normal or even subnormal

[1] All. Wiener Med. Zeitung, 1887, page 306. [2] Loc. cit.

in the morning. Towards the end of February there was a return of the pain and tenderness in the abdomen. Early in March, signs of pleurisy on the left side and a friction murmur developed near the left nipple, thought to be pericardial. By the 17th of April, there was well-marked effusion into the left pleura. The heart impulse was felt to the right of sternum. The abdomen became more distended, a little hard; no ascites. On the 30th, 1½ litres of serum were removed from the left chest. By May 7th, the fluid had re-accumulated and he was again aspirated. Death took place on the 19th.

Autopsy.—(Case 795, Post-mortem Records of Montreal General Hospital.) Much emaciation. Abdominal organs and coils of intestines completely glued together. Peritoneum studded with innumerable whitish masses, the size of small marbles. On section they were firm and caseous. Pericardium was adherent to sternum and there were tuberculous nodules infiltrating the parietal layer. The visceral layer was smooth; no tubercles. In left pleural cavity 2 litres of fluid. The pleura was covered with tubercles; the lung was airless and lay close against the spine. There were no tubercles in the substance of either lung. The abdominal organs were normal. There were vegetations on the aortic valves. The brain was normal. Dr. Ross, in commenting on this case,[1] notes particularly the abrupt onset of the acute peritonitis, which under appropriate treatment rapidly disappeared.

The disease may set in with pronounced *gastric symptoms* and simulate ulcer or cancer, as in the following case already published in my Pathological Reports, Montreal General Hospital, 1878.

CASE II.—*Acute tubercular inflammation of the peritoneum. Persistent gastric symptoms. Small caseous mass in left lung. Right-sided pleurisy.*

J. McT., aged 35.—Had been a soldier for twelve years, latterly a sailor; admitted to Montreal General Hospital in September, 1876, complaining of weakness, loss of appetite, and frequent attacks of vomiting. No albumen in urine. Blood normal. Systolic murmur at apex. No enlargement of abdominal organs. Tenderness on deep pressure along right costal border and ensiform cartilage. The vomiting became more marked, and he had occasional attacks of diarrhœa.

[1] Canada Medical and Surgical Journal, Vol. XIII.

The symptoms pointed, though vaguely, to disease of the stomach, either round ulcer or cancer. The vomiting was with difficulty controlled, and patient became very weak and anaemic, the skin slightly icteric. He gradually got so feeble that he was unable to move from bed, and the vomiting was so persistent as to necessitate feeding per rectum. Through January and February the vomiting diminished, but the patient wasted slowly, and the case was regarded as malignant disease, involving perhaps the peritoneum. In the beginning of May the peritonitis became acute and general, and he died on the 25th, profoundly exhausted. For some weeks before death hemorrhages occurred in various parts of the skin.

Autopsy.—The peritoneum, contained 3 litres of a turbid, slightly bloody fluid, in which were flocculi of lymph. Here and there the coils of intestines were matted together by easily separable adhesions. The transverse colon and stomach were in this way glued together; the former covered also the anterior border of the liver. The entire peritoneum, except the portion over the stomach, was of a dark red color, infiltrated, sodden, and readily stripped off from the subjacent tissues. Localized patches of lymph occurred here and there upon it. The whole membrane presented a great number of small white areas, flat, not projecting above the surface, and ranging in size from a hemp seed to a split pea. As a rule they were isolated, but occasionally groups were seen. They existed in about equal numbers over the intestines, mesentery, and parietal peritoneum. Beneath the latter were from eight to ten larger white patches, which, on section, had a caseous appearance, were firm to the touch, not encapsulated, and extended to the depth of about four millimetres. On examination of these small and large white masses, they were found to be almost entirely subperitoneal and composed of aggregations of lymphoid corpuscles, a little smaller than the colorless blood corpuscles, and with one, rarely two, nuclei. In sections through those on the intestinal wall, the corpuscles were seen to infiltrate to some extent the muscular coats. The mesenteric glands were but little enlarged.

The heart showed numerous ecchymoses on pericardium; the walls were flabby, the muscle pale; very little blood in the chambers.

There were 2 litres of turbid fluid in right pleural sac. Visceral and parietal layers congested, and covered with flakes of lymph. A few cc. of fluid in left sac.

The right lung was crepitant, except at extreme base, the lower lobe collapsed. The organ contained a good deal of serous fluid. The left upper lobe was crepitant, the lower collapsed and œdematous. At the anterior border of upper lobe was a firm block of condensed tissue, somewhat triangular in shape, which on section was made up of a small cavity, looking not unlike a dilated tube. There were one or two caseous nodules in the lung. There were no miliary tubercles in either lung.

The spleen weighed 150 gms. unaltered.

The liver weighed 2000 gms., was anæmic and yellowish in color.

The kidneys were normal in size, but very firm in texture. In the cortex of the right were several small purulent foci, about which the substance was much congested.

The stomach did not present any trace of cicatrices or of tumor. It contained about a litre of fluid.

The small intestines contained yellowish, liquid fæces; the walls were thick, owing to an infiltrated, swollen condition of all the coats. The mucous membrane was dark in color. Peyer's glands were not enlarged.

A more common mistake is confounding tubercular peritonitis with *typhoid fever*, which it may simulate very closely. R. L. MacDonnell,[1] of Montreal, has recently called attention to this, and has reported several cases. In the following instance, also in Case IV, this mistake was, I believe, made.

CASE III.—*Attack of acute abdominal disease; gradual recovery; latent pleural effusion. Pronounced tuberculous history.*

Miss G., aged about 30, fairly well nourished, seen in October, 1888, on account of shortness of breath and cough. The family history was bad; several members had died of tuberculosis. She had herself always enjoyed fair health. In August she began to have abdominal pains and an irregular fever, in which the temperature rose as high as 102.5°. She was thought to have typhoid fever, though there was no diarrhœa and spots were not found. The most marked symptoms were the distension of the abdomen and the tenderness, chiefly on the right side. The temperature chart, which I

[1] Canadian Practitioner, 1888.

saw, showed an irregular fever range, not at all characteristic, the temperature sometimes dropping to normal. After persisting for about six weeks, these symptoms subsided, the fever left, and she got up and began to gain strength; but shortness of breath became a marked feature and she remained pale and developed a slight cough, and it was for these symptoms that I was consulted. The abdomen was a little full, tympanitic, nowhere tender, no signs of any effusion. On inspection of the chest, it was seen that the right side scarcely moved; the apex beat was far over in the left axillary line. There were dullness and other signs of extensive exudation in the right pleura. Temperature was normal. She was aspirated with great relief and two weeks later fluid was again withdrawn. She improved rapidly and by the middle of December, the breath sounds were well heard over the greater part of the right lung, but percussion resonance was defective over the lower half, and at the base quite flat.

Considering the nature of the abdominal attack, the patient's family history and the gradual onset of the pleural effusion, there can be but little doubt that this was a case of tubercular peritonitis, mistaken for typhoid fever.

Ascites is a frequent symptom but it does not as a rule become very marked; thus Biat,[1] in an analysis of eighty-one observations, found only thirteen instances with extensive ascites. In the acute miliary tuberculosis with rapid exudation the effusion may be bloody, but judging from the published records and from my personal experience this is not so common as in cancer, though the opposite statement is usually made. It has frequently been mistaken for the effusion in connection with cirrhosis, of which, indeed, it may sometimes be a complication. It is somewhat remarkable with what frequency acute tuberculosis of the serous membranes occurs in this disease. Moroux[2] and Wagner[3] have called attention to the involvement of the peritoneum, which in my experience is not so often affected as the pleura. I have notes of six cases in which acute tubercular pleurisy occurred as a final complication in cirrhosis.

Cases with extreme *tympanites* are also common. This condition, the result of impairment of the tone of the muscular coats, is a very constant feature in all forms of the disease. There are instances in

[1] Paris Thesis, 1884.
[2] Paris Thesis, 1883.
[3] Deutsches Archiv f. Klin. Medicin, Bd. xxxiv.

which it seems to be particularly marked, as in Case VI, to be referred to later.

Of special symptoms, I wish to speak of two only; one of which has not received the attention it deserves.

Sub-normal temperatures.—Many writers refer to the fact that the temperature in tubercular peritonitis may be normal, but it is not generally known that the temperature may be subnormal for weeks or months at a time. My attention was called to this fact about four years ago by my colleague Dr. Musser, at the Philadelphia Hospital, who has made a number of observations on this point. In the cases of fibrous tubercle, without much inflammatory process or effusion, there is as a rule very slight fever and subnormal temperatures are common. Thus, in Case VII, to be fully given under another section, the temperature during the patient's entire stay in the Hospital was subnormal for a greater part of the day. In the early morning the thermometer rarely indicated more than 96° or 96.5°; a gradual rise occurred through the day, and the normal point was reached late in the afternoon. The same was noticed in a second case, upon which laparotomy was performed, Case VIII. During her convalescence, for days at a time, the temperature did not once reach 98°; thus during November 28th, 29th, 30th and December 1st, the temperature was taken every two hours, day and night. On the 29th and 30th it ranged between 97° and 98°, but twice registered at 96°. Throughout December 1st, 2d and 3d it only once reached 98°; the range was between 96° and 97.5°. In the diagnosis of doubtful cases this symptom may prove of great value.

In a case of Sir Edward Sieveking's, at St. Mary's Hospital, London, reported by J. F. Payne,[1] the patient's temperature from March 21st to April 16th, ranged from 95.6° to 96.4°. Such references as this occur in the literature, but they are by no means common and the fact is not widely recognized.

Pigmentation.—An increase in the skin pigment, particularly on the face, is an occasional symptom in tuberculosis of the peritoneum. It was specially described by Guéneau de Mussy in 1879,[2] but I remember in the session of 1872–73, that Sir Wm. Jenner, at University College Hospital, pointed out this condition as simulating Addison's

[1] Transactions of the Pathological Society of London, Vol. XXI.

[2] Étude sur la Pigmentation de la Face dans la Tuberculose abdominaire. Paris, 1879.

disease in a case of extensive abdominal tuberculosis. It was present in a marked degree in Case VII, and I have seen one other instance. In Case XII of Boulland's paper, the symptoms of Addison's disease were pronounced and, post-mortem, tubercles were found in the suprarenal capsules as well as on the peritoneum. I think the condition may be present when the tubercles are confined to the peritoneum, and an increase in the pigmentation does not necessarily mean that the adrenals are affected.

II.—Tumor Formations in Tubercular Peritonitis.

To the occurrence of tumor-like formations in tubercular peritonitis we are indebted for much of the increase in our knowledge on this subject, as the errors in diagnosis have shown the frequency with which these tumors occur and also how amenable the condition is to surgical treatment. The question has not been fully considered by any recent writer, yet its importance may be gathered from the fact that in 96 cases in which laparotomy was performed, in 37 the diagnosis was tumor, ovarian or otherwise.

One of the best and most suggestive, and perhaps the first, of the papers to deal with this question was by Dr. W. T. Howard, of Baltimore.[1] He reviewed the literature of ovarian disease with special reference to this point, and showed how little attention had really been paid to it; yet, even in 1885, before laparotomy had become so common for peritonitis, he was able to refer to several instances in which the mistake had been made of confounding encysted effusion with ovarian tumor. As he remarked, the standard works on gynecology did not allude to the subject, and with the exception of a brief note in Kaulich's[2] monograph, there was no reference in general medical literature. Busey[3] had previously reported a case in which an encysted peritonitis simulated ovarian cyst, and Gardner[4] an instance in which the diagnosis of a suppurating cyst was made.

More recently Van der Warker[5] reported an interesting case and discussed the propriety of laparotomy in tubercular peritonitis.

[1] Transactions of the American Gynecological Society, 1885.
[2] Prager Vierteljahrsschrift, 1871.
[3] Gaillard's Med. Journal, May, 1880. Quoted by Howard.
[4] Canada Medical and Surgical Journal, 1885.
[5] American Journal of Gynecology, 1887.

Among the numerous monographs and papers on the operative treatment of peritonitis in recent French and German literature, I have not met with one which discusses as it deserves the question of these tumor-like formations.

We may recognize anatomically, and possibly clinically, four groups of cases in which with tubercular peritonitis tumors occur and may be felt on examination: First, omental tumor; second, sacculated exudation; third, retracted and thickened intestinal coils; fourth, mesenteric glands.

(*a.*) *Omental Tumors.*

On the thin and delicate layers of the epiploon tubercles will be found if present at all on the peritoneum, but they do not often form large masses which can be felt through the abdominal wall. The omental tumor in connection with this form of peritonitis results from a slow tubercular process which gradually puckers and rolls the membrane, until it forms an elongated firm mass attached to the transverse colon lying athwart the upper part of the abdomen. This condition, perfectly well recognized by clinicians, is in many cases peculiar and distinctive. I call to mind at least four instances, in two of which the diagnosis was confirmed post-mortem. Of these, two did not occur in my own practice. In the third, a man at the University Hospital, Philadelphia, with a tuberculous history and symptoms which pointed to gastric trouble, the abdomen was moderately distended, painless, and there lay across the upper zone a ridge-like tumor, readily separated from the liver and spleen. It was not possible to exclude cancer but the diagnosis leaned rather to tuberculosis, and this was confirmed some months after on the death of the patient, which took place outside the Hospital. The fourth case is of interest, as it occurred in a man over eighty, who presented simply a condition of general enfeeblement with moderate wasting and slight enlargement of the abdomen. Here, too, there was an elongated mass in the upper part of the umbilical region, which proved on post-mortem to be a solid omental tumor caused by chronic tubercular inflammation. There were no tubercules in the lungs or pleuræ in this case, which illustrates also a condition which is more common than is supposed, viz: tubercular infection in the aged.

These cases often occur without much exudation and result from

a slow, latent process which may run its course without exciting serious symptoms. To diagnose this condition from cancer is often difficult. A pronounced tubercular history, subnormal temperatures —which are not I think so common in cancer, and which are specially likely to occur in these more chronic cases of tuberculosis—and the existence of disease in the pleuræ or lungs are suggestive indications. The impossibility of avoiding error is illustrated by a case of Gairdner's[1] in which an omental tumor was thought to be mesenteric. In connection with the subject this writer says that "it would be easy to show that in most of the text books the diagnostic characters and significance of thickening of the great omentum have been strangely overlooked; although the mere anatomical fact has long been known."[2] Cases I and IV in the appendix to his lectures are of special value as indicating the gradual resolution in children of these tubercular omental tumors.

Fagge[3] calls attention to the existence of a resonant percussion note above the mass, which sometimes feels as if attached to, and indeed has been mistaken for, the edge of the liver roughened and nodular. This point is of some importance in the diagnosis of the omental tumor. It must be remembered, too, that when the mass lies close to, or even upon, a distended colon firm percussion may elicit flat tympany. Crozer Griffith[4] has recently reported an interesting case in a man, aged 64, in whom a tuberculous omental tumor complicated rather than simplified the diagnosis.

R. L. MacDonnell has given me the notes of the following case in which the omental mass formed a prominent tumor in the right iliac and lumbar region—an unusual situation.

Emma S., aged 30, admitted to the Montreal General Hospital, April 5th, 1887. A thin delicate woman with a history of scarlet fever at fourteen, rheumatism at seventeen, followed by some pulmonary trouble. She had always been subject to constipation, neuralgia and general indisposition. Some years ago she had a foot

[1] Loc. cit.

[2] The justness of this criticism is appreciated after a perusal of Péan's large work (Tumeurs de l'abdomen, 1880, Tome I) in which he devotes, of twenty-eight pages, just a half a page to tubercle of the omentum and does not even allude to this most common form of tumor.

[3] Practice of Medicine.

[4] University Medical Magazine, October, 1888.

amputated on account of disease of the ankle joint. About three weeks previous to admission, her present illness began with an attack of severe pain in the abdomen. With this she had vomiting, particularly after taking food. The bowels were obstinately constipated. On admission there was severe abdominal pain; dorsal decubitus, with knees drawn up; pulse small and frequent; temperature normal; tongue heavily coated; abdomen distended, no fluctuation, no tenderness, except in the left lumbar region over the descending colon. Heart and lungs negative.

May 3rd. The condition remained practically the same. Much pain and tenderness over the abdomen. A hard tumor could be plainly felt in the right iliac and lumbar regions, lying quite to the right of the middle line. She was removed to a private hospital and Dr. Gardner performed laparotomy. A large tubercular mass was found in the omentum, occupying the position above noted, in some places it was adherent to the intestines. A fæcal fistula resulted and she died of exhaustion.

Klebs[1] describes an extensive fibro-caseous thickening of the peritoneum which in one case formed a dense, opaque yellow mass a hand's breath in width attached to the parietal layer and stretched across the abdomen just below the navel. Such a mass might be readily confounded with an omental tumor. Fenwick says[2] that the thickened capsule of the spleen may produce a tumor-like body in the left hypochondriac region. More common I should think would be the tumors associated with thickening of the capsule of the liver to which he also refers. Here an exudation sacculated between the capsule of an enlarged liver—and, as Strümpell notes, this condition is not uncommon in tubercular peritonitis—and the anterior abdominal wall may produce a localized tumor of great distinctness.

There might possibly be in tubercular disease a cystic accumulation within the layers of the great omentum. Péan[3] cites such a case in which there was an enormous tumor in front of the intestine, containing a brownish semi-purulent fluid and gas, the walls of which were evidently formed by the layers of the omentum. Obliteration of the foramen of Winslow by tumor or by chronic peritonitis has been followed by encysted hydrops between the epiplooic layers.

[1] Handbuch der Pathologischen Anatomie, Berlin, 1869.
[2] Loc cit.
[3] Loc. cit., p. 338.

(*b.*) *Sacculated Exudations.*

These are the most common, as they are undoubtedly the most puzzling of the abdominal tumors produced by tuberculous disease; so puzzling, indeed, that, as a long list of cases shows in which the operation for ovariatomy has been performed, the very elect among gynæcologists may be deceived.

In these cases a sero-fibrinous or purulent exudation is confined and limited by adhesions formed between the intestinal coils, the parietal peritoneum, the mesentery and the abdominal or the pelvic organs. What is felt as tumor may be entirely fluid or it may have an irregular nodular character from the presence between the coils of large caseous masses.

These sacculated tumors, due to tuberculosis, may, as in other forms of peritonitis, be met with in the upper, middle or lower abdominal regions. In the upper zone, which includes the stomach, liver and spleen, encysted collections of fluid are extremely common. Thus, we have the localized peritonitis associated with gall bladder disease, and with various affections of the stomach and of the liver and spleen. The effusion in these cases may be limited entirely to the upper region of the peritoneum. In the tubercular disease by far the most common sacculated exudation occurs here with peri-hepatitis, and as in the case of Emma G. (p. 99) over the surface of an enlarged liver, may lead to the suspicion of a gall-bladder tumor projecting below the edge of the ribs. I think, however, from an analysis of the cases, that these encysted peritoneal tumors are less common in the upper abdominal region.

In the middle zone, which includes the peritoneal cavity from the level of the transverse meso-colon to the false pelvis, and which embraces the omentum and intestine, these encysted tumors are much more common and as the record of operations shows are very frequently mistaken for ovarian tumor. In reviewing a list of such cases, it seems that they fall into two divisions, those in which the entire anterior portion of the peritoneal cavity was occupied by a large collection of fluid and those in which a more limited sacculated exudation was found on one or the other side of the abdomen or in the middle line. The following remarkable case reported by Gardner,[1] of Montreal, illustrates the former :—

[1] Canada Medical and Surgical Journal, Vol. XIII.

A. B., aged 23, unmarried, was sent to him by Dr. Ross for examination, as there had been a suspicion of pregnancy. She could give no definite account of the date at which the present abdominal enlargement began, but it had been noticed for three or four months and had rapidly increased. There was pain in the abdomen; the general health and strength had declined and she had become emaciated. The menses had been absent for three months.

Examination.—The abdomen was much enlarged; well marked fluctuation in the anterior and antero-lateral aspects, with dullness on percussion in these areas. In the flanks and epigastrium, the bowel note was present; no firm or solid part to be felt anywhere. The anterior aspect of the abdomen was quite uniform. The uterus, measuring two inches, was pressed upwards and forwards. The patient was admitted to the General Hospital, when it was found that she had fever of a septic type, the temperature running very high. In the centre of the anterior part of the abdominal wall about the navel, there was œdema and a red blush. The diagnosis of suppurating ovarian cyst was made. At the operation, on reaching the peritoneum, no separation of parietal from visceral layer could be made. The knife entered a collection of fluid, passing through what seemed to be a thickened, closely adherent cyst wall. The cyst was drained and irrigated. The general condition improved for ten days. The temperature then rose and she developed a cough with purulent expectoration. She sank rapidly and died six weeks after the operation.

Autopsy.—(No. 825, Post-mortem Records, Montreal General Hospital). Moderately emaciated girl. A two-inch wound between the navel and the pubes contained a drainage tube which passed through Douglas' fossa into the vagina. On opening the cavity of the peritoneum, a large mass the size of a man's head, occupied the false pelvis. This and the parietes were covered by a grey, rough membrane half an inch in thickness. The transverse colon, although firmly adherent upon the surface was also bent upon the liver. Drawing this mass and the liver towards the right side, a collection of pus was found below and by the side of the spleen, and another small collection lay under the left lobe of the liver. On careful examination it was found that the anterior peritoneal cavity was converted into a suppurating cyst, extending from the liver to the pubes. The pelvis was nearly filled by the globular mass referred to above.

This consisted of all the intestines except the transverse colon, closely matted together by recent soft adhesions, which were studded with miliary tubercles. Everywhere the walls of the cyst appeared older than the internal adhesions and had all the appearance of unhealthy granulating membrane. The walls and viscera of the true pelvis were covered with the same membrane.

The lungs contained many grey tubercles but no cavities. Both lungs were universally adherent.

The intestines were normal.

In this remarkable case the sac occupied a large part of the peritoneal cavity and pushed the intestine into the pelvis. It is interesting to note the œdema and redness about the navel, at which point in these cases of tubercular peritonitis spontaneous perforations sometimes occur.

These large purulent exudations simulating ovarian tumor are not necessarily tubercular but, as in the remarkable case described by Dr. Ewing Mears,[1] may be puerperal.

In a larger number of these cases the tumor is more localized and either lateral or central in position, and it may be quite impossible to make a diagnosis from developing ovarian tumor. The following is a case of the kind to which additional interest is added by the gradual and complete disappearance of the tumor.

CASE IV.—*Illness simulating typhoid fever; development of an abdominal tumor which gradually disappeared. Rapid pulmonary tuberculosis.*

Early in November, 1884, I was consulted by a young lady from Montreal, from whose statements and from the account of her physician, R. L. MacDonnell, the following history was obtained: No tuberculosis in the family; she had, though somewhat delicate, enjoyed average health. Early in June she was confined to bed with a low fever, thought to be typhoid. The temperature ranged from 100° to 102°. The abdomen gradually became distended. By the end of July it was evident that there was fluid in the peritoneum. The dulness, however, was not movable but persisted in the left iliac and right lumbar regions when the patient was turned on her

[1] Transactions of the College of Physicians, Philadelphia, 1875.

right side. The urine became very copious in amount, of low specific gravity—1005. The question was discussed whether the patient had not an ovarian tumor with mild typhoid fever. Throughout August she improved. The abdomen diminished in size and became irregular in outline. The left side gradually became more prominent. On the 26th of August, Mr. Lawson Tait examined the patient and said that the tumor might be one of three things: tubercular peritonitis, parovarium cyst or a congenital subperitoneal cyst, working its way up in front of the abdomen. He predicted gradual absorption and recommended incision and drainage when the fluid became thickened. Throughout September she improved very much and the tumor reduced in size. On September 20th, Dr. MacDonnell noted that "beyond a doubt an encysted tumor, as large as an adult head, lay on the left side of the abdomen." I saw the patient on the 10th of November. The abdominal symptoms had almost disappeared and there was left nothing more than an obscure sense of fullness and thickening in the left side. I could scarcely believe from the examination that there had been the large tumor described and sketched by Dr. MacDonnell. The lung symptoms were marked and the patient was rapidly failing. She returned to her home and died in December.

The majority of the cases in which encysted effusions have been mistaken for ovarian tumor, have been of this kind. The exudation is sacculated either between the intestinal coils, in which case it may be deep-seated and give only a sense of obscure fluctuation or, as is more usual, the parietal peritoneum forms the anterior wall of the sac and the collection simulates an ovarian cyst.

Lastly, there are the sacculated exudations within the pelvis proper in which case the disease almost always starts from the Fallopian tubes. The tubercular process may be exclusively upon the parietal peritoneum and the coils of intestines glued to the lateral walls may shut off completely the pelvic from the general cavity.

(c.) *Retracted and thickened intestinal coils.*

The matting together and thickening of several coils of the intestines may form a mass of great distinctness and even lead to the diagnosis of a solid tumor. This is most frequently met with in the

cæcal region. They are not necessarily fixed tumors but may be freely movable as in Case IV of Spaeth's paper.[1] The following case is a good illustration:

CASE V.—*Tumor in right iliac region, believed to be malignant. Gradual loss of flesh and strength. Pain and diarrhœa. Tumor formed of intestinal coils in cæcal region.*

Man aged 48. For twelve months he had had pain in the right lumbar region and in the right groin. Micturition was frequent and he had occasional diarrhœa. He had not passed blood in the stools, and there had been neither obstruction nor vomiting. There was a well-marked tumor in the right iliac region. Towards the end, a cough with muco-purulent expectoration developed and there was dullness at the base of the right lung. During the last three days of life the abdomen was tender and tympanitic. The tumor was believed to be malignant in character.

Autopsy.—Slight emaciation. Abdomen distended, 500 cc. of turbid fluid, with many flakes of lymph in the peritoneum. The coils of the intestines were matted together, but could be separated. A mass of adherent bowel filled up the right iliac fossa; several of the coils communicated with the colon, by perforations in the terminal part of the ileum. These coils and the ascending colon formed a firm solid mass which occupied the right iliac fossa and which had been mistaken during life for a tumor.

When slit open the lower two inches of the ileum were found to be extensively diseased. The walls were thickened and the mucosa ulcerated. The cæcum was much contracted, only admitting the thumb. The wall was nearly half an inch in thickness. In the upper part of the ileum there was a typical tuberculous ulcer. There was general tubercular peritonitis, and the serous covering of the liver was greatly thickened.

The lungs presented small cavities at the apices surrounded by fibrous tissue and groups of tubercles. The lower lobes were normal. The kidneys presented a few small tubercles.

Here no doubt the starting point of the trouble was in the cæcum, in which the disease was much more extensive and older looking

[1] Deutsche Med. Wochenschrift, No. 20, 1889.

than in any other part. The solidity and firmness of these tumor masses formed by the intestinal coils are very remarkable and as in this case are very apt to lead to error in diagnosis.

There is another remarkable form of intestinal tumor, the result of chronic peritonitis, not necessarily tubercular. The small intestine is shortened by puckering and thickening of the mesentery. The walls are enormously thickened and the entire coil may form a firm knot, lying close against the spine. When matted together by adhesions this coil of intestines may give on examination the idea of a solid mass. The following is a remarkable instance of the kind:

Sarah A., aged 82, admitted to the Philadelphia Hospital, December 22, 1887, with ascites, stated to be of several months duration. At first the effusion was moderate but it increased so that tapping was necessary. About five litres of a sero-fibrinous fluid were removed. The liver could not be felt, but presented about three inches of vertical dullness in the nipple line.

The spleen was not palpable. After withdrawal of the fluid, a rounded, firm mass about the size of a cocoanut, could be felt, and seen, in the central part of the abdomen. It was somewhat movable and a little irregular on the surface. The fluid reaccumulated and she was again tapped and an equal amount withdrawn. The tumor was centrally placed, and so readily separated from any of the abdominal viscera that I thought it very probably of retro-peritoneal origin.

The autopsy, January 26th, 1888, showed the peritoneum covered with flakes of moderately firm lymph. The tumor was seen to be made up of the small intestine greatly shortened and thickened, the coils closely united with each other forming a mass the size of a large cocoanut, closely adherent to the spine. It seemed scarcely credible that the small intestine, even puckered and thickened as it was, should form so firm and so small a mass. The mesentery was very greatly thickened. There was much pigmentation of the peritoneal coat, the muscular wall was greatly thickened and the mucous membrane of the ileum was thrown into thick folds, resembling the valvulæ conniventes. The transverse colon and sigmoid flexure were much contracted. There was thickening about the appendix and in the mucous membrane of the cæcum there were two small ulcers. The liver presented senile atrophy but no cirrhosis. There was extensive perihepatitis.

The other organs presented no special changes.

Tubercles were not found, and the case appears to have been one of chronic peritonitis, starting possibly from the cæcal region.

A very similar condition to this has been found in the chronic tubercular disease. Some years ago I performed a post-mortem for Howard, of Montreal, on a woman aged about 30, who had signs of chronic disease of the peritoneum with ascites. On opening the abdomen, the entire cavity was converted into a large fæcal abscess. The anterior wall of the cæcum was completely destroyed by the tubercular ulceration and the fluid fæces had passed directly into the peritoneal cavity. The small intestine formed a puckered and retracted coil which lay close against the spine, forming a firm bunch which, as in the other case, presented a strange appearance in contrast to the greatly distended peritoneal cavity.

Prochownick [1] reports a remarkable case in a girl of 16, who presented in the right side of the abdomen a hard somewhat nodular tumor, which extended from Poupart's ligament to a point above the navel. At the operation the mass was found to be composed of the entire intestinal tract, from duodenum to the beginning of the rectum, united in a single coil, closely matted together and covered with lymphoid granulations.

The coils may not form, as in these cases, a uniform tumor, but there may be a separation into three or four irregular masses, divided by fissures and covered with thick lymph.

It is possible for the coil to form a resonant tumor; thus Goodell writes that "in one of his cases of tubercular peritonitis the intestines were gathered up towards the sternum in a bag of false membrane, making a well-defined resonant tumor, which was very puzzling until the abdominal cavity was opened." [2]

(*d.*) *Mesenteric Glands.*

Less common, perhaps, in tubercular peritonitis than any one of the previous conditions is the presence of tumors caused by enlarged glands. So far as I can ascertain, in none of the cases of laparotomy did they lead to an error in diagnosis. Cases are, however, on record

[1] Deutsche Med. Wochenschrift, No. 24, 1889.

[2] Private letter, November 29th, 1889.

in which extensive tuberculosis of these glands formed palpable tumors, associated with ascites. One of the most accurately described is by Gairdner:[1] A man, aged 21, had nodular tumors "of varying distinctness, sometimes nearly superficial, sometimes over-lapped by intestines, not capable of being identified with any of the greater viscera, to a great extent mobile and chiefly felt in the left umbilical region, very dense, hard, irregular and somewhat nodulate, altogether having much of the position and some of the characters of mesenteric glandular tumors." The post-mortem showed these glands greatly enlarged, hard, inelastic; on section solid, no suppuration but presenting a yellow infiltrated matter. There was no disease of the lungs or of other organs, nor was the peritoneum involved. One cannot doubt the tuberculous nature of this case. I have not seen in the adult a similar one in which the tuberculosis, confined to the mesenteric glands, produced large tumors, but I have seen a precisely similar condition limited to the retro-peritoneal glands. (Philadelphia Hospital, Post-mortem Records, 1888, p. 220.) These are cases of the abdominal scrofula of the old writers. Bamberger[2] gives an instance, the only one in his experience, in which a woman, aged 60, who had vomiting, diarrhœa and signs of marasmus, presented nodular masses in the abdomen, above the navel, which were mistaken for gastric cancer. Post-mortem showed extensive tuberculous infiltration of the mesenteric glands without tubercles in other organs.

Besnier[3] states that Colin has described three cases in soldiers, in whom were found enormous tubercular tumors of the mesenteric glands without ulcers in the intestines.

Andral[4] records the case of a man, aged 29, with ascites, and enlarged cervical glands, in whom, with extensive tuberculous peritonitis, an enormous tumor was found, due to infiltration of the glands. Occasionally in phthisis there is great enlargement of these bodies without any indications during life. Such a case was in the Philadelphia Hospital last year (Post-mortem Records, 1888–89, p. 60), with enormous enlargement of the mesenteric glands, forming large irregular tumors. Tympanites may mask this condition, as in a case given by Henoch[5] in which a mesenteric tumor, the size of the child's

[1] Loc. cit.
[2] Virchow's Handbuch, Bd. VI, p. 708.
[3] Dictionaire Encyclopédique. Article Mesentery.
[4] Clinique Medicale, T. II, p. 648, 1839.
[5] Loc. cit.

head, was entirely concealed by the distension of the intestines. Sometimes, after the removal of the ascitic fluid, or when it is in slight amount, there can be felt irregular nodular bodies or cord-like thickenings of great distinctness, and it is not always feasible to determine whether these are glandular or large caseous masses between the coils of intestines.

A question of special interest relates to the association of mesenteric gland disease with tubercular peritonitis. Gairdner, in the lectures already referred to, has urged that in a large proportion of the cases of so-called tabes mesenterica, in which there is enlargement and hardness of the abdomen—the condition which the French speak of as *carreau*—there is involvement of the peritoneum. Jacobi has recently expressed the same opinion.[1]

The *diagnosis* of these peritoneal tubercular tumors offers difficulties which vary greatly in the different varieties. The omental tumor is probably a less frequent source of error than any other, but as an identically similar condition may exist in cancer, it is not always possible, unless there is marked tubercular disease elsewhere, to determine the precise nature; and, as we have seen, even an acknowledged expert like Gairdner may be led astray.

The lumpy, nodular character of the mesenteric tumors gives to them also a certain degree of distinctness. The mistake is sometimes made, nor do I think it can always be avoided, of confounding the large caseous nodules situated between the intestinal coils with the mesenteric glands. The possibility of their recognition depends very much on the degree of distention of the bowels, as extreme tympanites may completely cloak a very large tumor of this character.

The tumors formed by contracted and thickened intestinal coils usually lead to error in diagnosis, nor do I see, save in most exceptional circumstances, that this could be avoided.

The recognition of the saccular exudation, more particularly its differentiation from cystic ovarian disease, offers really serious difficulties, the extent of which may best be appreciated by the fact that of 96 cases of laparotomy in tubercular peritonitis, in not less than 30 ovarian disease was supposed to be present. Such being the case, it may be worth while to discuss briefly certain diagnositic details.

[1] New York Medical Journal, II, 1889.

There is no single criterion which enables us to say in a given case that the condition is one of encysted peritonitis, nor indeed is there any special group of symptoms which can be regarded as distinctive. It were folly to lay down, in parallel columns, differential rules in an affection in which again and again the ablest diagnosticians in our profession have erred.

It will suffice merely to touch upon the points most suggestive, in individual cases, of tubercular trouble:

First. The history of the patient and of the disease. Tubercular antecedents are common. Evidence may exist of old tubercular lesions. Gradual failure in health and strength may perhaps be taken into consideration, but it must not be forgotten that in many of the cases the patients have been robust and well-nourished. The mode of onset is in the majority of instances gradual, but this is such a variable factor that it is not of very much value; perhaps the most which can be said on this point is that there can usually be elicited a history of obscure abdominal pains, irregular febrile attacks and altogether a greater degree of gastro-intestinal disturbance than generally accompanies the slow evolution of ovarian cysts. If the case has been under observation for some time, the fever record should be of great assistance, as high or very low temperatures more commonly occur in this condition, though it is true that in inflamed and suppurating ovarian cyst there may be fever of a hectic type.

Second. The local physical signs. If possible, these are more deceptive than the history and symptoms. The question is not so much between the characters of a sacculated exudation and ascites, but it is the extremely nice one of discriminating between two varieties of sacculated effusion, ovarian and peritoneal. In typical cases, the physical signs have conformed in every particular to those of cystic ovarian disease. There are a few indications which may at times be useful; thus when the sacculated tumor is limited and small the outlines may not be so definite and clear as in ovarian disease. This is a point referred to by several writers. The position and form may be variable owing to alterations in the calibre of the surrounding intestinal coils of which in part the walls are composed. At the periphery of the tumor irregular, nodular bodies —cheesy masses—may sometimes be felt, which in several instances have led to the diagnosis of malignant disease. Depression of the

vaginal wall is not a safe indication one way or the other, as I find the condition mentioned as present in ovarian tumor as well as in encysted peritonitis.

Third. In every case the condition of the tubes and of the lungs and pleura should be most thoroughly examined. The association of a tubal tumor with an ill-defined, anomalous mass in the abdominal cavity should arouse suspicion at once. So also the evidence of involvement of the pleura or of the apex of one lung. It is rather surprising, in looking over the reports of cases, how little attention seems to have been paid to these most important and common concomitants of tubercular peritonitis.

III.—The Curability of Tubercular Peritonitis.

Until within the past few years, the general opinion in the profession has been that this disease is incurable; and in looking over the text-books of medicine, with but few exceptions—Fagge a notable one—the prognosis is given, as in the words of Flint, "always fatal." Henoch,[1] in his admirable account of this affection in children, says that when recovery has followed in certain cases in his practice, he has thought the diagnosis incorrect, and that the peritonitis had really been of the simple chronic form. Yet there exist not a few reports among the older writers, indicating that a form of chronic peritonitis, not to be distinguished from the tubercular, did occasionally get well. More recently McCall Anderson,[2] of Glasgow, in a clinical lecture published in 1877, reported three cases illustrating recovery in tubercular peritonitis. The history and the symptoms left no doubt as to the correctness of the diagnosis, but the cases were regarded as altogether unique. Gee,[3] in 1881, stated "that recovery from tubercular peritonitis is common." Gairdner[4] also has insisted upon the occasional cure in this affection, while admitting that there was a hiatus in our knowledge of the changes undergone in the progress towards healing. Ashby,[5] in his article on peritonitis in children, says "a large number of cases completely recover." Fenwick, in his recent lectures,[6] speaks less hopefully of permanent cure. The evidence

[1] Vorlesungen ueber Kinderkrankheiten, 4te Auflage, 1889. [2] Lancet, 1877.
[3] Lancet, Jan. 1st, 1881. [4] Loc. cit.
[5] Cyclopedia of Diseases of Children. Edited by Keating. Vol. III, 1890.
[6] Loc. cit.

has been rapidly accumulating to show that in a considerable number of cases, recovery in this disease is possible, either spontaneously or after operative interference.

(*a.*) *Spontaneous Cure.*

There is no inherent improbability why tubercles on the peritoneum should not undergo involution as they do elsewhere. Anatomically the peritoneal growth bears in its evolution a close analogy to the pulmonary, and this is still further borne out by the retrograde changes through which it passes. Just as the aggregations of miliary nodules in the lung may undergo the changes which we speak of as healing, becoming hard and fibroid, so in the peritoneum the tubercle tends in many cases to become sclerotic, and passes into a condition in which it is practically harmless. This beneficial result is more likely to be seen in cases belonging to the third group, in which, from the outset, the process is sub-acute and not associated with much exudation; but there are cases on record in which recovery has followed even after extensive effusion.

The anatomical changes are, in brief, these: fibroid and pigmentary induration of the tubercles, absorption of the exudate, transformation of the fibrinous material into connective tissue, with the union to a greater or lesser extent of the intestinal coils and of the peritoneal surfaces with each other. The following case illustrates this condition:

CASE VI.—*Chronic tympanites, with constipation; gradual development of pulmonary symptoms, death; adhesive peritonitis with fibroid tubercles. Pulmonary tuberculosis.*

W. C., age 38, colored, admitted to the University Hospital, Philadelphia on the 18th of January, 1888. His father died of phthisis. He had been a healthy laboring man of temperate habits. He had not had any serious illness. About four weeks before admission he first noticed distension of the abdomen and he found that it was difficult to button his clothes. For some time he had been very constipated.

Following note was made on admission: "The patient is fairly well nourished, says he has not lost in weight, complains of swollen abdomen and constipation; temperature 101.3°; pulse 82. On examination uniform enlargement of the abdomen, measuring 72 cm.; respira-

tion is costo-abdominal. On palpation, soft, no special resistance; percussion gives resonance anteriorly and in the flanks; in illiac regions resonance not so full; there is no dullness, no percussion wave. Neither liver nor spleen palpable. Area of liver dullness diminished; two inches of vertical splenic dullness." The case was regarded for a time as one of ordinary tympanitic distention, associated with sluggish and constipated bowels. The persistent elevation of temperature ranging from 99° to 102° and slight tenderness in the flanks, with recurring night sweats, aroused a suspicion of tubercular trouble, but the examination of the lungs was negative. Throughout the month of February, there was a daily elevation of from 1 to 3 degrees; he lost flesh and began to cough; there was, however, no expectoration, but examination determined a few scattered râles, most marked at the left apex, behind. During March he continued to lose in weight, the sweats were less troublesome, the temperature rarely rose above 101°; the condition of the abdomen remained the same; there was slight tenderness in the flanks; no dullness; measurement about 75 cm.; no signs of effusion could at any time be discovered; the local disease had at the left apex behind become more marked, the breathing was slightly tubular and there were numerous mucous râles. The constipation remained a marked feature, the bowels were never moved without a purge or an enema. He gradually failed without any further development of the pulmonary symptoms, and death occurred on the 19th of March. The post-mortem showed disease of the left lung, partly old, with slight fibroid change and many recent tubercles and cheesey masses. In the abdomen, the peritoneum was obliterated by universal adhesions between the layers. The coils of small intestines were united together by old fibrinous bands; here and there in the adhesion were pigmentations and small, hard, dark tubercles. Numerous adhesions existed over the liver, uniting it strongly to the diaphragm, and in these, too, there were many old fibroid tubercles.

Here the peritoneal disease was practically cured, but the ill effects remained in the weakening of the intestines. The pulmonary not the abdominal affection caused death.

Similar cases might be drawn from the records of any pathologist of large experience. In Cases XIII and XIV of my series,

an identical condition existed. In both, death took place from pulmonary disease, and the peritoneum presented universal adhesions in which were hard, deeply-pigmented fibroid tubercles.

In this connection the cases which Gairdner gives in the appendix to his lectures are of the greatest interest, as three of them illustrate this gradual improvement in undoubted tubercular disease. In Case I, a child, aged 8, presented signs of peritoneal disease, with moderate effusion, and later, thickening of the great omentum. The improvement within three months was remarkable, though slight induration of the omentum remained. The improvement continued and two years subsequently the patient was well. In Case III, the improvement was also most striking under simple treatment; the effusion disappeared, but evidence of omental thickening persisted. Case IV is still more remarkable. A child, aged 9, presented well-marked thickening of the omentum, and other symptoms pointing to peritoneal involvement. During the two years she was under observation, the general health improved and a gradual resolution of the omental tumor took place.

No writer has dealt with this aspect of the question, so fully and clearly as Boulland.[1] He has ransacked the literature of the subject, and in his collection of eighty-one cases in which tubercle occurred in the pleuro-peritoneal membranes, there are at least twenty cases of peritoneal tuberculosis in which recovery took place. He places the number of recoveries much higher than this, but I have excluded many doubtful cases on his list. In many instances, of course, this may have been only a temporary improvement, but in three instances quoted from Bucquoy, the good health persisted ten, twelve and seventeen years after recovery. The subsequent history of operative cases removes all grounds for skepticism—reasonable perhaps a few years ago—as to the genuineness of these cases. One of the most interesting of the cases quoted by Boulland is from Louis. A man aged 24, with great enlargement of the abdomen, signs of pleural affection and extreme marasmus, was attacked with Asiatic cholera. He nearly died from the excessive purging, but the abdominal effusion disappeared and he ultimately made a good recovery. In reading the details of the long list of cases given by Boulland, one receives the impression that the cure of tubercular peritonitis cannot be a very

[1] Loc. cit.

uncommon event. Case III, to which I have already referred, as simulating typhoid, is an illustration, I have no doubt, of a clinical group by no means rare. The following is an interesting example of marked improvement in, if not actual healing of peritoneal tuberculosis:

CASE VII.—*History of an obscure abdominal affection with fever and loss of flesh. Gradual improvement. Ill-defined abdominal tumor. Local disease of the lungs. Pigmentation of the skin. Marked improvement.*

A. B., aged 31, merchant, admitted to the Johns Hopkins Hospital May 18th, 1889, complaining of swelling and distress in the abdomen, with weakness and loss of flesh.

Family history is good. Father and mother living and healthy; two brothers living; two sisters died when children.

He had dysentery 15 years ago and with that exception has always enjoyed good health until October, 1888, when, after exposure to cold, he had an attack of obscure trouble in the abdomen. There were swelling, tenderness and a sense of distension and weight, particularly in the region of the liver. There was no diarrhœa, rather constipation. He lost flesh and became extremely weak. At Christmas he was up and about, and in January attended to his business. The strained, distressed feeling in abdomen persisted. Throughout February and March he remained pretty well, though far from his usual condition of health. The swelling of the abdomen subsided greatly. Early in April the distention increased again so that he could not button his trousers, but he had neither pain, diarrhœa, nor fever. He again lost flesh rapidly.

Condition on admission: Large boned man, 5 ft. 11½ in height; marked emaciation; orbital fat much wasted; eyes sunken, with deep, dark rings about them; cheeks very hollow. The forehead, cheeks and chin were distinctly pigmented; this darkening in color he had noticed gradually coming on since October. The skin of abdomen and backs of hands were also pigmented. The chest was large; ribs prominent. Expansion was deficient at left base. Percussion was clear with the exception of the left base, where the resonance was slightly defective and here fremitus was diminished. There was also slightly defective resonance at right apex and the right clavicle was more prominent than the left. On auscultation there was feeble breathing

with fine râles in the lower axillary and infra-scapular regions. The contrast between the two sides was most marked. At the right apex there were moist sounds heard just beneath the clavicle, and behind in the upper part of inter-scapular area.

Abdomen was moderately distended, uniform. No fluid discoverable. Flanks were tympanitic. The resonance was defective just below and to the left of the navel, in an area equal in size to the palm of the hand. On palpation, no tenderness, but in the region below and to the left of the navel there was an ill-defined, tumor-like mass, resistant, not painful but slightly tender on deep pressure. It was readily separable from liver and spleen. Below, the margin was well defined.

Liver dullness not increased. Edge of spleen not palpable. Inguinal glands not enlarged. No tenderness in renal regions. The temperature was subnormal. Urine negative, not increased in amount. He had slight morning expectoration, muco-purulent in character, which did not contain tubercle bacilli, but in which once elastic tissue was found.

Patient improved rapidly in Hospital. Abdomen reduced in size. He gained in weight. June 6th he went to Atlantic City, where he improved in a remarkable manner. He returned on the 19th, having gained over 25 pounds since his first entrance to Hospital. He had no cough. The color had improved and he had lost the characteristic abdominal facies. The examination of the lungs showed that the note at the left base was clearer; there was a dry friction rub in the lower left axillary region. Râles still persisted at the apex. The abdomen was a little full, though not so much so as at first. There was a distinct prominence to the left of the navel, and here the same obscure tumor-like mass could be felt. In the right inguinal region about two inches above Poupart ligament, there was also a distinct, ridge-like projection which was not noticed at previous examinations.

The temperature range of this patient during his stay in the Hospital was very carefully studied. For days at a time two hourly observations were made. Unfortunately the charts were mislaid, but the general results may be stated as follows: The range was between 96° and 99°. The temperature fell throughout the morning hours, and by 6 or 8 A. M. reached the minimum, then gradually rose through the fore-

noon and only reached a normal point in the late afternoon hours. The persistent low temperature was one of the most striking features of the case.

The patient returned to his home in a Western State, and has remained well ever since. He was seen by Dr. Toulmin in October, when the condition of good health persisted.

The attack in 1888, with swelling and tenderness of the abdomen and loss of flesh, was, without question, I should say, tuberculosis of the peritoneum. The existence of the tumor-like mass, the sub-normal temperature curve, the signs of involvement of the pleura and of the lung, the diffuse pigmentation—all point to the existence of this affection. The striking improvement which occurred throughout May and June has persisted, and I see no reason why a permanent cure should not be established.

The cases which are most likely to terminate favorably are those in which the infection is limited to the peritoneum, the inflammation of moderate grade and the effusion slight in amount and sero-fibrinous. The instances I have given in illustration of the lateney of the disease would seem to indicate that an adhesive inflammation, as it is termed, may accompany the process from the outset, and that a gradual selerosis may overtake the tubercles and render them harmless. Case-ation and ulceration, with a sero-purulent exudation, preclude the possibility of spontaneous cure. Extension to the pleura and lungs and the co-existence of intestinal or tubal disease are conditions equally unfavorable to permanent recovery.

(*b.*) *Cure by Operation.*

The beneficial effects which, in a number of cases, followed the opening of the peritoneum when a saceulated exudation was mistaken for ovarian tumor, encouraged surgeons to perform laparotomy in ordinary cases of tubercular peritonitis accompanied with much effu-sion. Sir Spencer Wells, in 1862, performed laparotomy on a patient believed to be the subject of ovarian tumor, but in whom the condi-tion was found to be tubercular peritonitis. The effusion was with-drawn and the patient recovered. She married and at last report, twenty-five years after the operation, maintained her good health. The operation, thus unintentionally carried out in this and many

subsequent cases, was advocated strongly by Hegar[1] and by Koenig[2] in Germany, by Lawson Tait in England, and has since been practiced by many surgeons in Europe; and in this country by Homans of Boston, Mundé of New York, Goodell of Philadelphia, Kelly of Baltimore, Gardner of Montreal, and others.

In two cases recently under treatment in the Hospital, laparotomy has been performed, in one for tubercular peritonitis, though a doubt existed whether or not a tumor was present; in the other an ovarian tumor was found accidentally to be complicated with a latent peritonitis. The first case presents features of very special interest, as rapid amelioration followed the removal of the fluid, while the death from acute disease, after convalescence was established, enabled us to study the changes in the peritoneum which are associated with the healing of tubercular processes.

CASE VIII.—*History of obscure abdominal trouble for several months; acute exacerbation with high fever. Doubtful abdominal tumor. Laparotomy, drainage; rapid improvement. Discharged, feeling well. Return with acute pneumonia, death. Chronic tubercular peritonitis in process of healing. Syphilis of rectum. Amyloid liver.*

Emma G., æ. 28, admitted August 28th, complaining of pains in abdomen.

Father and mother probably living, one brother and one sister living; two sisters and two brothers dead, none of them of lung disease. Had whooping-cough and measles as a child; ten years ago had pleuro-pneumonia, was ill five months and has not been perfectly well since. For five years she has had a cough, on and off, and on several occasions has spat blood; has had no special illness since the attack ten years ago, but several times in the spring or autumn she has been in bed with weakness and shortness of breath. Her present trouble began about six months ago with swelling of abdomen, which has been variable in extent and has on several occasions almost disappeared. She has generally been constipated, has been short of breath and has had palpitation of the heart. She had been working up to a few days before applying to Hospital. On admission the following note was made: "Temperature 101°. Patient is a well-

[1] Loc. cit. [2] Centralblatt für Chururgie, 1884.

grown, not emaciated woman. The tongue is coated white. The abdomen is much distended, measures 86 centimetres; it is symmetrical, extremely tender to touch in the upper zone, particularly below the right costal margin. The lower zone is more flaccid and less tender. On percussion, when lying on back the flanks are dull, umbilical region resonant; on changing posture, flanks become resonant and the fluid gravitates towards the centre of abdomen. The liver dullness reaches from fifth rib to nearly two inches below costal margin. Both percussion and palpation in this region very difficult on account of the exquisite tenderness in epigastrium. There is dullness from the ensiform cartilage 7 cm. downward. There are nodes on the tibiæ. Inguinal glands slightly enlarged. The heart sounds are normal. Lungs, percussion clear anteriorly; resonance is defective at the extreme base on the right side; there is tenderness here on palpation." The temperature range until September the 4th was from 100° to 103°.

Both Dr. Lafleur, who first saw the case, and Dr. Atkinson, who joined him in consultation, regarded it as one of peritonitis. There was, however, a doubt about the extremely tender area below the right costal margin, and here Dr. Halsted thought there were indications of a distinct tumor, possibly a gall bladder. On the 4th an exploratory laparotomy was made. The incision extended from the costal border 2.5 cm. to the right of median line. The peritoneum was found filled with a bloody serum. The liver seemed enlarged. The capsule was studded with tuberculous nodules. The intestines were matted together and the layers of the peritoneum presented tubercules. The cavity of the abdomen was drained and then washed out with sterilized salt solution. Histological examination by Dr. Councilman showed the tuberculous character of the peritoneal growths.

The temperature on the evening of the 4th was 104°. She rallied well from the operation. The temperature fluctuated from 99° to 102° until the 14th, when it fell to 98°, from which date until the 30th the range was from 98° to 100°. Her general condition improved very rapidly and she was up at the end of a month. She had no cough and expressed herself much better. She was about the ward, and on the 22d of October, six weeks after the operation, the following note was made: "General condition continues good; she is

up every day ; the abdomen is still a little distended, and on palpation is tender on right side, and there is here between costal margin and illiac region a well-defined firm swelling, slightly resistant and very tender. On percussion there is tympany in umbilical and left lateral regions almost to the back ; to the right there is dullness from 5 cm. beyond the navel. On firmer percussion flat tympany can be elicited except in the extreme right flank where it is dull." She continued to improve through November, and on December 12th she was discharged. The following note was made :

"Patient went out to-day feeling quite well. All signs of tumor have disappeared ; the abdomen is soft, but in the right hypochondriac region a little more resistant than elsewhere ; here, too, it is now tympanitic."

The temperature had been normal and sub-normal for weeks.

The patient was re-admitted January 8th, with fever and urgent dyspœna.

She stated that she had been at work since her discharge. On December 30th, she had a slight chill, followed by fever and cough. On January 4th, she had another chill, with quite high fever, and on that day went to bed. On admission her temperature was 102°, respiration 60, pulse 120 ; physical signs showed an extensive area of consolidation in the right lower lobe, which extended anteriorly to the nipple line and as high as the fourth rib. The sputum was mucopurulent, a little blood-tinged and contained numerous pneumococci but no tubercle baccilli. The abdomen was not specially distended, but was quite tender in the upper zone. On the 11th and 12th she seemed better but the physical signs persisted. Temperature was not high, never reaching above 102.5°. On the 14th, she passed blood in the stool, and in the evening she had a profuse hemorrhage from the bowels and died at 10.20 p. m.

The following is a condensed report from the autopsy record by Dr. Councilman : A well-built, well-nourished woman. A smooth cicatrix extended diagonally across the abdomen, 14 cm. in length. Pigmented macular scars over the entire body, more marked on the anterior surface.

Peritoneum adherent to anterior abdominal wall over the liver. A few slight adhesions with the omentum. The adhesions over the liver

were firm, and contained a good deal of fat. Here and there in the adhesions were firm, whitish nodules, which varied in size from a pin's head up to 3 mm. in diameter. The omentum was thickened, its upper surface smooth, its lower surface covered with numerous small, up to 2 mm. in size, firm, nodules, especially numerous along the thickened inferior border. Most of these were pigmented. No adhesions between intestinal coils. Over peritoneal surface, numerous small, firm nodules slightly pigmented. Many of these were seated flat on the peritoneum, others in small connective tissue bands, attached by one end to the serous surface. The tubercles were generally seated at the end of these. They extended, with about the same frequency, along the entire length of small intestine, but were most numerous for 75 cm. above the valve. The large intestine on its surface contained very few of these nodules. The mesentery contained numerous tubercles, partly seated on the membrane, partly along the intestinal border, in a few places matted together. The surface surrounding them was thickened and puckered as though from slight cicatricial formation. Nearly all of these contained in the tubercle dark pigment. The posterior surface contained a few, and generally smaller tubercles than on the omentum.

In the right pleural sac, 400 cc. of purulent fluid with flakes of fibrin. The pericardial membranes were adherent, slightly thickened but presented no evidence of either tubercle or caseation. The heart showed no special changes.

Lungs. The left was bound down by old, tolerably firm adhesions. The tissue was crepitant. Muco-pus could be squeezed from the small bronchi. Right lung slightly adherent at base, somewhat compressed by the pleuritic exudation. The entire pleural surface covered with fresh exudation which could be stripped off. The lower lobe, the middle lobe and part of the upper lobe were solidified. Cut surface smooth and reddish in color, and from it a reddish fluid could be squeezed. The posterior parts of the upper and middle lobes were grayer in color than elsewhere. Portions excised sank in water. The bronchial glands large, pigmented, not caseous.

Liver was large, weighed 2910 grammes; the entire surface, especially the upper, was covered with adhesions, in which and in the capsule there were numerous tubercles, either single firm nodules or flattened masses. Even when these were apparently situated in

the liver surface they could be stripped off with the capsule, which was very much thickened. In reality this was not the capsule, but a thickened and newly formed connective tissue membrane over the entire organ.

Spleen. Capsule slightly thickened and presented numerous adhesions, in most of which were small nodules. Kidneys showed no special changes. The mesenteric glands were enlarged, firm, whitish-gray in color, a few of them slightly pigmented. No caseation. No tubercles. Small intestines showed no special change. In the rectum there was a loss of substance encircling the entire bowel with much cicatricial tissue about it and two recent-looking, deeper ulcers from which apparently the haemorrhage had come. No tuberculosis of the tubes.

The microscopical examination showed the liver to be intensely amyloid. The tubercles in the peritoneum were composed of numbers of sub-miliary nodules, very fibrous, containing few cells in a firm tissue. In the middle of the masses, giant cells with mural nuclei and fatty granules; no caseation in the nodules. Tubercle bacilli were very abundant.

This case presented in turn many points of interest to the physician, the surgeon and the pathologist. In the first place it is a good example of primary tuberculosis of the peritoneum; not even in the pleura or pericardium, both of which showed old adhesive inflammation, were there granulations, and a most rigid search failed to find tubercles elsewhere. Surgically, the operation was a success as the symptoms were relieved, the general health improved and she left the Hospital looking and feeling well. Then the accident of an acute pneumonia gave an opportunity of studying the condition of the peritoneum four months after an acute exacerbation and showed the tubercles undergoing fibroid change but still retaining their characteristic structure and still very rich in bacilli.

The other case illustrates the latency of peritoneal tuberculosis and the extent which it may reach before inducing serious symptoms.

CASE IX.—*Gradual swelling of abdomen; tumor on left side. Ovariotomy. Extensive tubercular peritonitis; recovery.*

Bridget N., age 42, admitted to the gynæcological ward October 17th. Married 19 years, has had 8 children. Has been ill, on and

off, ever since the birth of her last child 5 years ago. Has had metrorrhagia. She has had successive attacks of abdominal swelling, and within the past year has noticed a lump on the left side, which has gradually grown larger, and it is for this she sought relief. On inquiry she states that every winter she is apt to have a cough, and has had pleurisy on the right side. Her mother died of pulmonary hemorrhages. Other members of her family healthy.

Dr. Kelly operated October 18th; removed a tumor of the left ovary, the size of a cocoanut. On the right side the ovary was as large as a lemon, cystic and the tube greatly dilated. The ovarian tumor and the entire peritoneum, visceral and parietal, were covered with miliary tubercles. The intestines were in places matted together. There were 500 cc. of fluid in the peritoneum. The tubercular nature of the growths was demonstrated microscopically. The nodules were firm and hard, some of them pigmented. She did well after the operation and was sitting up out of bed by the 6th of November, with the wound perfectly healed. The temperature ranged for the first ten days from 98° to 100°. After the 28th the range was between 98° and 99.5°. On Dec. 18th the following note was made: "She has gained in flesh and looks well. The abdomen is a little distended but is not tender and there are no signs of effusion. There are dullness, râles and feeble breathing at the base of the right lung where she has had pleurisy. The apices of the lungs are clear."

The statistics showing the results of this operation have lately been collected by several writers, particularly Kuemmel[1] and Maurange.[2] This last writer has made an elaborate analysis of the cases recorded to date, seventy-one in all, with the following result: There died after the operation, six; by generalization of the tubercle, seven; there recovered sixteen cases, of which no further mention than this fact was made; fifteen cases were alive at the end of six months, and twenty-eight cases had survived a year.

Of the American cases, Maurange includes those of Homans (3), of Van der Warker (1), Morrill and Bradford (1), Cabot (2), Goodell (1), and Bruen (1). To these I can add the following cases. Goodell writes[3] that he has operated upon four cases, in all of which the

[1] Archiv. f. klinische Chirurgie, 1888. Bd. XXXVII.
[2] Thèse de Paris, 1889.
[3] Private letter, Nov. 28th, 1889.

ascitic fluid was recognized, but in addition ovarian disease was suspected. In none of the cases were the tubes or ovaries diseased. So far as he could ascertain, all of the cases got well. One of them, however, after six months excellent health, returned with a pelvic tumor and ascites. She refused an operation and is now probably dead.

Mundé writes[1] that he has operated on three cases, in all of which there was ascites, and the diagnosis of obscure tumor was made. In one case the patient recovered from the operation and died two months later of pulmonary disease, which was not evident at the time of the operation. In the other two cases, the recovery was temporary and they died afterwards of exhaustion. In all three, a distinct abdominal tumor appeared to exist; in two general, in the third in the left ovarian region. There was no doubt in any of the cases as to their tuberculous nature.

Kelly has operated upon four cases.[2] The first case was in 1886. There was temporary improvement. Some months after a second operation was performed. The patient is at present alive and well. The operation in this case was performed for tubal disease and peritonitis was found. In the second case there was no definite diagnosis but a tumor mass was evident. An encysted purulent peritonitis was found which was drained. Patient recovered temporarily and died one year after of phthisis. In the third case, the diagnosis was a parovarian cyst. The first operation was in May, 1889. The abdomen was drained, improvement followed for a time, but the fluid re-accumulated and on three subsequent occasions, at intervals of about six weeks, the peritoneum was incised and drained. At the last operation the tube and ovary of the right side were removed. The patient is still under observation and has evidence of some fluid remaining in the peritoneum. The fourth case has already been referred to, in which the tubercular disease was found as an accidental complication with an ovarian tumor.

Homans'[3] fourth case, operated upon March 19th, 1889, left the Massachusetts General Hospital in June quite well. His second case, included in Maurange's statistics, operated upon April 20th, 1887—referred to at page 44 of his statistical account of three hundred and

[1] Private letter, Nov. 18th, 1889.

[2] From notes given by Dr. Robb.

[3] Private letter, November, 1889.

forty-four laparotomies[1]—is of great interest, as Dr. Cutler examined the peritoneal growth and found it to be tubercular. In May, 1889, more than two years after the operation, she remained perfectly well.

Two cases operated upon by Gardner, of Montreal, have already been referred to in previous sections of this paper (pp. 80, 83.)

H. P. C. Wilson, of Baltimore,[2] has operated upon one case in which the disease was thought to be a cystic ovarian tumor. The entire peritoneum was studded with miliary tubercles. The patient recovered from the operation but died six months afterwards.

Dudley, of Chicago,[3] operated upon one case in 1884. There was double ovarian disease as well. She recovered but a fistula remained. Death occurred in 1888. G. E. Shoemaker[4] reports a case of recovery.

To these cases, for statistical purposes, may be added the four reported by Spaeth,[5] as they are not referred to in Maurange's paper. Of these, one died after the operation; the second, three months after of acute phthisis; the third, four months after of tuberculosis of the intestines, and the fourth, at the time of report, had intestinal disease. M. Schmidt[6] has reported two cases, one of which recovered completely and was well more than a year after the operation, the second was benefited temporarily but death occurred five months after. Imlach[7] states that he has had five cases, all of which had resulted in apparent cure.

Of these additional twenty-six cases, the results cannot be said to be on the whole so satisfactory, as fourteen cases were dead at the time of the report, one of an intercurrent pneumonia.

The majority of writers on the subject speak hopefully of the operation in suitable cases, and from what we know of the natural history of the disease and from a study of the cases in which laparotomy has been performed, whether specifically for tubercular disease, or by accident, we may regard it as not only justifiable but urgently indicated in many cases.

Secheyron[8] concludes from an analyses of forty-two cases of lapa-

[1] Boston. Sawyer & Sons, 1887.
[2] Private letter, Nov. 11th, 1889.
[3] American Journal of Obstetrics, Nov., 1889.
[4] Medical and Surgical Reporter, April 13th, 1889.
[5] Loc. cit.
[6] Centralblatt f. Gynäcologie, 1889, No. 32.
[7] British Med. Journal, Dec. 14, 1889.
[8] Nouvelles Archives d'Obstétrique et de Gynécologie, No. 11, 1887, quoted in American Journal of Obstetrics, Vol. 21, p. 447.

rotomy, that interference is not called for in the acute or chronic disease when generalized, whether with or without sero-purulent effusion, and thinks that the operation is only called for when symptoms of strangulation or of perforation of the intestines appear. He acknowledges that encysted tubercular peritonitis calls for surgical intervention as the condition is really one of cold abscess.

Spaeth, too, does not write very encouragingly, but in a disease heretofore believed to be incurable the statistics of Maurange show such a percentage of recoveries, that we may place the operation among the triumphs of recent surgery.

Two questions remain for consideration, what cases are most suitable for operation, and how can we explain the beneficial influence?

Undoubtedly the cases of the first group, those with fresh eruption and considerable effusion, whether free or sacculated, offer the best chance of recovery, as the disease is more likely to be primary in the peritoneum, the general condition is usually better, and the subsequent chances of general infection are much slighter. When the Fallopian tubes are extensively diseased, and when the process has extended through the diaphragm to the pleura, the condition is of course less favorable. The existence of marked omental tumor, in the form of a transverse ridge, need not necessarily be an objection to operation, as we have seen that in two of Gairdner's cases, spontaneous resolution of such masses took place. In cases then with somewhat sudden onset, rapid development of ascites with fever of moderate grade, we may be most sanguine of success.

In the class of cases with extensive caseous masses in the peritoneum and a purulent exudation, the outlook is necessarily less hopeful, but even in such instances, particularly when the exudation is sacculated, laparotomy may be advised as a palliative measure.

In the chronic adhesive form, no benefit could be expected to follow the operation, which could only be intended to remove an omental mass or to open a sacculated effusion. In the majority of the cases of this group nature is effecting a cure in which she scarcely needs outside assistance; and the danger lies not so much in the peritoneal disease as in the risk of pulmonary affection.

It is difficult to explain the beneficial results of the operation. It is interesting to note that not alone in tubercular peritonitis, but in

other forms with effusion, the simple opening and drainage of the cavity has seemed to exercise a very beneficial effect on the subsequent course of the disease. Thus, Homans reports a case[1] in which an exploratory laparotomy was performed in a woman, aged sixty, with enormous ascites: Forty pounds of fluid were removed and a soft tumor was found attached to the sacrum and right ilium. The abdomen was sponged out and sewed up, as it was found impossible to remove the tumor. The patient recovered rapidly, was greatly relieved and the fluid never re-accumulated. Death occurred a year subsequently, and at the autopsy a sarcoma was found filling the pelvis. This would indicate that the thorough drainage of an ascites, even of enormous extent, may so alter the condition of the peritoneum that the fluid is not re-formed. More remarkable still are the cases which indicate that the mere opening of the abdominal cavity modifies in some way the development of new growths. Gairdner states[2] that Sir Spencer Wells informed him of a case of apparently cancerous peritonitis, in which, after an exploratory incision, the symptoms subsided and the woman got well. Mr. Lawson Tait[3] comments at some length on this remarkable tendency of abdominal neoplasms to undergo retrograde changes after an exploratory incision.

His statements on this point are most interesting and deserve the careful consideration of physicians as well as surgeons. He says that he has seen tumors disappear after laparotomy in cases of disease of the liver, spleen and head of the pancreas. He does not specifically mention cancer of the peritoneum. His remarks deserve quoting, as they bear directly upon this subject.

"The cases are far too numerous, and the results indicate sequence far too clearly, for us to dismiss the phenomena as a mere coincidence; nor can we accept the explanation of subsequent medical treatment as having brought about this much-desired ending. I am satisfied that the mere opening of the peritoneal cavity has a direct influence in setting up the process of absorption of the tumor, and my conviction in this direction has increased my confidence in the principle of exploration. That some emphatic physiological change is at once set up by opening the peritoneal cavity is clearly

[1] Loc. cit., page 40.
[2] Loc. cit., page 46.
[3] Edinburgh Medical Journal, Nov. and Dec., 1889.

indicated by the uniform onset of a most distressing thirst, which lasts for days, and is not seen so markedly after any other operation known to me. Let the incision in the abdominal wall be made down to the peritoneum, but let the serous cavity remain unopened and this thirst is not marked. But let the peritoneum be opened but a finger's breath and the result is marked. That a therapeutic change is effected in the peritoneum itself by the mere opening of the cavity is now universally recognized in the treatment of what we call tubercular peritonitis by abdominal section. I have now had a large experience on this point, and can say positively that we can cure permanently and speedily cases that have gone even as far as suppuration, by opening and cleansing. But in the bad cases in all probability the cleansing is never complete, no matter how much time and care are spent on it. And, in the non-purulent cases, I very often do no cleansing at all, but merely empty out the serum and put in a drainage-pipe. Yet the great majority of these cases are cured by these simple means."

Evidently, in whatever way brought about, the opening and drainage of the peritoneum favors in a remarkable way the regression of the tubercles; and it does more than this, for, as has been frequently noted and as is well indicated in the history of Case VIII, with an improvement in the local symptoms the fever reduces and the general condition of the patient rapidly improves. In some way the operation renders the condition of the peritoneum more favorable to the fibroid changes by which alone healing is induced.

There are on record several cases from which we may get an idea of the condition of the peritoneum some months after the operation. The case of Emma G., so often referred to, is probably as good an example as could be obtained of healing tuberculosis. The effusion had disappeared, in the neighborhood of the liver the adhesions had become fibroid, the tubercles were hard and pigmented, and there was nowhere any congestion about them. In the literature there are several cases of this kind. Thus, Hirschberg[1] narrates the case of a woman upon whom laparotomy was performed for peritoneal tuberculosis, and in whom the abdominal symptoms subsided completely. Eight months after, the patient died of phthisis, and there were no traces of the numerous granulations which had existed on

[1] Quoted by Kuemmel. Loc. cit.

the membrane at the time of the operation. Another case, also quoted by Kuemmel, a girl aged 17 with ascites and tubercles in the peritoneum died six months after the operation. The autopsy showed that the effusion had not been reproduced and that healing had occurred.

A third case of Ahlfeld's[1] is still more interesting, in which he found, during the performance of Freund's operation, the peritoneum covered with granulations. At the autopsy, a year and a half afterwards, there was no trace of the tubercles.

Several views have been advanced in explanation of the beneficial effects of the operation. Thus, Cameron, of Huddersfield, thinks that the curative action is due to the removal of the ptomaines which accumulate in the ascitic fluid and the absorption of which is responsible for the constitutional disturbance. Possibly it may be by a reduction in the activity of the inflammatory processes about the tubercles, which some have supposed are kept up and encouraged by the ascitic fluid, but it is more reasonable to suppose the existence of the latter to depend upon the activity of the former. I scarcely think we are at present in a position to give a thoroughly acceptable explanation why incision and drainage should in these cases of tubercular and other neoplasms so remarkably inhibit the growth and often induce retrograde curative changes.

Are all of these cases of cure truly tubercular? Spaeth[2] raises this question and throws doubt upon the diagnosis in the absence of the proofs afforded by the discovery of the bacillus, or the infective nature of the growths as demonstrated by inoculation. I cannot see that in practice this is an entirely forcible objection; for, as a rule, the peritoneum is the seat of miliary and nodular growths in only two affections, cancer and tubercle—the former a very rare, the latter a very common occurrence, and without histological examination, it may be impossible in certain cases to say which of the two conditions is before us.

Spaeth makes the interesting statement that there are numerous cases of other chronic diseases of the peritoneum which, at first glance, look like tuberculosis, but which on examination prove to be simply chronic peritonitis with nodular thickenings or lymphomatous growths.

[1] Quoted by Kuemmel, from Deut. med. Woch., 1880.

[2] Loc. cit.

My colleague, Dr. Welch, informs me that his experience coincides with this, and that there is a form of chronic peritonitis, usually associated with much effusion, in which the peritoneum is studded with fibroid or lymphomatous nodules. He has, in Flint's Practice (6th Edition, 1886), described these nodules as occurring in chronic serous peritonitis and speaks of the difficulty in the diagnosis between this condition and tubercular peritonitis.

The point is one not often referred to by pathologists.

Birsch-Hirschfeld[1] speaks of fine fibrous nodules occurring in large numbers on the peritoneum in chronic inflammation, similar to those which are seen upon the pleura.

Rokitansky,[2] too, speaks of papillary fibrous growths of sub-serous connective tissue as a result of hyperæmia of the peritoneum.

Prochownick,[3] in a paper upon laparotomy in chronic peritonitis, has some very interesting observations upon this subject. Two of his five cases were regarded as tuberculous until an examination was made. In the first case there were two elastic tumors by the side of the uterus. At the operation extensive union of the omentum with the pelvic peritoneum was found. There was a hemorrhagic effusion. The tumors were made up of encysted exudation. Over the intestines there was a grayish granular deposit. Although he states that this was regarded as tuberculosis, I do not see that he mentions the existence of any tubercle-like granulations or nodules. The examination of portions removed from the omentum showed that tubercles were not present, and it was evidently a case of simple peritonitis. A second case, much more remarkable, occurred in a girl of sixteen years, with a well-marked tumor in the left side of the abdomen, which upon operation was found to be composed of the coil of intestines. The entire peritoneum was covered with hundreds of small nodular tumors. On examination these were found to be made up of a lymphoid tissue, chiefly seen at the outer margin of the nodules, the centres of which had in many places undergone softening. Mundé was present at the operation in this case and refers to it (American Journal of Obstetrics, Vol. 19, page 899) as one of multiple *carcinosis* of the parietal and visceral peritoneum. The

[1] Lehrbuch der Pathologische Anatomie, 2te Auflage.

[2] 3te Auflage, Bd. 3, p. 138.

[3] Deutsche med. Wochenschrift, 1889, Number 24.

patient, it may be mentioned, made a rapid recovery, but I see no note as to the subsequent history.

J. F. Payne[1] describes a case of minute fibrous granulations of the peritoneum associated with disseminated growths throughout the liver, possibly syphilitic, and fibrous thickening of the walls of the portal vein and bile duct. The patient, a man, aged 52, was admitted to St. Mary's Hospital under the care of Sir Edward Sieveking and died with symptoms of dropsy. The peritoneum was covered over with miliary granulations without any larger nodules and without general thickening or adhesion. There were a few litres of fluid in the cavity. Payne remarks that the peritoneal granulations were certainly not like cancer, tubercle or any generalized growth which commonly occurs in the form of a miliary eruption. They were essential fibrous outgrowths of the peritoneum and not of its serous epithelium. He says they resemble somewhat the fibrous outgrowths met with in the capsule of the liver or spleen.

I have never seen cases of this kind, unless, indeed, as is possible, I have mistaken some of these cases for fibroid tubercles. On the other hand, it is equally possible that those who have described these cases of chronic nodular peritonitis, may have confounded this condition with the healed tubercular disease. Indeed, in reference to Emma G., Case VIII, Dr. Welch tells me that had not Dr. Councilman, at the date of the operation, examined the nodules removed and demonstrated their tuberculous nature, he would, at the autopsy, which occurred four and a half months subsequently, scarcely have regarded the nodules as tubercular, so hard and fibroid had they become. In this respect the case is one of the greatest importance, as it shows how essential the examination of the nodules is, taken fresh at the time of the operation.

It must not be forgotten that in certain cases the bacilli are very difficult to find in peritoneal tuberculosis, though they may, as in the case just referred to, be most abundant even when the tubercles are very hard and fibroid. In all cases, when possible, the inoculation of a rabbit or guinea pig should supplement the histological examination.

The important practical point, however, is the relief and cure of

[1] Transactions of the Pathological Society of London, Vol. XXI.

these cases by laparotomy, and the surgeons may well leave to the pathologist the minor question of determining the nature—whether fibroid, lymphomatous or tubercular—of the chronic peritonitis.

Among the conclusions which follow from the foregoing considerations, are:

First, that tubercular peritonitis is often a latent affection, localized in the peritoneum, which may even run its course without inducing special symptoms.

Second, that as in other local tubercular processes there is in this a natural tendency to healing, which takes place more frequently than has hitherto been supposed.

Third, that statistical evidence shows laparotomy to be in many cases a palliative, and in a certain number a curative, measure.

ACUTE NEPHRITIS IN TYPHOID FEVER.

By WILLIAM OSLER, M. D.

Occurring early in the course of typhoid fever, nephritis and pneumonia are very apt to cause error in diagnosis, and too often the post-mortem examination gives the first intimation that there has been a general disease, masked entirely by prominent local symptoms in lungs or kidneys. There are few physicians who have not puzzled over these cases of so-called pneumo-typhoid and nephro-typhoid and have been undecided whether they had been dealing with a pneumonia or an acute nephritis with adynamic symptoms, or whether the disease has not been typhoid fever with early and unusually well marked pulmonary or renal lesions.

In my experience, the cases of typhoid fever which have set in with lobar pneumonia, and in which the symptoms of this disease have dominated the entire course, have been more common than those in which nephritis was a complication. The latter is by no means frequent, and during the ten years in which, as pathologist or physician, I was connected with the Montreal General Hospital—one of the largest fields for the study of typhoid fever on this continent—I do not remember to have seen an instance of the kind.

The renal complications which we meet with in typhoid fever may be grouped as follows: first, febrile albuminuria, usually not of much moment, even though casts be present; second, acute nephritis, often hemorrhagic, which sets in early and which gives the prominent clinical features to the case; third, a late nephritis, occurring during convalescence and which is analogous to that which follows other infectious disorders; fourth, a lymphomatous (Wagner) nephritis, also occurring late; and lastly may be mentioned, as the urinary symptoms are well marked, a post-typhoid pyelitis.

Of these, the second, acute nephritis—the *nephro-typhus* of the Germans, the *fièvre typhoïde à forme rénale* of the French—occur-

ring at the onset or quite early in the disease, is especially likely to cause difficulty in diagnosis and forms a serious complication.

The following cases illustrate many of the clinical features of this condition.

CASE I.—*Onset with rigor. Persistent high fever. Hæmoglobinuria with albumen and tube casts. Delirium. Symptoms of perforation. Death on the 14th day of illness. Typhoid lesions in ileum; perforation. Nephritis.*

John T., aged 26, oysterman, colored, admitted to the Johns Hopkins Hospital, June 11th, 1889, complaining of pain in the lumbar and hypochondriac regions, with cough and shortness of breath. He had been ill since the 5th, when he caught a heavy cold and had pain in the back, chest and limbs, and from the description he must have had a severe rigor. Though feeling miserable he kept at work until the 10th, the day before his admission. He says that he has eaten nothing for three days.

On admission, he was complaining of lightness of the head and pain in the back. Temperature was 104°. Pulse 84, strong and full. Respirations 38, shallow. The tongue was dry and brown; the skin very hot and dry. He coughed very frequently and expectorated slightly blood-stained mucus. The abdomen was not distended; it was a little tender to the touch in the right iliac region. The lungs and heart were normal.

He was ordered antipyrin—5 grs.—and to be sponged every three hours and given a fever mixture; and, if the temperature reached 105°, to be given a graduated bath.

12th.—Passed a restless night. Temperature at 9 a. m. 102°. Cough troublesome and expectoration slightly tinged with blood. Examination of the lungs negative. The condition of the urine was as follows: Amount passed about 500 cc.; dark reddish brown in color; acid in reaction; moderate amount of greyish sediment; specific gravity 1024; albumen present. Microscopical examination showed numerous epithelial and granular casts, and much granular débris; no blood corpuscles.

Towards evening the temperature rose again to 105° and was reduced by a graduated bath.

13th.—Patient passed a restless night. Temperature between 104°

and 105°. He had a liquid and slightly blood-stained stool. He was conscious; pulse 110, dicrotic. Tongue dry. Examination of the abdomen negative. The blood was examined on several occasions with negative result. The urine presented the same characteristics, but was perhaps a little higher in color.

14th.—Temperature at 9 o'clock 104.4°. Patient did not seem so well; was delirous; passed urine involuntarily.

15th.—Temperature again 105°, reduced by a graduated bath to 102.4°. Urine presented the same dark color; specific gravity 1022, acid in reaction; numerous tube casts, no red blood corpuseles; abundant hæmoglobin.

16th.—Temperature lower, not reaching 104°. Patient conscious; pulse 104, no longer dicrotic. Tongue swollen and moist, uniformly furred. Abdomen not distended, soft, no tenderness, a little gurgling in the right iliac fossa. Splenic dullness began at the lower border of the 7th rib and extended four finger's breadth vertically. Edge not palpable. Heart sounds clear. Examination of the lungs negative. 700 ounces of urine passed in the 24 hours; specific gravity 1018; color deep blood red. It contained albumen, granular and epithelial casts, hæmoglobin, but no blood corpuscles.

17th.—Temperature not above 103°. Passed a very comfortable night; was delirous at times. Pulse 120. Tongue moist and furred. Conjunctivæ a little jaundiced. Abdomen not distended. Heart sounds clear. Urine cherry red, not quite so dark but contained a larger amount of sediment; specific gravity 1016.

18th.—Patient seems better. He complained of pain in the abdomen for which he was ordered a turpentine stupe. In the evening, at 9.30, he had a rigor. The temperature fell to 97°, but after the chill it rose again to 102°. Between 8 and 11 o'clock he had four loose stools. The abdomen became very painful and a little swollen. At 3 a. m. the temperature was 104°. There was great pain in the abdomen. There was no special distension. At 7 o'clock the temperature was 104°.

19th.—At 10 a. m. the pulse was 120, and extremely feeble, scarcely to be felt. The patient seemed rational. There was no special hardness of the abdomen, no great distension. Dr. Lafleur diagnosed perforation and the propriety of a laparotomy was discussed and negatived.

The liver dullness was almost obliterated in parasternal line. Pulmonary resonance ended at 6th rib. In 6th and 7th interspaces there was a flat tympanitic note. In mid-axillary line there was a slight liver dullness. The stomach tympany reached high to the 5th rib in the left anterior axillary line. The splenic dullness was pushed very far back. The patient became comatose and died on that day.

Post-mortem, by Dr. Welch.—In peritoneum 25 cc. of offensive brownish-yellow fluid. The lower coils of the intestines were ecchymosed in places and there was exudation of fibrin on the surface. The liver had fallen back from the abdominal wall. The diaphragm on the right side corresponded to the lower margin of the 3rd rib on the left to the upper margin of the 5th.

In thorax there were no adhesions.

In pleura there was a slight amount of blood-stained serum in each cavity. The heart weighed 325 gms.; the valves were normal, the muscular substance flabby and pale. There was general pulmonary œdema in the lungs; no foci of pneumonia.

The spleen was large and soft; and weighed 550 gms.

The capsule of the kidney was not adherent. The left weighed 226 gms. The cortex was pale-yellow. The striæ were obscured. There were no ecchymoses. The right organ was in the same condition. Both of them showed signs of decomposition.

The liver was soft and pale. The stomach presented nothing abnormal.

In the intestines the first ulcer in the ileum was 130 cm. from the valve. From this point the ulcers were numerous. Many of them were transverse, some presented the remains of shreddy, yellow sloughs. A large ulcer, 7 cm. from the valve, was irregular in shape, 6 cm. in length and $4\frac{1}{2}$ cm. in breadth, with undermined edges and a sloughy, moderately congested floor. Near the centre of this were two perforations about 2 mm. apart and about 2 mm. each in diameter.

In the upper half of the large intestine there were a few scattered elevated patches with yellowish surfaces and infiltrated margins.

Microscopical examination showed in the substance of the kidney epithelium of the tubules, granular and much broken containing fatty globules of small size. There were numerous straight, thick, non-motor baccilli.

The heart muscle showed fine granules and a few oil globules.

This case offered much difficulty in the diagnosis. We thought at first it might be malarial remittent fever but as the examination of the blood proved negative, this was excluded. The persistence of the fever at a high level and the dicrotic character of the pulse favored typhoid fever. The latter symptom was regarded as very suggestive, but it is curious that several writers have noted, particularly in these forms of renal typhoid, the absence of dicrotism. The occurrence of profuse hemoglobinuria, with his severe initial chill again suggested malaria, but we relied upon the negative character of blood examination to exclude this. There were practically no abdominal symptoms other than slight pain. It was not until the seventh day in the hospital that he had diarrhœa and this followed the chill, associated with the perforation. The rigor, the collapse temperature, the pain in abdomen with slight swelling and more particularly the almost complete obliteration of the liver dullness in the mammary line, led Dr. Lafleur to the diagnosis of perforative peritonitis.

CASE II.—*Gradual onset, with fever and cough; no rigor. Restless delirium, diarrhœa; well marked rash. Much albumen and many tube casts in urine. Remarkably low temperatures. Acute otitis media. Death about 22nd day. Extensive ulceration in ileum. Acute nephritis.*

Josie H., aged 25, was admitted to the Philadelphia Hospital on October 9th in a condition of delirium. From her friends the following history was obtained.

She had enjoyed good health with the exception of an illness of three months duration, eight years ago, which had followed the birth of a child.

She had been complaining for a few days of headache and of a feeling of fatigue and loss of appetite. She had a slight cough, but no expectoration; was feverish at times in the evening and her sleep was disturbed. She kept at work until Saturday the 5th and on Sunday the 6th took to her bed, the fever becoming more marked.

On admission, the temperature was 104.2°, pulse 123, not dicrotic, respirations 22. The patient answered questions, but rambled at times. The tongue was dry and tremulous; examination of the

viscera was negative. There were a few bronchitic râles in the upper lobes of the lung. On the three next days the fever ranged from 102° to 103.8°. She had slight diarrhœa—two stools on the 10th, three on the 11th and three on the 12th. They were watery and yellow in color. She was very restless, constantly trying to get out of bed. The pulse ranged from 100 to 130, and on the evening of the 12th rose to 160. There was incontinuance of urine on the 10th and 11th and none was obtained for examination. The amount of urine was uncertain as it was passed involuntarily. On the 12th the patient was catheterized and six or seven oz. were withdrawn which was found to contain albumen and numerous tube casts. On the evening of the 12th the quantity had been so small that Dr. Talley, the resident physician, ordered the infusion of digitalis in half ounce doses, and a digitalis poultice on the abdomen. On the 11th rose spots were seen on the lower thoracic and epigastric regions. She continued restless and delirious, and when dozing subsultus tendinum was marked.

On the 13th she refused to take nourishment. The temperature at 3 a. m. was 100.8°; at 12 m., 101.6°; at 4 p. m., 101°; at 6.30 p. m., 97.4°. The temperature remained low all night, at 10 p. m. it registered 97.4°; at 4 a. m., 97.2°; at 7 a. m. 96.4°. The pulse was small, 115 to 120. She took nourishment better and there were 250 cc. of urine passed on the 13th.

The following notes were made of her condition at the mid-day visit:

"Face looks haggard; eyes sunken but bright; she has a distressed, frightened look; features pinched; tongue red and dry; pulse rapid and small; abdomen not distended; eruption distinct; vertical splenic dullness of four inches; urine turbid and high colored with deposit of a heavy sediment of mucus; specific gravity 1022; reaction acid; with nitric acid, a copious precipitate of albumen, one-third by bulk in settling; microscopical examination showed numerous large and coarsely granular tube casts. They were so coarse that at first they were taken for pseudo-casts of sediment. Numerous specimens were seen with the upper portions composed of mucus alone with a few particles, while the lower parts consisted entirely of these coarse granules; in the casts were also remnants of epithelium cells and, in a few, leucocytes. In the urine freshly drawn from the bladder there were

numerous bacilli, some of which seemed to be in the tube casts. Here and there red blood corpuscles were seen but they were not numerous."

On the 14th the temperature, which had been subnormal at 7 a. m. rose by noon to 100.4°, and for the remainder of the day it kept between 104° and 105.5°. She passed 440 cc. of urine in the twenty-four hours and slept better. She also took more food.

On the 15th the temperature at 8 a. m. was 97.3° ; at 2 p. m. it rose to 101.4°, and the pulse ranged from 120 to 140. There was a discharge of blood-stained fluid from the right ear ; nothing to be seen in the meatus and no tenderness over the mastoid process. In the evening the temperature again sank below normal, and at 10 p. m., 1 a. m. and 4 a. m. it stood at 97.8°.

On the 16th the temperature was 99.2° in the morning. She had had a restless night, but looked better in the morning. She had passed urine involuntarily and the quantity for the twenty-four hours was therefore doubtful. The discharge from the right ear continued and there was no special tenderness on either side of the head.

The anomalous temperature curve and the discharge from the right ear suggested a doubt as to the true nature of the case. Puncture of spleen was made with a fine hypodermic needle and cultures prepared from the fluid. After midnight the temperature again sank.

On the morning of the 17th the temperature was 97.8°, remained about 99° all day, but at 8 p. m. sank to 97.4°. The pulse was 120, very feeble ; passed a very quiet day and seemed to recognize her friends.

On the 18th the temperature at 1 a. m. was 97° and by 8 a. m. rose to 98.8°. The urine presented the same features as before, but the granular casts were less numerous ; the amount of albumen was large, and bacilli were still seen in the urine withdrawn with careful antiseptic precautions. The continued low temperature necessitated the constant application of hot cans. The bowels had not moved for several days. The delirium persisted.

On the 19th, the temperature at 5 a. m., was 96.4° ; at 8 a. m. 96.8° ; pulse very feeble 140. She was given an injection which brought away a partly formed yellowish stool. At 2 p. m. the thermometer in the axilla could not be made to register more than 95°. The patient seemed very dull, heavy and lethargic. At 3 p. m. the temperature rose to 96.4° and by 5 p. m. it was 98.4°. She had

hiccough through the day and more rapid respiration. The temperature at 8 p. m. was 97°; at 10 p. m. 96.4° and death took place at 3.30 on the morning of the 20th, eighteen days after taking to her bed.

Autopsy, eighteen hours after death.—The body was that of a well-made, well-nourished young woman; the skin was pale; considerable discharge from the right ear.

Abdomen. The peritoneum was smooth; the lower coils of the intestines were deeply congested and the mesentery was swollen.

Thorax. There were numerous adhesions in the right pleura; the left pleura was smooth. Pericardium was normal. The heart was of medium size and contracted, with dark clots in the right chambers; the valves were normal; muscular substance looked a little pale. Beneath the endocardium of the left ventricle there was hæmorrhage, forming a continuous layer on the septum and specially abundant about the muscular papillæ.

The lungs showed no change beyond slight hypostatic congestion at bases.

The spleen was slightly enlarged and the pulp softened; no trace on the capsule of the needle puncture.

Stomach and duodenum showed no special changes. The jejunum presented a catarrhal condition; the mucosa was thickened, and at its lower part Peyer's patches were swollen. The ileum was swollen and congested. In the upper portion there were half dozen small ulcers on the patches; the bases were formed of muscular tissue, and the edges were elevated and deeply hæmorrhagic; the lower foot of the ileum was very thick and heavy, livid in color. Three or four large large ulcers with swollen deeply hæmorrhagic edges were seen. One next to the valve was fully two inches in extent. Here and there portions of yellowish sloughs were adherent on the ulcers. The cæcum presented one or two small ulcers. The large intestine was full of yellowish-brown, liquid fæces. With the deeply hæmorrhagic character of the ulcers, it is interesting to note the absence of even a bloody tinge in the fæces.

The mesenteric glands were greatly enlarged and deeply congested. One presented a soft cheesy centre. The liver was large, the vessels full of blood, the substance rather soft.

The kidneys were enlarged and weighed together about 400 grammes; the capsules were thin and readily detached; the surface

was pale and mottled by the presence of numerous stellated veins. On section, the substance was moist and from the larger veins blood flowed freely. There was marked contrast between the cortex and pyramids, the former being greyish-white and uniform. The tubuli Bellini appeared swollen and presented only here and there a full vessel or congested Malpighian tuft. No localized opaque areas. The pyramids were congested and the vessels and veins at the bases were distended with blood. Histologically the changes found may be thus summarized: (1) Glomerulo-nephritis involving both the vascular and capsular epithelial lining. The tuft was often partially compressed by granular débris and rounded cells which stained badly. (2) Dilatation of the convoluted tubes with extensive necrosis of the epithelium, which, as granular matter, filled the lumen. In places large tubes were distended with the pale round cells noticed in the capsules. (3) In spots atrophy of the tufts with fibroid change about them—probably an older process.

Uterus normal. Bladder tightly contracted; mucosa hyperæmic.

There was reddish, grey exudation in the right tympanum; the drum was perforated. The inflamation had not extended to the mastoid cells.

The brain showed congestion of the cortical veins; substance normal; no extension of inflammation from the ear.

This case presents an entirely different clinical picture from the first. The slow onset, fever, dry tongue, bronchitic râles, slight diarrhœa, left very little doubt at the time of her admission that the case was one of typhoid fever. The extraordinary ranges in the temperature, with the occurrence of an otitis media and the renal symptoms, shook this opinion somewhat for a few days, and it was then that Dr. Shakespeare was asked to make cultures from a blood drop from the spleen, in which were characteristic typhoid bacilli. By far the most interesting feature in this case, possibly associated with the nephritis, was the extremely irregular temperature; thus, on the 13th, the fourth day of her admission, after the temperature had been ranging from 102° to 104°, it fell at 6.30 p. m. to 97.4°, and remained about this point all night, registering at 7 a. m. 96.4°. I was afraid, at the mid-day visit, that hemorrhage or perforation had occurred. She rallied, however, and by the evening the fever was higher than it had reached previously, 105.5°. On the mornings of the 15th, 16th, 17th and

18th, the temperature was also subnormal. It usually rose in the evening to 103° and 104°. Throughout the 19th, the thermometer only once registered 97°.

These cases, both unhappily fatal, illustrate the main features of this serious complication. Practically we have to deal with an acute, in most instances, a hemorrhagic nephritis. Naturally it adds much to the gravity of the case, and the prognosis is always rendered more dubious. Wagner,[1] however, has had five cases of recovery in succession, but the high mortality mentioned by Amat—10 deaths in 12 cases—is the more common experience.

A discussion of the relation of this form of nephritis to the typhoid poison—whether induced directly by the bacilli or by their ptomaines or the result of a mixed infection—would be beside my present purpose, which is solely clinical; nor do I think the materials are yet available for a solution of this problem, one of the most complex in the pathology of the infectious diseases.

[1] Deutsches Archiv für Klin. Med., Bds. XXV and XXXVII.

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ON THE AMŒBA COLI IN DYSENTERY AND IN DYSENTERIC LIVER ABSCESS.

By WILLIAM OSLER, M. D., *Professor of Medicine, Johns Hopkins University.*

The first observation on rhizopods, as human parasites, was made by Lamb in the year 1859,[1] who found in the mucus of the bowel in a child dead of enteritis, amoeboid bodies and other rhizopods belonging to the *difflugia* and *arcella* types. Leukart doubts whether these forms could be definitely regarded as parasitic. The first satisfactory studies on the subject were made by Losch,[2] of St. Petersburgh, who found the parasites in the stools in a case of ulcerative inflammation of the colon. They were in extraordinary numbers and presented all the characters of amœbæ. The movements were extremely active and the elaborate description which he gives, might have been written from a study of the specimens in which we have here been interested. He injected the stools containing amœbæ into the rectum of three dogs, in one of which, at the end of eighteen days, the amœbæ were found in large numbers in the mucus of the bowel and at the basis of a small ulcer which had formed.

Kartulis,[3] stimulated by the observations of Koch, who found, during his cholera investigations in Egypt in 1883, amœbæ in sections of the intestines of persons dead of dysentery, examined 150 cases in a period of two years and in every one found these organisms in the stools. In twelve post-mortems the amœbæ were present in the ulcers in every case.

They were present in all stages of the disease, in both acute and chronic cases.

He has extended his studies on this question to the liver abscesses, which occur so often in connection with dysentery.[4] In an examination of twenty liver abscesses he found the amœbæ in sections of the walls in every case. In one instance he found a living amœba in the pus of the abscess, examined fresh after death. They presented the same characters as the parasites which he had found in the large intestines. In Virchow's Archiv, Bd. 108. he gives a fuller account of his observations. He has met with the parasites in more than 500 cases of dysentery, and in all the cases of liver abscess due to this disease which he has examined. In thirteen of twenty-two instances of these abscesses cultures were made, eight of which

[1] Quoted by Leukart, Parasiten, zwte Auflage, Lief, I, p. 233.
[2] Virchow's Archiv, Bd. 65.
[3] Virchow's Archiv, Bd. 105.
[4] Centralblatt für Bakteriologie und Parasitenkunde, 1887, p. 745.

were negative; in three there were *staphylococci*, in one the *bacillus fœtidus* and in one the *proteus vulgaris*. He holds that the amœbæ, which exist in all the layers of the intestines in dysenteric ulceration, pass with the micro-örganisms and detritus through the portal veins to the liver. The micrococci excite the suppuration, but only in consequence of the lesions induced by the amœbæ. The pus seems to die rapidly in the abscesses, but the amœbæ remained alive for a much longer period, often over two months. Histologically, Kartulis describes three zones in the abscess wall,—first, the detritus zone, containing fibrous granulations and amœbæ; second, the cell zone, consisting of young cells which stain deeply and between which can be seen portions of liver tissue, liver cells and capillaries, and third, the limitation zone, separating the disease from the intact liver tissues. His most recent communication is in the Centralblatt für Bakteriologie, No. 2, 1890, in which he reports two cases of dysentery which had originated in Athens, in both of which amœbæ were present in the stools, similar in character to those met with in the Egyptian dysentery.

Massiutin[5] has studied this question under Losch's supervision. He has found the parasites in five patients—one, a case of chronic dysentery of seven years standing; the second, a man with chronic intestinal catarrh; a third, a case of typhoid fever with late diarrhœa and much mucus in the stools; the fourth and fifth were cases of diarrhœa with fluid mucoid stools. The amœbæ presented active movements and seemed to have the same characters as those described by Kartulis. He doubts their connection with the intestinal condition. He thinks that they gain access to the intestine through the water and find in the mucus of the colon situations suitable for their growth.

Baumgarten[6] comments as follows upon the view of Kartulis that the amœbæ constitute the exciting agents in the disease. "We will not contradict this view, although, as many old and recent observations show, very similar amœboid forms occur in other intestinal affections and even in normal fæces. We regard it, however, as unlikely that the amœbæ could induce all of the conditions in the dysenteric processes. Dysentery consists anatomically in a combination of diphtheritic and purulent inflammation, which induces rapid and deep ulceration of the affected part. We have no analogy to show that amœboid parasites can induce ulceration and we rather believe that the pyogenic micro-organisms, well known as exciters of ulcerative processes, are concerned with the amœbæ in the causation of tropical dysentery."

This practically embraces the entire literature of the subject. I had, after the publication of Kartulis' paper, made several examinations in Philadelphia with negative results. During a visit to the Hospital, Dr. Lutze,[7] last October, stimulated our interest in the matter as he stated that he had frequently met with the parasites in tropical dysentery. We

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[5] Abstract in Centralblatt für Bakteriologie, Bd. 6, p. 451.

[6] Lehrbuch der pathologischen Mykologie, Bd. 2, p. 937, 1890.

[7] Now the government medical officer for the study of leprosy in the Sandwich Islands.

have since had opportunities of examining several instances of the local dysenteric attacks, and in one case we thought we had found the parasites but we were not very confident. Recently, however, a case has been under observation in which the amœbæ have been found, not only in the stools, but in enormous numbers in the pus of abscesses of the liver. The details of the case are as follows:

Dr. B., age 29, resident in Panama for nearly six years, where he had had several severe attacks of dysentery, or indeed, more correctly speaking, a chronic dysentery, came north in May, 1889, and after remaining for a short time at his home in Baltimore, went to Germany. He had intervals of freedom from the diarrhœa but in Vienna it recurred severely. He returned to this country in December, and shortly afterward began to have an irregular fever with occasional chilly sensations and sweats, to lose flesh and to have a very sallow complexion. These symptoms persisted through January, and about February 15th I saw him in consultation with Dr. Friedenwald. His general condition was very good, considering that he had had severe dysentery and an irregular fever for more than two months. The liver was slightly enlarged anteriorly but not specially sensitive. Posteriorly, there seemed to be a very distinct extension of the dulness upward. He had six or eight mucoid stools with traces of blood daily. I saw him subsequently on four occasions and the symptoms remained practically the same. The temperature rose each day to about 103°. There were no positive chills but occasionally toward the afternoon he complained of sensations of cold. The diarrhœa lessened and his appetite improved, but in spite of this he had lost flesh and strength. Anteriorly, the liver dulness was not much increased, but behind it extended nearly a hand's breadth above the normal limit. There was distinct sensitiveness on deep pressure below the edge of the right costal cartilages, and he complained of a dragging pain whenever he turned upon his left side. The suspicion entertained at first that he had abscess of the liver was gradually confirmed, and on March 22nd Dr. Tiffany aspirated, and then incised and drained two large abscess cavities in the right lobe of the liver. The pus was thick, of creamy consistence, in color, in places slightly bile-stained, but it had not the reddish-brown and anchovy-sauce-like appearance presented by the pus in many cases of hepatic abscesses.

I made an examination of the pus at the Biological Laboratory, within three-quarters of an hour of its withdrawal and found in it, in large numbers, the amœbæ which Kartulis had described. The material was taken at once to the Pathological Laboratory where Prof. Welch and Dr. Councilman confirmed the observation. On each succeeding day, at the time of dressing, pus was removed from the drainage tube before irrigation was begun. On the first two days the amœbæ were quite numerous and very active. For the three following days they were still found, but moving forms were not so common, probably owing to the fact that stronger solutions of bichloride were used for irrigation. Subsequently they were very numerous, and we found them each day, in the pus as it came from the drainage tube, until his death on April 5th.

After the operation the dysenteric symptoms did not abate in the slightest; he continued to have from eight to sixteen movements daily. They varied a good deal in character, some were entirely mucoid streaked here and there with pus and presenting a few grayish shreds. Some were made up of a greenish, pultaceous mass, in which, on several occasions, there were large irregular sloughs. These mucous stools were usually slight in amount. Occasionally there was a large brownish liquid evacuation, in which could be seen small grayish-white masses embedded in blood-stained mucus. On each day there were found in these stools many characteristic examples of the amœbæ. They were most abundant in the small grayish-white shred masses, which in some places seemed almost infiltrated with them.

Description of the amœbæ.

(*a*) From the liver. The size ranged from 10 μ. to 20 μ., which appears to be somewhat greater than indicated by Kartulis. When at rest the outline was usually circular, occasionally ovoid, but when in motion they presented, as shown in the figures, the extreme irregular contour of moving amœboid bodies. The protoplasm could be distinctly differentiated into a translucent homogeneous ectosarc or motile portion and granular endosarc containing the nucleus, vacuoles and granules. The hyaline ectosarc was, as a rule, very distinct and in many examples the granular protoplasm of the interior was surrounded by it as a distinct rim. Occasionally a form was seen in which this portion was much less developed and the greater part of the organism seemed composed of granular substance. Within the endosarc, the vacuoles constituted the most striking feature. Sometimes the interior substance appeared to be made up of a series of closely set, clear vesicles of pretty uniform size. As a rule one or two larger vacuoles were present, the edges of which were not infrequently surrounded by fine dark granules. I never saw a true contractile vesicle which displayed rythmical pulsations but the larger vacuoles underwent at times changes in size. The nucleus was plain enough in some examples, in others very difficult or impossible to detect. It was usually pale, ovoid or rounded in outline and with a very delicate contour. No distinct nucleolus was seen, though there were sometimes coarser granules which possibly represented it.

When once recognized, there was not the slightest difficulty in distinguishing these bodies, even when at rest, from the pus elements, not only by their size but by the entirely different appearance of the protoplasm. The movements, however, constitute their most interesting and distinctive feature. From any portion of the surface, a rounded hemispherical knob would project and with a somewhat rapid movement, the process extended and the granules in the interior streamed towards it. As in the pond amoebae, the clear ectosarc seemed to initiate and play the important part in the movements. Though sometimes slow, many examples were found in which the alterations in contour and the change in locality were quite as striking as in the large active forms of pond amœbæ. The processes were always rounded, never angular or linear as in the white blood corpuscles. Motile forms were found each day in the pus during his life. They seemed

at times more active apparently than at others, and the movements went on at the average laboratory temperature, but seemed increased by heat. They continued active for hours at a time. Twice the movements were observed to continue in the same organism for more than ten hours.

(*b*) The amœbæ from the stools. During the month or more in which the patient was under observation, the diarrhœa was a marked feature. Tenesmus was rarely present and the frequency of the stools was from four to twelve in the twenty-four hours. The character varied very much. Sometimes he had a large brownish fluid evacuation with little or no mucus; more frequently three or four ounces were passed at a time and scattered through the brownish liquid mucus, blood and small whitish sloughs could be seen. On several occasions, the stools seemed to be made up of a gelatinous mucus, streaked with blood, and twice large grayish sloughs were found. Experience showed that the amœbæ were rarely found in the brownish liquid stools. In the mucus they were more frequent, but they were met with in large numbers only in the small grayish fragments, portions, no doubt, of sloughs which were present in variable numbers in almost every mucoid stool.

The general character of the amœbæ corresponded in every particular with those found in the liver. A greater variation, perhaps, in size was noticed, but in the appearance of the protoplasm, the character of the movements, and the arrangement of the vacuoles, no essential difference was noted.

It is impossible to speak as yet with any certainty as to the relation of these organisms to the disease. The subject is deserving of extended study, and a point of special interest will be the determination of their presence in the endemic dysentery of this country.

[Reprinted from THE MEDICAL NEWS, December 20, 1890.]

ON THE FORM OF CONVULSIVE TIC ASSOCIATED WITH CORPROLALIA, ETC.

Clinical remarks made to the Post-graduate Class in Medicine, Johns Hopkins Hospital, Baltimore, October 11, 1890.

BY WILLIAM OSLER, M.D.,
PROFESSOR OF THE PRINCIPLES AND PRACTICE OF MEDICINE, JOHNS HOPKINS UNIVERSITY.

GENTLEMEN: There is a curious disease—or perhaps, more correctly, symptom-group—met with chiefly in children, to which attention has been called of late by French writers, which is characterized by irregular, spasmodic movements, the utterance of involuntary explosive sounds or words, and mental defects of various sorts. It is not a very common affection in this country, and I take this opportunity to bring to your notice a case which we have been studying for the past few weeks.

The cases have usually been described as chorea, or "habit-spasm," both of which conditions are simulated very closely by the irregular movements; certain instances also have been reported as hysteria.

Unfortunately Charcot and his pupils, Guinon and Gilles de la Tourette, have given to this affection the name *maladie des tics convulsifs*. I say unfortunately, for here and in England we use the term *convulsive tic* to characterize a totally different affection, involving usually the facial muscles and of either central or peripheral origin, but not necessarily coming on in childhood and not characterized by the other features presented by the disease of which we are at present speaking; and thus it happens that if we turn to the

time past he has not felt as well as usual. On November 1st, while at his supper, in a restaurant, he found that he could not read the daily paper. He was sure that this came on quickly, and had been his chief annoyance, as he was an ardent politician. He had no definite headache, but

recent editions of French books we find under *tic convulsif* a disease very different from that described by the same name in English and American works.

Case I

The history of our patient is briefly as follows:

Mary ——, aged thirteen years, applied at the out-patient department, July 10th, and was under observation there until September 16th, when she was admitted to ward G. Her mother brought her to the hospital on account of irregular involuntary movements and curious barking-sounds.

Her family history is good. Her mother is a bright, intelligent woman, a German by birth, and has had ten children, none of whom have been affected as is this girl—the third child. There is no tendency to mental disease in the family. The birth of the child was normal and there is no history of convulsions in infancy. She has had scarlet fever, but has not had rheumatism.

Since her fifth year she has been subject to involuntary jerking movements of the arms and head, which vary very much in intensity, sometimes better, sometimes worse, and they have usually been called by the doctors chorea. They have not interfered with her development or her education. She has not yet menstruated. For the past year she has been making curious sounds; beginning by saying "hah" very frequently. Sometimes she would bark like a dog. She would also call out the names of people, and if she heard a new name she would be apt to repeat it.

Her condition on admission was as follows: A bright, intelligent child; well educated, writes nicely, takes an interest in her books and has evidently been ambitious at school. She is nervous, the right arm occasionally twitches and the head jerks. There are no grimaces, but on several occasions she seemed to mimic movements of the face. Every now and then she calls out "hah," "Bridget," or "stools," or says in a clear tones, "bow, wow." There are no disturbances of sen-

sation, and the special senses are unimpaired. Examination of the heart and lungs was negative; the thyroid gland is slightly enlarged.

Throughout the latter part of July and August attempts were made to treat the case by hypnotic suggestions, at first with success, but subsequently without any improvement.

On September 8th her mother wrote the following letter, which illustrated a new phase of the child's malady:

"Mary makes use of words lately that make me ashamed to bring her to you or to take her out of the house; it is dreadful; such words as ——, ——, ——, etc. She was always a modest child, and it almost kills me for to hear her use such words."

Her mother was asked to bring her again and was told that this was really a part of the affection, and, like the movements, involuntary in character. The child seemed more depressed, had lost flesh and, her mother said, had changed mentally. She was very obstinate, and almost invariably did what she was told not to do, and had threatened to take poi She will say the bad words aloud or mutter them to nerself.

On admission to the hospital she was placed in a room by herself, kept in bed, and encouraged in every way to cease making the sounds and to stop the use of the bad words. During the first two weeks she improved very much. The movements were reduced in frequency and sometimes during my visit they would not be noticed at all. They most commonly affected the right arm, which, with the hand, was drawn up in a sudden electric-like jerk. The head and neck would jerk simultaneously or alone. Sometimes there was combined movement of the neck and chest-muscles. The involuntary expressions of which she made use were those mentioned above; a sharp bark was the most frequent sound,

time past he has not felt as well as usual. On November 1st, while at his supper, in a restaurant, he found that he could not read the daily paper. He was sure that this came on quickly, and had been his chief annoyance, as he was an ardent politician. He had no definite headache, but

which, from its ringing quality, could be heard at a considerable distance.

She was so much better that she was allowed to get up and another patient was placed in the room with her. This seemed to excite and worry her, and shortly afterward the barking sounds became much more frequent, occurring every one or two minutes, and she complained of great soreness of the muscles of the chest and abdomen. The movements, however, did not increase. She was again placed in seclusion and in bed, and again improvement followed, but she still barks and she has not given up entirely the use of bad words.

She is a docile, intelligent child, and seems anxious to get well. She has kept a diary, which displays no special peculiarity. She writes verses, which are not worse than those usually composed by girls of her age.

The patient, as you see, is a bright, intelligent child, and there are still to be seen occasional lateral jerkings of the head, and now and then the right arm is elevated with great quickness. You have also heard the peculiar sharp sound which she makes from time to time, which sometimes resembles a hiccough. More commonly it has a barking quality, which is not nearly so marked as it was some weeks ago, when usually two of the sounds succeeded each other with rapidity. In addition, this child has presented several of the symptoms which Charcot and his pupils regard as characteristic of the affection.

I have just spoken of the emission of involuntary sounds and words. The use of bad words, for which the ingenious expression *coprolalia* (fæcal speech) has been invented, is present in very many of the cases, forming a feature very distressing to the relatives.

You can judge from the letter of this child's mother how grievously troubled she was over our patient's "slips of the tongue." She cried bitterly when she told us of it, and said that she wished her daughter

would die. In some of the reported cases, even children of five or six years have persistently used words of the most obscene character.

A second peculiarity of a similar nature is the repetition of any sound or word heard, for which the name *echolalia* is employed by Charcot. It is a veritable echo, and the word is repeated by the patient so soon as heard. In our case this did not often occur, but, on hearing a new name, she would be apt in a short time to repeat it very often; thus, on first coming into the hospital, she used for some time the word "nurse," which she was constantly hearing.

The facial mimicry was noticed on several occasions, but has not been a special feature. This curious imitation of muscular movement has been described, not only in the face muscles, but in those of the extremities, and simulates closely those of the remarkable Malay disease known as *latah*. The term *echokinesia* has been applied to this mimicry of movements.

So far, our patient has not presented any symptom of mental disorder, unless indeed her extreme obstinacy and her addiction to poetry could be so considered. Upon this aspect of the affection Charcot lays great stress, and thinks that sooner or later the cases invariably show psychical changes. By far the most common mental change is the existence of fixed ideas, and Guinon, whose article in the *Dictionnaire Encyclopédique* is the most extensive on the subject, describes these as very often a fear of impending trouble, or a fear of places (*agoraphobia*). In other instances there is "*folie pourquoi*," in which the patient incessantly demands the reason for the performance of even the simplest actions of life.

"*Folie du doute*" and the curious, irresistible impulse to touch certain objects, may also be present. Another form of this obsession which has been noted in some instances, is what has been termed *arithmomania*, in which the patient is possessed with an irresistible desire

time past he has not felt as well as usual. On November 1st, while at his supper, in a restaurant, he found that he could not read the daily paper. He was sure that this came on quickly, and had been his chief annoyance, as he was an ardent politician. He had no definite headache, but

to do some special mathematical problem, or to count up to a certain number before doing a certain action.

In brief, the main peculiarities of the disease are: the involuntary movements, the uttering of words or cries, coprolalia, mimicry of words or movements, and, in very many instances, mental symptoms, chiefly some form of obsession. The majority of the cases present only the first two or three of these features, and it is not until the more advanced stages that the mental symptoms become marked.

The prognosis, according to Charcot and his pupils, is extremely grave, and very few cases recover, but years may elapse before the onset of mental symptoms. The diagnosis is easily made in cases such as the one before you; but there are several conditions which in certain features simulate the disease very closely. Thus coprolalia and the irresistible tendency, on all occasions, even the most solemn, to use obscene words have been described apart from any motor phenomena. There is the oft-quoted case of the Marquis of Dampierre, who, from early youth to his ninetieth year, involuntarily uttered, even under circumstances the most solemn, the words "*merde!*" and "*foutu cochon!*"

Still more common is the existence, particularly in children and youth, of a fixed idea. One of the commonest is the "*délirie de toucher*," which impels the individual to touch certain objects, and of which the great Dr. Johnson, as is well known, was a subject. One of the most graphic accounts, probably autobiographical, of this imperative impulse to touch objects is given by George Borrow in his *Lavengro, the Scholar, the Gypsy, and Priest*, in which the practice was followed in order to prevent evil happening to the lad's mother.

In many points the affection has a close resemblance to the common habit-chorea or habit-spasm, with which indeed the involuntary movement of convulsive tic is identical. I do not remember, however, to have seen at

the Philadelphia Infirmary for Nervous Diseases, among the numerous cases of habit-spasm which came to our clinics, particularly to the clinic of Dr. S. Weir Mitchell, a single instance in which other symptoms developed.

I had one case with facial spasm, in which the lad put his middle finger into his mouth and bit it severely, and at the same time with the index-finger compressed the tip of his nose. This habit had continued for a long time, and had resulted in the production of a thick callosity on both surfaces of the second phalanx of his finger. A somewhat similar trick is reported to have been practised by Hartley Coleridge when a boy, only, if I recollect aright, he was in the habit of biting his arm. And quite recently there was at the clinic a girl nine years old, who, during convalescence from chorea, developed the curious trick of first smelling and then blowing upon anything she took into her hand.

With hysteria the relations of the disease are not thought to be very close by Charcot and his pupils. The affection usually sets in at a period of life earlier than that at which hysterical symptoms begin, and very many of the cases show no manifestations of hysteria. The utterance of loud involuntary cries and anomalous sounds is, however, a special feature of certain cases of hysteria which may thus present a resemblance to this form of convulsive tic. They, however, are not necessarily associated with involuntary movements, and are usually of a more bizarre character. I remember a remarkable case of the kind which was brought into Professor Wagner's clinic at Leipsic. A child, aged about fourteen years, had for several weeks uttered the most remarkable inspiratory cry, followed by a deep-toned expiration, both of which were audible at a great distance. They persisted during the day with each respiration, but ceased during sleep. The child was worn to a skeleton.

Dr. Capen, of Omaha, brought to the hospital last

time past he has not felt as well as usual. On November 1st, while at his supper, in a restaurant, he found that he could not read the daily paper. He was sure that this came on quickly, and had been his chief annoyance, as he was an ardent politician. He had no definite headache, but

year a phonographic cylinder, on which was recorded a most remarkable hysterical cry which the patient, a young girl, had been in the habit of uttering for many months, and which was loud enough to be heard at a distance of several blocks. These cases, however, usually present other features which make the diagnosis clear.

As was the case in this patient, the affection begins at an early period, in the majority of the cases, according to Guinon, from the sixth to the twelfth year. They are commonly regarded as chorea.

An hereditary neuropathic taint has been present in many instances.

We have treated this child in the hospital by seclusion and rest in bed, and have made moral rather than physical efforts to improve her condition. She is certainly better, particularly in the matter of the use of bad words.

Extracted from
The American Journal of the Medical Sciences for March, 1891.

A CASE OF SENSORY APHASIA—WORD BLINDNESS WITH HEMIANOPSIA.

By William Osler, M.D.,
Professor of the Principles and Practice of Medicine, Johns Hopkins University, Baltimore.

This case illustrates the following points: (1) The association of word-blindness with disease in the parieto-temporal region; (2) The paraphasia which so often accompanies this condition; (3) The occurrence of hemianopsia from interruption of the fibres of the optic radiation, without disease of the occipital lobe.

Clinical Summary.—*Inability to read a newspaper the first symptom; typical word-blindness, retention of intelligent hearing; misplacing of words and sentences—paraphasia; right homonymous hemianopsia; no paralysis; persistence of this condition for over two months, with gradual loss of muscular strength and mental power. For thirty-six hours before death, paralysis of right arm and leg.*

Anatomical Summary.—*Necrotic softening in the left hemisphere of the supra-marginal and lower part of angular gyri, of the posterior part of the first and second temporal, and of the two connectant convolutions uniting the first temporal to the parietal lobe. Complete transverse softening of the white matter between these convolutions externally and the lateral ventricle. The gray and white matter of the occipital lobe uninvolved.*

John W., aged seventy-two years, Scotchman, bookkeeper, applied at the Philadelphia Infirmary for Diseases of the Nervous System, November 14, 1888, complaining of uneasy sensations in his head. He was a healthy, vigorous-looking man, perfectly intelligent, and spoke well and clearly. It was not thought at first that there was anything the matter with him, beyond slight headache; but it was noticed that he had occasional difficulty in getting the word he wished, and this circumstance led to a more careful examination. He says he has been a temperate man, and has always enjoyed excellent health. He has not had syphilis. For some time past he has not felt as well as usual. On November 1st, while at his supper, in a restaurant, he found that he could not read the daily paper. He was sure that this came on quickly, and had been his chief annoyance, as he was an ardent politician. He had no definite headache, but

complained of a diffuse, uneasy sensation, and sometimes placed his hand upon his head saying, "It is all wrong here."

Present condition: Vigorous-looking man for his age; face intelligent; speaks clearly and rapidly, with occasional interruptions; no paralysis; movements of the arms, legs, and face perfect; no loss of sensation on either side; no incoördination; he stands well with his eyes shut; reflexes normal.

Speech: Though he speaks clearly and intelligently, and utters some sentences without interruption, replying promptly and fluently to questions, and evidently understanding everything, there is very distinct speech-disturbance; thus, for some time he could not give the address of his residence. He says he knows where it is, but could not pronounce it. He told the first name of the man with whom he lived, but could not say the second. He could not name his own occupation, but said, "Keep, keep, keep. Oh, you say it for me." When told—bookkeeper—he repeated it distinctly. He occasionally misplaces words. In referring to a wetting which he had spoken of, he said, "Deliberate attacks of wet dress." When a printed or written page is presented to him he does not appear to comprehend the words. The word Philadelphia at the head of a hospital blank, he read P, r, i, n, g, r, e, k. When told that it was Philadelphia, he replied, "Oh, certainly it is, I've known it for sixty-five years." His age, 72, written on a slip of paper, he read 213. He did not recognize the words "Cleveland and Harrison" at the top of a newspaper column, but when read to him, said, "I know all about them," and began making some very shrewd observations. He can write his name, but says that since his failure to see he does so with difficulty. He writes as well with his eyes shut as when they are open, but does so with hesitation. He wrote the name of the hospital, and the words "Philadelphia Record." He could not read the words of his name after he had written them. He names objects held before him quite readily.

Dr. de Schweinitz examined the eyes, and reported the presence of right lateral homonymous hemianopsia. Dr. de Schweinitz's report is here annexed:

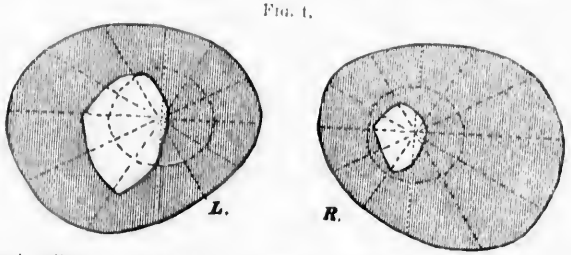
Right eye: An oval optic disk, with the scleral ring plainly followed all round, and both superficial and deep layers very gray; the veins full and dark, the arteries unchanged in size; a fine retinal haze veiled the upper and lower margins of the disk; there were no splotches or hæmorrhages in the general eye-ground, and no changes in the macular region.

Left eye: An oval optic disk, with well-marked scleral ring, more visible than on the opposite side, because the retinal haze seen in the opposite eye was less apparent. A similar appearance of the retinal circulation and an absence of gross changes in the retina and choroid; the disk was also gray, but not so devoid of color and capillarity as that upon the opposite side.

November 21, 1888. Patient was admitted to hospital with no essential change in his condition, though he did not seem to misplace words so often. He could not say his age, 72, but said "60 and 10 above that and 2 above that—that's 72." He knew the day of the week and of the month, and what year it was. He was asked how many years after Burns's death he was born, and said 5000, but at once corrected himself and said "No, no; I do not mean that—twenty-five." The state

of word-blindness persisted. He was given a newspaper, the Philadelphia *Record*, and asked to read its title. He said "Christian Observer." It was difficult to get him to write, and it was impossible for him to do so from dictation for any lengthy sentence. He wrote the word "Record" when told to, but after he had written it he spelled it "Freedom."

FIG. 1.



The oval outline of each figure is the average normal field of vision: the shading represents the blind areas. The asterisk is the fixing-point which is not exactly bisected by the line of division, but this passes a little to the right, although touching the fixing-point. There is decided contraction of the left half of each field, most marked upon the right side; that is, upon the side opposite to the lesion. The fields were taken with a one-centimetre square of white, pasted upon a dead black surface.

For the first two weeks in hospital there was no special change. He seemed to speak with rather fewer errors. He kept very quiet, and did not care to talk with the other patients. When asked how he felt, he generally placed his hand upon his head and repeated several times the phrase "All wrong here."

December 6. For several days he has vomited frequently.

8*th*. The following note was made: "Talks less freely. Speaks intelligently and plainly at first, but after a few minutes it is difficult to understand what he states. No additional ocular changes. The grip in the hands is equal. He walks with a somewhat tottering gait, though there is no actual paralysis."

For the next three weeks the condition remained practically unchanged. Early in January he became distinctly weaker.

On the 4th the following note was made: "Patient has been in bed for several days; no paralysis of motion or of sensation. He seems to understand and usually answers correctly, though, as was frequently noted, he would not give his age correctly, saying any figures. When first spoken to, his speech is clear and distinct, and then in a few minutes becomes very incoherent and mumbling. Lately he has been very noisy and restless at night, getting out of bed and walking about the ward."

On the 12th the note was: "Remains in the same condition; no fever; no paralysis; talks without difficulty; answers some questions correctly, others in a senseless manner. Says continually 'Lord, have mercy.' No disturbance of sensation."

On the 15th the note was: "Has been very wakeful for the past two days. This morning could not be roused. He lies with his head turned to the left, but sometimes moves it to the right. No conjugate deviation of the eyes. Pupils equal and of medium size; react feebly to light. Muscles of the right side of face seem to act as well as those on the left.

There is complete paralysis of the right arm, which has come on within the last twenty-four hours. He moves the right leg, but when lifted it falls more rapidly and with more dead weight than the other. He is in a semi-comatose condition. There are loud bronchial râles." He sank and died on the afternoon of the 16th.

Post-mortem, five hours after death: Body moderately well-nourished; no rigor mortis; calvaria thick and symmetrical.

Dura was normal and very closely adherent to the skull; sinuses contained recent blood-clots; a moderate amount of fluid escaped on removal of the brain. At the base the membranes were normal. The carotids were stiff and atheromatous; vertebral and basilar arteries in the same state. Nerves at the base normal.

Cortex: Pia moderately injected; the posterior part of the left hemisphere looked fuller and the convolutions were paler than on the right side. This was particularly marked on the parietal and temporal lobes, portions of which look softened. More accurately determined by sight and touch, the superficial soft areas were as follows:

1. The entire supra-marginal and the lower part of the angular gyri.

2. The posterior part of the first and second temporal gyri, which bulge distinctly, and the veins of which are much distended.

3. The two annectant convolutions joining the first temporal gyrus and the parietal convolutions, only evident after separation of the fissure of Sylvius.

Though these parts were softened and contrasted by touch, in a marked manner, with the rest of the brain, superficially they did not look very different, and were only a little paler in color.

The cortical arteries were stiff, and when slit open were found free to the finer ramifications. They presented occasional flakes of atheroma and recent soft blood-clots, but no thrombi. The posterior cerebrals presented several atheromatous patches. The branches passing to the cuneus were free. The lateral ventricle was not distended on the left side. The caudate nuclei and thalami looked normal. On the outer wall of the left ventricle, just at the point of divergence of the descending and posterior cornua, there was a grayish-white swelling, presenting congested bloodvessels here and there, and which looked like a region of thrombotic necrosis; behind, it extended into the posterior horn, anteriorly it did not reach the pulvinar. The ependyma of the posterior horn was soft, but the deeper white matter of the lingual gyrus and of the convolution at the junction of the parieto-occipital and calcarine fissures was not involved to any depth.

The organ was injected with and hardened in Müller's fluid, and then horizontal sections were made.

Section 1, half an inch above the corpus callosum.

The white matter of the centrum ovale on the left side presented a slight reddish-brown color in the fibres of the parietal lobe.

Section 2, at level of the corpus callosum.

An area of softening in the posterior-external part of the centrum ovale of about four centimetres in antero-posterior extent. Externally, this section passed through the angular gyrus, the gray matter of which was firm, but the white matter was uniformly softened.

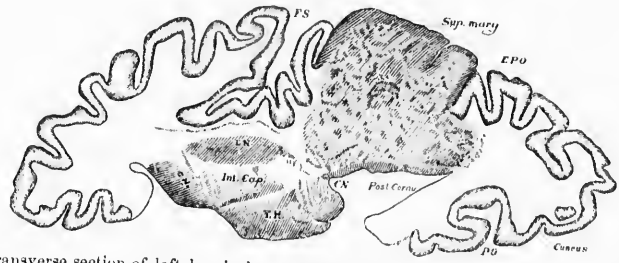
Section 3, at the level of the middle of the basal ganglia.

The softening occupied a large area between the posterior horn and

the middle of the outer aspect of the hemisphere, involving the entire white matter of this region (see figure). Anteriorly it reached to the posterior part of the internal capsule, which appeared somewhat softened but not changed in color. Posteriorly, the softening did not extend behind a line drawn across the level of the parieto-occipital fissure. The white matter of the occipital lobe was firm, and the gray matter of the cuneus was uninvolved.

Section 4, passing through the outer third of the left crus.

FIG. 2.



Transverse section of left hemisphere passing through supra-marginal convolution, showing the area of softening. F. S., fissure of Sylvius; L. N., lenticular nucleus; C. N, caudate nucleus; C. N., tail of caudate nucleus: Int. Cap., internal capsule; T. H., optic thalamus; P. O., parieto-occipital fissure; E. P. O., an external parieto-occipital fissure (?); Sup. Marg., supra-marginal gyrus.

The softening is more extensive. It reached nearly seven centimetres in the antero-posterior direction, extending anteriorly, and just involving the fibres behind the end of the lenticular nucleus and the tail of the caudate nucleus, where it passed into the descending cornu. Posteriorly, the white fibres of the occipital lobe were not involved. Internally, the softening reached to the ependyma of the posterior horn, which was dark in color. Externally, it touched, but did not involve the gray matter of the convolutions.

The internal capsule, the lenticular nucleus, the thalamus, and the crus seemed normal.

Section 5, at the level of the upper margin of the uncinate convolution.

Large area of softening, two inches in thickness and one in breadth, in the temporo-sphenoidal lobe, reaching to within two inches of its apex. Externally, it touched the gray matter of the third and the base of the second temporal gyri.

The corresponding sections of the other hemisphere were normal. The softened area has a grayish-yellow appearance, interspersed with patches of extravasation. It appeared to be ordinary necrotic change. The vessels were carefully withdrawn; no miliary aneurisms were found, but many of the smaller ones were blocked with thrombi. At the lower part of the temporo-sphenoidal lobe the margin of softened area was unusually firm. The branches of the posterior cerebral artery were free.

The drawing was made from a section which passed through the lower portion of the supra-marginal gyrus, at half an inch from the termina-

tion of the Sylvian fissure. The softening here was more superficial than at any other point, and seemed to involve the gray matter. In the posterior part of the first and second temporal the softening reached to the gray matter, but did not enter it. In the section from which the drawing was taken a deep fissure is seen, which crossed the hemisphere, and seemed to separate the parietal and occipital lobes. The angular gyrus lies at a higher level than shown in the section; the white matter of it was softened, but the gray looked very natural. The drawing is an exact representation of the specimen, made by placing tracing-paper upon the section.

RUDOLF VIRCHOW: THE MAN AND THE STUDENT.[1]

BY WILLIAM OSLER, M.D.,
Physician and Professor of Medicine in the Johns Hopkins University.

By his commission the physician is sent to the sick, and knowing in his calling neither Jew nor Gentile, bond or free, perhaps he alone rises superior to those differences which separate and make us dwell apart, too often oblivious to the common hopes and common frailties which should bind us together as a race. In his professional relations, though divided by national lines, there remains the feeling that he belongs to a Guild which owes no local allegiance, which has neither king nor country, but whose work is in the world. The Æsculapian temple has given place to the hospital, and the priestly character of the physician has vanished with the ages; still there is left with us a strong feeling of brotherhood, a sense of unity, which the limitations of language, race, and country have not been able to efface. So it has seemed meet and right to gather here this evening to do honor to a man — not of this country, not of our blood — whose life has been spent in the highest interests of humanity, whose special work has revolutionized the science of medicine, whose genius has shed lustre upon our craft.

The century now drawing to a close has seen the realization of much that the wise of old longed for, much of which the earnest spirits of the past had dreamt. It has been a century of release — a time of the loosening of bands and bonds; and medicine, too, after a long enslavement, ecclesiastical and philosophical, received its emancipation. Forsaking the

[1] Remarks made at the Virchow celebration, Johns Hopkins University, Baltimore, October 13, 1891.

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traditions of the elders, and scouting the Shibboleth of schools and sects, she has at last put off the garments of her pride, and with the reed of humility in her hand sits at the feet of her mistress, the new science. Not to any one man can this revolution be ascribed: the *Zeit-geist* was potent, and like a leaven worked even in unwilling minds; but no physician of our time has done more to promote the change, or by his individual efforts to win his generation to accept it, than Rudolf Virchow.

And now, as the shadows lengthen, and ere the twilight deepens, it has seemed right to his many pupils and friends, the world over, to show their love by a gathering in his honor, on this his seventieth birthday. To-day, in Berlin, a *Fest* has been held, in which several hundred members of the profession in this and other countries have been participants, as subscribers to the fund which was organized for the occasion. It seemed well, also, to his pupils who are teachers in this university, and to others, that the event should be marked by a reunion at which we could tell over the story of his life, rejoice in his career, and express the gratitude which we on this side of the Atlantic feel to the great German physician.

Let me first lay before you a brief outline of his life:

Rudolf Virchow was born October 13, 1821, at Schivelbein, a small town in Pomerania. Details of his family and of his childhood, which would be so interesting to us, are not available. Educated at the Gymnasium in Berlin, he left it at Easter, 1839, to begin his medical studies, and graduated from the University of that City in 1843. The following year he became assistant in pathological anatomy to Froriep; and in 1846 he was made prosector, and in 1847 a lecturer at the university. In 1849, on account of his active participation in the political events of the previous

year he was dismissed from his university positions, and, as he mentions was only *mit grossen beschränkungen* reinstated, largely in fact by the efforts of the profession of Berlin, and particularly of the medical societies. In August, 1849, he received a call to the chair of pathological anatomy at Würzburg, a position which he held until 1856, when, by the unanimous vote of the faculty, he was recommended for, and received the appointment which he still holds, namely, professor of pathological anatomy at Berlin. Prior to leaving Berlin he founded, in 1847, his celebrated *Archiv*, which now in its one hundred and twenty-eighth volume, is the greatest storehouse of facts in scientific medicine possessed by us to-day.

Externally, at least, an uneventful, quiet, peaceable life with few changes.

As an illustration of the successful pursuit of various callings, Virchow's career is without parallel in our profession, and this many-sidedness adds greatly to the interest of his life. Dr. Welch will speak of his special labors in the science of pathology; and other aspects will be considered by Dr. Chew and Dr. Friedenwald. I propose to indicate briefly a few traits in his life as a man of science and as a citizen.

From the days of the great Stageirite, who, if he never practised medicine, was at least an asclepiad and an anatomist, the intimate relation of medicine with science, has in no way been better shown than in the long array of physicians who have become distinguished in biological studies. Until the gradual differentiation of subjects, necessitated by the rapid growth of knowledge, the physician, as a matter of course, was a naturalist; and in the present era, from Galen to Huxley, the brightest minds of the profession in all countries, have turned towards science as a recreation or as a pursuit. Alas! that in the present

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generation, with its strong bent toward specialism, this combination seems more and more impossible. We miss now the quickening spirit and the wiser insight that come with work in a wide field; and in the great cities of this country we look in vain among practising physicians for the successors of Jacob Bigelow of Boston, Holmes of Montreal, Barton of Philadelphia, and others — men who maintained in this matter an honorable tradition, whose names live in natural history societies and academies of natural science, in the founding of which they were mainly instrumental.

In anthropology and archæology the name of Rudolf Virchow is almost as well known as it is in medicine. Very early in his work we find evidences of this bent in the memorable studies, now forty years ago, on Cretins and on the development of the skull. Not a year has passed since that time without some notable contribution from him on these subjects; and those of us who know only his professional side may well marvel at the industry of the man whose name is quoted and appears in anthropological memoirs and journals as often as in our technical works. In recognition of his remarkable labors in this department, a special anthropological institute was organized in 1881, on the occasion of the twenty-fifth year of his professoriate. In 1884, on returning to Berlin for the first time since my student days, I took with me four choice examples of skulls of British Columbian Indians, knowing well how acceptable they would be. In his room at the Pathological Institute, surrounded by crania and skeletons, and directing his celebrated *diener*, who was mending Trojan pottery, I found the professor noting the peculiarities of a set of bones which he had just received from Madeira. Not the warm thanks, nor the cheerful, friendly greeting which he always had

for an old student, pleased me half so much as the prompt and decisive identification of the skulls which I had brought, and his rapid sketch of the cranial characters of the North American Indian. The profound expert, not the dilettanté student, has characterized all of his work in this line. Even an enumeration with a brief report of his published writings in anthropological and archæological subjects would take more time than has been allotted to me. Of his relations with Schliemann I must say something, which I could not do so well as in the words used by his friend, Dr. Jacobi, ten years ago: "Schliemann, by whose modern witchcraft holy old Troy is just leaving its tomb, invited Virchow to aid him in his work of discovery of the buried city. He went — partly to aid, partly, as he says, to escape from overwhelming labors at home — only to be engrossed in just as hard work, though of a different nature. In regard to the latter, Schliemann's recent book on 'Ilios' contains some very interesting material. But what has engaged my attention and interest most has been to observe the humanity and indefatigability displayed by the great man in the service of the poor and sick. To read of his constant, practical exertions in behalf of the miserable population of Hissarlik; how he taught the aborigines the efficacy of chamomile and juniper, which grow about them, unnoticed and unused, in rare abundance; how a spring he laid open for archæological purposes has been called by them 'the physician's' and is believed to have beneficial effects; how he was, on leaving the neighborhood, loaded with flowers, the only thing they had and knew would please him, has charmed me intensely. To admire a great man for his professional labors, eagerly undertaken and successfully carried out, is a great satisfaction to the scientific observer; to be able to love him, in addi-

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tion, for his philanthropy and warm-heartedness, is a feast of the soul."

Virchow's life-work has been the study of the processes of disease, and in the profession we revere him as the greatest master that has appeared among us since John Hunter. There is another aspect of his work which has been memorable for good to his native city. From the day when, as a young man of twenty-seven, he was sent by the Prussian government to Upper Silesia to study the typhus epidemic, then raging among the half-starved population, he has been one of the most powerful advocates in Germany for sanitary reform; and it is not too much to say that it is largely to his efforts that the city of Berlin owes its magnificent system of drainage. His work in this department has been simply monumental, and characterized by the thoroughness which marks the specialist.

To his exhaustive monographs on camp-diseases, cholera, military medicine, and other cognate subjects, I cannot even refer.

It will be generally acknowledged that in this country doctors are, as a rule, bad citizens, taking little or no interest in civic, state or national politics. Let me detain you a moment or two longer to tell of one of us, at least, who, in the midst of absorbing pursuits, has found time to serve his city and his country. For more than twenty years Virchow has sat in the Berlin City Council as an alderman, and to no feature in his extraordinary life does the Berliner point with more justifiable pride. It is a combination of qualities only too rare, when the learned professor can leave his laboratory and take his share in practical, municipal work. How much his colleagues have appreciated his efforts has been shown by his election as Vice-president of the Board; and on the occasion of the celebration in 1881, the *Rathhaus* was not only

placed at the disposal of the committee, but the expenses of the decorations, etc., were met by the council; and to-day comes word by cable that he has been presented with the freedom of the city.

The years succeeding to Virchow's student days were full of strong political feeling, and with the French Revolution, in 1848, came a general awakening. In Germany the struggle for representative government attracted many of the ardent spirits of our profession, and it was then that Virchow began his political career. The revolution was a failure, and brought nothing to the young prosector but dismissal from his public positions. His participation might have been condoned had he not issued a medico-political journal, *Die Medicinische Reform*, the numbers of which are even now very interesting reading, and contain ideas which to-day would be called liberal, but were then revolutionary. It is a striking evidence of the deep impression which even at that time Virchow had made upon his colleagues and the profession, that he was reinstated in his office at the urgent solicitation of the medical societies of the city. He relates in his "*Gedächtnissrede auf Schönlein*," who was the Court physician and not at all in harmony with the views of his prosector, that on one occasion in 1848, at a post-mortem, in which the diagnosis of hæmorrhage into the brain had been made by the professor, Virchow demonstrated an obstructing embolus in the artery. Schönlein turned to him in a half-vexed, half-joking manner and said, "Sie sehen auch ueberall Barrikaden." His active political life dates from 1862, when he was elected to the lower house from one of the Berlin districts, and has, I believe, sat as member almost continuously from that date. The conditions in Germany have not been favorable to a man of advanced liberal views, and Virchow has been attached

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to a party which has not been conspiciously successful; but he has been an honest and industrious worker, a supporter of all measures for the relief of the people, a strenuous opponent of all class and repressive legislation, and above all an implacable enemy of absolutism as personified in Bismarck. A man of such strong individuality would make his presence felt in any assembly; and he always commanded the attention of his colleagues, and oftentimes his speeches have been reported fully both in England and in America.

As an illustration of his capacity for varied work, I recall one day in 1884, in which he gave the morning demonstration and lecture at the Pathological Institute, addressed the Town Council at great length on the extension of the canalization scheme, and made a Budget speech in the House, both of which were reported at great length in the papers of the next day.

Naturally, amid such diverse occupations, it has been impossible for him to enter with his old vigor into the minutiæ of pathological anatomy, and his attitude of late years has been critical rather than productive; but his interest in all that pertains to our profession is unabated, and is a feature of his character to which I must allude. Too often with us, in our gatherings and society meetings, the "men of rathe and riper years" are conspicuous by their absence. In this respect our great master has set a notable example. Amid cares and worries, social and political, with a thousand and one ties and duties, he has never held aloof from his brethren; but as the weekly medical journals testify, no man in Berlin has been more active, and for years he has held the Presidency of the Berliner Medicinische Gesellschaft, one of the most important medical societies of Europe.

Surely the contemplation of a life so noble in its aims, so notable in its achievements, so varied in

its pursuits, may well fill us with admiration for the man and with pride that he is a member of our profession. The influence of his work has been deep and far-reaching, and in one way or another has been felt by each one of us. It is well to acknowled[illegible] debt which we every-day practitioners owe to the great leaders and workers in the scientific branches of our art. We dwell too much in corners, and, consumed with the petty cares of a bread-and-butter struggle, forget that outside our routine lie Elysian fields into which we may never have wandered, the tillage of which is not done by our hands, but the fruits of which we of the profession (and you of the public) fully and freely enjoy. The lesson which should sink deepest into our hearts is the answer which a life, such as Virchow's, gives to those who to-day, as in past generations, see only pills and potions in the profession of medicine, and who, utilizing the gains of science, fail to appreciate the dignity and the worth of the methods by which they are attained. As Pausanias pestered Empedocles, even to the end, for the details of the cure of Pantheia, so there are with us still those who, "asking not wisdom, but drugs to charm with," are impatient at the slow progress of science, forgetting that the chaos from which order is now appearing has been in great part dispelled by the work of one still living — by the man whom to-night we delight to honor.

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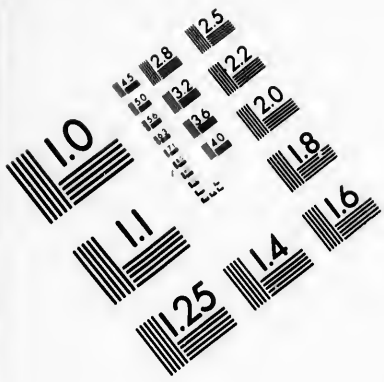

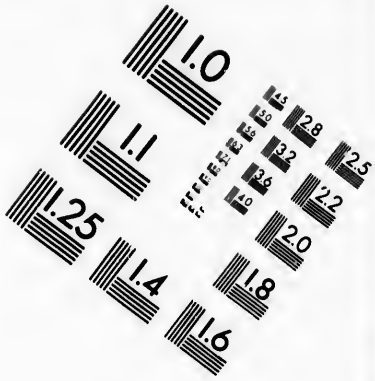

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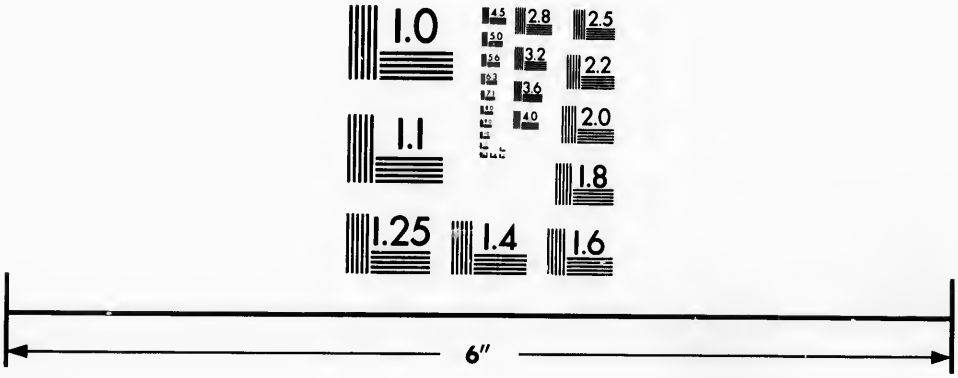

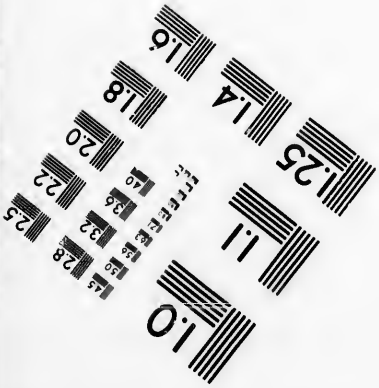

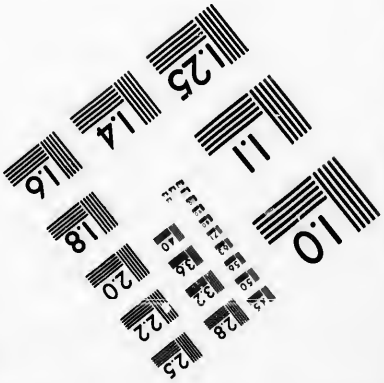

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DOCTOR AND NURSE

Remarks to the First Class of Graduates from the Training School for Nurses of the Johns Hopkins Hospital

By WILLIAM OSLER, M. D.

Physician-in-Chief to the Hospital

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DOCTOR AND NURSE.

REMARKS TO THE FIRST CLASS OF GRADUATES FROM THE TRAINING SCHOOL FOR NURSES OF THE JOHNS HOPKINS HOSPITAL.

BY

WILLIAM OSLER, M. D.,

Physician-in-Chief to the Hospital.

Mr. President, Members of the Board of Trustees, Members of the Graduating Class—Ladies and Gentlemen:—

There are individuals—doctors and nurses, for example—whose very existence is a constant reminder of our frailties; and considering the notoriously irritating character of such people, I often wonder that the world deals so gently with them. The parson never arouses these feelings—no matter what may be his views on celestial geography, his cloth and tie speak of dim possibilities, not of the grim realities conjured up by the names of the persons just mentioned. The lawyer never worries us—in this way. We can imagine in the future a social condition in which neither divinity nor law shall

have a place—when all shall be Friends and each one a Priest, when the Meek shall possess the earth; but we cannot picture a time when Birth and Life and Death shall be separated from the grizzly troop, which we dread so much, and which is ever associated in our minds with "physician and nurse."

Dread! Yes, but mercifully for us in a vague and misty way. In the shadows cast by the turrets of the temple of oblivion, towards which we travel, we play, like schoolboys, regardless of what awaits us in the vale of years beneath. Suffering and disease are ever before us, but life is very pleasant; and the motto of the world, when well, is "forward with the dance." Fondly imagining that we are in a Happy Valley, we deal with ourselves as the King did with Gautama, and hide away everything that suggests our fate. Perhaps we are wise. Who knows? Mercifully, the tragedy of life though seen is not realized. It is so close that we lose all sense of its proportions. And better so; for, as a great philosopher has said, "if we had a keen vision and feeling of all ordinary human life, it would be like hearing the grass grow, or the squirrel's heart beat, and we should die of that roar which lies on the other side of silence."

With many, however, it is a wilful blindness, a sort of fool's paradise, not destroyed by a thought, but by the stern exigencies of life, when the "min-

isters of human fate" drag us, or—worse still—those near and dear to us, upon the stage. Then, we become acutely conscious of the great drama of human suffering, and of those inevitable stage accessories—doctor and nurse.

If, Members of the graduating class, the medical profession, composed chiefly of men, has absorbed a larger share of attention and regard, you have, at least, the satisfaction of feeling that yours is the older, and, as older, the more honorable, calling. In one of the lost books of Solomon, a touching picture is given of Eve, then an early grandmother, bending over the little Enoch, and showing Mahala how to soothe his sufferings and to allay his pains. Woman, "the link among the days," and so trained in a bitter school, has, in successive generations, played the part of Mahala to the little Enoch, of Elaine to the wounded Lancelot. It seems a far cry from the plain of Mesopotamia and the lists of Camelot to the Johns Hopkins Hospital, but the spirit which makes this scene possible is the same, tempered through the ages, by the benign influence of Christianity. Many among the ancients had risen to the ideas of forgiveness of enemies, of patience under wrong doing, and even of the brotherhood of man; but the spirit of Love only received its incarnation with the ever memorable reply to the ever memorable question, Who is my neighbor?—a

reply which has changed the attitude of the world. Nowhere in ancient history, sacred or profane, do we find pictures of devoted heroism in woman such as dot the annals of the Catholic Church, or such as can be paralleled in our own century. Tender maternal affection, touching filial piety were there; but the spirit abroad was that of Deborah not Rizpah, of Jael not Dorcas.

In the gradual division of labor, by which civilization has emerged from barbarism, the doctor and the nurse have been evolved, as useful accessories in the incessant warfare in which man is engaged. The battle is ever against him, for the worst foes are in his own household.

Collectively, man, the race, with passions and ambitions, weaknesses and vanities, has made, by barbaric inhumanity, countless thousands mourn; and even to-day, when philosophers would have us believe his thoughts have widened, he is ready as of old to shut the gates of mercy, and to let loose the dogs of war. It was in one of these attacks of race-mania that your profession, until then unsettled and ill-defined, took, under Florence Nightengale—ever blessed be her name—its modern position.

Individually, man, the unit, the microcosm, fast bound in chains of atavism, inheriting not alone feature and form, but legacies of feeble will and strong desires, taints of blood and brain—what

wonder that many, sore let and hindered in running the race, fall by the way, and need a shelter in which to recruit or to die; a hospital, in which there shall be no harsh comments on conduct, but only, so far as is possible, love and peace and rest. Here, we learn to scan gently our brother man, and—chief test of charity in your sex—still gentler sister woman; judging not, asking no questions, but meting out to all alike a hospitality worthy of the *Hôtel Dieu*, and deeming ourselves honored in being allowed to act as its dispensers. Here, too, are daily before our eyes the problems which have ever perplexed the human mind; problems not presented in the dead abstract of books, but in the living concrete of some poor fellow in his last round, fighting a brave fight, but sadly weighted, and going to his account "unhousel'd, disappointed, unaneled, no reckoning made." As we whisper to each other over his bed that the battle is decided and Euthanasia alone remains, have I not heard in reply to that muttered proverb, so often on the lips of the physician, "the fathers have eaten sour grapes," your answer, in clear accents,—the comforting words of the prayer of Stephen?

But our work would be much restricted were it not for man's outside adversary—Nature, the great Moloch, which exacts a frightful tax of human blood, sparing neither young nor old; taking the child from the cradle, the mother from her babe,

and the father from the family. Is it strange that man, unable to dissociate a personal element from such work, has incarnated an evil principle—a devil? If we have now so far outgrown this idea as to hesitate to suggest, in seasons of epidemic peril, that "it is for our sins we suffer,"—when we know the drainage is bad; if we no longer mock the heart prostrate in the grief of loss with the words "whom the Lord loveth he chasteneth"—when we know the milk should have been sterilized—if, I say, we have, in a measure become, emancipated from such teachings, we have not yet risen to a true conception of Nature. Cruel, in the sense of being inexorable, she may be called, but we can no more upbraid her laws than we can those of the state, which are a terror only to evil doers; and so it is with the greater laws of Nature. The pity is that we do not know them all; in our ignorance we err daily, and pay dearly a blood penalty. Fortunately it is now a great and growing function of the medical profession to search out the laws about epidemics, and these outside enemies of man, and to teach to you, the public—dull, stupid pupils you are, too, as a rule—the ways of Nature, that you may walk therein and prosper.

It would be interesting, members of the graduating class, to cast your horoscopes. To do so collectively you would not like; to do so individually—I dare not; but it is safe to predict

certain things of you, as a whole. You will be better women for the life which you have led here. All women are good, naturally; the bad are made so by men. But what I mean by "better women" is that the eyes of your souls have been opened, the range of your sympathies has been widened, and your characters have been moulded by the events in which you have been participators during the past two years.

Practically there should be for each of you a busy, useful, and happy life, more you cannot expect; a greater blessing the world cannot bestow. Busy you shall certainly be, as the demand is great, both in private and public, for women with your training. Useful your lives shall be, as you will care for those who cannot care for themselves, and who need about them, in the day of tribulation, gentle hands and tender hearts. And happy lives shall be yours, because busy and useful; having been initiated into two of the three mysteries of the Great Secret—that happiness lies in the absorption in some vocation which satisfies the soul; that we are here to add what we can *to*, not to get what we can *from*, Life; and the third,—is still a mystery, which you may or may not learn hereafter.

Of the aims of the Founder and Trustees of this Hospital, one has been carried out during the past two years, in which, in the wards and dispensaries, over 33,000 sick received aid; another is accom-

plished to-day in the granting of these diplomas, and we await the completion of these aims in the establishment of the medical school.

Let me congratulate you as the first of the goodly bands which, year by year, shall distribute far and wide the blessings of this Institution.

I may express, Mr. President, on behalf of your medical staff, our gratification at the success of the Training School and our appreciation of the character of the work that has been done—in every respect in keeping with the high standard expected by the profession, the city and the country. I have been a hospital physician long enough to have watched the various steps in the evolution of the trained nurse, and can speak of the value of the great change which has been made. I can assure you, Sir, and the Members of the Board of Trustees, that the sick, for whose welfare you have been, through your deputies, directly responsible, have received at the hands of these, your graduates, every consideration, kindness and attention,—not that perfunctory, routine care which strains the very quality of mercy, but an interested devotion worthy of the spirit which we hope shall always characterize the work of this place.

And let me assure you, members of the graduating class, that although you go away out of our lives and that of the Institution, you still belong to us, and your welfare is our happiness. In

worries and anxieties of mind or of body it will be a privilege and a pleasure to help you.

And finally, remember what we are—useful supernumeraries in the battle, simply stage accessories in the Drama, playing minor, but essential parts at the exits and entrances, or picking up, here and there, a strutter, who may have tripped upon the stage.

You have been much by the dark river—so near to us all—and have seen so many embark, that you now know the old boatman too well to dread him; so

> "When the Angel of the darker Drink
> At last shall find you by the river brink,
> And offering his cup, invite your soul
> Forth to your lips to quaff—you shall not shrink"—

And why should you? Your passport shall be the blessing of Him in whose footsteps you have trodden, unto whose sick you have ministered, and for whose children you have cared.