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SECTION OF MEDICINE.

THOMAS BUZZARD, M.D., President.

A DISCUSSION ON INFLUENZA AS IT AFFECTS THE NERVOUS SYSTEM.

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INFLUENZA presents a greater variety in its symptoms than perhaps any other disease. The symptoms vary greatly not only in different epidemics but in different persons during the same epidemic. So great is the variation in different cases both as regards the grouping of symptoms and as regards their individual intensity that it is difficult to form an accurate conception as to what should be regarded as an ordinary or type case. In one set of cases the respiratory mucous membrane is mainly attacked, and nasal, laryngeal, and bronchial catarrh are the chief manifestations of the disease. In other cases the catarrh affects the gastro-intestinal tract, and a thickly-coated tongue, anorexia, vomiting, and diarrhœa are the main symptoms. Sometimes the heart appears to be predominantly affected, while in other cases nervous symptoms are conspicuous, and may be exclusively present.

A clearer idea of the disease is obtained by arranging and studying these various groups of symptoms than by attempting to frame an artificial type case. At the same time it is to be noted that in nearly every well-marked case of illness produced by the influenza bacilli there is abundant evidence that the nervous system is profoundly affected. Thus during the febrile stage the patient usually suffers from severe pains in the head, back, and limbs; he aches all over, his muscles are tender, often even to gentle pressure, and the skin, too, may be hyperæsthetic. Very often the patient is restless and unable to sleep, and there may be delirium. The subjective feelings of intense misery and depression are also in all probability the result of influenza toxins acting on nerve tissue. Moreover, in the types of influenza where nervous symptoms appear to be in abeyance there are often indications in the modification or the aggravation of symptoms associated with diseases of the viscera that certain parts of the nervous system are also affected by the influenza poison. For example, in some cases of pneumonia, paroxysmal attacks of dyspnœa and excessive delirium, sometimes maniacal in character, may be observed. Then when the main symptoms appear to be cardiac in origin attacks of tachycardia, of bradycardia and of various irregularities in pulse rhythm suggest that the nervous mechanism of the heart is profoundly affected. The cardiac symptoms which may occur in an influenza attack are indeed identical with those observed in diphtheria. Again, the gastro-enteric variety is frequently characterised by the severity of neuralgic pains and of tenderness in various parts of the abdomen; in some cases it is difficult to say whether the mucous membrane is primarily affected or whether the nerves supplying the alimentary canal are at fault. During the period of convalescence too nervous manifestations are very frequent, and, indeed, if we accept the evidence of reported cases, there is scarcely any variety of nervous disorder that may not occur during this period.

Having briefly alluded to the almost constant presence of nervous symptoms in influenza, let us direct our attention to cases in which the nervous system seems to be specially selected for attack by the bacilli and their poisonous products. Such cases may be broadly separated into two groups. In the first group we place nervous diseases which develop during or shortly after the febrile stage, and are sometimes the sole representatives of the effects of the influenza poison; meningitis and hæmorrhagic encephalitis are the best examples of this group. We assume, and indeed have proof, that in these diseases brain tissue is directly attacked by the bacilli. In the second group we place nervous diseases which usually occur after the attack has subsided; neurasthenia and multiple neuritis may be mentioned as good examples. Here we assume that the toxins produced by the bacilli are more dilute, less virulent than in the first group. Sometimes they are sufficiently powerful to initiate degenerative changes in nerve tissue, whereas in other cases they appear to be incapable of setting up definite histological changes, their power being limited to a disturbance of the functions of certain parts of the nervous system.

This division is not strictly accurate, because some of the effects of the diluted poison may be observed during the febrile stage, while inflammatory changes may be set up at a later period; still, from a clinical standpoint, the division is a convenient one.

Group I.—Of nervous symptoms belonging to the first group the most important are those which indicate a morbid condition of the brain. I shall venture to distinguish two types of cases—namely, the comatose type and the delirious type; not that they can always be sharply separated, but because the distinction is useful from a practical point of view.

The Comatose Type.—In a well-marked example a patient, with or without the usual symptoms marking the onset of influenza—namely, prostration, pyrexia, headache, and nasal catarrh—gradually becomes drowsy and apathetic; he answers questions with difficulty, and in a few days becomes comatose. Recovery may occur, but a fatal termination is more common. An examination of the brain in such cases may reveal nothing abnormal, or there may be congestion of its surface, or a purulent meningitis with or without an encephalitis, which is usually hæmorrhagic in character. In cases that recover and in those where no morbid changes are found *post mortem*, we must assume that during life there was a toxæmic condition of the brain, or the presence of definite lesions which were slight and temporary.

Of severer cases, where a meningo-encephalitis is usually found, the following is a good example; the patient was seen by my colleague Dr. Dreschfeld, to whose kindness I am indebted for permission to bring it before your notice.

The patient, a clerk, aged 31, was apparently quite well on Sunday. On Monday morning he went to business as usual but complained of headache, looked ill, and was unable to attend to his duties properly. His master was so struck with his looking ill that he told him to go home, and advised him to take a holiday. He went home, had some tea, and then sat near the fireplace. His landlady noticed that although there was no fire he held his hands out as if trying to warm them. The next day, Tuesday, he stopped in bed, and was unable to eat any breakfast or dinner. On Wednesday he was noticed to be very drowsy. Dr. Mackenzie saw him in the afternoon; his temperature was 102° and his pulse 110. He was drowsy, answered questions very slowly, put out his tongue when asked to do so; did not complain of anything. During the evening he passed his urine and fæces into the bed. On Thursday he was worse. Dr. Dreschfeld saw him in the evening. His temperature then was 105°, his pulse 120; he was unconscious, and unable to swallow any food. His limbs were quite rigid, the right limbs being stiffer than the left ones. Occasional twitchings of the arms and legs were noticed. The skin was dry; the pupils reacted to light. The knee-jerks were present, but the wrist-jerks and elbow-jerks and the superficial reflexes could not be obtained. On Friday afternoon he seemed to rally a little, and opened his eyes when spoken to. His temperature had fallen to 102° and his pulse to 110. On Saturday night Dr. Dreschfeld saw him again. His temperature then was 101°; he could swallow a little; the rigidity was less marked; he could put out his tongue; he tried to speak but could not get out any words. On Sunday morning he was worse, became comatose during the day, and died during the night.

A necropsy was made by Dr. Moore, Pathologist to the Manchester Infirmary, about eight hours after death. The following is an abstract of his report: On removing the calvarium the dura mater appeared tense, the superior longitudinal sinus contained fluid blood; its tributaries were engorged. The other sinuses were also engorged with fluid blood. Separation of the dura from the pia arachnoid was easy except on either side of the median fissure about midway between the anterior and posterior ends; here the two membranes were firmly united by inflammatory exudations. The whole brain was of a bright red colour, with here and there scattered patches of a yellowish white, these appearances being especially prominent over the anterior half of the right hemisphere. All the vessels of the pia arachnoid were greatly engorged; there were also œdema and irregular-scattered patches of yellowish-white fibrino-purulent exudation. The patches of inflammatory exudation were practically confined to the anterior aspects of the right hemisphere. On section of the brain (See Fig. 1) the grey matter had a pinkish appearance, the redness being most marked in the intermediate layers; the nutrient vessels were intensely hyperæmic. The white matter

presented scattered bleeding points and several small irregular patches of hæmorrhage in the anterior half of the right hemisphere. The other parts of the brain had a healthy appearance. There was no excess of fluid in the lateral ventricles. Microscopical appearances (See Fig. 2): The pia arachnoid was increased in thickness owing to con-

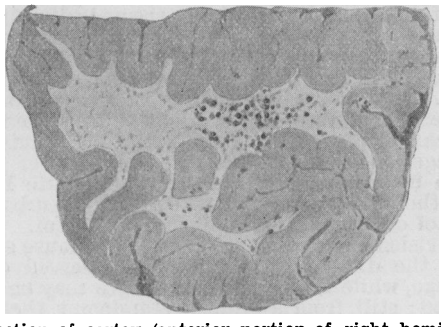

Fig. 1.—Section of cortex (anterior portion of right hemisphere).—Drawn by Dr W. E. Fothergill.

gestion of the vessels and distension of its lymphatic spaces, with inflammatory exudation. The lymphatic and especially the perivascular spaces were distended and occupied by well-marked networks of fibrin, in the meshes of which were leucocytes and many large endothelial cells derived from those covering the walls, which were proliferating rapidly and in places had accumulated in layers of some thickness. The inflammatory exudation was sharply limited to the pia and its cerebral offsets, the brain tissue proper being free. The vessels in the pia were engorged; some showed well-marked proliferative endarteritis which appeared to be of recent origin; some vessels contained thrombi. The same changes were seen in the nutrient vessels of the brain. In many instances hæmor-

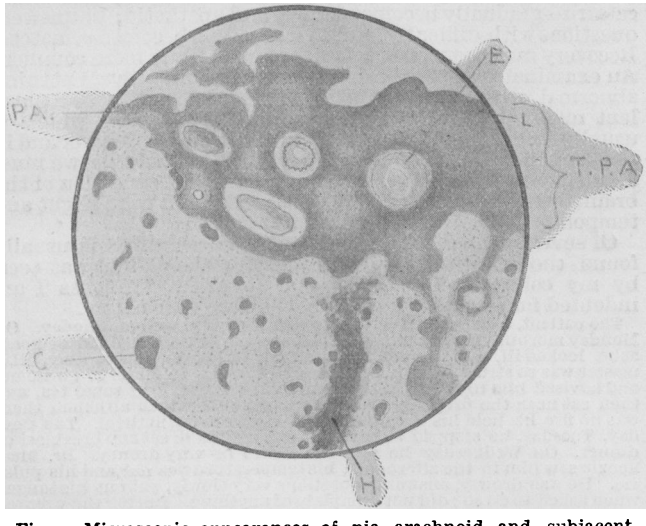

Fig. 2.—Microscopic appearances of pia arachnoid and subjacent tissues. P.A., pia arachnoid; T.P.A., thickened pia arachnoid; E., endarteritis; L., leucocytes and fibrin; C., engorged vessel; H., hæmorrhage.

rhages had occurred into the perivascular sheaths, and in some places had penetrated beyond the sheaths into the adjacent nerve substance. The nerve tissue showed much distension of the pericellular spaces, the nerve cells lying to one side of what appeared to be an empty space. As regards micro-organisms, in sections stained by dilute carbol-fuchsin, a few small bacilli-like bodies were seen in the midst of the exudation in the pia; they were very small; some appeared to be bipolar, and to resemble the influenza bacillus. In sections stained by Loeffler's and Gram's methods a few cocci-like bodies were also noted, and one typical diplococcus was present.

In this case we have a week's illness characterised by headache, pyrexia, and a rapidly-developing coma, symptoms associated with, and apparently dependent on, a meningo-encephalitis hæmorrhagica. The presence of Pfeiffer's bacilli in the diseased tissue was doubtful, but there are reasons for believing that the condition was a variety of influenza. In the first place the patient had been in contact with persons suffering from influenza; in the second place we have an acute illness in a comparatively young man, due to hæmorrhagic meningo-encephalitis and unassociated with any other lesion in any organ in the body. Many similar cases have been recorded, in some of which the influenza bacillus has been found in the meningeal exudation and in the inflammatory brain foci. In this direction the work of Fraenkel, of Nauwerck, and of Pfuhl is especially to be mentioned. Now, without pretending that acute hæmorrhagic encephalitis is pathognomonic of cerebral influenza, I would submit that its presence, in the absence of disease elsewhere, should be regarded as strong presumptive evidence that the fatal illness was due to influenza. Hæmorrhagic encephalitis is admittedly a rare condition; it is stated to occur in the course of some of the specific fevers, especially epidemic cerebro-spinal meningitis and in cases of ulcerative endocarditis. At my request Dr. Kelynack has very kindly made a careful search through the *post-mortem* records of the Manchester Royal Infirmary for the last ten years, but has been unable to find a single reference to any brain change resembling hæmorrhagic encephalitis. In Dr. Dreschfeld's case, apart from muscular rigidity, there were no motor symptoms. The absence of paralysis is explained by the localisation of the lesion to the frontal region of the brain, and perhaps there is a tendency in cerebral influenza for the anterior portion of the cortex to be attacked. It will, however, be readily understood that the symptoms will vary according to the situation of the inflammatory foci, to their number and size, and to the intensity of the process. Thus there may be a hemiplegia or a monoplegia, or a paralysis of one side of the face, or aphasia. I can recall one case of aphasia which came on during an attack of influenza, and was probably due to a patch of meningo-encephalitis in the neighbourhood of Broca's convolution.

The patient, a man, aged 35, was confined to bed with influenza and slight pneumonia; he began to exhibit a curious exaltation of ideas combined with exuberant spirits and self-assertiveness. Then he became aphasic, and had slight paralysis of the right side of the face. After recovering from the attack of influenza it was noticed that in addition to aphasia, the man's mental condition was decidedly altered; there was no gross impairment of the mind, but a subtle change as regards his mental attitude towards things in general. The aphasia as regards inability to give correct names to persons who were well known to him persisted for nearly two years.

Meningitis, as in Dr. Dreschfeld's case, is a frequent accompaniment of encephalitis, but it may exist alone. It is difficult in many cases to say how far some of the symptoms present are due to one or the other condition. The meningitis affects the vertex more frequently than the base, and is usually of the suppurative variety. Many of the reported cases have been in young children who have not presented the usual symptoms of influenza. Thus Fraenkel records three cases:

One, an infant, 10 weeks old, suffered from bronchitis, diarrhœa, and pyrexia, and died of exhaustion at the end of a fortnight. The *post-mortem* examination revealed a suppurative meningitis with much exudation in the subarachnoid space; typical influenza bacilli were cultivated from the pus. The second case was that of an infant, 9 months old, who after suffering for two weeks from bronchitis and digestive disturbances, developed symptoms of meningitis, and died three days later. A thick layer of pus was found between the soft membranes on the vertex and at the base of the brain in the region of the pons and medulla, and also on the posterior aspect of the cord. Here again influenza bacilli were cultivated from the purulent exudation. In the third case, a young child with pneumonia and empyema, suppurative meningitis and foci of hæmorrhagic encephalitis, were found *post mortem*. Typical bacilli were found in the pus and in the diseased portion of brain.

The meningitis may be secondary to a purulent otitis set up by influenza, or to a suppurative condition of the nasal cavities, the specific bacilli being conveyed to the brain either by the blood or by the lymph channels to the subarachnoid space. No doubt in many cases of meningitis there is a mixed infection, staphylococci and streptococci being found as well as influenza bacilli; we may assume that the influenza bacillus first attacks the brain, and paves the way for the entry of virulent streptococci. Our knowledge of the bacteriology of infective meningitis is still very limited, and the practical outcome of cases reported by Fraenkel, Pfuhl, and others is to direct our attention to the possibility of influenza infection as the cause of many apparently obscure cases of suppurative meningitis. A continued study of the results of lumbar puncture will doubtless in the future enable us to make a more accurate diagnosis than is at present possible. Before leaving the subject of meningitis I may mention that Krannhals has shown that a focal hæmorrhagic lepto-meningitis may occur in influenza without any serous or purulent exudation—a condition analogous to hæmorrhagic encephalitis. Kuskow also describes, under the title "hæmorrhagic influenza," cases of simple hæmorrhage into the membranes of the brain—an infiltration of blood into the pia mater without a trace of any inflammatory process. Besides meningitis and encephalitis,

other brain lesions may develop during an attack of influenza —namely, embolism, thrombosis, abscess of the brain, and hæmorrhage independent of encephalitis.

Cerebral abscess usually follows a purulent otitis which is not uncommon in influenza; in a case under my colleague, Dr. Steell, it was secondary to a collection of pus in the ethmoidal sinuses.

The patient, a young man aged 19, had an attack of influenza during and after which he suffered from severe pain in the frontal and occipital regions. His mental condition became very dull, and when admitted into the Manchester Infirmary about a month after the attack of influenza he was in a state of stupor; there was optic neuritis in the right eye but no neuritis in the left eye; the knee jerks were absent; the temperature ranged between normal and 102°; during the last four days of his life it gradually rose to 106°; he became unconscious and died about six weeks from the commencement of the attack. At the necropsy a large abscess was found in the right frontal lobe and a small collection of pus in the upper ethmoidal sinuses on the right side.

Cases have been reported by Bristowe and by Leichtenstern in which no primary focus of infection could be discovered.

The Delirious Type.—In contrast to the drowsiness, somnolence and unconsciousness which characterise what I have called the comatose type, we may meet with cases in which restlessness, irritability, delirium, and even mania are the essential features.

Dr. Dreschfeld has recorded the case of a boy, aged 15 years, who during an attack of influenza suddenly became restless and then maniacal, the temperature rising to 103°. He tossed himself violently about, and could only be restrained with difficulty. Chloral, bromide, morphine, and hyoscyamus had no effect whatever, and the boy died in 24 hours after the onset of the maniacal delirium.

In an unpublished paper read before the Manchester Society Dr. Dreschfeld related some cases that he had seen which seemed to suggest the occurrence of another variety of cerebral influenza. The symptoms were severe pains in the head, mental excitement, and various perversions of consciousness.

In one case, that of a lady who lived in a house where four people were laid up with influenza and one of whom she was nursing, violent headache and lassitude were quickly followed by strangeness in her manner; she was morose and very stupid. She lay curled up in bed with her knees drawn up and her chin on her chest. Then she had an attack of acute delirium and howled with pain and wanted to get out of the window. The next day she was drowsy and not easily roused, and passed urine into the bed. On the following night she had an attack of acute maniacal excitement. In some respects the symptoms resembled those of hysterical mania. After a few days of alternating moroseness and raving delirium she began to recover and quickly regained her usual good health.

In this case there was no elevation of temperature, and the absence of pyrexia was observed by Dr. Dreschfeld in other cases of this type. He believes that the prognosis is good, and certainly better than in the comatose type.

In infants an attack of influenza may be represented solely by pyrexia and convulsions. Very rarely a change in the mental condition precedes the outbreak of influenza. There may be depression and drowsiness or an exaltation and confusion of ideas passing into active delirium. These symptoms, which probably represent a toxæmic condition of brain, sometimes disappear when the actual feverish attack begins.

The Spinal Cord and its Membranes.—I have already mentioned a case recorded by Fraenkel, in which spinal meningitis accompanied the cerebral meningitis. As a rule affections of the cord appear to develop at a varying time after the attack of influenza, but in rare cases spinal symptoms show themselves during the attack and may constitute, as we have seen is the case in cerebral types, its salient features.

Some years ago I saw, in consultation with Dr. Duncan, of Tyldesley, a remarkable case, in which the symptoms suggested an inflammatory condition of the spinal membranes.

The patient, a man aged 34, during an epidemic of influenza was suddenly seized with headache and pains all over the body. When I saw him on the fifth day of his illness he complained of severe pain at the back of the head and along the spine, and of shooting pains along the limbs and round the body. The pain was much increased by movement and by pressure, indeed there seemed to be general hyperæsthesia of both skin and muscles. He was unable to turn his head from side to side, and the back also was rigid, with a slight tendency to opisthotonos. These symptoms were accompanied by pyrexia, the temperature ranging daily from 99 to 102°. After a fortnight's illness he gradually made a good recovery.

Group II. Nervous Sequelæ.—A greater variety of disorders of the nervous system may come after influenza than after any other disease. A study of the literature suggests that a complete list of the nervous sequelæ is most easily made out by enumerating every possible variety of functional, inflammatory, and degenerative diseases that may affect the nervous system. Thus, as regards the brain, we meet with neurasthenia, hysteria, epilepsy, outbursts of delirium, and every variety of psychosis; with meningitis, encephalitis, cerebral hæmorrhage, embolism, and thrombosis of arteries, veins, or sinuses. As regards the cord, almost every variety of myelitis or of degeneration of its various tracts may occur. Foa has recorded a case of disseminated hæmorrhagic myelitis, a condition analogous to that of multiple hæmorrhagic encephalitis. Finally, as regards the nerves, we may have neuralgia or neuritis in the territory of nearly every cerebral or spinal nerve, as well as the different forms of multiple neuritis. Here the occurrence of retrobulbar neuritis should be specially mentioned.

The paralyses which are related to disorders of the bulbar nuclei or of their nerves are of great interest, because they illustrate one of the striking peculiarities of influenza toxins—namely, the erratic way in which they seem to be distributed. Thus, while as in diphtheria there may be paralysis of accommodation associated with paralysis of the palate, there is a greater variety in influenza than in diphtheria as regards the grouping of muscles affected with paralysis. Thus we meet with isolated paralysis of the superior rectus or of the internal or external recti, with transitory dilatation of one pupil, with intermittent paralysis of accommodation, with paralysis of both thirds, or of both fourths, or of both sixths, or of both sevenths, or with paralysis of one side of the tongue. In these cases recovery is, I believe, invariable, hence the symptoms, whether of neuritic or of bulbar origin, must be assigned either to functional disturbances by the influenza toxins or to very slight changes in nerve tissue, inflammatory or degenerative in character.

The subject of post-influenzal nervous disorders is a very large one, and to-day it would be impossible for me to enter it further. Before concluding, however, I should like to briefly mention 5 cases that have come under my own observation, 2 relate to the brain, 2 to the peripheral nerves, and 1 case to the spinal cord.

Of the brain cases, one was that of a young man, aged 21, whom I saw in consultation with Dr. Nolan last June. He had an attack of influenza in February, from which he seemed to recover. Shortly after Easter he had a second attack, and suffered from headache and backache for a fortnight. Then he went to Llandudno, but returned home at the end of a week because he felt so poorly. When he reached home his temperature was 104°. In a day or two he improved, and was able to go out for a walk. On June 7th he became worse, and took to his bed; on June 9th he vomited several times. When I saw him on June 18th he was lying on his back, with his eyes half closed, and in a semi-conscious state. With difficulty he could be roused to answer questions. The optic discs were normal. The knee-jerks were present, though probably of less than normal activity. Beyond the stupor there were no other signs of disease. He rapidly became comatose, and died on the following day.

A necropsy could not be obtained, but I think there can be little doubt that the lesion was a meningitis or a meningo-encephalitis, which in all probability was set up by influenza. The interest of the case is that brain symptoms were not prominent till several weeks after the second attack of influenza.

The other case was one of, or what appeared to be, primary cerebral hæmorrhage following influenza in a lady aged 30, whom I saw several times with Dr. Brown, of Preston, in the year 1891.

The history of the case is briefly as follows: During the last week in May she had an attack presenting the features of influenza. Early in June she was able to go out-of-doors, but felt seedy, was subject to headache, to faints and to cramps, and aching pains in the limbs, and occasionally she had aching pains in the abdomen and slight diarrhœa. On June 12th she was seized with cramp in the right calf. This was followed by swelling of the leg. The condition, which persisted for some time, was thought to be due to venous thrombosis. On June 16th Dr. Brown allowed her to get up, but the leg was very painful. In the afternoon she was pouring out tea when she was suddenly seized with loss of speech, loss of power of swallowing, and great emotional disturbance. She could not put out her tongue; there was no loss of consciousness. She was very emotional during the rest of the day, but partially recovered her speech. I saw her on the 17th, and observed a little weakness of the right side of the face and of the right limbs. The tongue was protruded with difficulty and deviated very slightly to the right side. She spoke very slowly and with great effort, and laughed and said, "How ridiculous." The knee-jerk was present on the left side, but could not be obtained on the right side. During the next two days she complained of numbness in the left arm and in the right thumb and right index finger, also of a tingling sensation round the mouth, which made her feel very uncomfortable after drinking. She was not able to use the right hand quite as well as the left. The pupils and optic discs were normal. There was no vomiting. On June 20th she complained of numbness in the left thumb and forefinger, but no anæsthesia could be detected in any part of the limbs. She complained also of severe frontal headache, and it was noticed that the right pupil was larger than the left. On June 21st she was better, and the pupils were equal in size: in the afternoon she suffered from severe neuralgic

pain in the left side of the frontal region, and in the right arm. On June 25th she had an attack of hiccough and vomited; in the evening she felt giddy and had a frightened look, and was inclined to cry. On June 26th she suffered from nausea and had a sudden attack of pain in the left side of the neck and across the sternum to both clavicles. During the next ten days she suffered much from both frontal and occipital headache, and vomited nearly every day. On two occasions the right pupil became suddenly dilated for a time. There were times, however, when she felt fairly well. On July 10th she was seized with a sharp pain in the left popliteal space, and during the next few days the leg was much swollen. On July 11th she had a sudden pain on the right side of the chest; the next day the temperature was 99° to 100°, and a faint friction sound was heard at the right base. Two days later the chest symptoms were better, and there were no physical signs of pleurisy.

On July 16th she became semi-conscious; the pupils were widely dilated, the right being larger than the left. She was unable to speak or swallow. During the evening the left arm and leg became paralysed. The next day there was complete left hemiplegia; she became comatose and died a few days later.

At the necropsy a large cavity about the size of a walnut, filled with coagulated blood, was found in the white matter of the right hemisphere at the junction of the parietal and occipital lobes. The clot was recent; the walls of the cavity presented numerous hæmorrhagic points, but they were not softened to any extent, although the whole hemisphere was a little softer than the left hemisphere. The hæmorrhage had broken through the grey matter, and a little blood was effused along the superficial vessels in the pia mater. The cavity communicated with the right lateral ventricle which contained, however, only a small quantity of bloodstained fluid in the posterior cornu; there was scarcely any fluid in the left ventricle. A patch of pinkish white softening about the size of a shilling was found in the white matter external to the corpus striatum; all other parts of the brain were healthy. The venous sinuses were free from clot. On a branch of the posterior cerebral artery which ran up in the direction of the cavity there were three small aneurysmal dilatations; the vessel from which the hæmorrhage actually occurred was not discovered.

Time will not permit me to discuss the many interesting phenomena met with in this case, but I would especially draw your attention to the transient dilatation of the right pupil which was observed on three occasions; to the two attacks of venous thrombosis in the leg and to the frequency of emotional disturbance, the features of which made us often think that possibly the case was one of hysteria and nothing more.

The following is a case in which there was fair evidence that the lumbar portion of the spinal cord was involved:

A man aged 39 years, who was under my care at the Manchester Royal Infirmary four years ago, had an attack of influenza which was immediately followed by severe shooting pains down the legs. Then he noticed that his urine began to dribble from him, at first only during sleep, but subsequently during the day time also. There was also slight incontinence of fæces. The legs were weaker than natural, flexion of knees and ankles being weaker than other movements. There was no rigidity and no wasting of muscles; the knee jerks were absent. He had a sensation of numbness down the left leg; there was no distinct anæsthesia, although occasionally in various places he could not always distinguish between the head and the point of a pin. Three months later his knee jerks were still absent; he could hold his water for two or three hours. Soon after this his right knee jerk returned and then his left, and in about five months from the commencement of his illness he was quite well.

In the fourth case the nature of the complaint was not clear, but I was inclined to regard it as a variety of the irritative form of peripheral neuritis.

The patient, a governess, aged 31 years, who was much run down by overwork, had a severe attack of influenza and a few weeks later became subject, especially after exertion, to violent neuralgic pains in the body and limbs and to muscular cramps, which began in the legs and feet and then attacked the thighs and hands. Subsequently she suffered from numbness and tingling in the fingers, which were extremely sensitive to touch. During a severe attack of cramp the hands and feet assumed the attitude seen in tetany. Treatment by rest and massage, followed by a long holiday, resulted ultimately in complete recovery.

The last case that I would mention is one of almost complete paralysis of all four limbs in a girl aged 15 years, who was under my care about two years ago:

The muscles of both arms and legs were moderately wasted; some of the more atrophied ones gave the partial reaction of degeneration to electricity. The knee-jerks were absent; there was no sensory disturbance. After a few weeks' treatment with massage and electricity muscular power slowly returned. When examined one year from the onset of paralysis she appeared to be quite well, and no weakness could be detected in any of the movements of the arms or legs. The knee-jerks were still absent.

The paralysis was immediately preceded by aching pains in the back and limbs. One month after the onset of paralysis she noticed that her sight was affected; she had a difficulty in reading small print. This paresis of accommodation suggested diphtheria as a possible cause of the paralysis, but the most careful inquiries from her friends failed to obtain any evidence of her having suffered from this disease. The evidence as to influenza, it must be admitted, was very slight, consisting merely in the aching pains which ushered in the attack. Our President, Dr. Buzzard, showed a somewhat similar case at a meeting of the Neurological Society some years ago, in which the paralysis followed an illness having the characters of influenza. I have seen several cases of these widespread atrophic paralyses, in which sensory symptoms were insignificant or completely absent, and in which complete recovery suggested that they depended on a multiple neuritis. In one of my cases, complete paralysis of arms and legs was associated with symmetrical gangrene of the feet; the patient died and a microscopical examination proved the existence of a peripheral neuritis and the absence of any change whatever in the spinal cord. In two cases of this type I was unable to get the slightest clue with regard to their etiology. It may be that these and many other forms of paralysis are brought about by the action of organisms at present unknown to us. Hence we must not too readily assume during epidemics of influenza or of other specific diseases that an attack of paralysis unattended by the special features of the existing disease is more likely to be caused by it than by an agent, the usual effects of which are well known to us or by an agent of which at present we are completely ignorant.

II.—Sir W. H. BROADBENT, Bart., LL.D., M.D., F.R.C.P., F.R.S.

Physician Extraordinary to H.M. the Queen; Physician in Ordinary to H.R.H. the Prince of Wales; Consulting Physician to St. Mary's Hospital.

SIR WILLIAM BROADBENT said: I should not have thought of taking part in this discussion had not the President laid his command upon me. The opportunities I have had of seeing influenza have not been such as to permit of continuous observation or of following up the clinical symptoms to *post-mortem* examination, and I have not had time to keep up with the investigations of others. I can only relate some clinical experiences and refer to the speculations which have arisen in my own mind with regard to the way in which the nervous system is affected. It has seemed to me that some of these effects are due to the action of the toxin as, for example, neuritis and neuralgia, or neurasthenia which are common sequels of influenza, just as diphtheritic paralysis has been shown to be the result of the special toxin of this disease. Others appear to be directly due to the microbes, just as in the malignant form of malarial poisoning in which the meningeal capillaries are choked by the malarial parasites. There are, however, cases in which the results seems to be attributable rather to antecedent instability of the nervous system than to anything specific in the action of the influenza poison. I am disposed to explain in this way the cases of insanity which are not uncommon after influenza. Insanity occurs also after typhoid fever and other acute diseases. Such cases have not been frequent in my personal experience, but I have seen one example of acute dementia which followed influenza symptoms and proved fatal.

The comatose form of attack seems to me to be due to the direct action of the microbes. I have seen one case in which the onset of the coma was even more acute than in that related by Dr. Judson Bury. There was an outbreak of influenza on board a training ship near Portsmouth. The accommodation for the sick was limited, and I think was on the lower deck. Two or three hundred boys were attacked in rapid succession, and there was naturally overcrowding. Very shortly several boys—five in all, I think—after exhibiting the usual symptoms of influenza, in the course of a few hours became suddenly comatose, and two were already dead within twenty-four hours of the supervention of coma, and *post-mortem* examination had been made. The cerebral meninges were found to be intensely congested, as were the spleen and kidneys. I was called to Southsea to see the chaplain of the ship. He had been round the vessel in the course of his duty on a given day; he ate his dinner as usual, passed the evening with his family, and went to bed apparently well. At 6 A.M. he woke his wife, saying he was very ill. She went in search of something for him, and on her return found him quite unconscious; and in this condition he remained until I saw him early in the afternoon. The bowels had acted involuntarily, the bladder was full, and required the catheter. There was irregular rigidity of the limbs; the temperature was between 103° and 104° F.

It was thought that the best chance would be afforded to the

patient by subcutaneous injection of quinine, and he had two 10 grain doses of hydrobromate of quinine at an interval of three hours. There was apparent improvement within a few hours, and in the course of a few days consciousness was regained and hopes were entertained that he would recover. The case, however, proved fatal after about a week. In another very recent case syphilis and contracted granular disease of the kidney were present as complications. The patient had been out hunting on the Wednesday, had had a walk on Thursday, and in the evening was seized with symptoms of influenza. On Friday afternoon comatose symptoms set in attended with extreme restlessness. At the same time the urine became loaded with albumen and very shortly paresis of the left facial nerve supervened. I saw the patient in the night between Saturday and Sunday; he was unconscious, moaning loudly, the limbs rigid but in constant movement, the left facial paresis was peripheral and not central. Death occurred on the Sunday afternoon. A remarkable feature was that although there was no paralysis of the lower limbs, patches of herpes and of necrosis of the skin were present round the hips and buttocks, resembing those present in acute paraplegia, from which it was inferred that the lower end of the cord was implicated as well as the brain. In another case there was one-sided convulsion, which was not followed by paralysis, and the patient recovered after a period of sleeplessness and prostration. A very remarkable case of hemiplegia occurred in the first or second year of influenza, in which it seemed to me that thrombosis had taken place in the veins of the right hemispherical cortex while the patient was under treatment for influenza. Paralysis of the right limbs gradually came on in the course of about twenty-four years with stupor and confusion. An interesting point in this case is that although the attack occurred about 10 years ago, improvement is still taking place in the paralysed limbs year by year. There is rigidity, but it is not the rigidity of late hemiplegia, but an active spasm of the muscles that relaxes in some degree during sleep. Dr. Judson Bury asked if the respiratory muscles have been attacked in the multiple neuritis of influenza. I have seen one case in which in the course of a very general sensory neuritis, attended with severe pain and tenderness, death occurred from paralysis of the respiratory muscles.

III.—Sir PETER EADE, M D., F.R.C.P.,

Consulting Physician to the Norfolk and Norwich Hospital.

SIR PETER EADE said: I would first note that influenza is still being discussed by this Association ten years after its latest invasion. This is largely due to its prolonged continuance and to the special study of its nervous phenomena lately given to it. Let us not forget that influenza is primarily a local parasitic disease of the mouth, throat, bronchial tubes, etc., the special nervous symptoms being due to absorption of the toxin secreted by its special germ, Pfeiffer's bacillus. This toxin exerts a selective affinity for different parts of the nervous centres, with a strong tendency to largely affect the medulla oblongata, as specially noted by the late Dr. Althaus and others. In the spinal cord the sensory appear to be more affected than the motor portions, shown by the numerous special painful affections seen in cases of the disease. It is to be remembered that the so-called incubation period of hours or two or three days, is that in which the first portion of this toxin is formed, and that this often takes place before any sensation of illness is felt. The effect upon the nervous tissue unquestionably varies from mere poisonous irritation to actual inflammation, and the seriousness of the effects will vary with this. One of the best proofs of the special involvement of the bulb and the eighth nerve is the marked influence exerted upon the heart, as shown by the marked and often fatal asthenia observed in acute cases; also by the tachycardia and bradycardia seen in connection with the influenzal disease. I would venture here to remark that the noma or sleeping sickness occasionally met with is due to the slow or bradycardiac condition, which adds defective brain circulation to the already impaired nutrition of the nerve matter. A great multitude of varied secondary or tertiary symptoms have, of course, been observed by all in course of practice. There is no time to dwell upon special cases. But we must remember that they are all varying effects of the lesions of the different parts of the nerve centres or nerves—the organs most affected or specially attacked being, as Sir W. Broadbent has just said, those which have some inherent weakness or defect. The treatment of the nervous sequelæ must always be largely guided by our appreciation of general principles and of all-round knowledge of the disease.

IV.—THOMAS CLIFFORD ALLBUTT, M.A., LL.D., M.D., F.R.C.P., F.R.S.

Regius Professor of Physic in the University of Cambridge.

PROFESSOR CLIFFORD ALLBUTT said: The diagnosis of influenza can rarely be precise, and is often very indefinite indeed, so that any guidance to be had in cases of doubt becomes very important. One clinical feature, which may perhaps be called decisive, is the great suddenness, it may even be said the singular suddenness, of onset. Prodromal symptoms are often absent, the attack falling upon the patient all at once. The patient is riding at ease upon the high road, he is travelling between two stations by rail, he is walking briskly across a field, and in a moment is plunged into a state of illness so severe that he may be unable, or able with great difficulty, to move from the spot. As to the aid of bacteriology, it seems to be admitted that the influenza bacillus is very difficult to cultivate, if not indeed to find. I would urge that lumbar puncture should be practised in all cases of cerebro-spinal meningitis, possibly influenzal, and this at an early stage before the organism gets imprisoned, or, what is more likely, is overwhelmed by organisms, pyogenic or other, of mixed infections which are very apt to supervene. From site again, sites of election, some means of diagnosis may be obtained. Dr. Judson Bury is disposed to look upon the frontal cerebral lobes as preferentially attacked. My own experience leads in the same direction, and it is important that the precise lie of the mischief in influenza should be noted in all its nervous manifestations. Sir W. Broadbent's experience seems to have led him to think, on the other hand, that the disease is prone to fall upon parts weakened by some previous and independent causes. In regard to prognosis, I am was unable to give strong assurances of recovery in cases of severe influenza of the nervous system. However tediously, no doubt the large majority of cases end in recovery, but there is unfortunately a substantial remnant in which even recovery of the general health does not bring with it a restoration of the nervous parts permanently damaged by the attack, although some considerable degree of amendment is the rule.

V.—GEORGE NEWTON PITT, M.A., M.D., F.R.C.P.,

Physician to Guy's Hospital, Lecturer on Pathology in Guy's Hospital Medical School.

Dr. NEWTON PITT said: During the earlier years of the epidemic of influenza I saw seven cases of meningitis, which at the time were in each case thought to be part of an attack of influenza. In two there was found to be infection and distension of the frontal sinuses, from which apparently the meninges had been infected. These two may fairly be considered as the result of influenza. With regard to the others, the question is, Were they the result of influenza, or were they due to pneumococcal infection, or were they sporadic cases of cerebro-spinal meningitis? In one case the organism appeared to be pneumococcus, but we were not then cognisant of the diplococcus intracellularis of Weichselbaum. All the cases were fatal, but in several it was not possible to obtain a necropsy. I am not aware whether the organism of influenza has been found in any of the cases of meningitis with influenza. I should think it will most likely be found that in some of those cases in which the nasal sinuses have been inflamed, they have become secondarily infected with streptococci. Many of the cases of meningitis which have been attributed to influenza are not directly due to it; but after an attack of influenza patients are much more liable to take certain diseases against which previously they were immune; such as enterica, and probably in this way they more readily fall victims to the diplococci of Weichselbaum and of Fraenkel, for I believe that either may be the efficient cause of the meningitis.

The intensity of peripheral neuritis arising from influenza varies greatly. The most severe case which I have met with occurred in a powerful man, who was a professional long-distance runner. Some three weeks after the onset of a typical

influenza attack, he found he was becoming progressively weaker, so that he could no longer get about quickly. The weakness continued to increase, and he had marked wasting, with so much weakness of both extremities, that he was only able to shuffle across a room with assistance, while there was foot-drop, the grasp of the hand and the movements of the fingers were extremely feeble. There was great loss of expression in the face, but no facial or ocular paralysis. He complained of defective and abnormal sensation, but there was no complete anæsthesia. The muscles of the extremities showed partial reaction of degeneration. With rest in bed, galvanism applied locally, and strychnine given hypodermically, he gradually made a good recovery, and was able to walk well, but his career as a professor runner was over. In many of the cases of prolonged weakness with wasting which are occasionally met with after influenza, there is sometimes evidence of slight neuritis. There is another group of cases of neuritis in which the toxin has especially affected the facial and the ocular muscles, this has been associated with some peripheral paralysis, which, however, has not been general in the cases I have met with. The paralysis has not presented any characteristic features which would enable the cause to be diagnosed with certainty without a history of influenza. The great cardiac irregularity and failure not infrequently met with after an attack of influenza may be due to affection of the cardiac ganglia and nerves quite as much as to a lesion of the muscle; in a few cases, œdema and water-logging develop, with extreme disturbance of the heart's action. Not infrequently the cardiac disturbance and the profound depression which are met with are due to a marked dilatation of the stomach with decomposition of its contents; and not directly to any nerve lesion; these are most efficiently relieved by treatment directed to the dilated condition of the stomach.

VI.—JOHN M. MACCORMAC, M.D.Durh., L.R.C.P. & S.Ed.,
Physician to the Hospital for Diseases of the Nervous System, Belfast.

DR. MACCORMAC said: It is now ten years ago since my Observations Based on the Clinical Phenomena of Influenza were published in the *Medical Press and Circular*. Influenza at that time was regarded as a lung disease of microbial origin, and this view is still held by many in spite of the fact that we now recognise clinically throat, lung, stomach, intestinal, and it may be liver influenza. I ventured then to state that the morbid conditions were induced by atmospheric conditions rather than by microbial infection, and that the nervous system suffered specially and primarily. My subsequent experience of the disease has convinced me more firmly than ever of the validity of the conclusions drawn by me at that time, and has caused me to believe that influenza is not a distinct and specific disease; in fact, its symptoms are most varied, its origin has remained unproved, its differential diagnosis impossible, its prognosis most difficult, and there is no special treatment. Of course, I do not deny that bacilli may be detected in patients suffering from influenza, but I hold that they are accidental; in fact, it is hardly possible to believe that one definite and specific bacillus can cause such varied symptoms. If there be a specific microbe in the atmosphere so abundant as some would have us believe it is remarkable that it has never been detected in rivers, watercourses, or reservoirs. There is no evidence of infection being carried by water, and if the infection be airborne we might expect the throat and lungs to be always the primary and chief seat of the disease. It appears to me that influenza may cause throat, lung, gastro-intestinal, or skin troubles by a disturbance of the nervous system through atmospheric influences, and I think the most striking feature in influenza is its effect upon the nervous system as evidenced by the numerous and varied symptoms which may be produced, such as delirium, coma, convulsions, and paralysis of various kinds. In support of my views I may advance the following facts: There is no doubt that the disease is much modified by climate; in warm climates most of the cases are accompanied with great nervous prostration and eruptions (similar to that of measles), while in cold climates chest complications prevail. At Gibraltar during a certain time of the year (July, August, etc.) a wind known as the "Levanter" sometimes prevails, which is a moist east wind with heavy cloud over the Rock; and at that time the people, especially the inhabitants (Spanish) suffer from a group of symptoms which are very severe headache and great bodily and mental depression, which come on and pass off rapidly with the advent and departure of the Levanter. The so-called sirocco—a wind which prevails in Malta—is attended, I believe, by a similar group of symptoms. Might not this group of symptoms be dependent upon these east winds?

VII.—FRANK MONTAGUE POPE, B.A., M.B., M.R.C.P.,
Senior Physician to the Leicester Infirmary.

DR. POPE mentioned a case of the comatose type of encephalitis in a boy at an industrial school, and suggested that antecedent injury determined the site of lesion. He had reported a good many cases of nervous affections three or four years after the first epidemic, but on looking over the cases recently he could only find out of a considerable number of different nervous diseases a very few in which influenza was the cause, and he explained it by the hypothesis that in the first epidemic the majority of those whose nervous systems were liable to the infection were affected, and that there were consequently fewer so liable to get similar affections in later epidemics.

VIII.—SARAT K. MULLICK, M.B.,
Assistant-Physician to the Hospital of St. Francis, London.

DR. MULLICK wished to emphasise the fact that there was too great a tendency to accept influenza as the primary cause of the nerve lesions. A little examination would sometimes reveal the fact that there were other causes. He was very cautious in accepting influenza as the starting point of lesions, as there was often a history either of syphilis, alcohol, or rheumatism. He was inclined to believe that many cases which were quoted as influenzal were really due to these causes which had been revivified by influenzal toxins. Influenza generally attacked such a large area that it was difficult to withstand the conclusion that it attacked some specially weak spot in the nervous system, and through it brought about the general symptoms. At one time influenza was thought to be primarily an affection of the pulmonary system, but now the more accepted theory was that the nervous system was first attacked. He did not agree with Sir Peter Eade that influenzal toxins attacked sensory more than the motor areas. It was true that some sensory changes were present, but they were fleeting compared to the permanent changes from motor paralysis. Its effect on the heart was great, he was inclined to believe, through the nerve mechanism, because in many cases the tachycardia, bradycardia, and irregular action of the heart were so rapid in onset that it was difficult to believe that they could have been due to changes in the myocardium pure and simple. He quoted cases of narcolepsy and amaurosis, following influenza, and also referred to cases of locomotor ataxy and diabetes which had been reported as sequelæ. As regards the affections of other special senses, he mentioned cases of anosmia and loss of taste. Cases of aphasia more or less complete were also met with. Lastly he took a favourable view of the question of prognosis, especially in comparison with the disastrous nerve lesions due to other causes.

IX.—S. EDWIN SOLLY, M.D., M.R.C.S.,
Consulting Physician to St. Francis Hospital, Colorado Springs, Colorado, U.S.A.

DR. SOLLY related a case of right-sided hemiplegia occurring in connection with an attack of influenza. The subject was a young lady, aged 25 years, of previous good health and good family history. Investigation revealed no history of any other cause, and examination showed no disease of the heart or other organs. The urine was examined microscopically and chemically, and nothing abnormal found. The blood was also examined without result. The patient was a member of a household all of whom had in turn well-marked but not severe attacks of influenza; she was the last to take it. One morning she was taken with mild fever, nervous depression, pains, and catarrh of the respiratory and intestinal tracts, but did not go to bed. The following morning the hemiplegia appeared, there was motor and sensory paralysis of the right side of the body, facial paralysis and slight aphasia. After thirty-six

hours improvement began, first in the face and speech and then in the hand, and much more gradually in the foot. In twelve days the patient could walk across the room with the use of a stick; at the end of three months all evidence of the paralysis had vanished, except that she complained of a somewhat heavy feeling in the foot and ankle. She could walk two or three miles six months after the seizure, and she still had a slight but lessening sensation of weight in the foot, but otherwise was in good health.

X.—ROBERT SAUNDBY, M.D., LL.D., F.R.C.P.,
Physician to the Birmingham General Hospital; Professor of Medicine in the University of Birmingham.

PROFESSOR SAUNDBY said he could not identify the particular case of post-influenzal diabetes to which Dr. Mullick had referred, but he could say generally that he regarded post-influenzal diabetes as upon the same footing and as produced in the same way as the diabetes which followed other infectious processes such as typhoid, for example. He was a little surprised to hear influenza described by some speakers as a primary disease of the lungs or nervous system; an infectious process might localise itself in different organs and in different cases, a law which was illustrated less commonly in other diseases such as typhoid fever which, while generally localised in the intestine, sometimes assumed the ulmonary type (pneumo-typhus). As to the question which organ was affected in post-influenzal diabetes he had suggested that it was the pancreas, and that the interstitial pancreatitis, which was present in a considerable proportion of cases of diabetes, was due to the action of the toxins of infectious disease, but they did not possess the data to enable them to say that this was always the case; it was possible that in some cases these toxins might attack the nervous system or the liver itself.

XI.—Mrs. ELIZABETH GARRETT ANDERSON, M.D.,
Consulting Physician to the New Hospital for Women; Vice-President of the Section.

MRS. GARRETT ANDERSON said: While admitting fully the large number of morbid conditions of the nervous system caused by influenza, it is probable that many affections are wrongfully or hastily referred to influenza as their cause. Practically not much is gained by accepting a condition as due to influenza. A more important practical point is to consider how the influenza poison can be made less or more powerful. Crowding in its many forms seems to be the condition which more than any other increases the virulence of influenza, and it is in crowded houses, rooms, offices, and asylums that it is found in its worst form. She had seen two cases of diabetes and one of complete loss of taste after influenza.

XII.—JOHN HADDON, M.A., M.D.,
Denholm, Roxburghshire.

DR. HADDON looked upon influenza as a very peculiar infectious disease. Other infectious diseases might be followed by some one serious lesion, but influenza appeared to be followed by any disease. In diphtheria the primary fever lasted 48 hours, and then in 10 days might follow paralysis of various kinds. In influenza also the primary fever lasted 48 hours, but it might be succeeded by various paralyses or mania, pulmonary affections, diabetes, gastric disturbances, etc. The theory that it was through the nervous system that its evil effects were produced he believed to be correct, and that theory alone explained the protean diseases which might follow an attack.

XIII.—WILLIAM EWART, M.D., F.R.C.P.,
Senior Physician to St George's Hospital and to the Belgrave Hospital for Children.

DR. EWART dwelt upon the peculiarity of some forms of system diseases originating after influenza. Whilst the usual progress of sclerosis was slowly ingravescent those attacks evolved quickly, reaching early an intensity which belonged to an advanced stage of the ordinary affection. The later progress in these cases was not towards aggravation but partial recovery, much of the initial paralysis of the higher centres disappearing, whilst the special system symptoms might long persist. In connection with the etiology of the later post-influenzal paralysis, as also of the late post-diphtheria paralysis, he suggested that there might be a chronic influenzal intoxication due to micro-organisms remaining lastingly in possession in the upper aërial tract. In all patients but particularly in those who were subject to repeated attacks and who probably harboured the microbe permanently, sanitation of the nasal cavities was an important indication. As regarded the causation of the cardiac failure so often witnessed he agreed with Dr. Newton Pitt's remarks and had long recognised the evil effect of gastric distension, not in influenza alone but in many other conditions; at the same time, he could not but attribute a large share to the nervous factor as part of the general prostration of the nervous system which was so prominent in this disease.

XIV.—Sir JOHN WILLIAM MOORE, B.A., M.D., F.R.C.P.I.,
Senior Physician to the Meath Hospital and to the County Dublin Infirmary; Professor of Practice of Medicine in the Royal College of Surgeons of Ireland; President of the Royal College of Physicians of Ireland.

SIR JOHN MOORE drew attention to the remarkable mental state which so often appeared in the victims of influenza, and to which, perhaps, many of the supposed nervous lesions of the disease should be attributed. He considered that frequently the supposed nervous lesions were purely subjective—they were psychoses—and he instanced a case in illustration of this opinion. At the same time he had seen very many serious organic nervous affections during or subsequent to influenza. He thoroughly agreed with Dr. Newton Pitt's observation that the influenzal lesions of the heart had reference rather to the innervation of that organ than to changes in the heart muscle. He was also in accordance with Dr. Pitt as to the dangerous influence on the heart's action of a dilated stomach in this disease or in any other infectious process.

XV.—STCLAIR THOMSON, M.D., M.R.C.P., F.R.C.S.,
Physician to the Throat Hospital, Golden Square.

DR. STCLAIR THOMSON limited his remarks to his experience in one department of practice. He fully confirmed Mrs. Garrett Anderson's remarks on loss of smell. Cases of complete anosmia were not uncommon, and from the history and from the absence of local lesions there could be little doubt as to influenza being the causative agent. If such cases did not recover spontaneously in a few months, his experience led him to fear that the anosmia would be permanent. After referring to cases of paræsthesia of the pharynx, Dr. StClair Thomson dwelt on the occurrence of paralysis of the vocal cords. Abductor laryngeal paralysis frequently presented great difficulty as regarded determining the etiology; but a number of cases had been observed in which a paralysis of one cord, lasting sometimes for years, was undoubtedly due to a post-influenzal neuritis. While agreeing as to the frequency of merely subjective symptoms in the results of influenza, his own experience showed him the frequency and reality of objective affections of the throat, nose, and ear, paralysis, anæsthesia, anosmia, sinusitis, otitis, and abscess of the mastoid antrum. Finally, while sympathising with Dr. Ewart's observations on the nose as a channel of infection, he pointed out that we should not be tempted to try to render the nasal fossæ aseptic by the use of any chemical germicide. The healthy nose was automatically aseptic, and a lotion strong enough to be germicidal would only destroy the inhibitory action of nasal mucus, paralyse the ciliary action of the epithelium, and strongly irritate the sensitive Schneiderian membrane. At the same time he quite agreed that purulent, catarrhal, or obstructive affections of the nose should be remedied and the cavities rendered as clean and well-ventilated as possible.

XVI.—WILLIAM CALWELL, M.A., M.D.,
Physician to the Royal Victoria Hospital and to the Throne Consumption Hospital, Belfast.

DR. CALWELL drew attention to the importance of obtaining a history of recent influenza before the administration of anæsthetics, especially of chloroform; there had been large numbers of deaths from chloroform administration, and this was especially the case during influenza epidemics. Very suspicious cases had occurred, which were clearly explained by the depressed condition of the nervous system and of the

heart. As a practical matter it was important, and would perhaps cause postponement in operating in those cases where urgency was not an object.

XVII.—THOMAS BUZZARD, M.D., F.R.C.P.,

Physician to the National Hospital for the Paralysed and Epileptic; President of the Section.

DR. BUZZARD thought that the warmest thanks of the Section were due to Dr. Judson Bury for the admirable and lucid address which he had read. He felt, like others, the extreme difficulty of dealing in a very limited time with the interesting and important subject of discussion. His experience in regard to numerous points so nearly resembled that of Dr. Bury and others that it was quite unnecessary to repeat what had been already so well described by others. He thought, with Sir William Broadbent, that there was strong evidence to show that an attack of influenza was prone, by its depressing effect, to reveal previously existing flaws in the physiological condition of patients. As an illustration of this he mentioned a case of tabes of some years' duration, where the patient, who had so much improved as to find no difficulty at all in the use of his legs, was suddenly rendered completely ataxic by an attack of influenza. Similarly, patients with an inherited proclivity to mental disorder were apt to become maniacal or melancholic in the sequel of this disease. It was doubtless open to any one to believe that in every case in which organic disease of the nervous system succeeded influenza it was not a question of direct cause and effect, but merely an illustration of previously existing lesion being as it were displayed under the depressing influence of the attack. His own opinion was that, although this might account for a certain proportion of the nerve disease observed in the sequel of influenza, it by no means held good for the large majority of cases. The immediate incidence of an attack of influenza was distinctly upon the nervous system, and it was impossible to believe that the pain in the back, and bones, the aching head, and eyeballs, which would characterise the attack of a large number of persons simultaneously in a community did not represent the effect of a toxin upon previously healthy structures. And if this, as he thought, was certain, he failed to see any difficulty in equally ascribing the later disease, which not infrequently occurred, to the direct effects of a toxin.

There was another circumstance, too, to which no reference had been made by previous speakers, which he thought bore very strong evidence as to the grave and numerous diseases of the nervous system being a direct outcome of the toxæmia called influenza. In the early days of the study of syphilitic affections of the nervous system when writing upon the subject he had called attention (as Dr. Hughlings Jackson had done before him) to the not infrequent bizarre character of the symptom-complex in those diseases. There might be, for example, paralysis of an oculo-motor nerve alongside of paraplegia, paralysis of one arm perhaps with a like affection of the opposite leg or of both, and so on, pointing to the existence of multiple lesions—a condition which contrasted strongly with the usual picture presented by disease which was not directly of toxic character—and so in more recent times it had been found by Medin, of Stockholm, in Kentucky also, and by Dr. Pasteur in England, that in epidemics of so-called infantile paralysis, whilst the brunt of the attack might fall perhaps on the anterior horns of the cord, there would in many cases be concomitant affection of other parts of the cerebro-spinal axis—localised paralysis of a cranial nerve, lesion of the lateral columns, symptoms of encephalitis—indications, indeed, of an intense and narrowly-localised lesion in various parts of the nervous system. In many cases he had been struck with a similar bizarre distribution of symptoms in disease of the nervous system connected with influenza, and he could not help thinking that this peculiar character, in the circumstances, gave a very strong support to the view that the grave lesions observed in influenza, like those in syphilis and in epidemics of infantile paralysis, were dependent upon the direct effect of a toxin on healthy nervous structure.

He adduced a case, at present under his care in hospital, which well illustrated this. It was that of a previously healthy man who, immediately upon an attack of influenza in May, 1898, became affected with double optic neuritis, resulting in complete optic atrophy, later nystagmus, paralysis of the four extremities of the kind usually ascribed to multiple neuritis, along with marked intention tremor of the upper extremities pointing to lesion of the lateral columns, and absent jerks.

In another the patient, a man, aged 46, suffered only from a slight attack of influenza, but three weeks afterwards began to have sharp pains in the calves with numbness of the feet. This was followed by a gradually progressive paralysis, slowly invading almost all parts of the body, so that about fourteen months after his attack there was complete inability to move any limb, almost complete paralysis of the diaphragm, intercostals and muscles of the back, and for several days death appeared imminent. But improvement then began, and slowly and uninterruptedly a recession of symptoms took place, so that at the end of six years he was able to resume his occupation.

This was a case widely differing in its character and progress from an ordinary example of multiple neuritis. Another was equally remarkable. A young man of previous good health, influenza having been rife in the neighbourhood, suffered from intense headache, pain in the eyes, neck, and loins, with sharp darting pains in the extremities, a temperature of 101°, and pulse of only 76. In three days the acute symptoms subsided, but a day later a relapse took place, and he began to present a characteristic appearance of extensive multiple neuritis, involving also an oculo-motor nerve, with much articulatory difficulty, great sensory disturbance, and reduced electrical excitability. After a few days improvement occurred in these symptoms, and then, as Dr. Turner of York reported in an admirable account of the case: "A month from the beginning of the illness a curious change was taking place. The impaired sensation and motion continued, but in a less degree; the reflexes, instead of being almost absent, were now exaggerated, and his gait was that of spastic paralysis." Six months later, when he came under Dr. Buzzard's observation, he presented symptoms of spastic paraplegia, with ankle clonus, and at the same time some sensory disturbance and lowered faradic excitability, a strikingly anomalous combination of symptoms.

The earliest and perhaps the most remarkable case which he had seen was in January, 1890, at Margate, in consultation with Mr. Knight Treves, and this was one which could not be classed in any recognised category. The patient, a gentleman aged 65, presented to a remarkable extent the appearance of one in the algide stage of Asiatic cholera, with shrunken and blue hands covered with cold sweat, whispering voice, and vomiting. He was conscious, and perfectly calm. There was no pulse at the wrist, and it was very difficult to be sure that the sounds of the heart were heard with the stethoscope. He had no cramps or diarrhœa, but had been suffering for a few days previously with horrible pains in the chest wall, and there had been elevation of temperature. Death took place in a few days. In view of the symptoms, which pointed to bulbar lesion, Dr. Buzzard procured a microscopical examination of the medulla oblongata, and Dr. Colman, who kindly made this, found in the floor of the fourth ventricle marked changes in the vessels and in the ground substance of the grey matter with pigmentation of the vagal and hypoglossal nuclei.

He instanced also the case of a schoolboy who in May, 1890, felt giddy one evening and went to bed (there had been several cases of influenza just previously). Next day there was bad headache, and a temperature of 101°; two days later intense pain in cervico-dorsal region and also in the sciatic region, right side, with loss of power in the right arm and leg. The lad shrieked with the pain in the spine when lifted in bed. The symptoms of the attack appeared to point to one of spinal meningo-myelitis, with probably some multiple neuritis, and the patient had been left with dreadful deformity from permanent paralysis of the intercostal and some abdominal muscles, serrati, and rhomboids.

It appeared to Dr. Buzzard that ten years' experience of this widespread toxæmia made it necessary either to largely increase the nomenclature of disease of the nervous system, or (which he thought was better) to refrain as much as possible from the use of the existing terminology. Do what we could we were unable to cramp and confine examples of the grave nervous disorders of influenza in such narrow cabins as "encephalitis," "neuritis," "myelitis," "polio-myelitis," "meningitis," "Landry's paralysis," and the like.

In many of the instances the influence of the toxin had evidently been extensive, embracing widely separated sensory and motor neurons, and it was quite impossible to include the cases in any recognised category of diseases of the nervous system. He had seen various other cases which he was equally unable to tabulate.

It appeared to him, looking over a lengthened period of special experience, that the relative as well as absolute number of grave diseases of the nervous system ascribable to toxæmia had very largely increased during the last few years, and he was disposed to think that, although this increase was by no means to be attributed exclusively to the invasion of influenza (for he felt sure that there were many other as yet unlabelled toxins at work), yet that a large proportion must be credited to the direct influence of the disease under consideration.

A DISCUSSION ON THE PROBLEMS OF GASTRIC ULCER.

I.—JOSEPH FRANK PAYNE, M.D., F.R.C.P.,
Consulting Physician to St. Thomas's Hospital.

WHEN I was honoured by the invitation to open this discussion, I did so on the understanding that I should endeavour to raise points for discussion, without professing to have anything actually new to communicate. My attention during a long hospital experience has often been drawn to this disease, and I have been led to notice the imperfection of our knowledge respecting certain points, which I propose to call the problems of gastric ulcer.

The first problem, which arises from an inspection of the hospital statistics, is that gastric ulcer seems to be increasingly prevalent. The table which I show displays the statistics of

ST. THOMAS'S HOSPITAL.

Cases of Gastric and Duodenal Ulcer.

Periods of Years.	All.	M.	F.	Died.	M.	F.
1870-4	30	9	21	0	—	—
1875-9	38	14	24	4	3	1
1880-4	70	12	58	0	—	—
1885-9	103	23	80	11	7	4
1890-4	174	15	159	20	6	14
1895-9	216	37	179	24	11	13
Total	631	110	521	59	27	32
Duodenal ulcer	18	18	0	7	7	0
Gastric only	613	92	521	52	20	32

One fatal case of ulcer of the œsophagus.

Percentage of Cases at Different Ages.

Age periods	0-10	— 20	— 30	— 40	— 50	— 60	60 +	All ages.
Percentage of 530 living cases	0.7	13.4	47.4	22.8	10.6	4.0	1.1	= 100
Fatal cases { M.	0	5	16	42	16	21	0	100
Fatal cases { F.	3	10	58	16	10	3	0	100

gastric ulcer in St. Thomas's Hospital for thirty years in six periods of five years each. I pass over the first period, as the hospital was then in a state of transition, but observe that in the period 1875-9 the number of cases was about one-sixth of what it was in 1895-9. There has been some variation in the number of beds, but this would not exceed 10 per cent., so that the present number of admissions for gastric ulcer is at least five times as many as it was twenty years ago. Why this should be I cannot tell. The fact that some cases are now admitted with a view to operation accounts for very little.

I would only point out that there has been a corresponding increase in some other affections of the digestive organs. Thus typhlitis or appendicitis has increased in St. Thomas's hospital from 6 admissions in 1875-79 to 343 in four years 1895-98 (statistics for 1899 not being available), the number of fatal cases having proportionally increased. Now the greater frequency of operations for this disease cannot explain such an increase as this, nor can improved diagnosis altogether, for certainly fatal cases were recognised in the *post-mortem* room as precisely twenty years ago as they are now. It is also notable that cancer of the digestive organs has increased very largely of late years, and in a higher ratio than cancer generally. Again, it is strange that the form of continued fever which affects the digestive organs, namely, enteric, has supplanted the older continued fevers, typhus and relapsing fever.

We seem to be living through a period in which diseases affecting the digestive system, perhaps caused by food, or something introduced with food, are predominant. Without pretending to explain this, I suggest as the first problem of gastric ulcer, "Is it really more frequent now than formerly in this or other countries?"

DIAGNOSIS OF GASTRIC ULCER.

The second problem which I propose relates to diagnosis. Are all the cases recorded (if unverified by *post-mortem* examination) really cases of gastric ulcer? Are some real cases of the affection called by other names? In other words, Are our customary grounds of diagnosis adequate and certain?

The principles of diagnosis in this disease have not varied much since I was a student. Then, as now, we were taught that the cardinal symptoms are: (1) Pain in the stomach of a certain kind, at certain times, and referred to special situations; (2) vomiting of food, or gastric irritability; (3) hæmorrhage, shown usually by hæmatemesis, more rarely by melæna. This was regarded as the cardinal sign; and then, as now, some physicians would hesitate or refuse to make the diagnosis of gastric ulcer without it.

Beside these things we were taught that the diagnosis was more probable if the patient was young, female, anæmic, and especially if a domestic servant; while it was much less probable if the patient was a male, and middle-aged or elderly.

In the last 30 years but one new diagnostic element has been introduced, namely, that of hyperacidity of the gastric fluid, of which I shall speak presently, a few words may be said about the old grounds of diagnosis.

1. First with regard to *Pain*.—The particular kind of pain regarded as typical of gastric ulcer—coming on after food, sometimes limited to one spot, accompanied by limited tenderness, and so forth—is so well known that I need not minutely describe it. In looking over the notes of a large number of non-fatal cases in my own wards, I find that this particular kind of pain and circumscribed tenderness is only mentioned in a minority of cases—I cannot say in what proportion—but the line is obviously difficult to draw. But in most cases the pain recorded—if any—is not at all characteristic or typical. Out of 48 fatal cases confirmed by *post-mortem* examination, I find a record of some kind of pain in 33 cases. In 14 cases it is not definitely mentioned, while in 1 it is positively stated that there never was any pain.

2. *Vomiting*.—Independent of hæmatemesis from my own cases as I find the symptoms recorded in more than one-half or nearly two-thirds of the cases. Of the 48 fatal cases it is positively mentioned in 20, and definitely stated to have been absent in two. In the rest it was not a prominent symptom.

3. *Hæmatemesis*.—Having a strong impression of the frequency and importance of this symptom I was surprised to find it definitely recorded only in 17 out of 48 fatal cases. In 27 it was definitely absent, in 4 the records were imperfect. The statistics of more than 100 non-fatal cases in my own wards form a remarkable contrast; in these I find hæmatemesis nearly always recorded, that is, in from 90 to 95 per cent. of the cases. Possibly the proportion in my cases is somewhat above the average since I have always regarded this symptom as a *sine quâ non* of diagnosis. Many cases are admitted in consequence of severe and sudden hæmatemesis, which is, therefore, the one ground of the diagnosis. On the other hand, the fatal cases include a large number of sudden perforation, in which hæmatemesis would not occur. In two cases only was hæmorrhage the cause of death. The difference raises a doubt whether all the non-fatal cases with profuse hæmatemesis were really gastric ulcer.

4. *Hyperacidity*.—Some German workers, especially Professor Riegel, attach great importance to hyperacidity or, more accurately, excess of hydrochloric acid, as a diagnostic

sign of gastric ulcer. Riegel states that he has found in a long series of cases of gastric ulcer, with remarkable frequency, an excessive gastric secretion, or hyperacidity; also that the time of digestion is shortened rather than lengthened, as compared with the normal. He regards this hypersecretion as a predisposing cause of ulcer and especially as the chief cause which prevents its healing. But the ulcer may continue when this condition has passed away. Other observers, as Ewald, Gerhardt, Rosenheim, Dreschfeld have not found hyperacidity a constant feature, while admitting that this condition and ulcer are often combined.

I can say nothing from my own experience on this point, since I should not venture in any case in which gastric ulcer was strongly suspected to wash out the stomach, or use other means for removing its contents for analysis. But this has been done by German physicians and by some in this country; so perhaps we are over-timid on this point.

Therefore another problem which I present to the meeting is this: Is the existence of hyperacidity in gastric ulcer proved; and can it be ascertained without risk?

Conclusions as to Diagnosis.

The general conclusion seems to be that while hæmatemesis, if accompanied by other gastric symptoms already mentioned, is the most trustworthy sign, it is not absolute; it may be produced by many other causes.

One of the commonest is no doubt hæmorrhage from dilated œsophageal and gastric veins in alcoholic cirrhosis of the liver. This occurs most frequently in men at a later age than the average of gastric ulcer, and with other signs of alcoholism.

It may also be caused by strain or direct injury in healthy people. Such hæmorrhage may be apparently the starting point of ulcer, or of a wound in the stomach indistinguishable clinically from ulcer. I have had some well-marked cases. One was that of a nurse, aged 30, who after lifting a heavy patient had profuse gastric hæmorrhage. Symptoms like those of ulcer lasted for a month or two. She completely recovered. Another was that of a man, aged 30, employed on a railway. On lifting a heavy weight he felt sudden sharp pain in the stomach, which two days later was followed by profuse hæmorrhage, with tenderness, etc. He recovered. Injury was the cause in a married woman, aged 30, who was brutally beaten by her husband. Severe hæmatemesis followed, but she recovered. Another remarkable case was that of a man, aged 34, who eight years before had suffered from hæmatemesis following injury. When under observation he had gastric pain and other symptoms, with slight hæmatemesis. In this case injury was probably the starting-point of a chronic ulcer.

Aneurysm is an undoubted though rare cause of gastric hæmorrhage.

Moreover, there may be hæmatemesis without gastric hæmorrhage. When combined with hæmoptysis no difficulty is likely to arise. But there may be other causes. A man was brought into my wards with profuse repeated hæmatemesis and the provisional diagnosis of gastric ulcer.

There was no doubt about the facts, but I was struck with the peculiarity that the vomited matters were not acid. Examination of the throat showed a bleeding adenoid of the nasopharynx. The blood trickled down into the stomach, and was expelled by vomiting. Finally, there are many non-fatal cases of hæmatemesis where the diagnosis is very obscure. The St. Thomas's Hospital *Reports* give 102 cases in 20 years, diagnosed as hæmatemesis. The general impression I have derived is that many cases in men were due to cirrhosis of the liver, while in young women the symptoms mostly pointed to gastric ulcer, though no positive diagnosis could be made. It is a question whether the diagnosis of gastric ulcer can be made if there has been no hæmatemesis, and it is a further question whether even the addition of hæmatemesis to the other symptoms is sufficient. I feel very sceptical as to the certain recognition of cases in which there is no *post-mortem* examination, and propose the problem: Is our diagnosis of gastric ulcer, when not confirmed by *post-mortem* examination, quite satisfactory, with or without evidence of hæmorrhage?

Acute Gastric Ulcer.

The next problem is whether we can draw a clear distinction, as has been done by Dr. Samuel Fenwick and Dr. Soltau Fenwick in their very valuable book, between acute and chronic gastric ulcer. By an acute disease we mean one which is rapid in its onset and short in its duration; that is, the distinction is a clinical one. But in the disease now spoken of this is not enough, since we know that a gastric ulcer may be latent for an undetermined time till sudden symptoms occur. The only absolute criterion is that furnished by *post-mortem* examination, showing whether the condition was chronic or recent. On clinical grounds I propose to call those cases acute in which symptoms lasted one month or less, chronic those of longer duration.

Out of 48 fatal cases

Symptoms longer than a month	36
,, less ,, ...	12
	48

Judged from *post-mortem* appearances, there were

Cases of chronic ulcer	42
,, acute or recent	6
	48

There were thus 6 cases of recent ulcer with acute symptoms. Of these, 2 were males, aged 16 and 25: 4 were females, aged from 22 to 29. But there were also 6 cases with very acute symptoms, though the disease was found to be chronic. It thus seems that in fatal cases sudden or acute symptoms are quite as likely to indicate chronic as acute disease. In non-fatal cases, though the symptoms may be acute, it is very difficult to say how long the disease has lasted, since the statements of patients are vague and uncertain. Out of my series of non-fatal cases I find 34 per cent. (10 per cent. being males, 24 per cent. females) with symptoms lasting one month or less, that is, acute; and 66 per cent. (12 per cent. males, 54 per cent. females) with a history of symptoms over that time, that is, chronic. Three-fourths of the acute class and one-half of the chronic cases were under 30. It thus appears that in acute cases the proportion of females to males was $2\frac{1}{2}$ to 1, while in chronic cases it was $4\frac{1}{2}$ to 1; the proportion of females to males generally being about $3\frac{1}{2}$ to 1.

These results do not at all agree with those of the Doctors Fenwick, who state that acute primary gastric ulcer almost exclusively affects young female subjects, and that the proportion of female to male cases is nearly 10 to 1.

In my non-fatal cases the proportion of females to males in patients giving a history of chronic symptoms was much higher than that in those giving a history of recent symptoms; while in the only quite certain cases, namely, the fatal, this proportion was 2 to 1. A partial explanation may be that women pay more attention to their physical state than men; and thus are more likely to give a long history of symptoms. But the discrepancy cannot be thus entirely accounted for.

I must say I fail to find any evidence that the acute primary ulcer is essentially different from the chronic ulcer. It seems to me that an acute ulcer if it does not heal up or cause death becomes chronic; while a chronic ulcer is nothing more than an acute ulcer grown older. I propose, therefore, this problem: Is there an acute form of gastric ulcer different from the chronic form?

Etiology of Gastric Ulcer.

This very large subject can only be briefly discussed. My object is merely to show how imperfect our knowledge is. The absolute limitation of these ulcers to the stomach, with adjacent parts of the duodenum and œsophagus, is strong evidence that digestion plays a part. Hence the appropriate name "peptic ulcers." But it is not enough to conclude that the ulcer as we see it is the result of a solution of tissues by gastric juice. The further question is, why a particular part of the mucous membrane and deeper tissues should be thus destroyed.

Broadly, we can only say that it is due to loss of vitality, a local death of the tissues making them liable to digestion. It cannot be merely due to the loss of the alkaline reaction of circulating blood, since the alkalinity of the blood is very feeble, and quite insufficient to neutralise the reaction of the gastric fluid.

I need not relate the numerous observations and experiments by which these truths have been established. The question remains, What produces in a certain limited area,

this loss of vitality? It appears to me that this, the central problem of gastric ulcer, is entirely unsolved. The peptic theory explains very well why an ulcer persists, but not in the least how it originates. I have always thought it possible that the starting point may be different in different cases, though the subsequent course, dependent upon peptic conditions, may be the same.

Among the causes proposed is, for instance, arterial embolism, suggested long ago by Virchow—a good cause enough, were it shown to exist; but the conditions of embolism are present in an extremely small proportion of cases of ulcer. Capillary thrombosis, ecchymosis, congestion in certain areas, have also been brought forward as causes producing necrosis and digestion. But even were the existence of such conditions more certainly proved than it is, we should still have to ask what causes the congestion, thrombosis, etc. Dr. Hunter has shown that the administration to animals of certain toxic substances (for example, toluylendiamine), produced in the duodenum patches of congestion which might lead to peptic solution or ulcer. But after all they were not ulcers, and it did not happen in the stomach. So that this interesting experiment only furnishes a hint.

As is natural, microbes have been invoked as the cause of gastric ulcer. It used to be thought that bacteria soon perish in the stomach. But it has been shown that colonies may be found on various parts of the walls; though how long they live we do not know. There is no antecedent improbability in the idea of gastric ulcer being a specific bacterial disease. The centrifugal extension of the morbid process may be thought even to suggest some local infectivity. Once I made an observation which gave a hint of this. There were two ulcers in a stomach—one on the posterior aspect comparatively chronic, and one quite recent on the anterior aspect. On placing the organ in its natural empty position the two ulcers came into apposition, suggesting that the newer might have been produced by infection from the older.

There is, however, no evidence at present in favour of the bacterial origin of gastric ulcer.

Again, like many other organic diseases, gastric ulcer has been supposed to depend upon a "neurosis" or "disturbed ervation." But till this conjecture is put into a more definite shape so as to become a true hypothesis, it seems hardly worth considering.

Finally, there is the hypothesis of hyperacidity or excess of hydrochloric acid, to which I have already referred. But this condition, supposing it to be a real factor in producing the disease, ought to act uniformly, and would not account for an excess of solvent action at any special spot on the surface of the stomach. It might account for the continuance of an ulcer, but not for its commencement.

I should therefore conclude that we have not at present an even plausible explanation of the origin of gastric ulcer.

PREDISPOSING CAUSES.

Youth, the female sex, anæmia, hard work, poor nourishment are most generally accepted as predisposing causes; so that there seems to be an impression that this is chiefly a disease of chlorotic servant girls. Our tables show that this is a great exaggeration, but that women between the ages of 20 and 30 give the largest proportion. With respect to sex and age I may say that examination shows that the second half of this decade supplies the larger proportion. This is a little above the chlorotic age, and I do not think that chlorosis in a definite sense is often associated with gastric ulcer. On the other hand, a large number of the female cases are described in the notes as delicate, pale, weak, or anæmic (though the anæmia is sometimes secondary). Irregularity of menstruation is often noted.

With regard to occupation. It is not surprising that hospital statistics should show a large number of maidservants among the subjects of gastric ulcer, since that class forms a considerable proportion of the young women admitted to any hospital. But beside servants I find a large proportion of married women, and also young women in various other occupations, such as nurses, barmaids, shopgirls, and workers in different trades, and I doubt very much the predominance of servant girls, except as above explained. Some authors have found gastric ulcer specially common among cooks, and have given plausible explanations of this frequency. I have found 3 cases of cooks among 50 female cases specially examined, which seems a large proportion.

The occupations of male patients are so varied that it would be impossible to make any generalisation about them. With regard to alcoholism, I have found few records of this habit; not many even among male patients and hardly any among women.

Tuberculous disease of any kind was only recorded in a few cases. There were also a few of valvular disease of the heart; but the numbers were insignificant. Syphilis does not come into account. On the whole it would seem that gastric ulcer is a disease by itself, not produced or even favoured by any special constitutional condition, though more likely to occur in those who are delicate and badly nourished.

We find it generally stated that this is a disease of the poorer classes, rarely found among the rich or well-to-do. The same statement is made with regard to a great many diseases, but it is open to criticism. Suppose that a particular physician has observed many more poor than rich affected with any complaint. In order to make this statement of any importance we should have to consider what proportion of each class he has under observation. Most of those attached to hospitals see many more hospital patients than private patients, especially if they have been long in the out-patient room. Moreover, we must remember that in this world, such as it is, there are many more poor than rich. Can anyone say what the proportion of the poor or lower classes to the rich or upper classes is? Is it 10 to 1 or 100 to 1? I do not know, but till this is in some degree settled, the statement that a disease occurs more frequently among poor than rich is not convincing. Precisely the converse, I may say, holds with regard to diseases said to be common among the upper classes than the lower, such as gout, hay fever, nervous asthma. Here we may readily trust our general impressions, because we refer the larger proportion to a smaller number of patients.

Gastric ulcer certainly does occur in young ladies. I have seen several cases, and also in middle aged or elderly men of the more wealthy classes, but in what proportion I am quite unable to say.

PROGNOSIS.

The prospects of a patient with gastric ulcer will vary according to the stage, and according to the time that it has already lasted. Nothing can well be more alarming than the symptom of an acute ulcer leading to hæmorrhage, or, still more, to perforation. But experience shows that recovery takes place in most cases where there is no actual perforation. Hæmorrhage was the direct cause of death in 2 cases only out of 48 fatal cases.

Experience shows that a recent ulcer, if not rapidly fatal, tends to recovery; so that in the young the prognosis is on the whole good. But if the alarming symptoms result from a chronic ulcer, as is often the case, the prognosis is not so good. Persistence of chronic symptoms, and recurrence of acute symptoms is to be expected. And our only test of acute and chronic disease during life is the previous duration of symptoms, fallacious though it may be. It follows that the longer symptoms have been observed the worse is the prognosis. Indeed, a really chronic ulcer is probably seldom absolutely healed. Recurrence of grave symptoms may always be expected.

There is a remarkable difference in the proportionate mortality of men and women respectively. The percentage of deaths among male cases is about 22 per cent.; among female cases a little over 6 per cent.; and for both taken together $8\frac{1}{2}$ per cent. It follows that gastric ulcer, though rarer in men than in women, is a much more fatal disease in the former. Also, the liability of men to die of this disease goes on much later in life; having its maximum between 30 and 40; and being very considerable between 50 and 60. In women the liability to death is slight after 30, and very small after 40. If these rates were calculated according to the number of persons living at each age period, the discrepancy would be still more striking.

It would be interesting to know the subsequent history of cases in which there is apparent recovery. The experience of hospital and private cases is that recurrence may take place after several years, so that we cannot hastily pronounce any case permanently cured.

Morbid Anatomy.

So much has been written on the anatomy of gastric ulcer as recognised *post mortem*, that I will not dwell upon it. This is, however, the real foundation of what we know about this affection, and the only ground of definition, and therefore of diagnosis. It is difficult to attach much importance to the supposed recognition of gastric ulcer before *post-mortem* examinations were made.

Treatment.

This is a most important subject, but the limits of time imposed on the present occasion prevent me from making more than a very few remarks.

In acute cases, when profuse hæmorrhage is the marked symptom, the principles of treatment are clear enough. We want to give the injured organ the most complete physiological and mechanical rest. Beside perfect quiet and inactivity, we have to put the functions of the stomach, if possible, into complete abeyance for as long as possible. The only absolute method of doing this is to withhold all food by the mouth and sustain the strength as far as possible by rectal feeding.

Theoretical objections may be made against the possibility of absorption of food by the rectum. I remember the time when experienced physicians were extremely sceptical on this point. But experience has shown that life may be sustained by this method of feeding, though it is after all but a slow starvation. I believe that a great step has been made by the introduction of peptonised foods. It is probable that milk alone is hardly absorbed by the rectum, and beef-tea which was formerly given, we now know hardly deserves the name of a food. Eggs, whether it is the yolk or the albumen that is absorbed, appear to give better results. But I have come in the end to trust almost entirely to peptonised foods.

The general principles and methods of rectal feeding are too well known to need discussion. The chief points appeared to me to be to consider how long a patient can be nourished by this means, and by what method, if any, the possible period may be prolonged.

It is usual to interdict not only food of any kind, but even water by the mouth; and to try and relieve the sensation of thirst by giving the patient small lumps of ice, as recommended in every textbook. I maintain, on the other hand, that water, given in small quantities by the mouth, is not only not injurious, but decidedly advantageous. To begin with, ice does not really relieve thirst, as we may know by experience, and the quantity of water represented by a little lump of ice is absurdly small.

Moreover the patient who drinks water is able to support life under rectal feeding much longer than without. This is shown both by analogy and by direct experience. Rectal feeding, I have said, is but a slow starvation. Now nothing is more certainly established than that we are able to support starvation much longer with water than without. Men have been known to live without food, but, with access to water, for a much longer time than is required for rectal feeding as a therapeutic measure.

We find that rectal feeding for one week without water is a severe strain upon the bodily strength. Some patients cannot even bear it as long as this. But if they are allowed to sip water in moderation, I find that they can bear a fortnight's rectal feeding without more inconvenience than most patients find after one week without water. The danger in rectal feeding is not emaciation or want of nutrition generally, but failure of the heart. During this process or at least in the second week great care is required to avoid this accident. The patient must not be allowed to sit up, especially suddenly, nor to move for any purpose. With these precautions, and allowing water by the mouth, I have often prolonged rectal feeding for a fortnight or longer. We must not forget that the mere act of swallowing has been shown to be a stimulus to the heart. Of course we know that water may be absorbed by the rectum, but giving it by the mouth has this advantage among others. I propose therefore, as one of the problems of gastric ulcer, whether taking water by the mouth should be forbidden during rectal feeding.

There is one small point in connection with rectal feeding to which I should like to direct attention, namely, the occurrence of acetonuria, that is, the presence of diacetic acid or acetone in the urine. We know that this occurs not only in diabetes but in various diseases of the digestive system. The largest amount of acetone I ever found in the urine was in a case of extreme alcoholic dyspepsia. It has also been recorded in cases of gastric ulcer, but I do not happen to have observed it except when the patient was under rectal feeding, or under an extremely restricted diet. In many of my cases the observations were made by my then house-physician, Dr. Dixon, now well known as a physiological investigator, and some were carefully analysed in the hospital laboratory. Under these circumstances the condition can hardly be due to perverted gastric digestion since the stomach is not digesting at all. I have therefore regarded as the result of starvation, since it is known that acetonuria has been produced by artificial deprivation of food in animals; and in extreme alcoholism as in diabetes, the condition is one of virtual starvation. Further observation will show whether this explanation is mistaken. I therefore propose as a minor problem connected with gastric ulcer whether acetonuria is due not to the disease itself, but to rectal feeding or extreme restriction of diet.

About drugs in the treatment of gastric ulcer I have no time to say much. The most useful appear to be salts of bismuth and next nitrate of silver. Their action is, of course, entirely local, and their suitability appears to depend upon the fact that they are not absorbed (or, in the case of silver, very slowly), and therefore, unlike salts of zinc and lead, the local action of which is the same or stronger, they do not produce vomiting or any general toxic effect.

The results of treatment are certainly encouraging. The large number of cases with severe hæmorrhage and other serious symptoms which recover is satisfactory evidence of the success of treatment before perforation has occurred. When this terrible accident has actually occurred, we know of no method which gives any chance except an operation and suturing the perforation with surgical precautions, which I need not dwell upon. We have had some very successful operations of this kind at St. Thomas's, and others which, notwithstanding the greatest care and skill, were unsuccessful. I refrain from trying to state the results, because I could not give them completely, and an incomplete summary would be misleading.

The amount of success which has been obtained leads one to ask the question whether operative measures may not some day be applied to ulcers where perforation has not occurred, and the very probable fatal termination thus warded off.

Summary.

The following are the problems connected with gastric ulcer which seem to me most in need of elucidation:

1. Is gastric ulcer increasing in frequency?
2. Is the connection of hyperacidity with gastric ulcer proved; and can it be ascertained without danger?
3. Are our present means of diagnosis in non-fatal cases quite satisfactory, especially in cases where there has been no hæmatemesis, but even when this has occurred?
4. Is there an acute form of gastric ulcer, different from the chronic form?
5. Is the original cause or starting-point of gastric ulcer really known?
6. Is gastric ulcer so rare in the upper and middle classes as seems to be generally supposed?
7. During rectal feeding should taking water by the mouth be prohibited?
8. Is acetonuria a frequent accompaniment of rectal feeding?

II.—Samuel Herbert Habershon, M.A., M.D., F.R.C.P.,
Assistant Physician to the Hospital for Consumption, Brompton.

Dr. Habershon addressed his remarks first to the last problem enunciated by Dr. Payne. He showed diagrams drawn from some private cases of his late father, and compared them with Brinton's statistics, showing a gradual rise in the proportion of cases from early to old age, as related to the number of people of that age living at the time. He exhibited curves which showed the difference between the incidence of the disease in males and females, clearly indicating some potent cause of gastric ulcer—and probably of acute cases—occurring in young females between the ages of 20 to 35. With regard to the problem of diagnosis, Dr. Habershon described three classes of cases in which the diagnosis was difficult: (1) Cases

of gastric pain and vomiting in young anæmic subjects in whom no hæmatemesis is present. In these one may suspect but cannot always diagnose the condition, which is sometimes revealed subsequently by alarming symptoms. (2) Neurotic cases of irritable stomach and great hyperæsthesia, with the history of pain after food, sometimes introduced a great difficulty of diagnosis. Dr. Habershon described an aid to diagnosis of which he had heard and frequently found of practical value. If pressure was made with the finger upon the carotid artery on one side of the neck or the other, the tenderness and hyperæsthesia of the epigastrium was found to be remarkably diminished. He did not pretend to explain the observation or to do more than state it as an empirical fact, and as to whether the disappearance of tenderness was due to moral effect or to the effect of some control of circulation in the brain. A third class comprised certain rare cases in which the symptoms were anomalous, and consisted of pain not following but relieved by food, and occurring some hours after food, associated with retching and occasional regurgitation. Hæmatemesis occurred in two cases. In both there was an ulcer found after death, near the pyloric end of the stomach. As to the question of whether an ulcer was acute or chronic, Dr. Habershon suggested that acute ulceration was more likely to occur in young females, and that when certain late sequelæ of gastric ulcer were found upon examination—such, for instance, as signs of cicatricial tissue, evidenced by some thickening felt through the abdominal wall, or by some severe irregular pain occurring through the involvement of a branch of the pneumogastric nerve—it was more probable that the case was chronic, even though the symptoms were recent. Further dilatation of the stomach was a result of chronic ulcer of the stomach, though an acute dilatation sometimes occurred in the early stages in conditions of great prostration.

III.—WILLIAM GORDON, M.A., M.D., M.R.C.P.,
Physician to the Devon and Exeter Hospital.

DR. GORDON said: At first sight it seems strange that we have so little certain knowledge of the causes of gastric ulcer, but we must remember that until the last few years no one saw these ulcers until they had undergone not only the ordinary *post-mortem* changes common to dead tissues, but also (often, at least) more or less digestion by the gastric juice after death. When we remember this we shall have less difficulty in understanding how it is that we know so little.

Now we are entering on a new field of inquiry; for so long as some surgeons consider it desirable in select cases to excise perforated gastric ulcers, so long shall we have invaluable opportunities of studying these ulcers as they exist in the living body. It seems not unlikely that the systematic examination of excised ulcers would give us a far clearer insight into their causation than has been hitherto possible, and one cannot but feel surprised that apparently no one has yet thought it worth while to make the necessary investigation.

Eight or nine years ago I had an opportunity of examining a very typical example of acute perforating gastric ulcer. The specimen, which had been some time in spirit, showed a clean circular hole, punched out as it were, in the stomach wall, with no naked-eye evidence of inflammation or even swelling round it; and from the edge of this ulcer sections into the surrounding tissue, stained with methylene blue, showed a condition which was at least suggestive. The edge of the ulcer was confused and almost structureless, having apparently undergone digestion, a little way from the edge there was indication of a certain amount of inflammation with aggregation of leucocytes, and (what impressed me most at the time) beyond these leucocytes and reaching for some distance into the stomach wall, were numerous cells stuffed with micrococci and free groups of micrococci scattered in the tissue. On the free edge of the ulcer there were also microbes, but these were of various sorts, both bacilli and cocci. In the tissues there were cocci, and cocci only. One could not help wondering if the ulcer were caused by these cocci. I did not then pursue the investigation, for it seemed to me that without fresh specimens, specimens excised in life, no useful result could be arrived at, and eight years ago no one talked of excising gastric ulcers. Now, in certain cases the material has become available, although none of the cases which have come under my notice operated on by my surgical colleagues have been cases where excision was thought desirable. But I have searched the records of recent operations in the hope of finding some facts which might at all events suggest the true pathology of the disease, and it is to some considerations arising out of this rather limited inquiry that I would venture to ask your attention for a few moments.

The theories which have been advanced from time to time to explain the origin of gastric ulcer may be briefly stated thus:

1. Embolism with digestion of the damaged area. But in the vast majority of cases there is neither evidence of any source for an embolus nor of the existence of any embolism elsewhere in the body. This suggestion may be safely set aside except as a possible cause in exceedingly rare cases.

2. Thrombosis with digestion of the damaged area. But in the vast majority of cases there is neither atheroma nor syphilis, nor suggestion of thrombosis in any other vessels. Here, again, we may safely set aside the suggestion except as possibly true in rare cases.

3. Simple submucous hæmorrhage, with subsequent digestion. Here one fails altogether to understand how such a process could cause the destruction of the whole thickness of the stomach wall.

4. Trophic lesions due to some nervous abnormality. Perhaps this is the most unlikely suggestion that has been made, and rests, so far as I can discover, on no evidence of value.

5. Scalding food and corrosive poisons may in very exceptional instances give rise to this very common disease.

6. Mechanical pressure on the stomach, as by tight lacing. It seems scarcely conceivable that such a cause should be sufficient, protected as the stomach is.

7. Injury to the mucous membrane by swallowed substances with sharp edges. Judging by the rapidity with which stomach wounds heal, we can give no credence to this as a likely explanation.

In short, these theories have remarkably little to recommend them for the generality of cases; but there is another and as I think, a more probable view. There is evidence accumulating, experimental and pathological, that organisms can cause ulcer of the stomach as they can cause ulcer elsewhere. It is curious to see how hesitatingly this theory is put forward in some of our textbooks, and yet surely it is the theory which seems to bear upon it the stamp of probability.

I suppose it would be unscientific to say it is the only theory that in the light of modern pathology appeals to one's common sense. If one were to rub a pure culture of staphylococcus aureus into one's arm and produce a crop of boils there, what would one think of a pathologist who said they were embolic or thrombotic, or trophic or the results of petechiæ, when one knew that one's heart, vessels, and nervous system were free from any discoverable disease?

Now, what might we expect would happen if a culture of staphylococcus aureus were rubbed into the wall of the stomach? We are daily swallowing innumerable microbes, some of which must at least be capable of setting up suppuration in the tissues. These microbes are carried down in an alkaline medium of mixed food and saliva, and in an anæmic servant girl are associated with a surplus of saccharine material which should afford an ideal medium for their multiplication. Then they have twenty minutes or perhaps double that time in the stomach before the alkaline reaction is changed to an acid reaction, and during that time they are being rubbed and scrubbed all over the gastric mucous membrance by the muscular movements of the gastric walls and kept warm by the warmth of the organ which contains them. Should we be greatly astonished under such circumstances if "a boil"—to use a crude term—was produced in the stomach just as a boil may be produced on one's neck? And if there was a patch of gastritis or a mechanical erosion on the stomach surface would not such a result be even more likely to occur?

Next, let us for a moment assume that this might happen, and consider what would be the consequence. The gastric juice performs a twofold purpose. It is at once a digesting and a disinfecting fluid. According, therefore, to the virulence of the microbe and its point of entry we might have one of several results.

(*a*) A rapid and serious injury of an area of the stomach wall. If from the position of this area it were not speedily reached by the acid juice, the injury might easily proceed by acute inflammation of the whole thickness of the wall, which

would naturally tend to affect a circular area wider internally than externally, to a very serious extent and then if the gastric juice did reach it too late to act as a disinfectant, it would simply digest out the injured circle and we should have the acute perforating ulcer of the stomach with a clean punched out opening. The swelling of the surrounding tissue might easily have altogether subsided when we examined it *post mortem*, and as a matter of fact this subsidence of swelling after death has been actually observed. We would then find, microscopically, that the edge of the ulcer was digested, that some indications of inflammation existed round it, and that colonies of cocci were being carried away on all sides by the phagocytes which had enclosed them.

(*b*) Or a less virulent organism or one less fortunately placed would have time to cause only a slight degree of surface injury. The tide of gastric juice would then exercise its protective action by the digestion of the surface, the production of an erosion and the destruction of the microbes before they could accomplish more extensive damage.

(*c*) An intermediate result might follow. The gastric juice might effect an erosion, but fail to destroy the microbe, only succeeding in weakening it. We should then have a slow alternation of progress of the ulcer and digestion of the damaged tissue, together with irritation of the exposed surface both mechanically by food and chemically by the acid, so that inflammation would steadily advance beyond the limits of destruction, the ulcer produced widening and deepening simultaneously, adhering to neighbouring organs, and eating its way into their substance. In fact we should have an ordinary chronic funnel-shaped ulcer.

And there should be other peculiarities about the result of such processes. The part of the stomach where the gastric juice is free from hydrochloric acid at the moment of its secretion—where the secretion of the glands is alkaline—would suffer from ulcers, as Dr. Sidney Martin has pointed out in his valuable book. Therefore the pyloric region would suffer. And the part of the stomach which is most fixed—the part from which the organ depends—would be apt to suffer because it would tend to be away from contact with the acid contents of the stomach. Thus the lesser curvature would suffer. Also the parts of the stomach which are the most remote of all from the acid contents, and where the microbes would remain longest undisturbed by the antiseptic and digestive action should be just the parts where perforations could most frequently happen, whilst those parts which are most continuously or frequently bathed by the gastric juice should be just the parts where perforation would be most infrequent. Perforation ought, in fact—if my suggestion be correct—to occur most often on the anterior surface, and especially near the cardiac orifice, and least often on the posterior surface. And this is just what happens. The analysis of published cases makes that very clear.

It seems to me that a theory of microbic origin will explain the facts of gastric ulcer better than any other. The explanation of the infrequency of posterior perforations, which attributes this infrequency to less mobility, of that surface is very improbable, for it is by no means obvious that the back of the stomach moves less freely over other organs than the front. Moreover, the infrequency of anterior adhesions has been much underrated.

It rests with our surgical colleagues when they excise gastric ulcers to supply us with the material necessary to the solution of this problem. Such an ulcer could be cut in half, and one half hardened for cutting and staining, whilst the other might be immediately used, with suitable precautions, for bacteriological cultivation experiments.

IV.—William Calwell, M.A., M.D.,

Physician to the Royal Victoria Hospital, and to the Throne Consumption Hospital, Belfast.

Dr. Calwell emphasised the question of the necessity of preventive treatment in gastric ulcer. It was too much the custom to temporise with suspicious cases of dyspepsia. The patient was allowed to pursue ordinary avocations, and mild restrictions of diet with medicinal treatment were advised. It was imperative that this mode of treatment should not be pursued for long. The physician must be emphatic in his conduct of the case, and although the affection be but apparently a case of indigestion, if the patient be a young woman she should be put to bed, and an absolutely milk diet, duly prepared, insisted on. This offered the best possibility of preventing the formation of an ulcer, and if an ulcer had formed, it would tend to minimise the formation of adhesions, and so the best had been done to leave a healthy stomach, with the peristaltic action unimpeded. It was commonly believed that adhesions were a protection against perforation; but in some 14 of 16 cases lately operated on for perforation within the last couple of years in Belfast, there were found large adhesions, some of which were very indurated and extensive. This led to the question whether some so-called perforations were not really rents in the coat of the stomach due to the adhesions. The question of the possibility of adhesions to the pancreas being a cause of acute hæmorrhagic pancreatitis was important and as yet undecided. In operating on cases of perforated gastric ulcer, the surgeon could, by enlarging the perforation, and with the aid of a laryngeal mirror and reflector, inspect the mucous membrane of the stomach. The question of rectal feeding and of the return to ordinary diet was one of the greatest importance and the really vital point in treatment.

V.—Miss Julia Cock, M.D.,

Senior Physician to the New Hospital for Women; Joint Lecturer on Medicine, London (Royal Free Hospital) School of Medicine for Women.

Miss Cock said: I should like to report two cases which illustrate in a striking way the great difficulty in diagnosis which may arise when clinically some of the more important symptoms or complications of gastric ulcer are closely simulated in patients who are not, as a matter of fact, the subjects of gastric ulcer. Such cases are probably not extremely rare. These have been selected from others of a like nature occurring at the New Hospital for Women because in both diagnosis was brought to the test of actual examination. In Case I after death, in Case II by exploration of the abdomen on two separate occasions during life.

Case I.—A girl, aged 17; housemaid. Admitted to the New Hospital for Women, November 29th, 1895, with certificate from home doctor of urgent hæmatemesis.

History of Present Illness.—Quite well until November 14th (two weeks before admission), when she began to have pain after food in the epigastrium. No vomiting occurred till November 27th, when she vomited twice. On November 28th she became faint and giddy, and vomited "a large quantity" of bright blood.

On admission she was blanched, but not excessively; not collapsed; complained of no pain. Temperature 98.8°; pulse 88. Some epigastric tenderness, not marked and not characteristically localised. Examination of the chest showed nothing abnormal.

Treatment.—Absolute rest in recumbent position; nutrient enemata; sips of water by mouth. She did well until December 1st, when she vomited twice, bringing up first 10 ounces of bright blood, and an hour after 18 ounces, dark and clotted. After this she was blanched and faint. Pulse rapid and feeble 120. Restless, and complained of abdominal pain; temperature subnormal. She rallied, and on December 10th was taking milk by the mouth without pain, tenderness, or vomiting.

December 16th. Patient complained of sudden severe epigastric pain, and the temperature rose to 102°. In the evening the temperature was 105°, and marked epigastric tenderness developed. The abdomen was not distended except in the epigastrium, and moved with respiration in the lower two-thirds. From this time signs pointing to a small subphrenic abscess were developed, namely: (*a*) Fulness and marked tenderness and pain in the epigastrium; (*b*) temperature rising to 103° or 104° in the evening; (*c*) signs at the base of the left lung of pleurisy and pneumonia; (*d*) an area of tympanitic resonance over left lower chest. The question of surgical interference was discussed, but on the whole it was thought best to wait until the collection came within reach, and not to risk the conversion of a localised into a general peritonitis by premature operation.

On December 20th the patient became suddenly worse, and died of heart failure without any change in the physical signs.

The *post-mortem* examination showed the following condition: (1) The right lung and pleura were healthy. The base of the left lung showed pneumonia and pleurisy, marked involvement of the diaphragmatic pleura in the inflammatory process, with adhesions to diaphragm and base of lung. (2) The abdominal organs were normal; the stomach was healthy, and there was not the slightest trace of ulceration recent or chronic; there was no subphrenic abscess. The œsophagus and intestinal tract were healthy. The vessels of the portal area were normal. No source of hæmorrhage was found, and the body showed no trace of disease except that noted above.

This case seems worthy of record on account of the close and coherent simulation of gastric ulcer which it presented in the following points: (1) The age, sex, and occupation of the patient; (2) the history of pain after food, vomiting, and severe hæmatemesis, followed by a resemblance to perforation and subphrenic abscess, so exact as to mislead experienced observers, both medical and surgical.

It would be interesting to hear to-day some suggestion as

to the possible source of hæmatemesis occurring in young women who are not the subjects of gastric ulcer. Clinically, one strongly suspects that such hæmatemesis occurs in these patients more commonly than is usually believed, and in the case quoted the presence of severe and repeated hæmatemesis with no gastric ulcer was conclusively proved. The patient died of pneumonia, having already been debilitated by loss of blood; the source of that loss we did not discover.

CASE II.—A woman, aged 34. Charge nurse at the New Hospital for Women. Warded on December 19th, 1898, with acute epigastric pain, vomiting, and distension of abdomen.

Past History.—Always delicate. Eight years ago had severe hæmatemesis, and was treated for gastric ulcer. A year and a-half ago had pleurisy and congestion of lungs; ordered to Ventnor. While there had severe gastric pain and slight hæmatemesis. After six months went on duty as nurse at the North London Consumption Hospital. While there had three attacks of hæmatemesis. One night was seized with violent abdominal pain, collapse, and distension. Laparotomy was performed by a distinguished surgeon, under the impression that a gastric ulcer had perforated. No perforation was found, no adhesions, and no discoverable sign of gastric ulcer.

Since coming to the New Hospital for Women two months ago she had constant pain after food, with vomiting which only slightly relieved. On the 18th she was put to bed and treated by rest, rectal feeding, and afterwards by careful feeding by the mouth. Progress was unsatisfactory; pain and vomiting continued, there was almost daily distension of coils of intestine, the abdomen was resistent and somewhat tender. No fluid or definite masses could be made out. The temperature rose to 100° each night. Chronic peritonitis was thought to be present, either the result of inflammation set up by a slowly-perforating gastric ulcer, or due to tuberculous infection of the peritoneum, with adhesions hampering the stomach and intestines. As a month of careful treatment had failed to produce any improvement and the patient was losing ground, it was decided to open the abdomen a second time with the intention of searching for peritoneal adhesions, and if possible freeing the organs involved. Laparotomy was accordingly performed by Mrs. Scharlieb on January 22nd. Chronic peritonitis was found with numerous adhesions; two strong bands were attached to the greater curvature of the stomach. All adhesions were divided The stomach was carefully examined after freeing. Nothing to indicate disease of its coats was detected by the eye or with the finger. The peritonitis was thought to be simple and the result of mechanical interference with the peritoneum at the time of the first laparotomy. Subsequent microscopic examination confirmed this view. The patient made a good recovery and left the hospital on February 17th.

This case also shows how closely the graver complications of gastric ulcer may be simulated by other conditions. One would especially emphasise the hæmatemesis and the resemblance to symptoms of acute perforation at the time of the first laparotomy. It is worth remembering that an exploratory laparotomy may be followed by troublesome and even dangerous chronic peritonitis, as in this case, a fact which should have its weight in deciding on abdominal section for purposes of diagnosis.

VI.—GEORGE NEWTON PITT, M.A., M.D., F.R.C.P.,
Physician to, and Lecturer on Pathology in, Guy's Hospital.

DR. NEWTON PITT said: Undoubtedly the diagnosis of gastric ulcer is most frequently made in young women. Yet if we take *post-mortem* records, we find that at inspections the frequency with which gastric ulcer is found is far greater in old people than in the young; and, allowing for the proportion living at each age, it is found with increasing frequency for each decade of life, that is, a greater proportion of the population between the ages of, say, 60 and 70 die with gastric ulcer than is the case with those between the ages of 20 and 30. It is therefore clear that to reconcile these statements gastric ulcer in the earlier periods of life must generally end in recovery, whereas this is not the case in the later periods when the lesion more often proves fatal. In addition the question is raised whether the diagnosis may not often be at fault. It is generally asumed that whenever there is hæmatemesis in a young woman there is a gastric ulcer. We have, however, all met with cases where the patient has after an attack of hæmatemesis refused to submit to a strict diet, and yet no further symptoms have developed, and the patient has remained well. I cannot help feeling that not infrequently hæmatemesis occurs in young women independently of gastric ulcer, although the pathology of the condition is still obscure. I have twice made *post-mortem* examinations on patients who had died from hæmatemesis but in whose stomachs no trace of ulceration could be found, nor were any of the other lesions, such as cirrhosis of the liver, which might cause hæmatemesis, present; in fact, the bodies were free from any organic lesion which could account for the loss of blood. I am not prepared to satisfactorily explain the causation of the loss of blood in such cases, but would draw attention to the difficulty there is in discovering the seat of an epistaxis after it has ceased, and it is often not easy to find even while the nose is bleeding. Sometimes probably the mucous membrane of the stomach oozes blood in the same way without any actual ulcer. It has been shown that certain materials, such as opium, when circulating in the blood are excreted into the stomach. Possibly some such may be a cause of intense engorgement and or hæmatemesis, in the same way that toluylendiamine is capable of producing ecchymoses in the duodenum when it is being excreted by the bile. Still at present no such facts have been observed. Under the present circumstances it is most desirable that hæmatemesis in young women should not be assumed as necessarily connecting a gastric ulcer.

VII.—WILLIAM STUART-LOW, F.R.C.S.,
London.

MR. STUART LOW said: There are few affections around which medical and surgical controversy has more strenuously striven than that of the pathology and treatment of gastric ulcer, and with less profit either to the suffering patient or the perplexed practitioner. Here pathology has failed to point the way to a proper treatment, and therefore the therapeutics of gastric ulcer is still so much groping in the dark. A series of theories have been propounded, but each in its turn has failed to explain the malady, or serve as a foundation of a successful therapy. The clean, red, and sometimes angry or dry tongue, the clear, hyperacid, non-mucous and scanty vomit, and the constant constipation with the frequently dry scybalous stools, certainly point to deficient secretion of the normal juices of the alimentary canal, but more especially to a deficiency of the mucous secretion—the natural protector and lubricator of the entire passage. Noting these and other features in the semeiology, and the fact that many of my cases of gastric ulcer have been in patients suffering from the accompanying diseases of atrophic pharyngitis, and rhinitis, and amenorrhœa, conditions in which the pathology is admittedly clear, and the dominating feature is that of a deficiency of mucous secretion, I have for some time been treating my cases of irritable stomach, painful digestion, and gastric ulcer with mucin, and with most satisfactory and gratifying results.

I have had prepared for me, by the kind courtesy of Messrs. Burroughs and Wellcome, the mucin in powder form. They manufacture it from animal bile, which contains it in large amount. It is a dark brown powder, and almost tasteless and odourless, and therefore quite unobjectionable to swallow. This I give just before meals, or rather as *hors d'œuvre* at the beginning of the meal in cachet form, with an equal quantity (10 grains) of sodium bicarbonate.

The good effects of this are markedly evident in the immediate alleviation of all painful sensations in the gastric region, and in the establishment of regularity in the action of the bowels. That the constipation is relieved is a most important fact, and the value of mucin as an aperient is a great point in its favour as a therapeutic agent, and of much interest physiologically.

The diet is also carefully regulated and studied, and certain substances having a specially soothing and protecting action, such as animal jellies—calves' foot, mutton and chicken jelly—and thin cornflour, and the frequent use of a jujube of freshly-prepared marsh mallow is allowed. I have the feeding done regularly every two or three hours, according to the severity of the symptoms. The *rationale* of this method of treatment is to protect the irritable gastric surface, and especially the ulcerated part, from attrition by the food and constant worry by the hyperacid gastric juice; therefore the mucin is given first to form a gluey coating over the lining membrane, a kind of Unna's dressing is applied, and the surface thus soothed and protected. If there is any pain or uneasiness still after nourishment then another cachet is given, and thus the increased acidity counteracted. The ulcerated surface on the stomach wall is thus treated just as one on the surface of the body would be—protected from friction and rested, and given a chance to heal.

Mucin is a compound substance, being composed of a proteid and a carbohydrate called animal gum; it is the principal constituent of mucus, and is very widely distributed in the body, occurring in epithelial cells, goblet cells, and

mucous glands. There are probably several mucins, and they are all viscid and tenacious, and precipitated by acetic acid, and are dissolved by dilute alkalies. The contents of one cachet —10 gr. each of mucin and sodium bicarbonate mixed in a glass with a little water, and gradually heated to the temperature of the body—readily changes into a sticky glue, and this is the viscid solution that effectually protects the ulcer and the sensitive and inflamed gastric wall and regulates the bowels. The functions of mucin in the animal economy may be various, but one most certainly is that of the protection of the delicate membrane it pours over, not only from influences from without, but from the effects of other secretions as seen in the urinary and alimentary mucous tracts.

We know that any injury to the healthy gastric mucous lining is healed over with marvellous ease and quickness, because the wounded part is protected by the mucus present in the healthy state from the irritating influence of the gastric juice, and we also know that the gastric ulcers that bleed as evidenced by melæna and hæmatemesis are those that do not perforate but generally get well, as the effused blood, no doubt, takes the place of the deficient mucus, and thus shields the ulcered part, and allows it time to heal over effectually.

VIII.—PHILIP HENRY PYE-SMITH, M.D., F.R.C.P.,
Consulting Physician to Guy's Hospital.

DR. PYE SMITH said: Some statistics I collected nine or ten years ago revealed that the clinical records show a large proportion of cases in young women, while the *post-mortem* records show a much more equal distribution between the two sexes at different ages of life. The pathology of gastric ulcer is still obscure, but provisionally I would separate the acute perforating ulcer with perhaps venous (not arterial) thrombosis preceding it, from the superficial, extensive, chronic ulceration, and would regard hæmatemesis as sometimes occurring independently of ulceration or cirrhosis, as hæmaturia or epistaxis does. With respect to prognosis, I regard hæmatemesis as of little gravity, and it does not, I think, call for active treatment. As to treatment, I believe in rectal alimentation for a short period, and in using spoonfuls of warm water, and not pieces of ice, to alleviate thirst.

IX.—ROBERT SAUNDBY, M.D., F.R.C.P.,
Physician to the Birmingham General Hospital; Professor of Medicine in the University of Birmingham.

DR. SAUNDBY was not prepared to accept without hesitation the views of Drs. Pye-Smith and Newton Pitt that pathological facts contradicted the usual opinion, founded upon clinical experience, that gastric ulcer, etc., was most common in young women. He would suggest the need for collecting a greater number of *post-mortem* cases than had been done at Guy's, as the disease was relatively rare in the *post-mortem* room. He emphasised the difficulty of diagnosis which previous speakers had described, and pointed out the close resemblance of anæmic gastralgia with gastric ulcer, and the differential value of hæmatemesis. If, as Dr. Newton Pitt thought, which he was not prepared to deny, even this symptom might be present without ulceration, they must admit that it was impossible to affirm with certainty during life the presence of an ulcer of the stomach. He urged that in these doubtful circumstances the treatment of all cases presenting this group of symptoms should be uniform. The patient should be put to bed, and if hæmatemesis had occurred no food should be taken by the mouth for 48 hours, thirst being allayed by teaspoonful doses of warm water; but nutrient enemata or suppositories (1 egg beaten up, 1 teaspoonful of brandy with milk to 4 ozs.), might be given every four hours. After the lapse of this period feeding by the mouth should be resumed by giving 1 oz. of milk and lime water every hour, and this quantity should be increased every day, or every second day, until ordinary house diet was reached by suitable stages in the course of from three weeks to a month. The only medicine needed, as a general rule, was sulphate of iron, combined with sulphuric acid and magnesium sulphate in doses suitable to combat the anæmia and the constipation so usually present.

ON INTERMITTENT PULSE.*

By ARTHUR R. CUSHNY, M.A., M.D.,
Professor of Materia Medica and Therapeutics in the University of Michigan.

NONE of the ordinary symptoms are more readily appreciated than intermission of the pulse, and it is remarkable that while many less noticeable abnormalities in the pulse movements have been the subject of exhaustive treatises, hardly any attempt has been made hitherto to describe the different forms of intermission or to classify them on the basis of the cardiac physiology of the present day. According to the views entertained now, the contraction of the heart originates at the junction of the great veins with the auricles and passes throughout the latter almost instantaneously; there follows a short pause occupied by the transit of the impulse to the ventricle, which then contracts, and the open beat is succeeded by the arterial pulse. If the cycle be represented diagrammatically (Fig. 1.)

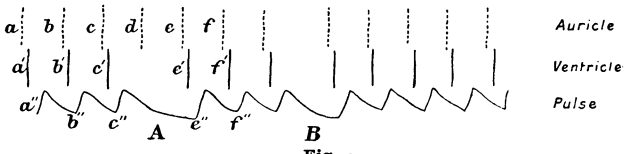

Fig. 1.

the broken lines may represent the auricular contraction, the unbroken vertical lines the ventricular systole and the familiar undulating line the arterial pulse tracing. The auricular contraction (*a*) is followed by the ventricular (*a'*) and this by the pulse elevation (*a''*), the auricular systole (*b*) by the ventricular (*b'*) and the pulsation (*b''*), etc. The auricular contractions are represented by broken lines because they can be appreciated clinically only in exceptional cases. Our diagnosis must as a general rule be made from what can be learned from those parts drawn in unbroken lines—the ventricular systole and the arterial pulse.

In the diagram (Fig. 1) two intermissions are represented as occurring at A and B, but these are not due to the same cause. Between the pulse *c''* and *e''* an auricular contraction *d* occurs, that is, an impulse has been emitted in regular course by the part of the heart which originates the movement (the orifices of the great veins); but this impulse has not caused a ventricular contraction, either through its failing to penetrate through some obstruction between the auricle or ventricle, or from the inability of the ventricle to contract in response to the impulse. The cause of the intermission lies not in the area controlling the rhythm, but in the ventricle, and the intermission may therefore be termed ventricular. In the case of the other intermission at B, the ventricle is able and ready to contract, but it fails to do so because the rhythmical area has failed to emit an impulse. In this case the fault lies not in the ventricle, but in the rhythmical area, and as this leads to a failure of the auricular systole, the intermission may be termed auricular in contradistinction to the ventricular. Hitherto no attempt has been made to distinguish between these two forms, and in fact, I am not aware of any distinct statement as to their existence. Some physiological experiments, into which I need not enter, suggested the possibility of diagnosing between these forms of intermission, and I find that most cases of intermission in disease may be relegated to one or other class without much difficulty. In the dog, when the ventricle fails to contract and the auricle maintains its rhythm, the intermission is exactly twice as long as the interval between two normal pulses; that is, in Fig. 1 the interval between *c''* and *e''* is exactly equal to twice the interval between *b''* and *c''* or *e''* and *f''*. This may be deduced from *a priori* reasoning also, for when the ventricle fails to respond to the descending impulse, as at A, it must simply wait until another reaches it and rouses it from its inactivity. But if the impulses descend at regular intervals, the ventricle must remain in diastole for twice the ordinary time when it has missed the first impulse.

On the other hand, when, as at B, the emission of the impulse is retarded from any cause, there is no reason why

* A more detailed account of the experiments and the analysis of the sphygmograms will be found in the *Journal of Experimental Medicine*, iv, p. 327.

it should be delayed for a whole cycle; on the contrary, it may be only a fraction of a second late, or may, as far as *a priori* reasoning indicates, be delayed indefinitely. The ventricular rhythm is dominated by the auricular while the rhythm of the originating area is uncontrolled. Accordingly an intermission due to ventricular disorder must of necessity be a multiple of the ordinary pulse interval, while an intermission from failure of the rhythmical area may be of any duration. In animals I have found the auricular intermission to be considerably shorter than two-pulse intervals, and in man I find practically only two forms of intermission: (1) Those in which the interval is about equal to two-pulse intervals and (2) those in which it is shorter than two-pulse intervals. The first I ascribe to ventricular failure, the second to auricular. In order to distinguish between them the sphygmogram must be accurately taken and carefully measured, and for this purpose I have used Jacquet's chromo-sphygmograph and curve analyser (Figs. 2 and 3).

Fig. 2.—Ventricular intermission. The figures beneath the tracing represent the length of the pulse in one-hundredths of a second. The intermission, 152, is exactly twice the length of the preceding pulse, 76.

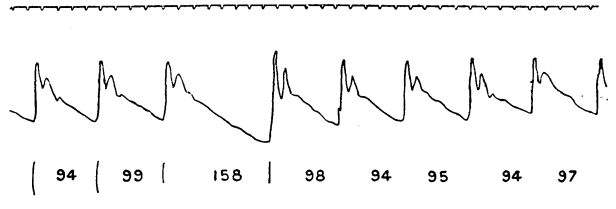

Fig. 3.—Auricular intermission. The figures beneath the tracing indicate the length of the interval in one-hundredths of a second. The intermission, 158, is much less than twice the length of the preceding pulse (2×99=198).

Every case of intermission of the pulse at the wrist does not indicate that the ventricle has failed to contract. On the contrary, such true intermissions are rare in comparison with those of another form first described by Wenckebach.[1] In most instances an intermission is due to a premature contraction of the ventricle, which occurs before the heart has recovered sufficiently from the last systole to allow of its full strength being developed or of the cavity containing enough blood to cause an elevation of the pulse. In Fig. 4 two such

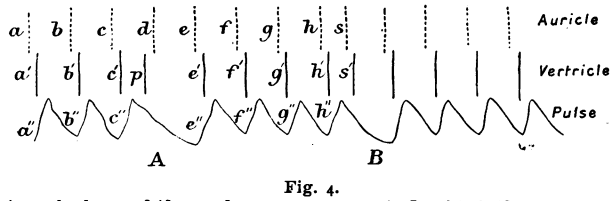

Fig. 4.

intermissions of the pulse are represented. At A the auricular systole *c* is followed by the ventricular systole *c'* and by the pulse *c''*, and the systole *d* would be followed by a similar cycle; but the ventricle contracts prematurely at *p* owing to some excessive irritability of its muscle. This contraction is too weak to expel much blood into the aorta, and the ventricle contains little blood at the time, but it is sufficient to exhaust the ventricle, so that it is unable to respond to the impulse corresponding to *d*, and there is therefore an intermission, the ventricle remaining quiescent until it is aroused by the impulse causing *e* descends from the auricle. At B a process in many respects similar occurs; but here the premature ventricular systole (*s'*) is not due to the excessive irritability of the ventricle, but to an impulse descending from the auricle, in which it has caused a premature systole (*s*). The result is similar, in that the amount of blood expelled by the ventricular systole is too small to cause an arterial pulse. Thus, the form of intermission due to a premature contraction may again be subdivided into two classes: (1) excessive irritability of the ventricle (ventricular intermission) or (2) excessive activity of the rhythmical area (auricular intermission); and the two forms may be distinguished by the length of the intermission in the sphygmographic tracing, the ventricular being exactly twice the ordinary pulse interval, the auricular being shorter. This conclusion may be arrived at by a consideration of the known facts regarding the physiology of the heart, and is confirmed by experiments on animals, in which a premature contraction is elicited by electrical or mechanical irritation of the ventricle or auricle.

Those forms of intermission in which the cause is not the failure of the heart to contract, but rather a premature contraction, may be called false intermissions to distinguish them from the first class, and may be diagnosed from true intermissions by several methods. In the first place the sphygmographic tracing often shows a slight elevation during the apparent intermission. Very often one such intermission occurs among a number of others, or there may be an elevation during each intermission (Fig. 5). But a simpler means

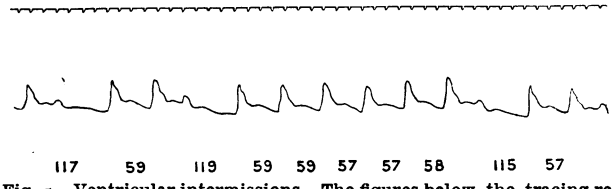

Fig. 5.—Ventricular intermissions. The figures below the tracing represent the length of each interval in one-hundredths of a second. During each intermission there is a distinct elevation, so that the irregularity is due to excessive irritability of the ventricle causing a premature systole.

of diagnosis is offered in the stethoscope, for in the true intermission there is no heart sound in the interval, while in the false intermission there is a dull muffled first sound corresponding to the premature contraction, and following immediately after the last normal systole. It often obscures the second sound of the heart, and may itself be followed by a weak second sound. It seems likely that some cases which have been described as instances of dissonance between the systoles of the two ventricles are really to be explained as examples of a normal beat followed very soon by a premature contraction of the ventricle.

Intermissions of the pulse may thus be divided into several classes, which can be diagnosed from each other tolerably readily:

1. True ventricular intermissions in which the pause is exactly equal to two pulse intervals, and during which there is no cardiac sound.

2. True auricular intermissions in which the pause is shorter than two pulse intervals, and during which there is no cardiac sound. This form is not infrequently seen in healthy persons, and these appear to be due to excessive inhibition, for it disappears on treatment with atropine which paralyses the inhibitory nerves. In other cases it may be due to auricular disease.

3. False ventricular intermissions, in which the pause is equal to two pulse intervals, but is often interrupted by a slight elevation. In every case a first heart sound can be heard during the intermission. This form appears to be caused by excessive irritability of the ventricle leading to a premature systole.

4. False auricular intermissions, in which the pause is shorter than two pulse intervals. There is often a slight elevation of the pulse during the intermission, and the stethoscope reveals a systolic sound very soon after the last regular pulse elevation.

5. Another form of intermission has been described by Wenckebach,[2] who attributes it to imperfect conduction of the impulse through the heart, perhaps especially in the auriculo-ventricular connecting fibres. It appears to be rarer than the other forms, though Wenckebach has had several cases in which it appeared. I have not yet had an opportunity of analysing a pulse of this form, and shall not enter on it. It often leads to allorhythmia, or intermissions recurring at regular intervals, but is not the only cause of this phenomenon,

for very often false ventricular or false auricular intermissions occur every fourth, fifth, or sixth contraction with unfailing certainty.

As regards the prognosis of these different forms of intermission, my experience is still too limited to admit of generalisations. The true auricular intermission seems to be of little significance when it arises from excessive inhibitory action, and is then merely an exaggeration of a physiological phenomenon.

The treatment of cardiac disease accompanied by intermissions may be rendered more exact by the careful examination of the pulse, for this may indicate whether the condition of the heart is one of excessive irritability or of deficient activity. When the intermission is of the true variety, some drug such as caffeine or digitalis appears to be indicated in order to increase the activity of the heart, while if the intermission is due to excessive irritability some sedative acting on the inhibitory mechanism might be suggested, such as aconite. But further experience is required before any definite statement can be made, though it would seem to be justifiable to demand a more careful examination of the heart than is generally performed before treatment is carried out.

REFERENCES.
[1] *Zeit. f. klin. Med*, xxxvi. [2] *Ibid.*, xxxvii, xxxix.

HEADACHES AND OTHER NERVOUS SYMPTOMS IN RELATION TO POST-NASAL ADENOIDS.

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HEADACHE, mental dulness, bad memory, languor, lassitude, defective nutrition, and stunted growth are some of the results of post-nasal vegetations. They are commonly held to be due to an imperfect aëration of the blood—that is, a deficiency of oxygen, an excess of carbonic acid, and the presence of organic impurities which should have been removed by the normal interchange in the lungs, the imperfect aëration being the consequence of an insufficient supply of air, and the insufficiency the outcome of the encroachment of the adenoids upon the respiratory channel. It is admitted that during waking hours the supply is sufficient, buccal respiration being then available and ample; but it is alleged that the supply is insufficient during sleep, that "in the vast majority of cases the air enters the lungs almost entirely through the nose during sleep, however great may be the difficulties, and though the mouth be kept wide open." The absence of buccal respiration with a widely-open mouth is ascribed to "a very overpowering instinct in favour of breathing through the nose, which during sleep, when the will power is suspended, strongly asserts itself." Mr. Parker, from whom I have been quoting, does not tell us of the condition, open or closed, of the mouth air channel, which might be mechanically obstructed—for example, by contact or proximity of the tongue and palate, the result of gravity and the suction of inspiration combined—even though the mouth was wide open. It is to be hoped that further investigation may enable our authors to drop the mysterious, to dispense with "a very overpowering instinct," and to give a simple explanation.

Whilst admitting that imperfectly aërated blood would give rise to various groups of symptoms, I submit that the idea that imperfect aëration is the cause—the only cause—of the symptoms is not warranted, for several reasons. First, the symptoms exist in cases (and these not few in number) where the growths are too small to give rise to respiratory insufficiency. Secondly, some of the symptoms are immediately cured or relieved by operation—a fact which is not explicable by the aëration theory. Thirdly, another explanation—complete or partial and applicable to all cases, to those with and to those without respiratory obstruction—is available.

There are some points to be kept in view when dealing with questions relating to adenoids. (*a*) That adenoids are only an accentuation of the normal condition, namely, of the lymphoid tissue composing the pharyngeal tonsil, and that the hypertrophic condition is not regarded as growths and requiring treatment until it has attained such dimensions as to cause derangement of some of the physiological functions. (*b*) That between the minimal quantity causing derangement and the maximum found, a quantity almost sufficient to fill the naso-pharynx, there is a very wide range, which doubtless finds its counterpart in the varying symptoms of the patients. (*c*) That the degree of obstruction depends upon the relation which the capacity of the post-nasal space bears to the size of the adenoids; that the capacity of the space varies with the individual, and in the individual with the age; and that the bulk of the adenoids not only varies with the age, but is subject to considerable fluctuation of a more or less temporary character from the various circumstances which lead to congestion. (*d*) That adenoids imply a diminution of the post-nasal space, but not necessarily such a diminution as to prevent the requisite quantity of air from reaching the lungs when the demands of the economy are at their lowest point, namely, during sleep. There are, therefore, two classes of cases—those in which the obstruction is so great as to lead to an insufficiency of air during sleep, and those in which it is not. In the latter, imperfect aëration could not be the cause of the symptoms; in the former, it is operative, but, as will presently appear, it is not the cause but only one factor.

What explanation can be offered in lieu or in aid of the insufficient doctrine of imperfect aëration? The condition of the tissues in the naso-pharynx and the nasal fossæ, with the consequent obstruction to the vascular and lymphatic circulation and pressure upon nerves, appears to me to be an important factor in the production of the headache and the allied symptoms. I have been led to this view by the following considerations: First, one of the immediate results of operation is the cure or relief of headache and some of the other symptoms. I have operated in a large number of cases without anæsthetics, and have found (*a*) that patients who had headache at the commencement of the operation were free from it within a few minutes after completion of the manipulation; (*b*) that where cerebral troubles were not complained of or were even denied, patients have immediately after operation, and sometimes spontaneously, spoken of the great relief they experienced, "as if a weight had been taken off the forehead," "as if a cloud had been lifted from the forehead," "feeling brighter," "feeling lighter," "feeling quite different." Whatever may have been the cause of the symptoms thus relieved instantaneously, one thing is clear, it was not imperfect aëration of the blood. Secondly, the removal of adenoids is, as a rule, attended by profuse hæmorrhage. Thirdly, headaches are often relieved or cured by epistaxis or by derivative treatment. Fourthly, the anatomical relations of the pathological area with the intracranial contents are so intimate that we could not expect the latter to be unaffected by the long-continued morbid condition of the former. The adenoids are situate on the posterior wall and roof of the naso-pharynx; their site is the seat of marked vascularity, and often of catarrh. Very frequently the nasal fossæ are likewise the seat of catarrh, and probably in all or the vast majority of cases there is more or less hyperæmia. The frontal sinus, the ethmoidal cells, and the sphenoidal sinus are so closely associated with the nasal fossæ and the naso-pharynx as also to suffer to some extent, probably from hyperæmia. The area thus involved extends from the posterior wall of the pharynx to the anterior boundary of the nostrils, comprising a series of cavities separated from the cranial contents by a very thin layer of bone. Fifthly, headache is a symptom of acute nasal catarrh and also of evanescent attacks of nasal congestion, but it is not caused by imperfect aëration of the blood. The conditions present in post-nasal adenoids are somewhat similar—vascular engorgement, tumefaction of the soft tissues, and pressure on nerves—and though from their long continuance they may be less resented by the economy, still their results should be analogous, that is, headache, etc. Sixthly, with headache resulting from nasal catarrh or nasal congestion there is a feeling of weight or oppression in the region of the forehead, an inability or disinclination for mental work or physical exercise, and a general depression of the vital functions. These concomitants of headache we find, as we might expect, in cases of adenoids, and their continuance, not for days or weeks or months only, but for years, affords a simple explanation of the baneful influence of adenoids on the economy as portrayed in the group of symptoms under consideration. Seventhly, the symptoms vary in degree, and the fluctuation

is explicable by the condition of engorgement, whether it be dependent upon the position of the body (recumbent or erect), climatic changes, or other accidental circumstances.

Normal nutrition requires that the nutrient fluid shall be (*a*) of good quality, and (*b*) normally circulated through the tissues. The advocates of the aëration theory have confined their attention to the quality of the fluid, and have ignored the question of circulation, although in the subject under consideration, a disorder in the circulatory mechanism, plays by far the more important *rôle*. Bearing in mind the relationship which has been established between the teeth, the eye, and the nose, on the one hand, and headache on the other, we recognise that our subject raises the question, Does reflex action play any, and if so what, part in the causation of the symptoms in question?

THE DIASTOLIC EXPANSION MOVEMENT OF THE VENTRICLES AS A FACTOR IN COMPENSATION FOR DISEASE OF THE MITRAL VALVE.*

By T. STACEY WILSON, M.D.Edin., M.R.C.P.,
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MY object in this paper is to bring forward evidence in favour of the heart having the power of enlarging its chambers by means of a true muscular expansion movement. The possession of this power would constitute the heart a double acting pump, instead of its having the power of single action only with which accepted theories credit it. It would then be able to fill itself by its own counterstroke, just as is the case with most of the pumps which the art of man has devised. The possession of such a power would mean that the heart is a much more perfect mechanism than if it had to depend upon some extraneous mechanism for the filling of its ventricles, as the ordinarily accepted theory asserts.

This view—that the ventricles of the heart possess the power of aspiration in virtue of a true vital expansion of its muscular fibres—was first definitely propounded by Dr. Lockhart Gibson, when assistant to the late Professor Rutherford, some sixteen years ago.[1] He pointed out that in the case of ordinary striated muscular fibre the phase of contraction, which results from a minimal stimulation of the muscle, is followed by a phase of sudden expansion, during which the muscle develops about one-fifth of the force it develops during contraction, but in, of course, the reverse direction. The possession of such an expansile power by the individual muscular fibres of the heart would cause a sudden and moderately powerful enlargement of the ventricles at the commencement of the diastole.

PHYSIOLOGICAL EVIDENCE AS TO THE NATURE OF THE EXPANSION MOVEMENT OF THE VENTRICLES.

So far as I have been able to ascertain, there is but little experimental evidence that the expansion of the ventricles is due to a muscular movement in addition to simple elastic resiliency. We know, however, that the muscular fibre of the ventricles remains active for an appreciable time after the closure of the semilunar valves, and does not at once enter upon its phase of relaxation. The most striking physiological evidence of the possession of such a power which I have been able to find is afforded by some experiments made by Stephani and quoted by Tigerstedt.[2] He found that section of the vagus nerve diminished the force of the heart's recoil after contraction. Where the vagus was divided, less force was required to prevent the diastolic enlargement of the heart than was necessary before section of the vagus.

The confirmation of this observation would seem to prove that the expansion of the heart is, in part at all events, a muscular movement under nervous control, and not simply a mechanical phenomena due to elasticity only.

CLINICAL EVIDENCE OF THE NATURE OF THE EXPANSION MOVEMENT IN THE NORMAL HEART.

Clinically we have little opportunity of studying the changes in volume which the heart undergoes during its phases of contraction and expansion. Were instantaneous radiography of the heart possible we should have an excellent means.

Our chief source of information is the cardiograph. There are difficulties and fallacies connected with the use of the cardiograph of which we must take account. Of these the interpretation of the cardiogram is perhaps the most important. This I have in large measure overcome by the simultaneous record of the cardiac sounds upon the cardiogram. This can be done by means of an electric time-marker, which makes an audible click as it rises and falls. It is quite easy in most cases to synchronise the clicks of the electric signal with the heart sounds, and thus to distinguish between the systolic and the diastolic portion of the cardiogram.

In the course of the last nine years, since I first used this method, I have had ample evidence of its reliability; and, further, I think I can claim that the beautiful researches of M. A. Chauveau upon the movement of the cardiac valves in relation to the intracardial pressure curves and the cardiogram,[3] fully confirm the interpretation of the cardiograms which I am about to give.

In using the cardiograph for the study of the expansion movement of the heart we must remember the limited area over which we can take tracings, and give due allowance for the changes in form which may occur apart from alterations in the volume of the heart.

EVIDENCE OBTAINED FROM THE STUDY OF THE HEART IN VALVULAR DISEASE.

When considering the process of compensation for incompetence or stenosis of the mitral valve, the possession of such a muscular power as we are discussing would be of very great service to the heart. In the case of mitral incompetence the occurrence of hypertrophy and dilatation would increase the aspiratory power equally with the expulsive power. If this were so we would expect in a case of compensated mitral regurgitation that there would be little, if any, backward pressure on the lungs or right side of the heart, and that the left auricle would have no more than a normal amount of work to do.

PATHOLOGICAL EVIDENCE.

In the only cases of mitral regurgitation with unbroken compensation which I have been able to examine *post mortem* there was evidently much regurgitation, and the left ventricle was much dilated, but the left auricle was of almost normal size, suggesting that the hypertrophy and dilatation called forth by the failure in expelling power was fully sufficient for compensation so far as aspiration also was concerned.

In the first of the cases the left ventricle held 165 c.cm. as against the normal 80 c.cm., while the left auricle held the normal 90 c.cm. In the other case the left ventricle held 235 c.cm. as against the normal 80 c.cm.; the left auricle only held 115 c.cm. Considering that it is quite usual for the left auricle to be dilated to the extent of 120 c.cm. in patients dying of pneumonia and other diseases without definite cardiac disease, these figures are remarkable, and cannot, so far as I can see, be explained by the ordinarily accepted theory of compensation in mitral regurgitation. They are, I consider, strong evidence in favour of what I may call the "*vis a fronte*" theory of compensation, namely, that the ventricle by increase in its aspiratory power compensates for the incompetence of the mitral valve, and that so long as compensation remains unbroken the left auricle and right side of the heart have very little extra strain put upon them.

In comparison with the above figures those of another case (Case IV) are striking. Here compensation had failed, and while the left ventricle only held 200 c.cm. as compared with the 235 above mentioned, the left auricle held 250 c.cm. as against the 115 where compensation was good. In such a case there was undoubtedly extra strain on the left auricle and right ventricle.

CARDIOGRAPHIC EVIDENCE IN MITRAL REGURGITATION.

In mitral regurgitation we have cardiographic evidence of increased diastolic expansion of the ventricles. I show some tracings taken from cases of mitral incompetence, and side by side with them some from normal hearts. The time of occurrence of the heart sounds is marked on some of them. In tracings taken over the apex beat the tilt of the heart's apex

* In part taken from a thesis (Gold Medal) for the degree of M.D. at the University of Edinburgh, 1892.

hides any movement due to change in volume, because, as has long been known, the apex remains pressed against the chest wall for an appreciable time after the closure of the semilunar valves. In tracings taken over the ventricle internal to the apex, the diminution in the size of the ventricle during systole causes the heart to recede from the chest wall, and we have more or less of a systolic depression in the cardiogram (*vide* Plate I, Case 1, Fig. 3. In such a situation the enlargement of the heart after the systole may also be expected to show as a rise in the cardiogram if sufficiently powerful. In taking my tracings I used a pressure of about $\frac{1}{4}$ lb. in the spring of my cardiograph, and therefore any elevation seen in the tracings I show implies that the heart wall was able to overcome a resistance of at least $\frac{1}{4}$ lb. in causing the elevation of the lever.

I show some tracings from a normal heart where there is some evidence of sudden enlargement at the time of the closure of the semilunar valves (Plate I, Normal heart Fig. 2).

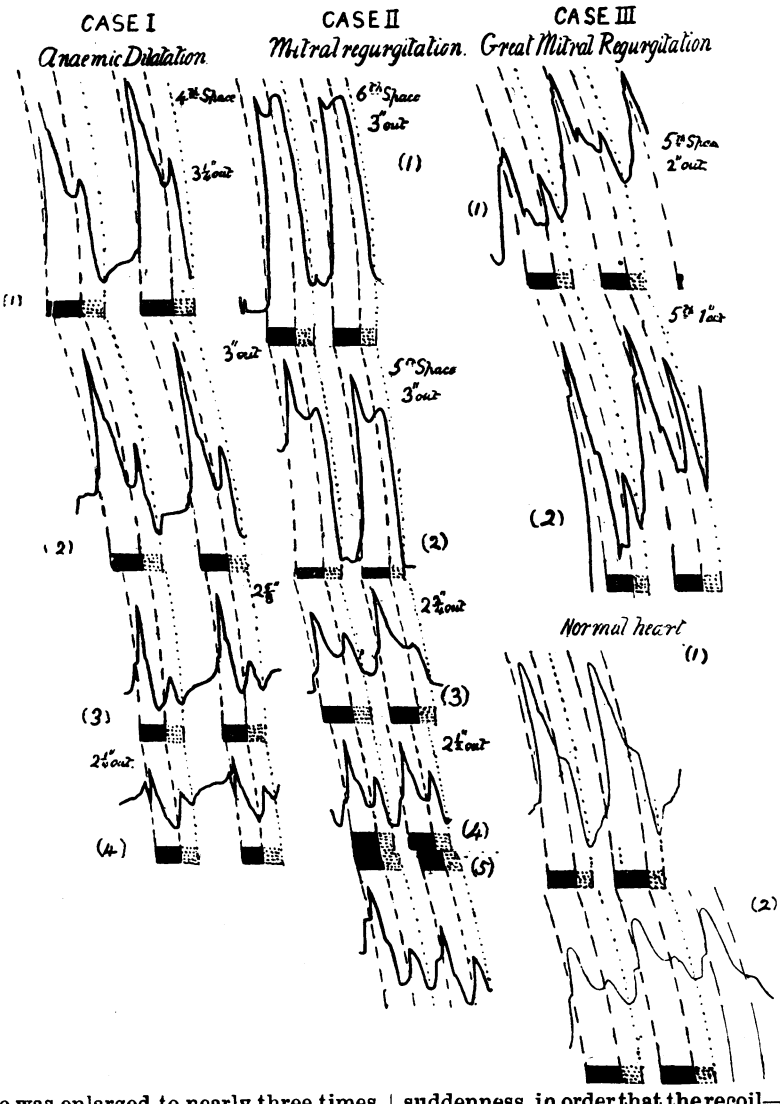
I also show some tracings taken over the right ventricle in a case of anæmic dilatation. They show how very well the sudden enlargement of the ventricle after the systole (Plate I, Case 1, Figs. 2, 3). The fact of the lever of the cardiograph rising so rapidly and powerfully is proof that the ventricular wall does not relax till after a certain amount of expansion has occurred, otherwise it would not have strength to lift the lever. I may say that this is quite an ordinary type of tracing. In comparison with these I show some tracings from a case of moderate mitral regurgitation. In this series the diastolic expansion wave is well marked (Case II).

In the next two series (Cases III and IV) there was very considerable regurgitation. In the first the systolic diminution in size of the ventricle is much more rapid than normal, as might be expected, and the diastolic expansion rise is proportionately more marked. In the next (Case IV) there was very extreme mitral regurgitation, the cavity of the left ventricle was enlarged to nearly three times its natural size, and its contents being 7 ounces (200 c.cm.) instead of the $2\frac{1}{2}$ ounces (90 c.cm.), the contents of the left auricle were 9 ounces (250 c.cm.). In this case the systolic diminution was so extreme and the diastolic expansion so great that the tracing is divided into two nearly equal halves by a deep notch.

CASE V.—Finally I show you some tracings taken over the right ventricle in a case of mitral regurgitation with extreme secondary tricuspid regurgitation. So extreme indeed was the regurgitation that a systolic thrill could be felt over the right auricle in the region of the right nipple. The tracings are extremely interesting, though complicated, and I have not time to go fully into them in this paper. I show you, however, a series from the outer part of the fifth left interspace.

I have proved the correctness of the interpretations given in the figures by means of many observations with the electric recorder of the heart sounds, and by the polygraph, and also by taking consecutive series of tracings $\frac{1}{8}$-inch apart over the available part of the heart. The diastolic expansion wave is here very high, and in tracings taken in the fifth interspace in the nipple line—the apex being in the axilla—this part of the tracing is far higher than the rest.

In Fig. 5 is shown a polygraph tracing taken with a Marey's drum cardiograph, with the heart sounds recorded on it. It shows that the closure of the semilunar valves occurs at the notch about halfway up the diastolic expansion rise. It is difficult to me to believe that these phenomena can be explained on the supposition of the expansion movement being simply a mechanical one due to the elastic recoil of the relaxing heart wall. There is far more and far stronger movement than could be explained except by a true muscular expansion movement.



CLINICAL EVIDENCE IN MITRAL STENOSIS.

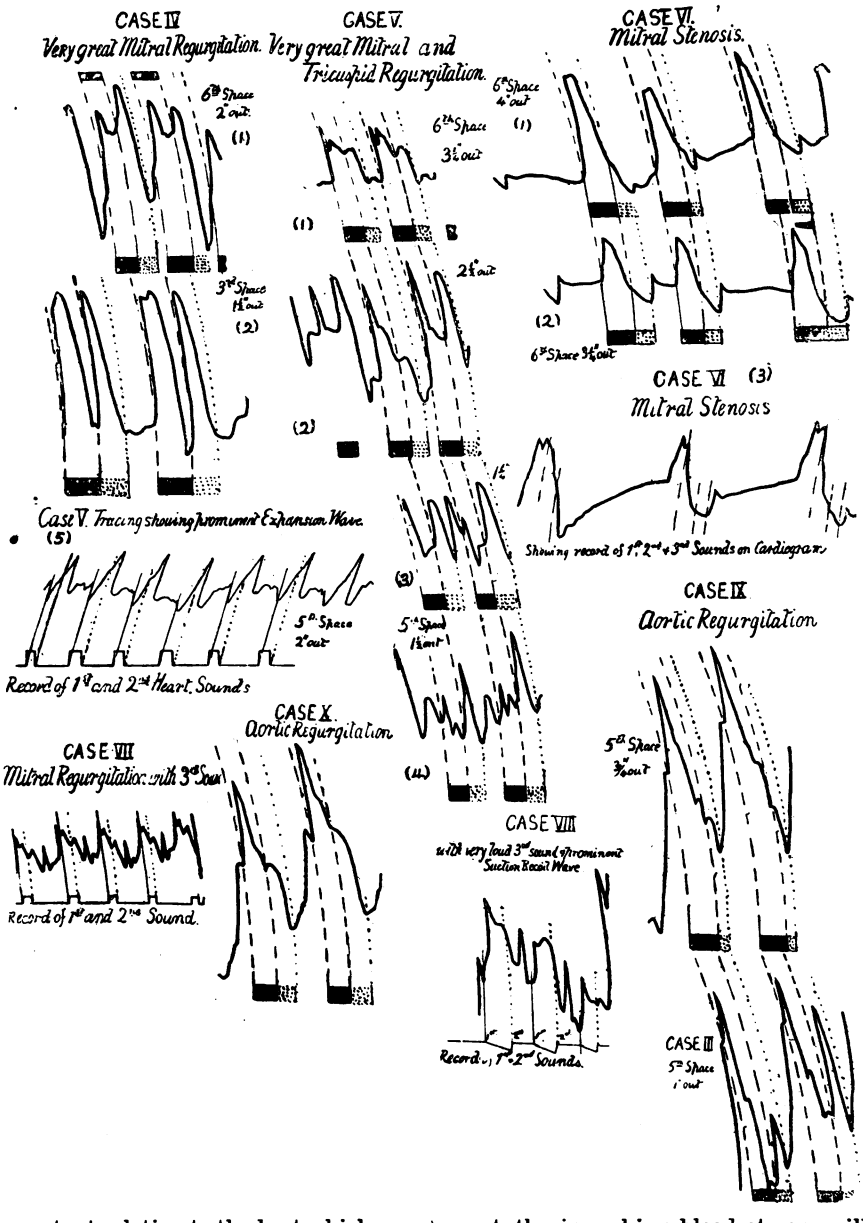
In mitral stenosis we have clinically various phenomena more or less indicative of increased diastolic activity on the part of the ventricles. In the first place there is sometimes *post-mortem* evidence that the left ventricle has increased work to do. Its wall sometimes seems to be slightly thicker than normal. Secondly, the first sound of the heart is louder than normal in mitral stenosis. Now the ventricle has, if anything, a diminished amount of work to do so far as its direct or forward work is concerned, owing to the hindrance to the filling of the ventricle, and we ought therefore to expect that the first sound would not be louder than normal. Thirdly, the first sound ends more sharply than normal.

The explanation of these facts is, I believe, that the ventricle alters its beat. It contracts with greater force and suddenness, in order that the recoil—both elastic and muscular—may be as great as possible, thus developing the maximum amount of aspiration. In this way the ventricle by its altered beat is able to compensate for the valvular disability, without there being any permanent need for increased action of the right heart. Every practitioner must know many cases of mitral stenosis which are fully compensated, and where there is no evidence at all of any increased blood pressure in the lungs. According to the ordinary accepted *vis a tergo* theory of compensation there must be increased pulmonary blood pressure in all cases of stenosis. According to the *vis a fronte* theory this is not necessary, and the clinical acts seem to me more in favour of the latter than the former.

I shall deal with the other clinical evidence of increased aspiratory action after dealing with the cardiographic evidence.

CARDIOGRAPHIC EVIDENCE IN MITRAL STENOSIS.

Owing to the ventricle filling more slowly than normal we expect the expansion wave to be less marked than normal, and we shall not expect it to show in the cardiographic tracings. This is so (*vide* Case VI, Figs. 1, 2, and 3.) Although the expansion movement itself does not show in the tracing we very often have an accessory wave which gives us very important evidence as to the presence of a powerful aspiratory action. I refer to a small sharp wave which occurs just after the diastolic expansion movement has ceased, namely, immediately after relaxation of the cardiac muscle has occurred. This wave is best seen at and near the apex (*vide* Cases VII and VIII) but is sometimes evident over a considerable part of the heart. The cause of this wave is, I believe, as follows: At the commencement of diastole the left auricle is naturally considerably distended with blood, and the ventricular aspiration causes it to rush into the ventricle with considerable force. Owing to the narrowness of the mitral orifice it enters more slowly than normal, and there is not time for all the blood to get through into the ventricle before the expansion movement ceases. When, therefore, relaxation commences there is still a strong stream of blood flowing into the ventricle. It is the impact of this stream upon the relaxed heart wall that causes the small rise referred to. (This wave is clearly not due to the auricle, because when the heart is irregular this wave maintains a constant relation to the beat which precedes it, while its distance from the following beat is variable.)



SUCTION RECOIL WAVE.

If this theory be correct we ought to see this wave (which I call the suction recoil wave) whenever the auricle is not able to discharge the bulk of its contents into the ventricle before the onset of relaxation. I show a tracing (Case VII) from a case where there was considerable mitral regurgitation with no stenosis, but where the ventricle could not dilate to its proper amount in consequence of pericardial adhesions. The cubic content of the left ventricle was 90 c.cm., and that of the left auricle 164 c.cm. In this case the suction recoil wave was most marked.

This suction recoil wave is closely associated with a diastolic cardiac sound which is, I believe, due like it to the aspiratory power of the ventricle. I refer to the so-called reduplicated second sound which is heard at the apex in mitral stenosis. This sound has no right to be called a second sound. It can easily be demonstrated that it is neither the aortic nor the pulmonary second sound. With a differential stethoscope it is frequently easy to hear all three sounds. This sound ought to have a name of its own, and I have christened it the third sound of the heart and called it so for many years. It has been described by some authors as the sound of the mitral opening. This is, I believe, not quite correct, for it is produced shortly after the opening of the mitral valve. I have in many instances recorded the time of occurrence of this sound on the cardiogram, and I find that it coincides exactly with the commencement of the suction recoil wave just spoken of. I believe that this sound is caused by the inrush of blood into the ventricle at the commencement of diastole as was suggested by Dr. Sansom twenty years ago,[4] and the exact mechanism of its production I believe to be as follows:

During the phase of diastolic expansion the auriculo-ventricular valve is kept more or less rigid by the rigidity of the heart muscles. As soon, however, as relaxation sets in the valve is free to move, and if the auricle has not already been emptied by the aspiration during the expansion movement, the in-rushing blood stream will flap the valve back against the ventricle wall in a manner calculated to produce the faint sound we are speaking of.

MITRAL DIASTOLIC MURMUR.

I now come to the last of the physical signs in mitral stenosis of which I wish to speak, viz., the mitral diastolic murmur. By this murmur I mean the one sometimes called post-diastolic, because of its occurring after the second sound, not with it as in the case of the aortic diastolic murmur. This

murmur is also sometimes, I believe, called a mid-diastolic murmur. It begins loudly and then fades away, although sometimes prolonged through the diastole. Its time relation to the second sound is constant, but its relation to the first is not constant, the reverse being true of the presystolic. This murmur is now, I believe, very generally recognised as being a suction murmur and due to ventricular aspiration, and the fact that it is very often strong enough to give rise to a palpable thrill is evidence as to the force of the aspiration.

On studying the relation of this murmur to the "third sound" of the heart it is evident that the two are closely related. The murmur occurs at the same interval of time after the second sound that the third sound does, and in cases where the third sound is audible a slight alteration in the rate or strength of the heart will frequently transform the third sound into the diastolic murmur and *vice versâ*. The diastolic murmur may accompany or replace the third sound. It never accompanies the true second sound. Also on recording the time of this murmur on the cardiogram it is found to coincide with the suction recoil wave just as the third sound does. The explanation given for the third cardiac sound holds true, I think, for this murmur. The valve segments are not free to vibrate in the blood stream till after the muscular relaxation has set in.

CARDIOGRAM IN AORTIC REGURGITATION.

The last point to which I wish to draw attention in this paper is the evidence given by the cardiogram in aortic regurgitation. If the diastolic expansion movement were purely a mechanical one it ought to be evident in aortic regurgitation as it is in mitral regurgitation. The cardiogram shows that this is not so. A marked feature of all the tracings I have taken in aortic regurgitation is the absence of the diastolic expansion wave. The tracings shown under Case IX, Fig. 1, and Case X, illustrate this point, and show the absence of the expansion wave.

In giving these tracings as typical of the cardiogram in aortic regurgitation I ought to add that my generalisation as to aortic disease is only based upon the cardiographic study of some 8 or 10 cases. There was, however, sufficient similarity in the tracings obtained to make it admissible to generalise from so few a number. The reason for this type of tracing is evident, for in aortic regurgitation increase of ventricular aspiration would only increase the amount of leakage. The heart, therefore, alters its beat so as to produce the minimum of diastolic expansion.

The tracings in aortic regurgitation therefore give us most important evidence that the expansion movement is one under nervous control and not a simple mechanical one.

In bringing this paper to a conclusion, I am conscious that much of it is theory, and therefore may be erroneous. But as a result of many years careful observation and research I have been unable to obtain any evidence except such as seems to point strongly in favour of the expansion of the ventricles being in large measure due to a true muscular movement.

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THE ORIGIN OF GOUT.

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THE discovery of the presence of uric acid in the blood of patients suffering from an attack of acute gout led to the formation of the theory that the symptoms which make up the disease we know as gout are caused by this presence of uric acid. This theory has led most investigation into the cause of gout into a series of inquiries as to the various ways in which uric acid can be formed in the system, ingenious in themselves, but giving no definite results as to the cause of gout, or much practical information as far as the treatment of the disease is concerned.

The object of this paper is to show that the symptoms of gout are not due to the presence of uric acid in the blood, also to suggest another explanation both for the symptoms of gout and for the formation of uric acid in this disease.

When the fact that uric acid was present in the blood in gout was first discovered, it was naturally supposed that the symptoms of this disease were due to the presence of this body, especially so, as when gout becomes chronic it is so often accompanied by the formation of deposits, either of sodium urate in various parts of the body, or uric acid deposits in the kidneys and bladder. A natural corollary of this proposition would be that if a certain proportion of uric acid in the blood was the cause of gout, then gout would be caused whenever this proportion of uric acid was present in the blood, yet we know that this is not the case. In leucocythæmia, for instance, the blood contains a large quantity of uric acid for a long-continued time, and no symptoms of gout arise, the same occurs occasionally in cases of malnutrition in children, yet no symptoms that we can put down to gout occur, although the excretion of uric acid may be sufficient to form uric acid calculi. It is said that gout does not arise in these cases because there is free elimination; there may be free elimination of uric acid, but still there is a higher percentage of uric acid in the blood in some of the cases, and for a longer time than there is in gout, yet no symptoms of gout arise; elimination can make no difference, unless it diminishes the percentage of uric acid in the blood, neither can it if the formation of uric acid still goes on; in short, elimination can do no good unless it diminishes the amount of uric acid in the blood.

Taking the various symptoms of gout, I think it can confidently be said that, with the exception of the presence of uric acid deposits, there are none of them which can be ascribed to the action of uric acid on the organism.

Take one of the commonest—headache. There is no positive evidence that uric acid will produce headache; there is plenty of negative evidence that it will not. In most of the diseases other than gout in which uric acid is found in the blood, headache is absent. The same can be said for almost every symptom of gout. Uric acid is said to be the cause of the headache, the digestive troubles, the lassitude, the high tension pulse, the acute joint troubles, the heart failure, etc., because it happens to be in the blood to be a symptom of gout, not because there is any positive evidence that it can produce any of these symptoms; on the contrary, all these symptoms are conspicuously absent in many diseases in which uric acid is found in the blood in large quantities.

Taking, again, a typical case of acute gout—inflammation of the metatarsal joint of the great toe—it is very difficult to conceive how the presence of uric acid in the blood could cause such inflammation, or, if it does do so, why should it not do so in cases such as I have mentioned before—namely, leucocythæmia and malnutrition in children? The supposition is that uric acid is deposited in gout in this joint for two reasons: one that the joint is one much used and far from the centre of the circulation; the other that the presence of uric acid in the blood leads to a deposition of uric-acid crystals in the delicate tissues of the joint. This attack frequently occurs in people in vigorous health with good circulation. If due to deposition of uric acid from the blood, then such deposition would be more likely to occur in diseases such as I have mentioned above, in which a high percentage of uric acid is present in the blood. and in which the circulation is slow and feeble, which would much assist such a process.

The constitutional disturbance also in a case of acute gout is out of all proportion to the region injured. The explanation given by the holders of the theory that uric acid is the cause of the symptoms of acute articular gout is that a sudden deposition of crystals of sodium biurate occurs in the synovial fluid and delicate tissues of the joints, thus causing the extreme pain and other symptoms of acute articular gout, and that no such constitutional disturbance occurs in the interval between the attacks, because, the deposition of urates being gradual, the tissues become used to them; yet we have frequent acute attacks in the same joint with slow deposition between them.

It is, too, against the usual laws of Nature that, if an irritant foreign body remains in any organ, the symptoms should quickly subside while the irritant actually increases, for after each attack, and during the intervals between the attacks, the deposits of such biurate enlarge.

It is, I think, much more probable that the deposition of sodium biurate which occurs in these cases is secondary to the attack; that inflammation precedes deposition of urates. The

deposition of urates found in the synovial membrane and structures beneath it are shown to be deposited from the synovial fluid. Assuming for a moment that the inflammatory process is not due to the uric acid in the blood, we have a joint rapidly and acutely inflamed quickly distended with synovial fluid rich in sodium quadriurate; as the disease progressed for some days the sodium quadriurate would become converted into sodium biurate, the synovial fluid would also decrease from absorption, the less soluble biurate would be deposited in the tissues surrounding the synovial membrane, especially the edges of cartilaginous structures in which the circulation is most sluggish. The conversion of sodium quadriurate, in which form uric acid exists in the blood, to sodium biurate, the salt of uric acid which forms the deposits in the joints, may take a long time—up to two or three days. The deposition first occurs in that part of cartilage or other structures of the joint immediately under the synovial membrane. At the commencement of an attack the synovial membrane is excreting a fluid rich in sodium quadriurate; after an attack has gone on a for a few days it is absorbing a fluid in which the sodium quadriurate is being converted into sodium biurate, in which process is the deposition of sodium biurate most likely to occur? Obviously during the absorption. Although the presence of uric acid in the blood in cases of gout is undoubted, there is no evidence that an attack of acute gout is preceded by a sudden increase in the amount of uric acid present. The evidence of the latest observers on this point is that uric acid is not increased during the attack. It is difficult to find out whether the amount of uric acid in the blood is actually increased during, say, an attack of acute articular gout, as the attack coming on rapidly there is not often an opportunity for procuring a specimen of blood some days before an attack. The value of the symptom of the presence of uric acid in the blood during the attack, would depend on the comparison with the amount present during the attack, contrasted with the amount present some days previous to the appearance of acute symptoms. As I have said above, the latest observations on this point go to show that there is no such increase.

When one comes to think of the various symptoms that constitute gout, symptoms affecting almost every organ of the body, one must conclude that the cause of gout is some morbid constituent of the blood, even if it is not due to uric acid. The chemical constituents of the blood are so well known that any of the known contents are unlikely to be the cause.

It must also be granted that whatever be the cause of gout, it must be produced in the digestive tract. The one common symptom of all cases of gout is digestive disturbance. Gout is one of the charges we pay for the luxuries of civilisation. In an uncivilised community in which presumably the digestive secretions are normal, no diet, not even a purely proteid one, will produce gout. On the other hand, once the digestion becomes deranged, almost any diet will cause this disease. It must cause it by some product of digestion, either absorbed from the digestive tract or produced by an alteration in the metabolism going on in some of the digestive organs. The only disturbance of metabolism that we know is produced in gout is the increased formation of uric acid, probably from the liver. As we have seen, it is extremely doubtful if uric acid has anything to do with the causation of gout. We are then forced to look further back as it were, for some cause. There must be some body formed in the intestinal canal capable both of causing the symptoms of gout, and also so altering the metabolism of the liver as to cause increased formation of uric acid. It is the fashion at the present time to put a great many diseases down to toxins, but I consider the symptoms of gout are those which are essentially toxic in character—the headache, the depression and irritability so frequently found, are the commonest toxic symptoms we know.

The symptoms are widespread, the nervous symptoms are well marked, and we have the grave symptoms of irregular gout which are, I think, undoubtedly due to a toxin acting mainly upon the nervous system. We know that many toxins have a distinct tendency to attack joints, the causes usually given for the selection of the metatarsal joint of the great toe for attack, namely, the distance from the centre of the circulation and consequent diminished resisting power, and the frequency with which the cartilage of this joint is found damaged would explain why the metatarsal joint should be attacked more than another. An attack from this cause would much more likely be attended with great pain and constitutional disturbance than that from the deposition of sodium urate, which is non-irritating when deposited in other regions of the body. I have already given my reasons for believing that the deposition of urates is secondary to the joint inflammation.

I consider a toxin to be the cause of this disease. If so, such toxin must be formed in the intestine. As the symptoms of gout are constant it must be a definite toxin, the product of a definite bacillus acting upon the intestinal secretion. As gout is capable of being induced in any subject it must be one of the bacilli normally found in the intestinal canal.

The toxin of a bacillus varies with its food. It has been shown that the normal intestinal bacilli can produce most virulent toxins when the character of the intestinal secretion is changed. The normal bacilli living in the intestinal canal produce toxins which have no pathological effects upon the organism owing to their being a normal constituent of the intestinal contents. If through long-continued intestinal derangement, such as a specific catarrh of the intestinal canal, helped by a hereditary tendency to change in the intestinal secretion, a condition would be formed in which normal bacilli present in the intestines would produce a definite toxin having a toxic effect on the organism.

The process, then, which I consider produces gout in a patient for the first time is as follows: Owing to continued digestive trouble, sometimes aggravated by a sudden change in the mode of life, a catarrhal change takes place in the intestinal canal often indicated by few symptoms. This gradually becomes sufficient to cause the formation of altered bacterial products, which have a toxic effect upon the organism. This tendency would be transmitted to his offspring, and by their starting life with it they would in all probability have gout earlier and in an aggravated form. My theory is a simple explanation of the cause of gout, and if accepted would indicate a definite line of treatment, would explain the sudden production of gout by an error in diet, and would explain the hereditary tendency of gout to appear unless checked by the most careful regulations of diet. It would explain, moreover, the tendency of gout to attack civilised communities; how the diet which checks gout is that which best approaches to simplicity; how that the empirical treatment of gout which we know to be most successful by experience is that which is most calculated to restore the intestinal canal to a normal condition.

The blood in gouty subjects always contains uric acid, but whether it increases in amount during the actual attack of acute gout is extremely doubtful; its presence is only a symptom of gout, and would be produced by the action of the toxin upon the liver changing the metabolism in that organ. That uric acid is produced in the liver is the most probable solution of the problems that attend the formation of that body. The balance of evidence, clinical and experimental, is against its formation in the kidneys.

The action of two drugs must always be taken into consideration when speculating upon the origin of gout—the action of colchicum in arresting its symptoms, and that of lead in inducing gout. How colchicum acts is unknown; its only definite action in moderate doses is on the intestinal canal, in which it increases the intestinal secretion. It may also cause some change in the constituents of this secretion. The first action of lead when taken in very small doses over a long-continued period is a gradual contraction of the intestinal blood vessels and a diminution in the intestinal secretion, which favours an attack of gout. The action of these two drugs would favour my theory. Certainly neither of them has any influence on the formation or elimination of uric acid.

The supreme test of any theory is its effects upon the treatment of the disease it is applied to. Although it is not within the scope of this article to enter into my treatment of gout I may venture to say that gout treated as due to a toxin produced by an altered intestinal secretion will give better results than if treated in any other manner. If my theory is correct gout cannot occur if the gastro-intestinal secretions are normal.

Therefore, the object of treatment in gout should be to shorten the digestive process as much as possible, especially gastric digestion; to select a diet which will be quickly

digested; to forbid alcohol during treatment; to try to obtain a normal condition of the intestinal canal—this can be done by careful attention for some months and will break that habit of an altered intestinal secretion, which I am convinced is the true cause of gout.

CONCLUSIONS.

1. Gout is not due to the presence of uric acid in the blood, (2) the symptoms of gout are due to a toxin, (3) the concurrent presence of uric acid is due to the action of the toxin on the liver, (4) the toxin is formed by the action of one of the intestinal bacilli on an intestinal secretion specifically altered by diet, this alteration being assisted by hereditary disposition.

Dr. SAMUEL BARTON said: Evidently some other factor besides excess of uric acid in the blood is necessary to explain acute attacks of arthritic gout. The ordinary everyday cases of lithiasis do not develop arthritic gout. Children who commonly get excess of uric acid do not get the arthritic disease. Excess of lithic acid is very common in Norfolk, while arthritic gout is comparatively rare. I agree that the extra factor is probably associated with dyspeptic troubles, and believe that arthritic gout is not now such a common disease as 20 years ago, owing to the fact that people are better educated as to how digestion is best carried out. As to treatment gastric disorder should be avoided by temperance in food and drink, a mixed diet should be enjoined, and the action of the eliminating organs should be encouraged.

Mrs. GARRETT ANDERSON thought it impossible to accept the toxic theory of gout. She could not understand how any toxin could appear again and again at very short intervals under certain conditions, which conditions could be readily reproduced at will by the patient. She believed gout to be a fault of metabolism, the elimination of waste materials being imperfect, and varying with the habits, mode of life, and age of the patient.

SUBCUTANEOUS SALINE INFUSIONS IN PNEUMONIA.

BY

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THE following cases may be worth recording in connection with the occasional use which has recently been made of this method in the treatment of pneumonia, and particularly in connection with the results published by Dr. Clement Penrose of Baltimore[1].

The various kinds of treatment which have been adopted from time to time have been repeatedly shown by statistics not to have modified materially the mortality from pneumonia. Most of the methods have not yielded better results than those obtained by careful nursing without drugs; whilst some have not even come up to the latter standard. This means that a certain proportion of cases recover independently of treatment, and that the percentage of fatal cases is not reduced by any form of treatment below a certain minimum which corresponds closely to that obtainable by proper nursing and the expectant plan, and that the effects of potent drugs is more obvious in the direction of danger than of relief.

Since the prognosis seems to depend chiefly upon the individual features of each case rather than upon the mode of treatment, cases may be classified early in the attack into two groups: (1) The cases likely to recover (pneumonia in children, in healthy young people and in temperate robust adults); (2) the cases almost certain to be fatal (double pneumonia in old age, in confirmed alcoholism, or complicating severe constitutional diseases); (3) the cases with uncertain and exceedingly anxious though not hopeless prognosis (severe pneumonia in unhealthy or debilitated subjects of all ages, but particularly after 30).

The first group does not lend itself to any profitable therapeutical investigation. The second is probably beyond the capabilities of any remedies likely to be available in the near future. But in the third group, if only the suitable remedy could be found, the balance might conceivably be turned in favour of recovery. It is in these cases, in which sometimes, judging from outward appearances, all seems at first to be serene, that a sudden change for the worse supervenes, often about the fourth day of the disease, perhaps owing to the liberation and the absorption of toxins.

The cases reported belong to this third group. The idea which guided their treatment was that since infusion has been found of service in cases of severe collapse and in cases of pneumonia at a late stage, it should be, *a fortiori*, yet more efficacious if administered at an early period, and might conceivably modify in a favourable way the course of the pathological changes. With that view the cases were submitted to treatment as early as possible in the attack. They were all hospital cases, selected because of their gravity. The injections in all of them were administered with strict antiseptic precautions by Dr. Beaumont Percival from a bottle such as is used for intravenous transfusion.

CASE I. *Post-influenzal Apical Pneumonia: Recovery.*—M. B., aged 37, a cook, had influenza commencing on April 3rd, accompanied by coryza and pains all over her body, took to her bed on April 6th, and was admitted into St. George's Hospital on April 9th. No rigor. She was well nourished, with flushed face, rather dusky lips, and some dyspnœa. Pulse 140 full, respirations 42, temperature 103°. Labial herpes present. There was a dull note behind over the whole of the right lung, chiefly marked at the apex. In front the right apex was also dull. On auscultation fine crepitations and tubular breathing were audible, in addition to coarser *râles*, bronchophony and whispering pectoriloquy were present. Saline infusions were carried out as follows: April 10th. A pint of normal saline solution of temperature 110° F., containing NaCl 3j to 1 pint of water, was infused under the skin in the right subclavicular region of the chest by means of a hypodermic needle at 6 P.M. Shortly after the infusion, which occupied an hour, she was reported to have been rather blue and dyspnœic, but this soon passed away. April 11th. She seemed much better, the cyanosis of face was less and respiration easier. The *râles* in the chest were much less noticeable. The infusion was repeated at 11 A.M. No ill results followed. A third infusion was given at 6 P.M. On April 12th a fourth infusion was given at 11 A.M. The patient seemed to be much improved, and the crepitations had almost entirely disappeared. The pulse was firmer, the temperature was falling, and on the next day the temperature fell to normal and remained so afterwards.

Local Effects of the Infusion.—There was absolutely no tenderness or swelling on the right side of the chest. The infusions had been given alternately on the right and on the left. In the second left interspace a small, round, smooth swelling developed, somewhat tender and hard, about the size of half a pigeon's egg. After persisting for several days this gradually disappeared. It was evidently a small hæmatoma caused by injury from the needle. She was discharged on May 2nd, with both lungs apparently normal. No other treatment was given except an expectorant mixture, purgatives, and small doses of brandy.

CASE II. *Pneumo-typhoid Fever in an Alcoholic Subject: Death: Necropsy.*—J. S., aged 21, a metal polisher, a well-nourished man, rather dusky-looking in the face, with laboured respiration, mouth and tongue dry and covered with sordes, was admitted on May 2nd. After an imperfect recovery from influenza he had felt too weak for work, and had vomited on April 28th; no rigor. Respirations 44, pulse 130, temperature 104°. There was no marked dulness on percussion. Numerous rhonchi were heard on both sides, but no tubular breathing. The abdomen was rather tumid, but moved well with respiration; no pain or tenderness. The spleen could not be felt. May 3rd. The diagnosis of early pneumonia having been made, he was infused at 7.30 P.M. with two pints of saline fluid, one in each subclavicular fossa. May 4th. Patient not so well, delirious, and has taken his milk, etc., badly. He was again infused with saline fluid (2 pints) at 6 P.M. May 5th. Patient is more cyanosed and delirious. Vomiting set in, and rectal feeding had to be resorted to. The rhonchi were now less abundant; but on the right at the lower part of the axilla and at the back from just below the angle of the scapula downwards there was dulness and loss of breath sounds; vocal fremitus was present, but there was no tubular breathing. May 6th. An infusion of 1 pint was administered with the addition of a fifth part of a 10 per cent. solution of hydrogen peroxide. The patient is still very heavy and drowsy. Numerous spots have appeared upon the abdomen and chest, most of them not characteristic of typhoid. May 7th. The patient is perhaps a little better, more sensible, and of better colour. At 1 P.M. upwards of a pint of oxygen gas was injected with due precautions under the skin of the left leg. Widal's reaction gave a negative result. May 8th. Patient much worse; is in a typical typhoid state with much cyanosis. He died in the night.

Necropsy.—Slight emphysematous swelling of the left leg, extending up to the thigh. On the front of the chest between the clavicles at the seat of the infusion with peroxide of hydrogen a small swelling was noticed. This contained a small cavity filled with a glairy greenish fluid showing under the microscope crystals of fatty acids. The pleuræ presented many petechiæ. The base of the left lung was congested; the right base intensely congested and almost entirely solid, with slight collapse. The solid lung did not float in water. Spleen enlarged, soft, and diffluent. The blood in the vessels was not coagulated. Swollen Peyer's patches in the lower ileum and cæcum were just beginning to ulcerate. These were obviously due to typhoid.

CASE III. *Pneumonia, Empyema, Subsequent Peritonitis, and Secondary Salpingitis.*—L. H., 14, dressmaker, a well-nourished girl with flushed face, complained of pain in the left side and cough; had not been well for several weeks, suffering from catarrh of nose, etc. On April 6th she had a rigor accompained by general pains, and was sent to the hospital. She had never menstruated. April 8th. On admission the pulse was 120, small, respirations 50, temperature 103°. The urine was acid of specific gravity

[1] *Johns Hopkins Hospital Bulletin*, July, 1893.

1025, and contained albumen. The chlorides were absent. On examination, at the left upper front there was marked skodaic resonance, and lower down dulness and loss of vocal fremitus and of breath sounds. Behind, the chest was dull as far up as the spine of the scapula, where œgophony was heard. The right lung was normal. The heart's apex was displaced slightly to the right. The abdomen appeared normal. April 9th. Ten ounces of straw-coloured fluid with shreds of lymph were withdrawn from the left side of the chest by aspiration. The fluid contained many diplococci, but no streptococci or staphylcocci were found. April 10th. Patient worse, with pain and some distension of the abdomen. There was also some diarrhœa, with offensive motions. April 11th. Diarrhœa continued and vomiting set in. She commenced to menstruate for the first time, nothing abnormal being noticed. April 12th. Condition much the same. At 6 P.M. a pint of saline fluid was infused. The abdomen was more distended. April 13th. Much worse; abdomen rigid and tympanitic; much pain, which was relieved by morphine. At 10 A.M. infusion of one pint of saline solution. At 3 P.M. the infusion was repeated with the addition of one-fifth part of a 10 per cent. solution of peroxide of hydrogen. The infusion seemed to give some relief to the breathing. April 14th. She became worse in the night, and vomited many times some fluid which was bilious but not fæculent. She died at 8 A.M.

Necropsy.—The posterior surface of the left lung was covered with a thick layer of yellow lymph. Between the lung and the diaphragm was a small localised empyema containing 6 ounces of pus. The lung was intensely congested and partly solid, but there was no grey hepatisation. The intestines were congested, and covered with flakes of purulent lymph. The Fallopian tubes were congested and contained pus. Uterus normal. Hymen intact. The case appeared to have been one of pneumonia and of secondary pneumococcal pleurisy and peritonitis.

CASE IV. *Double Pneumonia in an Alcoholic Subject: Death: Necropsy.*—J. G., 39, potman. At work up to June 2nd, when he had a rigor at 10 A.M., and went to bed; later in the day he got up and came to the hospital. He was a strong-looking man, with dusky face, and had marked dyspnœa. His lung signs were as follows: At the left posterior base, which was the part chiefly affected, there was dulness and nearly complete absence of breath sounds; fine *rdles* and pleuritic friction were heard in the axilla. No tubular breathing. In the right lung some *rdles* were audible over the base behind, and the resonance was impaired. Respirations 60, pulse 136, temperature 103°. The disease ran an acute course, with hyperpyrexia and sleeplessness, and at times delirium. June 4th. The first infusion (1 pint of normal saline solution) was given at 11 A.M., in the subclavicular region, and did not appear to be followed by any bad result; he seemed a little easier after it. He received a second infusion at 6 P.M., this time in the thigh instead of the chest, as it was thought that possibly the subcutaneous swelling caused by the infusion might hamper his breathing. June 5th. He had two more infusions morning and evening, both in the thigh. June 6th. He was again infused at 10 A.M. During the day he became more cyanosed, and had an attack of very severe diaphragmatic pain relieved by morphine. Death took place on the morning of June 7th. The other measures of treatment employed were mostly symptomatic; leeches to relieve the pain, cold sponging, and morphine.

Necropsy.—There was recent pleurisy with a thick pad of lympth over the lower lobe. Both lobes of the left lung were solid and the upper lobe in a state of grey hepatisation; some serous fluid could be squeezed from it, but no purulent fluid. The centre of the lower lobe was in a state of red hepatisation surrounded by a zone of crepitant emphysematous lung. Numerous petechiæ were scattered over the right lower lobe. At the apex and base of this lung one or two deep-seated patches of consolidation were in a state of hepatisation. The whole lung was much congested. The other organs appeared healthy. The marks of the punctures remained but no trace of inflammation or swelling could be found.

CASE V.—*Severe Double Pneumonia in an Alcoholic Subject: Death: Necropsy.*—H.S., 51, plateman at a club, was admitted into the hospital on May 6th. He had been in bed about a week. On admission he was in a very exhausted semi-typhoid condition, with dry tongue, low delirium, picking at the bed clothes, etc. A superficial examination only was possible. The base of the left lung seemed to be the part most affected with tubular breathing and dulness. Temperature 102° F., pulse 120, respirations 42. He was infused at 1 P.M. in the subclavicular region with a pint of normal saline solution with no definite effect. An injection of morphine was given to attempt to procure rest, but he rapidly became worse, more cyanosed, and in spite of stimulants and of an injection of strychnine, he died about 4 P.M. apparently of heart failure.

Necropsy.—There were a few old adhesions about the right base and general old adhesions with recent pleurisy and lympth over the affected area of the left lung, and the left pleural cavity contained about half a pint of serous fluid. In the left lung the entire lower lobe was consolidated and in a condition of ordinary red hepatisation. Here and there there were patches where the pneumonia appeared older and in a state of early grey hepatisation. The right base was congested, with patches of red hepatisation.

CASE VI. *Chronic Bronchitis, Granular Kidney, Acute Pneumonia, and Bronchitis: Death: Necropsy.*—G. O., aged 63, medical school porter, gave a history of chronic cough and expectoration through the previous winter. He had had swollen legs for the last three months. On April 5th he became very short of breath and took to his bed, where he stayed until April 10th, when he was admitted into the hospital. He was a well-nourished man, with a red face, not deeply cyanosed, but orthopnœic, with much wheezing and rapid breathing. Owing to the pulmonary emphysema there was very little expansion of the chest. *Râles* and rhonchi were heard all over the lungs. Respirations 42; pulse 104; temperature 101°. Urine 1019, acid, albuminous. He was treated with expectorants, stimulants, steam tent, etc. April 12th. Signs of pneumonia were found at the back of the right upper lobe, with tubular breathing and dulness. He was delirious at times. At he was becoming much worse and as it did not appear that he could survive many hours a pint of normal saline solution was infused in the infraclavicular region at 6 P.M. This was well borne, and perceptibly relieved his dyspnœa as he himself acknowledged. April 13th. The night was restless, with much delirium, but he seemed quieter and better this morning after another infusion given at 11 A.M. He was again infused at 6 P.M. April 14th. A fourth infusion was given this morning at 11 A.M. His breathing became worse in the afternoon and he became much cyanosed. At 2 P.M. he was infused with one pint of normal saline fluid containing one-fifth of a 10 per cent. solution of peroxide of hydrogen; but no marked improvement occurred. Later in the day his abdomen became distended, and death took place at 7 P.M.

Necropsy.—Abdomen much distended. The tissues over the front of the right side of the chest were slightly emphysematous from the infusion of peroxide of hydrogen. Many old pleuritic adhesions occurred on the right and left side, with recent pleurisy at the right apex. The upper lobe of the right lung was in a condition of grey hepatisation, the rest of the lung in a condition of hypostatic congestion, as was also the left lung. The kidneys were small and their capsules adherent.

REMARKS.

Although a final judgment as to the value of subcutaneous infusion cannot be drawn from so limited a number of cases, nor from material presenting no strict uniformity, nevertheless partial conclusions may be based upon the cases taken together and upon the observations made in each of them. The decidedly favourable result obtained in Case I coincided in time with the treatment, and may fairly be thought to have been partly due to the latter. This is the only case in the series in which recovery occurred, and may possibly have been aided by the timely administration of the infusion. Case II was a case of complications, the patient being alcoholic and the disease proving to be typhoid fever with pneumonia. This case could not, therefore, be strictly classified with those of simple pneumonia. It is a question to what extent the typhoid poison itself may have accelerated the fatal result; but the typhoid lesions were not of a fatal order. On the other hand, the pneumonia was extensive, but it did not present the characters usually found at the relatively advanced stage at which the patient died. There was no grey hepatisation, but the solid lung was intensely congested and sodden. It is impossible to say whether this was due to the stage of dry consolidation having passed away or to its never having been reached. It is equally impossible to say whether this anatomical peculiarity was in any way connected with the form of treatment adopted. It, however, represented the kind of result which it is sought to obtain—namely, the avoidance of the degenerative stages known as grey hepatisation. Case III was also one of severe complications. The secondary occurrence of empyema and of acute peritonitis renders it useless as a test of the capabilities of treatment in simple pneumococcal pneumonia. The reviving effect and comfort experienced after the first infusion were not perceptible after the others, probably owing to the rapidly-increasing stupor of the patient. Case IV may be regarded as a fair case of its kind. The first infusion and some of the others appeared to revive the patient, but there was no permanent result, and the advent of grey hepatisation was not prevented, the lung presenting after death the appearances usually found. In Case V the disease had progressed beyond the early stage at which the infusion would seem most likely to be of use. Death was brought about partly by the exhaustion incidental to the violent delirium which supervened, and partly, perhaps, by the effect of the morphine injection which was administered for its relief. Case VI, with chronic renal and pulmonary disease, cardiac debility, and chronic anasarca, was specially unfavourable. The first infusions had a decidedly reviving effect when the symptoms seemed to be almost hopeless, and the patient survived three days; but the conditions were incompatible with recovery, and after death the consolidated parts were found in grey hepatisation.

The general impression gathered from these cases is that the infusions are not followed by any unfavourable complications, and that they would seem rather to delay than to accelerate the fatal result. This was also the experience of Penrose, whose infusions were bulkier than ours. They were not resented by the patients, and by some of them they were acknowledged to be comforting, although they proved powerless to check the fatal results of toxic absorption. The question remains whether infusions of a different composition or of a greater bulk or frequency might not have been more successful. The instalment of relief which was observed in some of the cases reported suggests that in cases of anxious prognosis, but not actually of the worst type, this mode of treatment might be capable of making a favourable and perhaps a life-saving impression upon the attack.

The therapeutical position of the method would be more clearly defined if answers could be given to the following questions: (1) Does it cure pneumonia? (2) Does it act in any detrimental way? (3) Is there any pathological evidence

of its effect on the influencing the morbid changes special to the disease? (4) Is there any clinical evidence that it either mitigates or shortens the disease, or that it prolongs its duration?

On the limited basis of the few cases observed the first two questions cannot be answered without hesitation. Injections such as those which were administered even when resorted to fairly early do not avail to save the worst cases. On the other hand, though carefully looked for, no indications were noticed of the injections having given rise in any of the cases to unfavourable symptoms, much less to a fatal result. No evidence was obtained of the anatomical morbid conditions having been modified in any marked degree by the treatment. Grey hepatisation was found much as usual in most of the fatal cases, and in the case of double pnemonia the early beginnings of this change in the older patches were associated with quite recent extensions of the congested stage of hepatisation, and this seemed to suggest that neither the late developments nor the early lesions were prevented by the infusion.

The clinical evidence suggests that the symptoms were mitigated, the resistance raised, and the fatal result probably delayed. This conservative tendency was particularly marked in Case VI, for the patient seemed as though he must have died within a few hours upon the day of the first infusion; but after the latter he rallied markedly for a time. Again in Case IV where the pulmonary affection was most extensive, although the symptoms were not of the worst type, the patient appeared to be improving until a few hours before he died, his death coming as a surprise to us.

As to the effect upon the duration of the disease, so long as practically hopeless cases are exclusively selected we shall not be able to decide whether the course of the disease is influenced by infusions in the direction of a prolongation or of a shortening of the attack. Upon this point we are unable to speak with any certainty, although in Case I, which recovered, the improvement after the infusions was rapid and that complete resolution was not delayed.

It must be borne in mind that these are merely provisional inferences, and that the failures were perhaps the inevitable consequence of the gravity of the cases, and perhaps also of the mode of application of the method which was adopted by us. The latter may be capable of various modifications and improvements which may add to its efficacy.

CONCLUSIONS.

Briefly stated the practical conclusions are as follows: (1) In the severe cases treated no unfavourable results were observed from the saline infusions; (2) these seemed to delay rather than to accelerate the fatal termination; (3) they were not resented by the patients, and by some of them they were acknowledged to be comforting; (4) they were powerless to check the fatal course of the pneumonia in the worst type of cases; (5) they do not seem, except in Case IV, where no pus but clear serum exuded from the cut surface of the grey hepatisation, to have made any difference in the characteristic appearances of the pulmonary changes.

At the same time, whilst our results have been disappointing they do not suffice to prove that saline infusions are absolutely useless. A different composition, a larger bulk, or a greater frequency of administration might lead to very different results. The cases reported were exceptionally severe, and may have been incapable of recovery. The effects noticed were, nevertheless, in our estimation such as to recommend the method for a more extensive trial in cases with anxious prognosis; for among them cases may occur which are not of the worst type, and in which an instalment of relief, such as that observed in some of the cases reported, might be sufficient to save life.

THE PROGRESS OF THE SANATORIUM TREATMENT OF CONSUMPTION IN ENGLAND.

By JANE H. WALKER, M.D.,
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IT was once remarked by Sir Charles Lyell that when any novel yet otherwise certain deduction in science appears, the first step objectors take is to assure us that it is not true, the next to tell us that it is wicked and absurd, and, lastly, when they are quite shut up and defeated, their ready but sadly disingenuous assertion is that it was made long before. In 1855 Dr. Henry MacCormac, of Dublin, published a treatise on the absolutely poisonous and infective character of re-breathed air, drawing attention to the prevalence of consumption where conditions of vitiated air exist, to the amelioration of the state of a consumptive individual when he is removed from bad air and surroundings, and also to the possibility of the prevention of consumption by an abundant supply of pure fresh air.

In 1863 a paper by him was read before the Royal Medical and Chirurigcal Society on the true nature and absolute preventability of tuberculous consumption. In it he reiterated his conviction as to the deadliness of re-breathed air and the absolute importance of pure air in the prevention and cure of pulmonary consumption. The *Lancet* of May 1, 1863, reports that, in the discussion which followed, the paper was variously characterised as a waste of time, as stating a truism, which was well-known and more than 500 years old, and finally, the report goes on to say, the meeting concluded with a refusal to pass a vote of thanks to Dr. MacCormac.

We are all more or less in the habit of regarding Germany as the fountain-head of the sanatorium method of treating consumption, but this method was advocated in a book published in 1840 by Dr. Bodington, of Sutton Coldfield, called *The Treatment and Cure of Pulmonary Consumption*. He anticipated the sanatorium treatment of consumption in England by about fifty-two years. He took a house adjoining his own in Warwickshire, a county which has lately been shown by Sir Hugh Beevor in his Hunterian Oration last year, to have a lower mortality from consumption than any other county in England. He there made systematic arrangements with regard to exercise, diet, and general treatment, and himself daily and almost hourly watched over the patients' condition. He lays great stress on the importance of inducing, as far as possible, nervous quietude, and draws attention to the great tendency of the consumptive patient to nervous excitement, both local and general. This must be the experience of all practitioners who have seen much of phthisical patients. Dr. Bodington says, stating in a nutshell the principles of the open-air treatment as we understand it in its completer form at the present day, "the nutrient muscular and sanguiniferous systems must be maintained in the highest perfection that is possible, the nervous system quieted down, subdued and rendered obtuse."

This treatment consisted in a varied and generous diet, of which wine always formed a part, sedatives in the form of morphine, and, the greatest sedative of all, fresh air. He gives six cases which were evidently far advanced, and five of them did extremely well, while the sixth was still under treatment at the time his book was published. He placed very special emphasis on the value of quite early morning air, and impresses upon his readers that no weather is too bad or inclement to cause a patient to remain indoors. He may thus be looked upon as the father of the sanatorium treatment in England. In spite of the encouraging results obtained by Dr. Bodington, all consumptive patients were banished from England in every case possible as a matter of routine, and first a long sea voyage, then moist warmth such as Madeira, next dry warmth, such as Egypt and the Riviera, and, finally, dry cold, such as the higher Alps and the Andes, held the field as far as medical counsel and practice were concerned. Now, finally, we seem to be reaching the belief that climate is unimportant, and that, given suitable arrangements and surroundings, it is possible to cure consumption in any climate.

The advance in medical opinion as to the suitability of various climates for the cure of consumption is shown to be on the right lines by some statistics given in Solly's *Medical Climatology*. He states that consumption is most prevalent in climates in proportion to the temperature and humidity as follows: (1) damp cold climates—for example, some parts of a sea voyage; (2) damp hot climates—for example, Madeira; (3) dry hot climates—for example, Egypt; (4) dry cold climates—for example, the Alps. That is, damp cold is more prejudicial than damp heat to the consumptive, and dry heat than dry cold. The variability of the temperature with dry air has had no bad effects on cases of consumption, but varia-

bility with dampness predisposes to phthisis. The great cause of consumption is overcrowding, and it results infallibly where overcrowding exists, even in climates where it would be otherwise unknown. In the cure of phthisical patients it is not the place nor the climate which plays the principal part, but the mode of treatment. Of course, there is no doubt that a perfect climate for consumptives—by which I must be understood to mean a dry cold climate—is of immense advantage in helping a patient round a bad corner; but still, other things being taken into consideration, it is advisable to cure consumptive patients in the climate in which they will ultimately have to live.

This brings me to speak of the present movement in favour of the sanatorium treatment of consumption in England. With the exception of a few isolated instances, myself among the number, this method of treating consumption is, as far as England is concerned, only two years old. I have treated patients, mostly of the hospital class, since 1893 on a small scale, in a farmhouse in Norfolk, and my results there were so encouraging that I opened a house for better class patients in the beginning of 1898, and finally formed a small company to raise the necessary capital, and to build the sanatorium at Nayland, in Suffolk, which is now approaching completion. At the same time sanatoria are cropping up in various parts of the country, and one has only to read the advertisements in the JOURNAL of the Association to learn how numerous they have become. There is, however, the danger of these establishments being managed by people who do not thoroughly understand the subject.

The sanatorium treatment of consumption is a minute and elaborate system made up of endless details, all of which are important. It is not enough to say, "Open all windows wide in all weathers, and all will be well"; it is not enough even to add, "Feed all patients very plentifully, put them through a process of 'superalimentation,'" as I saw in one of the advertisements of sanatoria. With these two points, essential as they are, must be united careful regulation of exercise and rest and constant medical supervision. No two cases can be treated on exactly the same lines; we must consider not only the "individual sickness but also the sick individual," by which I mean that the reaction of the patient to his environment is a very important variant in the cure of phthisis. The qualities which most aid consumptives in recovery are, first, strength; secondly, wisdom; thirdly, equability of temperament; therefore the essentials of the general treatment of phthisis are to preserve and strengthen the physique, to enforce prudence, and to induce placidity. In a way it is an unfortunate thing that patients in the first stage improve so much. It is hard, though it is the solemn duty of a medical officer of a sanatorium to do so, to convince a patient who has unmistakable signs of phthisis that, although he feels quite well, he is not so in fact, and is in no sense fit to leave the sanatorium or to lead an ordinary life either working or idling, but that he must stay on until he is lifted on to a higher plane physically, and until a higher standard of health is established. Patients are apt to return to their former manner of life, believing themselves to be cured when they are very far from this condition. Especially are patients prone to leave off treatment too early when they are at a paying sanatorium, yet a prolonged stay is often necessary if the improvement gained is to be maintained. Certainly there are incipient cases of phthisis for which a comparatively short period of change in climate and surroundings is all that is required, but these cases need to be very carefully watched for several years after their return home, and all their departures from health require to be most promptly attended to and their daily hygiene raised to as high a standard as possible.

In considering the length of time residence at a sanatorium is necessary, attention must be paid not only to the arrest of the disease but to the permanent raising of the standard of the patient's health, in order that recurrent attacks may be warded off.

Early recognition of phthisis is highly important, and watchfulness as soon as the diagnosis is made. It may seem presumptuous of me to urge upon such an assembly as the present the necessity of examining the chest of every patient who is getting in any way below par without any very obvious cause. But from my own experience I have found that the chest is not listened to by the regular general practitioner with the frequency which is really advisable. Patients are constantly brought to me who have been ailing for months and even for years, who have been constantly attended by medical practitioners, and who have never had their chests examined at all. Some, it is true, have been listened to through their clothes, and others occasionally have been made to take a deep breath with the medical practitioner's hands on their shoulders, but large numbers of the patients have not had any examination of their chests at all. The results of this neglect are most serious.

The recovery of a patient with phthisis in the second stage (by which I mean the stage of cavity formation with septic symptoms) is not only much less certain, but the process is of a much more lengthy and expensive description.

The prognosis in cases of consumption is extremely difficult. Dr. Walther, of Nordrach, whose experience is very considerable, told me a couple of months ago that he felt that time was the only thing that would give any data as to prognosis, and that no opinion of any value could be given on seeing a case for the first time. My own experience has led me to very much the same conclusion. Still there are some points of course which are of bad significance as far as prognosis goes. They are a permanently frequent pulse, a reversed high temperature, diarrhœa, and sickness. But some patients with apparently very slight disease go rapidly downhill, whereas others with widespread local mischief and great general exhaustion hold out for years. There are also points of good significance in prognosis; they are steady gain in weight, dropping of temperature, increase of strength, and improvement in the pulse. Gain in weight *per se*, although such stress has been laid on it as to constitute it an article of faith almost, is not of very favourable import, unless it proceeds *pari passu* with other signs of improvement. It is worse than useless to burden a patient with three or four stones additional weight if at the same time he is not helped to regain the strength necessary to enable him to turn this increase to his advantage, by giving him carefully-regulated exercises to deepen his breathing capacity and to give extra vigour to his heart and muscular system generally. "It is indeed often a matter of pure conjecture to decide whether, and how rapidly, and how severely the existing catarrh may produce ravages. It is only he who has attentively observed his patient for a long time, and has made himself acquainted with all his peculiarities, who can give any opinion as to the effects of treatment on a patient."[1]

The sanatorium treatment of consumption is after all a system of elaborated common sense, applied to a long and tedious illness, and for it to be a success all the factors which make up the convenient term "hygiene" must be introduced: a permanent supply of fresh air, a large quantity of nourishing and digestible food, carefully regulated exercise and rest, and the removal of all causes of worry and anxiety. The medical element is, of course, paramount, and the medical attendant must be of a particularly hopeful and cheerful disposition, and be capable of communicating his hopefulness to his patients. Still, after all, it is but a human agency, and as such, cannot be expected to work miracles. If I may venture to say so, Mr. Gibson's articles, good and useful as they were in educating public opinion, erred very much in the direction of leading the public to suppose that in the open-air treatment is to be found a certain cure for all cases of phthisis, and they gave false hopefulness to many. People in practically a dying condition came to Nordrach from Australia and many other distant parts, on the strength of those articles, and the mortality was considerably increased, and there was thereby some danger of bringing discredit on the whole sanatorium movement.

The sanatorium treatment is capable of still further expansion. For example, children of tuberculous parents, whose physical resistance is presumably below par, might very usefully spend some time in a suitable sanatorium, from prophylactic considerations. There should be sanatoria for children who are definitely tuberculous, and with these should be combined some arrangements for education for those who are able to avail themselves of them. The cure of tuberculosis in growing children is a far slower process than in people whose growth is completed.

What I may call for brevity "maternity sanatoria" might be formed with great advantage to the community. By this I

mean sanatoria where tuberculous pregnant women might be received for three or four months prior to their confinements, and remain there for the necessary period afterwards.

The provision at the present moment for consumptives in England is as follows:—9 urban chest hospitals for consumptives, 7 country chest hospitals for consumptives, 1 urban home for consumptives, 7 country homes for consumptives, 4 sanatoria for the poor, 4 more projected, 22 sanatoria for paying patients and 2 more projected.

My own cases from 1892 to June, 1900, are as follows:—

Total No. of Cases.	Still under Treatment.	Recovered.	Improved.	Going back.	Died.	Lost Sight of.
177	29	45	54	13	27	9

The mortality among these cases is 15.5 per cent.

REFERENCE.

[1] Rohden's article in Julius Braun's book on *The Curative Effects of Baths and Waters.*

Dr. CHOWRY-MUTHU said: I have listened with great interest to Miss Walker, who has been one of the pioneers of the open-air movement. If foul air and overcrowding increase the virulence of infectious diseases, fresh air is highly beneficial in these cases, as I have proved in influenza, scarlet fever, typhoid, etc. The results of the open-air movement in the sanatorium with which I am connected have been so satisfactory as to convince me that it is the remedy that at present holds out the best chance of success in phthisis. As for early diagnosis of phthisis, I have found a single click heard at the end of inspiration to be the most reliable physical sign in the very beginning of the disease. The prognosis very much depends upon the state of the stomach, the state of the pulse and the heart, and the duration of the treatment. We shall have very much better results if patients are early diagnosed and treated, and the duration of the treatment is prolonged at least from six to nine months. Though some cases can be treated satisfactorily at home, a well-conducted sanatorium with a resident physician offers the best chance of cure for the majority of patients. Consumption cannot be cured by fresh air and good feeding alone. Sanatorium treatment includes thorough organisation, strict discipline, and strong generalship, without which the open-air system will be a failure. The secret of the success of the treatment depends upon the strong will and personality of the doctor who takes the different elements, as pure air, exercise, feeding, etc., and distributes them according to individual requirements, who commands the obedience and regulates the life of the patient in every detail, inspiring him with his hope and enthusiasm in the treatment.

Dr. BURTON-FANNING said that Dr. Jane Walker's insistance on the necessity of wisdom on the patient's part reminded him of Brehmer's dictum, "that consumptives only died of their character." As regards results of the sanatorium treatment everything depended on the selection of cases, and the sanatorium doctor had less to do with the obtaining of recoveries than the doctors outside the sanatoria. Dr. Jane Walker referred to cases whose chests had not been examined and who came for treatment unfortunately late in the disease, but Dr. Burton-Fanning hoped that practitioners would not wait till physical signs developed which could be detected by the stethoscope. He hoped that more dependence would be placed on the clinical thermometer, the weighing machine, and the examination of sputum, and that cases would be placed under adequate treatment before signs had occurred in the lungs. By this he did not mean to say that improvement was not likely to occur in more advanced cases, but the best results were, of course, to be obtained in the very earliest cases. He did not feel any gratitude to the writer of certain popular articles who had prepared patients to consider that three months was the longest time required for a cure, and that 90 per cent. of all cases were cured at one sanatorium. If a year was stated as the time likely to be spent in obtaining the greatest amount of benefit, and if 90 per cent. improvements were substituted for 90 per cent. cures the truth would be better expressed. Dr. Jane Walker's description of the sanatorium treatment as consisting of "elaborated common sense" was a good one.

CONSANGUINITY AS A FACTOR IN THE ETIOLOGY OF TUBERCULOSIS

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THERE has long existed a belief that consanguineous marriages are detrimental to the resulting offspring. Morgan in *Ancient Society* declares that exogamy was due in olden times to the observed evil effects of marriages of near kin, and also because it was known that the intermixtures of stocks increased both mental and physical vigour. Sir H. Maine in *Early Law* agrees with Morgan on the ground that mixed marriages would give a better constitution. Sir John Lubbock in *Origin of Civilisation* says that one of the causes of exogamy was "the inferior energy of the children sprung from in-and-in marriages." Howitt in *Kamilaroi* considers the Australians introduced the prohibition against the marriages of near kin to avoid observed evil effects. Much has been written to prove the ill-effects of inbreeding among stock, and authorities are pretty well agreed that enfeebled constitutions commonly result.

The chief diseases that we may expect to find resulting are those that are transmitted hereditarily. We can readily understand how this comes about, as hereditary influence is bound to be intensified when both father and mother transmit the failings of a common ancestor. Dr. Mitchell, in a memoir read before the Anthropological Society of London as far back as 1886, gives an instance of a village on the North-East coast of Scotland. The fishing population was estimated at 779, and contained 119 married couples, of which 11 couples were first cousins and 16 were second cousins. Of these 27 marriages of near kin, 3 were barren, and from the remaining 24 105 children were born, or nearly 4.4 for every fruitful marriage. Of these 105 children, 38 were dead (of which 35 died in childhood) or 33.4 per cent.; 4 were deaf-mutes, or nearly 6 per cent.; 4 were imbecile and 4 were slightly silly; 1 was paralytic, and 11 or a little over 16.4 per cent. were scrofulous and puny. The children of those who were first cousins were described as all of them neither strong in mind nor body. Sir Thomas Watson says of the Faroe Islands that phthisis is very rare, but mental derangement is common, as many as 1 per cent. being thus afflicted. Inbreeding obtains to a great extent there. The *Pall Mall Gazette* for August 5th, 1872, in a biography of the late Mr. Augustus Smith, for a long time owner of the Scilly Islands, says that he removed some of the inhabitants of the outlying islets to better neighbourhoods. On some of these the scanty resident householders—never forming connections out of their own island—had, it is said, degenerated into a condition approaching that of imbecility. The Hon. G. Monson, in the consular reports 1871, No. 4, finds an unnatural frequency of idiocy and enfeebled constitution among the Azore Islanders, which he considers to be due to the prevalence of consanguineous marriages. Without spending more time on the opinions of others, I wish to direct your attention for a short time to the condition of things existing in the Isle of Man.

The Manx of to-day are the outcome of the amalgamation of the original Celts with the conquering Norse. The Norse descents took place during the tenth, eleventh, and half of the twelfth centuries. Since then, although various conquerors have subdued the Manx, they have had very little admixture of foreign blood. A patriotic and clannish spirit arose that resented the introduction of strangers, and so jealous did they become that they went to the extent of enacting a law prohibiting ships' masters from landing foreigners on their shores under a heavy penalty. To all intents and purposes, then, we have a little nation some 10,000 or 15,000 strong, living for 600 years an isolated and detached existence. This in itself would not have been so bad had there been a free and general mixing together amongst them. This was not the case, however. The central mass of mountains formed a natural barrier between the north and south of the island. Intercommunication could only be carried on along the narrow strips of lowland

bordering the eastern and western coasts. But a greater barrier than the physical one existed in the natural aversion in which the norther and southerner held each other. Although speaking the same language, and having the same religion, customs, and laws, they were descended from different races. Even to this day the types are distinct, the fair-haired, tall Scandinavian, being represented by the northener, while the more swarthy and thick-set Celt has left his mark upon the southerner. From time to time fierce and bloody battles were waged between them, and enmity existed for centuries. Midway between the two, situated on the east and west coasts respectively, are the village of Laxey and the ancient city of Peel. Laxey, undoubtedly, until recently, was in a particularly isolated condition. The roads, both north to Ramsey and south to Douglas, were simply rugged bridle paths, winding along between the hills and the steep rockbound shore, and continually crossing the narrow glens, through which ran the brawling mountain streams. It is only within the last half dozen years that the old-fashioned coach has given way to the electric tramway, which has brought Laxey into touch with the rest of the island. Peel was not quite so isolated, for as it was the only port on the west, and being from time immemorial a place of residence for the Lords of Man, it had dealings with both north and south.

We thus see that a small nation, isolated by its own independence and by a stormy sea, becomes further broken up into four portions by its physical conformation and racial antipathies—namely, that portion north of the mountains, that portion south of the mountains, and the small aggregation of farmers and fishermen that clustered round Peel and Laxey. But a further subdivision still existed, for the people grouped themselves into the various parishes, and it was very rarely indeed that they migrated from one parish to another. Great resentment was felt against any man who married a wife from any but his own parish. When we come to study the surnames that are most frequently met with in the various parishes, we have very strong corroborative evidence of this consanguinity. To compare in an old directory the surnames met with in a southern and a northern parish one might well believe the two to be a thousand miles apart. The same thing holds in a lesser degree with contiguous parishes; in fact each parish seems to have a few families that may be considered native to it. Thus we have the three families of Christian, Joughin, and Kelly which comprise among them a third of the inhabitants of Bride; and the Corlettes, Quayles, and Teares which comprise a third of the inhabitants of Ballaugh. Many of the farmsteads have been in the hands of the families who now own them for 300 years and more according to the records, and how much longer still we have no means of knowing. The consequence is that undoubtedly these families married and intermarried with their immediate neighbours again and again. It is only when one has dwelt among this people that the extent of this inbreeding becomes apparent, and it is no exaggeration to say that three-parts of the inhabitants are related to each other, and even where relationship is not acknowledged it is often found to exist unknown to the persons interested.

To sum up, we may say, that geographical positon, physical conformation, racial antipathies, and parish prejudices have been at work for hundreds of years, with the result that a very high degree of consanguinity has been attained by the Manx people. Having proved the consanguinity, do we find any of the alleged ill-effects resulting therefrom in the Manx people? The scope of the present paper only admits of our discussing one of these results, namely, tuberculosis.

My investigations cover fifteen years, and prove the average annual mortality-rate for phthisis to be 25.7 per 10,000 living. Roughly speaking, this is about double of what obtains in England and Wales. Such an excessive amount of tuberculosis must be due to some exceptional cause or causes. I shall endeavour to prove to you that the great amount of consanguinity and the great amount of tuberculosis bear to each other the relationship of cause and effect. In order to do this it will be necessary to briefly review the recognised causes of tuberculosis, and show that these are in no way accountable for this special prevalence, but rather that the causes pertaining to the external surroundings and life-conditions of the individual would tend to produce a low phthisis mortality. Full details of the climate, soil, etc., will be found in a short treatise on Manx phthisis, published by me last year. At present I must rest content with a brief summary. The temperature of the Isle of Man is more equable than that of any part of the British Isles, the extreme variation being 17.1° F., while the annual mean is 49.0°. By a comparison with the chief watering places of England and Scotland, we find that it is characterised by its cold springs, cool summers, and mild autumns and winters. There is comparatively little frost and snow, and fog is almost unknown. Its sunshine is much greater than in any surrounding district, and stands third on the list of the British Isles. The winds seem similar in velocity to those on the mainland, though being freely exposed on all sides no doubt one feels them more. The combination of mountain and sea air seems to be conducive to an excess of health-giving ozone, and certainly has a most invigorating and bracing effect on the system. From a life-long experience of the island, both as layman and practitioner, I have come to the conclusion that we have a climate eminently suitable for the treatment of lung diseases. The soil of the island is dry and fairly well drained. I have never yet come across a case of malnutrition due to poverty in town or country, and, as a rule, the natives are well nourished in body and happy and contented in mind. The two chief occupations of the people are agriculture and fishing. A very large number also follow the calling of mariners; lead mining is carried on, but not to any great extent. In no part of the island are the men and women herded together in any numbers, either for industrial or any other purposes. The dwellings of the Manx are neither better nor worse from a sanitary point of view than those of their class in England, and I am sorry to say that they have the same aversion to open windows and good ventilation.

In considering these general conditions under which the Manx live, we fail to find any adequate reason for the marked amount of tuberculosis, and so we are driven to conclude that there must be something in the constitutional idiosyncrasy of this people that renders them peculiarly liable to the onslaughts of the tubercle bacillus. With regard to the geographical distribution of phthisis in the Isle of Man, we consider it of comparatively little importance. The whole population, from the Point of Ayre to the Calf of Man, lives under circumstances, as regards climate, soil, and occupation, so similar in character that the slightest variations in the amount of consumption in the parishes from time to time are by no means of a significant character, and are due undoubtedly to a great extent to chance. There is, however, one fact that stands out clearly, and that is, that there is a notorious amount of consumption in Lonan, which parish contains the village of Laxey, and an equally remarkable freedom from it, comparatively speaking, on the western side of the island. This seems to suggest a distributive cause, and we believe this cause to be consanguinity. As I pointed out, Lonan has been exceptionally isolated, owing to its geographical position. This fact has been responsible for a very great amount of inbreeding, in fact we may safely say that Lonan is more consanguineous than any other parish in the island, and here we have the heavy phthisis roll of 41.17 per 10,000 persons living. I also pointed out that Peel and the western parishes lying midway between north and south, and being easy of access from both, and also from the fact of the political importance of Peel, and its being the chief outlet and inlet for the island for many centuries, naturally had more opportunities of introducing fresh blood, and consequently would suffer less from inbreeding than the other towns and parishes. We therefore expect to get a low phthisis rate, and such is the case throughout the whole western division, namely, 21 94, as against 24.19, 28 15, 24.53 for the northern, eastern, and southern divisions respectively; and we also get the lowest parish phthisis rate, namely, Michael, with 15.19.

After a careful study of the whole question I have come to the conclusion that the chief factor in producing the high mortality from tuberculosis in the Isle of Man is consanguinity.

Dr. R. MURRAY LESLIE considered that Dr. Davies's able paper was an exceedingly important one to those who had to deal with the treatment of phthisis. He asked if phthisis wer

more common in families of royal personages than in persons belonging to the general community?

Dr. Gore asked whether the conditions other than consanguinity that caused the prevalence of phthisis on the West Coast of Ireland prevailed in the Isle of Man, such as deficient ventilation. In Ireland, in the cottages of the poorer classes, the windows were usually not made to open, there was great overcrowding, many people sleeping in the same room, and this was an important factor in the production of phthisis there.

Dr. Davies, in his reply, proved that the lead mining in Laxey had no influence whatever on the high phthisis rate obtaining there, as the female phthisis rate was more pronounced than the male. He also briefly discussed Dr. Havilland's theory of wind causation, and showed that the windiest parish in the island was also the freest from phthisis.

A CASE OF FATAL MALIGNANT ENDOCARDITIS AND RIGHT EMBOLIC HEMIPLEGIA,

APPARENTLY DUE TO INFECTION FROM DENTAL CARIES AND STOMATITIS, TREATED BY ANTISTREPTOCOCCUS SERUM AND BY SALINE INFUSIONS.

By William Ewart, M.D.Cantab., F.R.C.P.,
Senior Physician to St. George's Hospital and to the Belgrave Hospital for Children.

The case to be narrated, although it stands alone, may provide an explanation for many others which may be observed and reported in the future. It is worth recording, in spite of the negative bacteriological result, because it is in other respects complete and clinically conclusive. It is also of interest in respect of the measures of treatment which were adopted, but which proved ineffectual.

J. C., aged 26, groom, was admitted into St. George's Hospital on April 9th, shortly after a sudden seizure whilst at work which left him aphasic and paralysed on the right side. He looked fairly well nourished and healthy, had never been laid up with illness so far as known, and had been fit for his work; but no history was obtainable from himself and there was no other source of information. A careful physical examination could detect no abnormality, thoracic, abdominal, or circulatory, except a systolic mitral murmur. The case ran the following course: The temperature, raised on admission, oscillated from an average of about 100° usually to above 101° in the evening and sometimes nearly to normal in the morning. The pulse ranged from 80 to 100, and at the end to 120; respirations from 24 to 34. There was a trace of albumen in the urine. On April 16th when general and cardiac aggravation occurred he vomited five times and on the 17th once. He had also vomited just before admission. The pyrexial and other peculiarities of the case suggested a complication of diseases, and Dr. Percival, my house physician, suspected during the first few days enteric fever in association with the hemiplegia. The discovery later on of a changing and increasing murmur defined the case as one of vegetative endocarditis. No improvement took place under treatment although he seemed to be progressing fairly favourably; and his rather sudden death was unexpected.

The mental state, except during the initial stupor, was one rather of limitation than of obscuration. There was no delirium. His aspect and gaze were intelligent. He seemed to understand all that was said, but "the way out" was completely blocked; he answered "Yes" to everything to the last. His paralysis was considerable though not absolute. Knee-jerks not present at first were afterwards obtained, but the plantar reflexes were very active on the right. He could move the leg and the arm slightly, but for several days was not able to feed himself. The right side of the face was markedly paralysed and he never recovered the power to whistle. There was apparently no pain.

On admission the apex beat was normal, with an undulatory heaving precordial impulse. A harsh systolic murmur was audible universally, but loudest in the third and fourth spaces to the left of the sternum. On April 16th the patient looked decidedly worse, ghastly pale, and vomiting occurred. On examination that day a diastolic aortic murmur was distinctly heard to the left of the sternum, and a double murmur at the apex. The spleen was found to be rather enlarged. On the 17th a diastolic rumble was heard at the apex. The aortic reflux had become much louder and a Corrigan pulse had developed. The aortic murmur could be heard to the right of the sternum and across it for some distance towards the apex.

The bowel and kidney functions presented no noteworthy abnormality. The blood was examined by Mr. Spitta for micro-organisms, but none could be found. A persistent hiccough began on the 17th and lasted for a few hours On the 25th an antitoxin rash developed. On the 26th there was œdema of the right hand, perhaps due to the rash. On the 27th a hard and painful swelling had formed on one of the ribs and two others on the inner aspect of the right arm. There were not at the site of the needle punctures, and at the necropsy they proved to be pyæmic abscesses.

The state of the mouth was unusually bad. Besides stomatitis there was an exceedingly foul condition of numerous stumps. The fœtor of the breath was intense and reminded one of the worst smell of decaying or macerating dead bone. Some of the hollow teeth contained plugs of offensive decomposing material. There were no glandular enlargements at the angle of the jaw.

The case was diagnosed as one of embolic hemiplegia due to vegetations and ulceration or detachment of the aortic valve, with either vegetations upon the mitral valve or the condition producing Flint's murmur. The same physical signs persisted with minor modifications to the end, which came rather abruptly.

The diet consisted of light food, milk, eggs, light pudding, and subsequently fish; and on the 27th pounded fish. Brandy was ordered (3 ounces daily) on April 16th.

The medicinal treatment consisted of calomel and senna; sanitas (1 in 6) as a mouth wash; carbolised oil for the nose; and potassium iodide with tincture of iodine internally. On April 16th, in addition to other treatment, antistreptococcus infusion 20 c.cm. was given; on April 17th two 10 c.cm. injections of the same; on the 18th two injections; on the 21st one injection; and on the 22nd one injection. On April 23rd one pint of saline infusion containing sodium cacodylate gr. $\frac{3}{4}$ was administered; this injection was repeated twice on the 24th, and once on the 25th and 26th. On April 30th and May 1st 10-grain doses of sulphate of quinine were prescribed.

The *post mortem* examination was performed by Dr. W. J. Fenton forty-two hours after death. Except three small subcutaneous abscesses (at the midsternal, the right mammary, and the posterior brachial region) the external appearances were normal. Abundant fluid was found in both pleuræ, but no pulmonary lesion except moderate bronchitis. The heart weighed 12 oz. About 1½ oz. slightly turbid fluid in the pericardium; a few petechiæ over the posterior surface of the left auricle; mitral and tricuspid valves normal. Aortic valves: A large, rough, greyish vegetation was attached to the ventricular surface of the left posterior aortic cusp at the point of insertion of which an ulcerative perforation had formed. Ragged vegetations also occurred on the right posterior cusp. The myocardium was free from disease. The liver weighed 4 lbs. 8 oz., and was slightly nutmegged. The spleen, 15 oz., was free from infarcts. A large anæmic infarct occurred in the left kidney; no other renal lesions. The genito-urinary organs were free from lesions. In the cranial cavity an adherent decolorised clot was found in the left middle cerebral artery, about 1 inch from its origin. The tip of the temporo-sphenoidal lobe and the subcortical tissue of the island of Reil as far as the outer edge of the lenticular nucleus were softened. The latter softening extended in an antero-posterior direction for about ¾ inch in the tissue of the brain.

N.B.—The small abscesses described above did not occupy the situation of the punctures made by the infusion needle. The mouth was in an unhealthy condition, and most of the molars in an advanced state of decay. The nose, throat, and ears, like the rest of the body, presented normal appearances. The middle ear was not opened, as there was no sign nor any clinical observation suggesting middle-ear disease. The only abnormalities found after careful search were those which have been described.

Remarks.

By most recent writers on infective endocarditis the etiological factors are given in almost identical terms. Von Jürgensen, in his monograph on *Endocarditis*[1] enumerates the micro-organisms which have been found in the vegetations. The most common are the staphylococcus pyogenes aureus, the streptococcus pyogenes in its various forms, and the diplococcus pneumoniæ. In addition to these the gonococcus has been met with, and Weichselbaum has found the following occasionally: Bacillus endocarditis griseus, the micrococcus endocarditis rugatus, and the micrococcus endocarditis capsulatus, and he also mentions, as admitted by some, the bacillus fœtidus (Passet) and another non-mobile fœtid bacillus that of Fraenkel and Sanger. G. Klemperer has also described the diplococcus tenuis. Besides all these, various microbes have been seen which could not be cultivated; and opinion is divided as to the possible share of the typhoid bacillus, of the bacterium coli, of the tubercle bacillus, and of the syphilitic contagium.

Ludwig Herzog,[2] in his collection of cases of ulcerative endocarditis, refers like the rest to cases where no portal of infection is traced, and these are supposed to belong to the group of "primary ulcerative endocarditis." No reference is made by him to dental disease as a possibility of infection, but it is significant that in Case viii of his series hæmorrhages from the gums had preceded the attack for a long time. This hæmorrhagic tendency is much insisted upon by Herzog, but as a complication rather than an etiological factor in the case, the derivation of which remained unexplained.

A "primary infective endocarditis" is also admitted by Dreschfeld in his article on Infective Endocarditis[3] by the side of the infective endocarditis arising as a complication of septic diseases (pyæmia, septicæmia, puerperal affections, traumatism) of that set up in pneumonia or meningitis by the diplococcus pneumoniæ, and of infective endocarditis as a

mixed infection due to septic organisms secondary to acute and infective fevers, or secondary to rheumatic endocarditis and to sclerotic changes in the valves. In connection with the digestive tract mention is made of ulceration of the intestine, enteric or dysenteric; and in connection with the respiratory tract the view of Thiroloix that ulcerative bronchiectasis may be a source of septic endocarditis is referred to. Bronchiectasis itself, as suggested doubtless by others as well as by myself, probably suffers infection from septic conditions of the mouth. This would explain recurring periods of fœtor in the expectoration of these patients.

Gibson[4] refers to disease of the middle ear as a source of the disease. The nearest approach to any connection having been suggested between infective endocarditis and infection in the mouth is, so far as I can find, a statement quoted by Dreschfeld[5] from Brissaud and Gilbert, that in one of their cases gangrenous stomatitis and ulcers on the tongue and lip were observed.

In connection with the instance which has been narrated, the choice lies between classing it in the group of "primary or idiopathic" cases, because, had all examination of the mouth been omitted, no disease, recent or old, would have been discovered throughout the body; or, on the other hand, giving full recognition to the fact that the mouth was profoundly diseased, that it was infested with organisms, and that it presented large ulcerated surfaces through which access to the circulation must have been given to infection. To recognise the exclusive presence side by side of these two intense local infective processes, and to fail to admit the possibility of some connection having existed between them, would be to neglect the method of pathological inference which has hitherto been followed with so much success in the etiological study of disease. I have therefore ventured to place this case on record as one in which, though it was not proved, yet it was highly probable that the septic condition of the mouth was the direct cause of the malignant endocarditis.

REFERENCES.

[1] Nothnagel's *Spec. Path. und Therap.*, Vienna, 1900. [2] Neun Fälle von ulceroser Endocarditis: *Deut med. Woch.*, November 10th, 1898, p. 716. [3] Clifford Allbutt's *System of Medicine*, vol. i, p. 1896. [4] *Diseases of the Heart and Aorta*, 1893. [5] *Loc. cit.*, p. 333.

Dr. ALEX. R. COLDSTREAM had met with a similar case some years ago. In a girl of 13, symptoms of ulcerative endocarditis, fever, joint pains and delirium, with a fatal result in four days, followed on a gumboil which was incised. The ulcer of the endocardium was on the tricuspid valves. The case seemed to be a commentary on Dr. Ewart's case, as having a dental origin, and served to show the great importance of mouth and teeth hygiene. There was no other possible source of infection discovered.

Dr. HADDON related his experience of ulcerative endocarditis, three cases of which he saw at Eccles near Manchester within a stone's throw of each other, one after another in a short time, In these cases no cause was suspected. In another case a lady had had several teeth removed under chloroform, and had never been well since, and there might be some connection between the operation and the disease. Whatever the true cause of this disease might be he was inclined to think that like other infective diseases, the germ might enter by the mouth. He could not believe that a decayed tooth or gumboil was to be regarded as a possible cause of ulcerating endocarditis without introduction of some specific cause.

Dr. R. MURRAY LESLIE considered Dr. Ewart's suggestion that the mouth might be the source of infection in some cases of ulcerative endocarditis exceedingly important. The case he quoted certainly went far in support of this theory. Many, if not all, of the so-called idiopathic or primary cases of ulcerative endocarditis were probably simply cases where the source of infection had not been discovered, and in not a few of them the mouth might constitute the source of infection. He thought that dental caries in young persons should be immediately treated so as to avoid such untoward sequelæ.

NOTIFICATION OF TUBERCULOSIS IN THE UNITED STATES.—The Board of Health of the City of Trenton, New Jersey, proposes to include pulmonary tuberculosis among notifiable diseases. The Board has further passed ordinances making spitting in the streets and public places a punishable offence.

SECTION OF PATHOLOGY.

E. KLEIN, M.D., F.R.S., President.

THE PRESIDENT made some introductory remarks on Bacteriology in Relation to Pathology, which were published in the BRITISH MEDICAL JOURNAL of August 4th, p. 291.

A DISCUSSION ON THE PATHOLOGICAL DISTRIBUTION OF THE DIPHTHERIA BACILLUS AND THE BACTERIOLOGICAL DIAGNOSIS OF DIPHTHERIA.

I.—F. W. ANDREWES, M.A., M.D., F.R.C.P.,

Pathologist and Lecturer on Pathology at St. Bartholomew's Hospital.

MOST pathologists will admit that Bretonneau's definition of diphtheria requires modification in the light of modern bacteriological knowledge. It requires in one direction limitation, for there are grounds for supposing that not every membranous sore throat or laryngitis is due to infection by the Klebs-Loeffler bacillus; while in another direction it requires extension, for it is clear that many mild and non-membranous sore throats do depend upon infection by this organism. It is the presence or absence of the specific bacillus which is now held to decide whether or not a given case is to be regarded as one of diphtheria.

This being so, a consideration of what is and what is not to be regarded as the diphtheria bacillus becomes an essential preliminary to the discussion of the subject. There exists a fairly definite group of bacteria often spoken of as "diphtheroid organisms," which has with propriety been systematised as a definite genus under the name "Coryne-bacterium." Its members are characterised by a tendency towards a "clubbed" form, and by an irregularity in the staining properties of their protoplasm, due to the presence of granules which are commonly metachromatic, and may even admit of differential staining. Spore formation is not known in the group; its species are devoid of flagella and are non-motile; they stain by Gram's method, and do not liquefy gelatine; in certain cases true branching has been demonstrated.

It has been shown, beyond the possibility of doubt, that diphtheria depends upon the pathogenic action of a bacillus possessing the above characters. It seems also certain that there are allied bacilli which are non-pathogenic, or are at least not concerned in the production of diphtheria. It is thus of the first importance to find criteria by which we can distinguish between the true diphtheria bacillus and its non-pathogenic allies. Unfortunately, the genuine organism varies considerably in its morphological characters. A large well-clubbed form, a much smaller peg-shaped form, or any gradation between these types, may be met with in clinically typical diphtheria. The toxin produced by these different forms is practically identical, and their inoculation into susceptible animals gives the same result. Considerable variation in size and form may sometimes be found, even amongst the individuals composing a single colony. Some of the smaller types of the true bacillus bear so close an outward resemblance to allied species—for example, to the xerosis bacillus—that they may be morphologically indistinguishable. Less commonly, harmless species are found to mimic the large form of the diphtheria bacillus.

It follows that morphological characters alone are an unsafe guide for absolute diagnosis. There is, indeed, a structural character for which some diagnostic value has been claimed—namely, the differential staining of the granules present in the protoplasm by Neisser's method or its modifications. Young cultures of the true bacillus on serum or serum agar commonly show the granules well, while in corresponding cultures of other diphtheroid organisms they are usually feeble or absent. I have employed the test regularly for some time, and my experience is that while it is a useful confirmatory test, often helpful, it is not one upon which absolute reliance can be placed.

Much the same criticism applies to a common chemical test—namely, the production of acid in glucose broth during the first 24 or 48 hours. It is a test of very great value, but

it is not an absolute criterion. Individual strains of true diphtheria bacilli vary in their degree of acid production, and although the majority of allied organisms fail to produce acid, there are said to be some that do so.

A test of much higher value is furnished by animal experiment, and it is upon this that ultimate reliance must be placed. If a guinea-pig, inoculated with a suitable dose of the suspected bacillus, die with the characteristic lesions, the bacillus is pronounced to be the genuine diphtheria bacillus. If, on the other hand, no pathogenic effect whatever is produced, the bacillus is held to be some other species, however closely its remaining characters may approach those of the diphtheria bacillus. Short of a fatal result, the production of pathogenic effects, such as illness and local tumour, in the inoculated animal is consonant with the belief that the bacillus is an attenuated form of the true diphtheria bacillus.

Such are the opinions commonly accepted; but there are certain points as to the absolute reliability even of animal experiment which are open to argument. Is it, for instance, quite certain that if the guinea pig dies the suspected bacillus is necessarily the diphtheria bacillus? Or, in other words, may there not be other diphtheroid organisms pathogenic to the guinea-pig, yet unconnected with diphtheria? It is claimed that there are such organisms, and that hence absolute proof can only be attained by showing that known diphtheria antitoxin immunises a control animal against an otherwise fatal dose of the suspected microbe. Again, is it absolutely certain that absence of pathogenic power proves that the suspected organism is not the diphtheria bacillus? It is certain that under such circumstances no one can affirm that it is that organism; but that is a different thing to affirming that it cannot be. What we know of loss of virulence in artificial cultures may well make us hesitate to deny that such non-pathogenic forms may be lineal descendants of pathogenic bacilli.

It may be that, in searching for absolute criteria, we are striving after the unattainable. No evolutionist need marvel that, amongst the lowliest forms of life, specific distinctions are vaguer and more elusive than higher in the organic scale. After all, it is only in very exceptional cases that a skilled observer who is at pains to apply all the known tests, is left in serious doubt as to the nature of a given diphtheroid organism.

The practical application of the foregoing remarks leads to questions of the highest importance. The diagnosis of the diphtheria bacillus is required under two distinct conditions. It is justly demanded of the man who puts forward new facts about the bacillus, as, for example, about its pathological distribution, that he should neglect no attainable proof as to its identity. The demonstration of this needs several days, perhaps a week or even longer; but scientific work demands it imperatively. Far more frequently, however, the bacteriologist is confronted with the problem of clinical diagnosis. He knows that the tests for absolute diagnosis require several days, a delay which the physician cannot tolerate. For the physician is aware that every day's delay in the administration of antitoxin means an added risk to his patient, and he is responsible for questions of isolation and disinfection. He naturally asks prompt assistance from the bacteriologist, for it is of little service to him unless it is prompt. He wants an answer by telegram in twenty-four hours. The bacteriologist does his best to comply with the request. The physician gets his report, and if we may judge from the increasing demand for such reports, finds it of assistance in diagnosis. But it is of great importance that practitioners generally should apprehend the precise nature and limitations of such a report. It can only represent a pious opinion on the part of the bacteriologist, based on the somewhat uncertain foundation of morphological, tinctorial, and cultural characters. In the hands of a competent and experienced observer the probability that such a report is correct may be very high, and more than enough to justify the practitioner in taking decisive action. It is therefore of obvious utility, but the practitioner must take it only for what it is worth; it has not the value of certainty too often attributed to it; and the report should, in my opinion, be more cautiously worded than is frequently the case. Every bacteriologist who has done much work of this kind has probably, at one time or another, placed himself in a false position by too hasty an assumption as to the nature of the bacilli he has found; for, as a rule, he knows little or nothing of the source of the material sent him, which may be from a suspicious sore throat, but may equally come from a healthy nose, or even from some non-human source. Malicious tricks have been played on bacteriologists often enough.

It may be urged that the practitioner wants an authoritative answer upon which final diagnosis may be based. If so, the sooner he is educated out of that expectation the better. There is a growing tendency to place the responsibility of diagnosis in diphtheria upon the shoulders of the bacteriologist, without furnishing him with any clinical details, or allowing him time for necessary tests. This is partly the fault of bacteriologists themselves, for they have loudly proclaimed that they alone can tell what is diphtheria and what is not. It is true that, given the requisite time for experiment, they can assert the presence or absence of pathogenic diphtheria bacilli, but ultimate diagnosis must always rest with the physician who knows all about the case, and not with the bacteriologist, who may know little or nothing. Virulent bacilli may be present in the throats of healthy persons who have been in contact with diphtheria cases, and it is obvious that this does not constitute diphtheria. Bacilli closely resembling diphtheria bacilli may be abundant in the healthy nose. In every case the ultimate responsibility of diagnosis must rest with the physician and not with the bacteriologist, though the help which the latter can give is of the highest value and importance. In one small branch of practice it is my good fortune to combine the two functions, for I am at once Pathologist to St. Bartholomew's Hospital and medical attendant to the nursing staff, amongst whom sore throat is common. For the diagnosis of such cases the combination is ideal, and I can bear emphatic testimony to the fact that it is from a combination of all points of view that a just and sane diagnosis is most readily attainable. At the same time it is fair to say that the bacteriologist is less liable to error than the physician; indeed, very much less liable to error if he is at pains to control his results by animal experiment. Five years ago I carried out, with the late Professor Kanthack, an investigation of some 70 consecutive cases of sore throats of all kinds amongst nurses—clinical and bacteriological—controlled by animal experiment. We found that, on clinical grounds, I should have made an erroneous diagnosis in one out of every nine cases of apparently simple sore throat.

In my opinion it would be a reasonable thing that the bacteriologist should always be furnished with clinical details concerning the material submitted to him. Much erroneous diagnosis is caused by his working in the dark. The practitioner seems to fancy that he gets a more unbiassed opinion if he withholds clinical facts, but I am sure this is a mistake. Within the last few months I have been concerned with a private school in which cases of diphtheria had occurred. The boys were sent home while disinfection was carried out, and no boy was allowed to return until cultivations from the throat and nose had shown the absence of diphtheria bacilli. Between 50 and 60 boys were thus examined: in no case were any suspicious bacilli found in the throat, but in about 10 cases reports came from different bacteriologists that diphtheria bacilli (or the more cautious report "bacilli morphologically indistinguishable from diphtheria bacilli") were present in the nose. These boys were all in perfect health, but the bacteriologists were not told that the material came from healthy noses, and they fell into the pit. But in no single case were the bacilli found to have any pathogenic effect upon guinea pigs, when more careful tests were applied. Eight out of the ten were submitted to me, and I found only Hoffmann's bacillus or some allied harmless species; the other two were tested elsewhere with similar result. Had the bacteriologists known the facts, the parents of the boys would have been spared a serious panic.

Another point worthy of consideration is the weight to be attached to negative bacteriological reports, especially in cases clinically regarded as diphtheria. It must occasionally have happened to most bacteriologists to find diphtheria bacilli at the second or third attempt when previous results had been negative. It has happened to me to fail in demonstrating the bacilli during life in a case of undoubted clinical diphtheria, in which tracheotomy did not avert a fatal issue—in spite of repeated and elaborate endeavours, and even after death to fail, except in a cultivation from the ventricle of the

larynx, in which the bacillus was demonstrable. Such instances make one hesitate to accept as final the cases of fatal membranous laryngitis which have been asserted to be non-diphtherial in nature. It must in any case be conceded that negative results are much less conclusive than positive ones.

I have felt it my duty, in opening the discussion on this very important subject, to deal with general principles rather than with details. I have no new or striking facts to bring forward as to the pathological distribution of the bacillus. It is generally admitted that it commonly remains limited to the original seat of infection, that by direct extension it may spread down the air passages or along the mucous membranes which are in continuity with the throat (so that it is commonly to be found in the lung in fatal cases), and lastly, that in cases of severe type it may be found after death in other parts of the body such as the spleen, usually in scanty numbers, and probably only as a terminal infection.

It is to be regretted that much of the work which has been done upon the distribution of the diphtheria bacillus, as, for instance, upon its occurrence in healthy throats, is vitiated by the absence of convincing proof as to the identity of the bacilli found. The question of the persistence of the bacilli in the throat after diphtheria is also of singular interest and importance. I have myself found bacilli present abundantly and in full virulence three months after the primary attack, and I believe that similar facts are on record. Another matter well worthy of discussion is the relation of the diphtheria bacillus to scarlatinal and post-scarlatinal diphtheria, a subject upon which, unfortunately, I have no personal observations to offer.

The opinions that I have ventured to express are the result of my own personal experience and represent my sincere convictions. But I do not doubt that, in a subject which bristles with so many difficulties and fallacies, there must be many present who will disagree with them, a circumstance which, I trust may lead to an animated discussion.

II.—THOMAS DAVID LISTER, M.D., M.R.C.P.

Registrar and Pathologist to the East London Hospital for Children.

DR. LISTER said: The bacterioscopic test which Dr. Andrewes described is sufficiently accurate for clinical purposes—that is to say, so far as the diagnosis of the presence of the Klebs-Loeffler bacillus is concerned, and is naturally the only one usually adopted for clinical purposes; in the exigencies of practice inoculation is not widely applicable. Cases in which organisms are found presenting the morphological characteristics described by Dr. Andrewes should be isolated and treated antiseptically, whether they present symptoms of true diphtheria or not. At the Royal Medical and Chirurgical Society on October 25th, 1898, I mentioned, in a discussion on a paper by Dr. Lambert Lack on Membranous Rhinitis, the frequency with which such bacilli are found in cases of chronic nasal discharge in infants and young children. I gave statistics of 125 examinations, in some of which a *post-mortem* examination confirmed the views expressed by Dr. Lack as to the relation of the Klebs-Loeffler bacillus to membranous rhinitis. Since then I have been able to trace three cases of true diphtheria following upon the presence of what I am accustomed to call Klebs-Loeffler bacilli in apparently merely chronic nasal discharges. These may of course have been infections by a different bacillus presenting similar morphological characteristics, but they may also have been due to the development of virulence in the organisms found in the nose, though what the factor is which may determine such virulence it is impossible to suggest.

III.—WILLIAM MILLER CROWFOOT, M.B., F.R.C.S.,

Vice-President of the Section.

DR. CROWFOOT said: I entirely concur with what Dr. Andrewes has said as to the necessity for the diagnosis of diphtheria being, in a large measure, dependent upon clinical as distinguished from bacteriological data. As an illustration of this statement I may mention a case which came under my notice. It was that of an individual who suffered from sore throat; a swab was taken from the throat and examined bacteriologically with a negative result. Nevertheless, several other members of the same family contracted the same disease, and I have no hesitation in saying that the cases, whatever they may have been bacteriologically, were clinically diphtheria.

IV.—ROBERT MUIR, M.A., M.D., F.R.C.P.E.,

Professor of Pathology in the University of Glasgow.

PROFESSOR MUIR said that Dr. Andrewes had treated the matter from the common-sense point of view, and he agreed in the main with what had been stated. He thought that the question had a twofold aspect—the strictly scientific and the practical. With regard to the former, the question as to what determined species, was involved, and that was a question in biology—moreover, a question which at present could scarcely be properly answered. An organism might give all the cultural and microscopic characters of the diphtheria bacillus and also produce the characteristic lesions on inoculation; with regard to it no doubt would arise, but another might be like it in all respects except that it was non-virulent to a guinea-pig and yet might produce small quantities of diphtheria toxin; this also would be called an attenuated diphtheria bacillus. But supposing that no toxin could be detected (the other characters being present), could it be said that it was not the diphtheria bacillus? From the biological point of view he thought not. With regard to clinical diagnosis, he thought that the proper course was for the bacteriologist to state the results of his investigations, and for the clinician to use these in association with the results of his own observation; it was only in this way that the best use could be made of the knowledge obtained in the two departments; the clinician ought at least to understand the bacteriology of the disease. It was a great mistake to divorce the two fields of investigation, as was sometimes done.

V.—W. S. LAZARUS-BARLOW, B.A., M.D., M.R.C.P.,

Pathologist and Lecturer on Pathology at the Westminster Hospital.

DR. LAZARUS-BARLOW said: I think there is nothing more certain than the fact that it is absolutely impossible to give a strictly scientific and certain diagnosis in a suspected case of diphtheria in twenty-four hours, and as the result of microscopic examination alone. The only thing that the physician has a right to expect is an opinion of a greater or less degree of probability. As a matter of fact, I decline to give an opinion unless I have been able to learn something of the clinical aspects of the case. Where experimental evidence is obtainable the probability of accurate diagnosis is, of course, enormously increased, so that while the rapid diagnosis must be more or less unsatisfactory, cases in which time is a somewhat less urgent factor can still derive the full benefit from a bacteriological examination. Cases of this description are to be found in the so-called mild cases in which throat symptoms are slight and fugitive. From the point of public health no less than from the point of the proper convalescence of the patient, definite knowledge as to whether the case has been one of true diphtheria or not is of the greatest importance; that is to say, the class of case in which bacteriological examinations are of value are of a somewhat different order than those for which we are commonly asked our opinion.

VI.—E. KLEIN, M.D., F.R.S.,

Lecturer on Physiology at St. Bartholomew's Hospital; President of the Section.

DR. KLEIN said: The opinions expressed by Dr. Andrewes and Dr. Muir are those which commend themselves to all scientific bacteriologists—namely, that the bacteriologist cannot at present do all that the clinician expects. I am of opinion that the sooner and the more forcibly this is placed before the physician the better for the physician, and particularly for the bacteriologist. After all the bacteriologist cannot go beyond what his methods and the particular state of his science allow. For example, diphtheria bacilli or bacilli conforming to all tests we are familiar with as characteristic of diphtheria bacilli occurred in milk, and yet the farm, its *personnel*, and the consumers of the milk negatived the conclusion that the bacilli were those that cause diphtheria.

A CASE OF PURPURA AND INTENSE ANÆMIA, WITH MARKED DEFICIENCY IN THE RED BONE MARROW.

By ROBERT MUIR, M.A., M.D., F.R.C.P.E.,
Professor of Pathology, University of Glasgow.

THE following case is recorded chiefly on account of the remarkable condition of the bone marrow—a condition which

may be of importance in throwing light on the nature of some cases of anæmia occurring in young subjects. The chief conditions found associated in this case were hæmorrhages from mucous membranes and purpuric eruptions, intense anæmia, marked deficiency in the amount of red bone marrow, and deposit of iron-containing pigment in the liver and in the kidneys. The relation of these conditions to one another will be discussed later.

The following are the chief clinical facts which appear of importance in relation to the pathology of the case. For these I am indebted to Dr. Finlayson, under whose charge the case was, and I take this opportunity of thanking him for his kindness in placing them at my disposal:

A boy, aged 14 years, was admitted on January 8th, suffering from bleeding from the nose, vomiting of blood, with purpuric eruption over his body and legs. According to the history he appears to have been healthy till about a month before admission, when he had a chill and suffered from a cough, with slight hæmoptysis. Four days before admission some spots had been noticed on his body, especially on his legs. On the evening of the following day, when in bed, he had severe bleeding from the nose and mouth, which was controlled with some difficulty. A day later he vomited a large quantity of partially clotted blood, of dark colour. The amount of blood lost was evidently considerable, as he fainted on endeavouring to rise from bed. There was nothing of importance in his family history.

On admission he showed marked anæmia. His lips and conjunctivæ were almost bloodless, and there was evidence still of a general oozing of blood from his gums. There were numerous small hæmorrhages all over his legs, trunk, and head. During his stay in the hospital he vomited blood from time to time, and administration of food by the mouth had to be stopped for a period. A slight general improvement resulted, and the purpuric eruption disappeared, but on February 23rd, that is about seven weeks after his admission, the spots reappeared. On the following day he vomited blood, and subsequently passed into a state of stupor, in which he died.

The blood was examined on January 15th, about a week after his admission, when the red blood corpuscles numbered 800,000 per c.mm., the hæmoglobin was 12 per cent., and the leucocytes equalled 7,000 per c.mm. On January 26th the number was practically the same, but on February 9th the number had fallen to 640,000. I examined films sent to me on February 10th, and the following conditions were noted: The red blood corpuscles showed little alteration beyond some variation in size and slight poikilocytosis; there were practically no megalocytes; there were no nucleated red blood corpuscles discoverable. The leucocytes were very scanty—in my opinion about 1,000—and there was a very marked diminution in the polymorphonuclear (neutrophile) forms these numbering only about 25 per cent of the whole. The lymphocytes numbered about 70 per cent., the rest being made up of the hyaline cells I could find no eosinophile cells. The blood plates appeared to be practically absent, a condition which has been observed in other cases of purpura, and on which importance has been laid by Denys. The urine was examined from time to time; it contained no blood or albumen throughout, and its colour was noted as straw-coloured or pale amber. It was of acid reaction, and its specific gravity varied from 1014 to 1020.

The following were the chief facts ascertained at the *post-mortem* examination:

The body was rather poorly nourished, and showed extreme anæmia; it was also poorly developed in proportion to the age of the patient. There were numerous very minute petechiæ on the trunk, especially over the anterior walls of the chest.

The Thorax.—The serous sacs were normal, with the exception of there being some ounces of serous fluid in each pleura.

Heart.—There were numerous petechiæ of various sizes in the epicardium all over the surface, but especially anteriorly; these appeared to be comparatively recent. The ventricles were contracted, and contained some pale *ante-mortem* clot. The heart muscle was extremely pale, and showed extensive fatty degeneration, this being especially marked in the inner half of the left ventricle. There were a few small petechiæ also in the endocardium. The valves were healthy. The left ventricle appeared very slightly hypertrophied. The lungs showed nothing worthy of note beyond some hypostatic congestion with œdema.

Abdomen.—The peritoneum was normal. The stomach contained about 10 ozs. of fluid material, with considerable admixture of altered blood. Its mucous membrane was rugose, and showed extensive patchy hæmorrhages in its substance, this condition being present throughout the organ, but specially marked posteriorly, where it had a diffuse character. The small intestine also showed a few hæmorrhagic patches in its mucous membrane here and there, and contained a considerable amount of altered blood, especially in its midd'e portion. There was no sign of hæmorrhage in the large intestine. There were no ulcerations or even abrasions discoverable in any part of the alimentary tract. The liver was of normal size, fairly firm in consistence, and showed a uniform brownish-yellow colour. On testing for iron pigment with hydrochloric acid and ferrocyanide of potassium, there was found to be a considerable quantity in the outer half of the lobules. The central part of the lobules showed fatty degeneration. The spleen was slightly enlarged, fairly firm, and on section showed nothing abnormal in appearance It gave no iron reaction. The kidneys were extremely pale and of a yellowish tint, and, on applying the usual test, a large amount of iron pigment was found to be present in the cortex, this giving a dark stain of somewhat mottled arrangement. The pancreas and suprarenals were anæmic, and evidently the seat of fatty change.

The brain was extremely anæmic, and showed one or two small subarachnoid hæmorrhages over the cortex of the hemispheres. It was also slightly œdematous.

BONE-MARROW.—When the marrow of the femur was examined, instead of showing the red appearance usually found in anæmic cases, it was found to consist almost exclusively of fat of whitish appearance. Here and there were hæmorrhagic patches, but there was no red marrow (in the proper sense) visible. A similar condition was found in the ribs, the marrow here being of almost pure white colour, and apparently composed almost exclusively of fat. A portion was fixed in formalin-alcohol solution, but, when passed into chloroform for purposes of embedding in paraffin, the marrow became dissolved, leaving scarcely a trace behind. In addition to showing this peculiar character, the marrow was deficient in quantity, the bone being distinctly thicker than normal, and also of unusually hard consistence; this condition of the bone was, in my opinion, distinctly pathological.

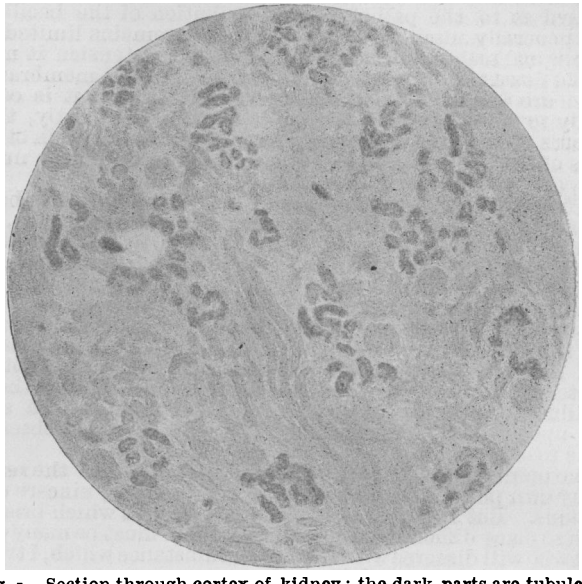


Fig. 1.—Section through cortex of kidney; the dark parts are tubules in which a deposit of iron pigment has occurred.

Microscopic Examination.—Portions of the various organs were examined, but only a summary of the results need be given. There was found very widespread fatty degeneration in the various organs—heart, kidneys, liver, etc, also in the small blood vessels—for example, in the heart wall. stomach, etc., where numerous hæmorrhages were present. The change seemed especially to affect the smaller arterioles, and was chiefly marked in the intima. In the blood vessels of the membranes of the brain a similar fatty change was present. Sections of the stomach wall were tested for the presence of iron pigment, but no trace of any was found.

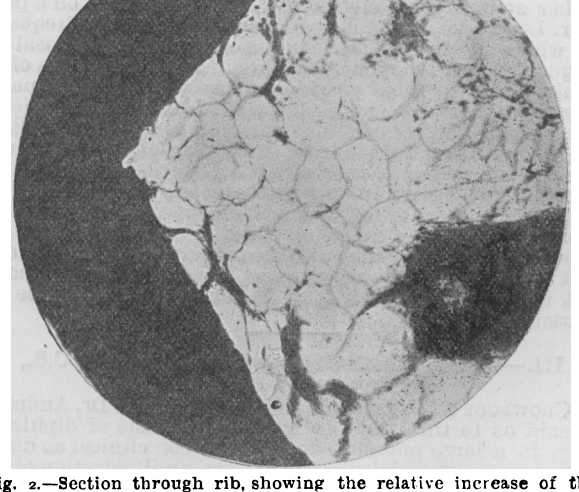


Fig. 2.—Section through rib, showing the relative increase of the adipose tissue, with great deficiency of the cellular elements. The dark part is sclerosed bone

Though the liver gave a well-marked iron reaction on naked-eye examination, similar to that met with in pernicious anæmia, only a small quantity of granular pigment was found on microscopic examination, the cells in the outer zone of the lobules giving merely a diffuse bluish staining with HCl and pot. ferrocyan. In the kidneys (Fig. 1) iron pigment was

found in larger quantities in the granular form within the epithelial cells, but in addition the cells gave here also a diffuse staining. The changes were not uniform, but occurred in patches, affecting chiefly the proximal portions of the convoluted tubules; the glomeruli were found to be quite free.

Film preparations of the marrow were made and fixed in the moist state in formalin-alcohol. In a large number of cases the film subsequently washed off, but in a certain proportion satisfactory specimens were obtained. The great mass of the tissue consisted of fat cells. Red blood corpuscles and the various forms of cells normally present were found in extremely small numbers. Only one or two nucleated red blood corpuscles could be found after a very long search. The finely granular narrow cells were also extremely scanty, and of smaller size than usual. No eosinophile narrow cells could be found. In addition to the usual fat cells there were also some cells of indeterminate nature containing small globules, and there were also a few amorphous broken-down cells. There was no evidence of pigment deposit in the bone marrow. As already stated, attempts to cut sections of the marrow expressed from the bone failed on account of its highly fatty nature. Sections, however, were obtained of the rib, showing the marrow *in situ*. In these sections (see Fig. 2) the marrow resembles adipose tissue, there being only small collections of cells round the capillaries here and there. The marrow from the femur showed a similar condition, cellular elements being there even more deficient. Films of the spleen pulp showed one condition of interest—namely, the presence of a considerable number of nucleated red blood corpuscles. In view of the conditions present in the blood and in the marrow, it is possible that their presence may indicate an attempt at compensatory blood formation in the spleen. The lymphatic glands showed nothing abnormal.

REMARKS.—It would be unwise to dogmatise in interpreting the changes found in this case, but one may with advantage discuss the relations of the more important lesions to one another.

First, as to the condition of the bone marrow: This I believe was a primary change, or, to be more correct, did not occur secondarily to any of the other lesions noted. For several years I have examined the bone marrow in a great many different conditions, and for more than a year I have been making a routine examination in almost every case. The condition of the bone marrow described above is quite new in my experience, and, so far as I can find, it has not been described before. I have spoken of it simply as a deficiency in the red marrow, and beyond this we cannot go, as we have no knowledge of any means by which such a change may be induced. It is well known that after hæmorrhage, as has been shown both experimentally and by observation on the human subject, the red marrow increases in amount, and nucleated red blood corpuscles become more numerous. The fact that in this case there were large hæmorrhages, and the marrow showed no increased regenerative power, emphasises more strongly the pre-existing abnormal condition of the bone marrow. Even in pernicious anæmia, as is well known, when the process of blood formation appears to be exhausted, the marrow is found to be of deep red colour and crowded with nucleated red blood corpuscles. There is in fact no evidence whatever that an accumulation of fat occurs as a result of the long-continued drain on the blood-forming functions. It is also to be noted that the bone was of unusually dense or sclerosed character, but I am not prepared to say how this should be regarded in relation to the change in the marrow.

Secondly, as to the anæmia: Though there is in the history no mention of advancing anæmia before the occurrence of the hæmorrhage, still I think that a degree of anæmia was present, and that this was due to the condition of the bone-marrow; this is almost certain from the fact that a week after the first hæmorrhages occurring on two successive days, the red blood corpuscles numbered only 800,000. The anæmia was of course in the main due to the hæmorrhages, but it is to be observed that after these had practically ceased, the number of red blood corpuscles showed no tendency to rise. The hæmorrhages may have been due to the fatty change in the vessel wall, or, as is more probable, some toxic or infective condition had been superadded. With regard to the iron pigment in the liver and kidneys, there is no need to look further than the hæmorrhages. These hæmorrhages occurred to a great extent in the disease, and it has been experimentally proved that in such conditions the iron-containing pigment resulting from disintegration of hæmoglobin is deposited in the liver, spleen, and kidneys. The large proportion of iron in the kidneys indicates, I think, a pretty rapid absorption of hæmoglobin or its derivatives; a similar condition may occur in paroxysmal hæmoglobinuria. In the present case, if the hæmoglobin was carried as such to the kidneys, the kidney cells were able to prevent its passage into the urine. The view that in pernicious anæmia the pigment in the organs is due to intravascular hæmolysis has been attacked by my colleague, Professor Stockman. It is not my purpose to discuss this question, but in the present case (which, however, differs in several respects from pernicious anæmia) there can be, I think, little doubt that the deposited pigment is due to the hæmorrhages. If this were not so, then there is no alternative but to assume that there were two independent lesions present—namely, a defect in the blood-forming tissue, and an increased blood destruction. My view, therefore, with regard to the case and its progress, is that the condition of the marrow had produced and kept up anæmia, and that, as a result of some intercurrent condition, the hæmorrhage and purpura occurred. From the fact that the patient had enjoyed good health before, it is probable that either the change in the bone marrow was not congenital, or if some congenital defect was present, it had recently become aggravated. The marked diminution of the the neutrophile leucocytes is also of importance, as, according to the opinion of Ehrlich and myself, these cells have their chief site of origin in the bone marrow.

Dr. LAZARUS-BARLOW said that he had had a case in the *post-mortem* room which, speaking from memory, bore a very close resemblance to that described by Professor Muir. It occured in a woman of middle age who during life had been supposed to be suffering from pernicious anæmia. At the necropsy the medulla of the tibia was found to be entirely converted into fat and a similar condition affected the marrow of the ribs, the liver and the kidneys showed a marked iron reaction. One difference between his case and that of Professor Muir lay in the fact that the bone in his own case was not sclerosed but on the contrary atrophied.

Dr. ANDREWES referred to a case in which the bone marrow was quite pale, though the anæmia was extreme. The interest of his case lay in the fact that it was not a case of primary anæmia but was definitely secondary to carcinoma.

Mr. ROGER WILLIAMS said: In cases of cancer attended with anæmia, he had often observed extensive degeneration of the marrow and bone of a similar nature to that described by Dr. Muir. These changes might be so advanced as to lead to spontaneous fracture in the absence of any secondary deposits, and he had generally regarded them as secondary to the blood degeneration.

Dr. CROWFOOT referred to a case of very severe anæmia in which there was an enlarged spleen and a great increase of the leucocytes in the blood (a case of leucocythæmia, probably) in which the spleen was removed to the great and lasting benefit of the patient.

Dr. KLEIN asked Dr. Muir to state the condition of the urine of his patient with regard to the presence in it of pigments.

Dr. MUIR, in reply, stated that in regard to pernicious anæmia he was familiar with cases in which the red transformation of the marrow was absent or very feebly marked in the long bones and in some instances recorded by others it had been found that the various long bones presented variation in this respect, for example, the tibia showing the change when the femur did not. But he had not met with any case of pernicious anæmia in the adult where there was an excess of fat in the marrow of the ribs. He was also familiar with the change occurring in cases of cancer, marasmus, etc., but these were also different. In view of all the facts mentioned his opinion was that the change in this case was not secondary to the anæmia or any other condition noted. With regard to the urine he had not had an opportunity of examining it; pathological urobilin might have been present, but from the notes it was clear that at no time had a dark colour been observed. He considered that the diffuse iron reaction preceded the deposits of iron-containing pigment granules.

UTERINE MYOMATA AND DEVELOPMENTAL IRREGULARITY.

By W. ROGER WILLIAMS, F.R.C.S.,
Clifton.

THE pathogenesis of tumours is one of the most interesting medical problems now pressing for solution, and of this problem the pathogenesis of uterine myomata is but a particular instance. It will be well, therefore, to refer briefly to the subject in general terms before discussing the par-

ticular case. It is now evident that out of the confusion of a transitional period but two conceptions as to the origin of neoplasms have emerged—the one based on the cell theory, and the other on the germ theory—and henceforth the struggle must be between these two. Briefly stated, the question now is, Do neoplasms arise, as Johannes Müller believed, through a modification of the formative process; or are they the outcome of the inflammatory process, as Broussais maintained, owing to the intrusion of microbes or other irritants *ab extrâ?* In other words are they essentially of intrinsic or extrinsic origin? I incline to the former alternative. I believe that neoplasms arise mainly from the play of forces generated within the body; and in what follows I shall endeavour to show that this is the case with uterine myomata.

The outcome of recent researches as to the genesis of these tumours indicates that in a large proportion of cases their origin is intimately associated with developmental irregularities; and conditions of this kind are probably the chief morphological factorsin their development.

Among the grosser uterine malformations with which myomata may be associated, special mention must be made of uterus duplex, instances of this having been reported by Galabin, Gow, Pick, Graverry, Falk, and others. In an interesting case by Clay, double uterus and vagina was associated with uterine myomata and absence of one kidney. In a uterus didelphys, Czerwenka found two myomata of the left corpus with cancer of the left cervix; and Jackson has seen myomata in an atresiac infantile uterus in which cancer was also present. Pick has met with a case in which the uterine malformation seemed to be due to the presence of a fœtal myomatous nodule, interfering with the union of the Müllerian ducts. Instances have also been reported of the development of myomata in the rudimentary horn of the uterus unicornis (Romiti, Routh, Doran, Mackenzie, etc.); while in a case described by Mundé similar tumours were present in the developed parous horn of a malformed uterus of this kind. In a pseudo-hermaphrodite, aged 50, in whom the female type appeared to predominate, Gruner found myomata of the malformed uterus; and in another defectively-developed person, aged 49, Howitz met with a tumour the size of a cocoanut, due to myomatous disease of the unicorn uterus. In the latter case the left tube was absent, the ovaries were represented merely by small nodules, remains of Gaertner's ducts were found in the vaginal walls, and there was hypospadias with hypertrophy of the clitoris.

Thomas has seen myomata with congenital anteflexion; and in a sterile woman, with an infantile uterus, Keiffer found a large myoma of the cervix.

Myomatous tumours have also been met with having in their interior diverticula from the uterine cavity, as in cases of "uterus accessorius"—bifid, trifid uterus, etc. (Recklinghausen, Ricker, etc.). Such conditions appear to be due to abnormal myomatous growth around persistent diverticula from the Müllerian ducts, such as Meyer and others have described.

Guyot has found uterine myomata associated with vaginal malformation; and Wetherill, in removing a large tumourof this kind, noticed supernumerary oviducts and hydatids. The concurrence of vaginal atresia and uterine myomata has been noted by Jenks.

Neumann has described myomata of the uterus and tube concurrent with Wolffian "rests" in both ovaries; and Russell has discovered Müllerian relics in the ovary, whence structures like utricular glands had evolved, that resembled the epithelial inclusions found in uterine myomata.

This leads me to remark on the frequency with which uterine myomata are complicated with ovarian cystomata (often bilateral), dermoids, and cysts of the adnexa (broad ligaments, round ligaments, etc.). Of his operated uterine myomata, Péan found associated ovarian cystomata in 12.5 per cent., and of Winckel's ovarian cystomata, 18 per cent. were concurrent with myoma uteri. Buffett has described a remarkable case of this kind in which the combined weight of the associated tumours amounted to no less than 216 lbs., the left ovarian cystoma weighing 180 lbs. and the uterine myoma 36 lbs. Leo has found myomata of the uterus coexisting with cystoma of the right ovary and polycystic disease of the left kidney. Thornton met with multiple uterine myomata associated with a large multilocular cystoma of the right ovary, a parovarian cyst of the right broad ligament, and multiple cysts of the left ovary; and in Hodge's case uterine myomata were associated with cystic disease of the ovary and broad ligament. Dartigues and Claisse have lately reported an instance in which a large uterine myoma coexisted with an enormous multilocular cyst of the left ovary and a dermoid of the right. Emmet has seen a large cystic myoma of the fundus, with several solid myomata adjacent to it, and a polypoid intrauterine myoma, concomitant with multilocular cystoma and dermoid of the right ovary.

The frequency with which uterine myomata are multiple might of itself lead us to suspect the association of developmental irregularity with the origin of these tumours, and the occurrence of cases in which the whole musculature is converted into a dense mass of small tumours—of which Emmet has described a remarkable example—points to the same conclusion.

Of like import is the finding of uterine myomata concomitant with similar tumours in the ovary, broad ligament, round ligament, tube, vagina, and in other situations adjacent to the uterus, of which many examples have been recorded. Thus, Neill has met with a case in which myomata coexisted in the uterus, broad ligaments, and ovaries; and Virchow long ago described an instance in which the uterus, ovaries, and vagina were concurrently affected.

I now pass to the consideratian of the connection between myomata and certain less obvious developmental flaws, to which Cohnheim has specially called attention. When Cohnheim first announced his theory of the origin of tumours from sequestrated fragments of the germinating tissues, very few facts could be adduced in support of it. No one then believed in the possibility of such an amount of developmental irregularity as it presupposed. The light of modern science has, however, effectually dissipated this misconception, and our eyes have been opened to the hidden defects of normality. Sequestrated fragments of the various tissues and organs have now been found to exist in every part of the body that has been specially examined for them. The urogenital system is no exception to this rule, for the track of the Wolffian and Müllerian ducts is strewn with *débris* of this kind.

Long before Cohnheim's time the tendency of tumours to originate at the seats of developmental defects had been recognised by Paget, Virchow, and others. Even as far back as 1853, referring to the proneness of melanomata to arise from pigmented moles, Paget said, "It seems a striking illustration of the weakness in resisting disease which belongs to parts congenitally abnormal.....This peculiarity may make us suspect that there may be other, though invisible, defects of first formation in our organs which may render them, or even small portions of them, peculiarly apt for the seats of malignant disease," etc. Recent observations show that most uterine myomata and cysts arise in like manner from dislocated myomatous elements connected with abnormally-evolving "rests" of Wolffian and Müllerian structures, or even of the uterine mucosa itself. Thus their initial multiplicity may be accounted for, as well as the similitude of their structure to that of the uterine wall. The discovery of epithelial inclusions in uterine myomata—for which we are indebted to Babes and Diestweg—was one of the earliest indications of the correctness of this interpretation; and several observers (Meyer, Ricker, Fischel, Coblenz, etc.) have found similar epithelial inclusions in the otherwise normal uterine musculature. By Babes and Recklinghausen these structures are believed to be Wolffian relics, while other pathologists insist on their Müllerian origin. But all such bodies are not necessarily either Wolffian or Müllerian residua, for they may be included sequestra from the uterine mucosa itself. Indeed, Ribbert has found deep in the uterine wall, not only sequestrated utricular glands, but even isolated fragments of the entire mucosa. In like manner the Nabothian follicles arise as sequestrations from the glands of the cervix.

Bearing in mind the developmental correlation between the uterine musculature and its numerous blood vessels—which are so extraordinarily interwoven—it is easily conceived how by a similar process these adenomyomatous inclusions arise, owing to the migrations and changed relations of the

parts incidental to ontogeny. Such is the manner in which I believe the germs of myomata originate, and thus may their association with the small arteries be accounted for.

A DISCUSSION ON THE PATHOLOGY OF CIRRHOSIS OF THE LIVER IN ADULTS AND YOUNG CHILDREN.

I.—ARTHUR VOELCKER, M.D., F.R.C.P.,

Assistant Physician and Lecturer on Pathology, Middlesex Hospital; Assistant Physician to the Great Ormond Street Children's Hospital.

DR. VOELCKER, in introducing this discussion, gave first a historical account of the pathology of cirrhosis of the liver. He considered it due to toxic action on the liver cells and connective tissue, and the degenerative or regenerative processes on the resisting power of the liver. The appearances described as newly-formed bile ducts suggested to him lymphatics or blood vessels. To ascertain what influence alcohol had as a cause of hobnailed liver, he examined the records of 2,020 necropsies made at the Middlesex Hospital; of these, 149 were cases of cirrhoses of the liver, which was hobnailed in 36. Of the 36 cases, alcoholism was acknowledged in 15, denied in 9, and not noted in 15. Of 4,278 necropsies made on children under 12 at Great Ormond Street, there were 23 cases, and hobnailing was present in 13. He concluded that alcohol played an important part in the production of cirrhosis, but in what way was uncertain. Large livers were rather more common in spirit drinkers than in beer drinkers, but the "gin-drinker's liver" could be produced by beer. He alluded to the effect of other poisons than alcohol in producing cirrhosis, and to the associated changes in the spleen, pancreas, and kidney. Points calling for discussion were: (1) Was it possible to distinguish between the various forms of cirrhosis microscopically and macroscopically? (2) What was the source of the newly-formed connective tissue? (3) What was the nature of the so-called newly-formed bile ducts? (4) Under what conditions could cirrhosis of the liver be experimentally produced? (5) Did cirrhosis in children differ essentially from cirrhosis in adults?

II.—LUDVIG HEKTOEN, M.D.,

Professor of Pathology in the Rush Medical College, Chicago.

MR. FOULERTON presented a contribution from Professor LUDVIG HEKTOEN on Experimental Bacillary Cirrhosis. Without entering upon the broad questions of the etiology and genesis of cirrhosis of the human liver, Professor Hektoen wished to refer briefly to some recent demonstrations made in his laboratory on cirrhotic processes in the liver of animals directly induced by two different bacilli. The observations seemed to him to be of some interest in their suggestiveness of a somewhat similar course of events in some instances of human cirrhosis. Similar more or less acute infections in man might induce a diffuse growth of new connective tissue in the liver. Then, whilst the bacteria might be destroyed, and the immediate effects of their presence pass away, the newly-formed tissue of the liver would remain; and as it contracted a vicious cycle was established, the pressure of the resulting fibrous tissue causing necrobiosis of the hepatic cells, which in turn led to renewed, more or less slow, but progressive connective tissue proliferation. With time, aided perchance by other superinduced factors, extensive contraction of the liver would result. One of the series of observations referred to was conducted by Dr. G. H. Weaver, and the main results had already been published under the title of Cirrhosis of the Liver on the Guinea-Pig Produced by a Bacillus and its Products.[1] The bacillus belonged to the colon group, and was isolated from a guinea-pig which died spontaneously. The bacillus lost its virulence rapidly, and before sufficient experiments had been made to establish clearly the relation between the necrotic and proliferative changes in the liver. With early death, necrotic and degenerative changes only were found in the guinea-pig; in those which lived longer proliferation of connecting tissue was associated with necrosis, and in other animals again cirrhosis entirely replaced the degenerative changes. These interesting changes were observed only in guinea-pigs, showing well the influence of species, and were caused by the inoculation of living as well as of devitalised cultures. The second series of observation concerned a bacillus that might be placed in the pseudo-diphtheria group. It was isolated from the lesions of a case of blastomycetic dermatitis of the back of the hand. Inoculations in various ways with this bacillus and its products had been found to produce with a fair degree of consistency more or less necrosis and diffuse cirrhosis of the liver in guinea-pigs and other animals. Unfortunately this bacillus also lost its virulence before many of the experiments planned could be completed. It would have been of great interest to follow out the subsequent course of the cirrhosis set up on some of the animals. After a description of the cultural characteristics of this bacillus, Professor Hektoen alluded to his animal experiments. In guinea-pigs the subcutaneous injection of about 1 c.cm. of bouillon culture produced, in from two to four days, a markedly hard infiltration, followed by the development of more or less extensive punched-out ulcers, which generally healed up. The animals became thin, and died in from three to five weeks. The essential change found was necrosis, with cirrhosis of the liver. The bacillus could usually be recovered from the internal organs and from the cutaneous ulceration. Occasionally the local reaction failed to take place, and the animals at times recovered. In a few cases local infiltration and ulceration took place, but no other changes were found. The general results with intraperitoneal injection were similar, but not so constant. With rabbits the intravenous or subcutaneous injection of 1 c.cm. of bouillon culture did not make the animals sick nor produce any change in the liver. Inoculation into the anterior chamber of the eye of a full-grown medium-sized rabbit resulted in great emaciation and death after 24 days with cirrhotic and other changes in the liver. The subcutaneous injection of 2 c.cm. of bouillon culture in a dog gave rise to a huge swelling which gradually subsided. The animal was killed with chloroform six weeks after the injection. The liver was of about normal size, finely uneven, with occasional single greyish dots or groups of dots. There was slight grating on cutting the organ. Microscopic sections showed numerous small intralobular islands of recent connective tissue cells, as well as of small cells with deeply stained irregular nuclei. There were also branching bands of recent connective tissue along the vessels. Inoculation of a grey mouse and of a white rat with 0.2 c.cm. and 0.3 c.cm. of a bouillon culture respectively made both animals sick for a time, but when killed on the twenty-first day the livers were found to be normal. [Photographs of microscopic sections were shown demonstrating the cirrhotic changes produced in the liver of the guinea-pig by both these bacilli described.]

[1] *Trans. Chic. Path. Soc.*, 1900, iii, pp. 221-335.

III.—SIMON FLEXNER, M.D.,

Professor of Pathology, University of Pennsylvania.

PROFESSOR FLEXNER said: Dr. Voelcker has so ably summed up our present knowledge of cirrhosis of the liver and so fully emphasised the problems that press most at this time for solution that in speaking on any topic of the discussion, one will hardly be able to avoid repetition. I shall ask your indulgence for a brief moment only to consider three points: the first, the experimental evidence that lesions of the liver cells precede changes in the connective tissue; the second, the nature of the new tissue formed in cirrhosis and its distribution; and the third, the common cause of death in the disease.

My own experiments cover the inoculation of animals—guinea pigs and rabbits—with poisons derived from bacteria, from the higher plants and other animals. The chief results were obtained with ricin and abrin, from the castor and jequirity bean respectively, and the blood serum of the dog injected into the circulation of the rabbit. In these experiments it was shown that the primary effects of the poisons were exerted upon the liver cells. Necrosis, consisting of a few or many cells and hyaline in nature, were common. In the animals which died from acute poisoning, they were the principal and, excepting for a moderate leucocytic infiltration, the only important lesions. Where the animals survived some weeks, proliferative changes in the connective

tissue, with the production of the so-called newly-formed bile ducts, were met with. When the new growth of tissue came from the surface capsule, indentations were produced suggestive of the granulations of atrophic hepatic cirrhosis. While these results were suggestive of the part played by a primary degeneration and necrosis of the parenchyma they failed entirely to clear up the question, in that they did not exactly reproduce the morbid appearances seen in human hepatic cirrhosis.

We have been in the habit of looking upon the new connective tissue found in hepatic cirrhosis as of the nature of white fibrous tissue. As a matter of fact, it is much more complex in structure. The liver normally contains at least three kinds of connective tissue: (1) White fibrous in the interlobular spaces and the surface capsule chiefly; (2) reticulum within the hepatic lobules; (3) elastic tissue chiefly about the blood vessels, and to a less extent the bile ducts in Glisson's capsule and in the surface capsule. Very rarely a minute quantity of this tissue may be seen in the walls of the central veins. A study of the tissues from cirrhosis by ordinary staining, then after digestion of the sections with pancreatine, and lastly after staining for elastica by Weigert's method, show that not one only but all the connective tissues enumerated are increased or altered. The most surprising result is the great amount of elastic tissue in the perilobular new growth of connective tissue, and now, for the first time, to be found within the lobules. There are differences in the amount and distribution of this tissue as well as in the alteration in the reticulum in the "atrophic" and "hypertrophic" forms of cirrhosis that time will not permit me to attempt to describe at this time, but the specimens which I pass around may enable you to appreciate.

Finally, I should like to remind you of a statement made by Professor Osler in his work on the *Practice of Medicine*. Somewhere in that volume he says, "It is paradoxical but true that few of our patients die of the diseases from which they suffer," etc. Professor Osler refers especially to the causes of death in chronic diseases, recognising that in the last event it is not the sudden failure of hepatic, or renal, or cardiac capacity that ushers in the terminal event. In most instances, as we now understand them, it is a bacterial infection. My studies of several hundred cases of chronic diseases, which had been investigated bacteriologically, convinced me of the importance of such terminal infections. The chief micro-organisms concerned are the pyogenic cocci. They may, moreover, occur as causes of local infections, especially inflammations of the serous membranes, or they may exist in the form of a general invasion-bacteræmia. The portal of entry may or may not be discovered clinically or at the necropsy. It may be an angina, an old ulcer (as in the leg) or the result of a trifling surgical operation, as in paracentesis, or it may baffle every attempt to discover it when we speak of the infection as cryptogenetic. I wish to thank you for the privilege of taking part in this interesting discussion, and to apologise for occupying so much of your valuable time.

IV.—W. S. LAZARUS-BARLOW, B.A., M.R.C.P.,
Pathologist and Lecturer on Pathology at the Westminster Hospital.

DR. LAZARUS-BARLOW said: I suppose that it is better, in a discussion of the present kind, that speakers should rather err on the side of dogmatism than on the side of uncertainty, and for this reason I propose to state my views in a somewhat more uncompromising way than truly represents my opinion. The two chief points upon which I should like to lay stress refer to the pathologies of atrophic cirrhosis in adults and in children. In the case of the atrophic cirrhosis of adult life I think that the old idea that the condition depends chiefly upon an undue indulgence in alcohol, and especially in the abuse of ardent spirits, is correct, and I do not propose to enter into the question of etiology at all. But when we come to the question whether the condition is "inflammatory," as was at one time the universal idea, and as is still held by some noteworthy authorities, I think we are on very doubtful ground. This question has for many years been an attractive one, and the idea of cirrhosis as being inflammatory has, to more persons than myself, been a severe stumbling-block. It is certainly curious that we should never be able, on the assumption that the change is inflammatory, to point out a specimen as showing an early stage of the fibrosis comparable with the early stages of true inflammatory fibrosis which is so common a condition, and one which carries such a definite microscopical picture with it. That we under certain conditions meet with an atrophic fibrosis which is accompanied with the presence of a small cell infiltration amongst the adventitious fibrous tissue is indubitable. Such cases are, however, in my experience extremely rare; and even then the fibrous tissue that is present is of a well-formed type, and is totally unlike the material composing a young cicatrix, for example. In these rare cases my own opinion is that we have to do with the superposition of a genuine attack of inflammation on a tissue which is already the seat of a chronic fibrosis, but I do not think they aid us in any other than a negative manner to arrive at a conclusion upon the pathology of the underlying fibrosis itself. Unfortunately, the results of experimenters upon the subject of hepatic fibrosis are more than usually discordant, and although one is aware of the logical fallacy of "arguing" from analogies, there is, I think, more to be hoped for in this direction at the present moment.

If we consider the fibroses as a distinct class of pathological change in which extreme chronicity is one of the predominating features, we can include under one heading (*a*) senile fibroses of all kinds, (*b*) cirrhosis of the liver, (*c*) chronic granular kidney, and (*d*) the scleroses of the nervous system. Whether the fibroses which are found at times in the muscle of the heart are to be included in the same group, is perhaps a question. Until this time last year I should have unhesitatingly so included them, but at the meeting at Portsmouth I had the honour of showing a specimen of gummata in the heart wall, in which true inflammatory products were present in the left ventricular wall side by side with definite fibrosis of the ordinary type in the muscle of the right ventricle. Since meeting with this specimen I have felt some doubt as to the nature of cardiac fibrosis, though it is most certainly true that it is only in the rarest cases that the coexistence of an acute inflammatory change with the chronic fibrotic change leaves us in doubt, and it is probable, therefore, that cardiac fibrosis must be brought into line with the other chronic fibroses to which reference has been made. Now in the case of the scleroses of the nervous system there has never been any tendency to consider the fibrotic change as inflammatory, but on the contrary, it has always been recognised that the adventitious fibrous tissue replaces nervous tissue which has degenerated. That is to say, the essential elements of the part degenerate first, and the overgrowth of neuroglia takes place subsequently to fill up what we may speak of as a potential lacuna caused by the death and degeneration of the nervous elements. It is unnecessary for me to pursue this matter further, as it is clear that I would wish to draw the inference that in the case of hepatic cirrhosis we have first a destruction of the hepatic cells themselves, be it as the result of the action on them of alcohol or some of the bacterial poisons, and that subsequently there occurs an overgrowth of the normal fibrous tissue of the liver to fill up a potential lacuna. Naturally, in any microscopic picture we shall find these features side by side, but since the destruction of hepatic cells must be a more or less gradual process—otherwise the onset of the disease could not be so insidious as it undoubtedly is—there is every reason to expect that signs of a rapidly forming and young fibrous tissue will be wanting, and this is just what we find to be actually the case. It may of course be urged against this view that the dead and degenerating hepatic cells, being foreign bodies, act as irritants, and that in consequence the fibrous tissue which arises subsequently is of the same nature as the fibrous tissue of a cicatrix. To these objections I would suggest that upon this view our conception of inflammation will have to be widened until it embraces the whole of pathology, with the exception of the new growths, and would ask whether we are to regard the umbilicus as inflammatory fibrous tissue—a claim to which designation it has in my opinion far more right than the chronic fibroses we are at the present moment considering.

While I would express my belief that the pathology of the fibrosis is as I have just indicated, I think that this is especially likely to be the case with the atrophic fibroses of the liver. With reference to the so-called unilobular or biliary cirrhosis, the matter is very difficult. Personally I have never

been able to satisfy myself of the separate existence of this variety as a distinct histological type. That one meets with large and fairly smooth livers of considerable weight, in which there is a widespread and small-meshed fibrosis, is true; though it must be noted that they are by no means common. But I have never been able to convince myself in the few cases that I have examined either that the condition is unilobular, or that it has any special relationship with the bile passages. For this reason I do not propose to refer to them further. Intercellular or pericellular cirrhosis is in a special class by itself, and that variety, too, I shall leave on one side. But there is a variety of hepatic fibrosis which is usually very intense, and leads to a more marked lobulation of the surface of the liver than any but the most extreme cases of adult atrophic fibrosis exhibit, and to these I should like to refer for a moment. The cases of which I am speaking are not very common; they affect children at an older age than is the case with intercellular fibrosis (usually the patients are 10 to 16 years of age), they are often associated with great ascites and with a well-marked jaundice of a greenish hue, and distension of the abdominal superficial veins is, as a rule, considerable. The cases are sometimes of long duration, at times extending into years, but they progressively become worse, and ultimately die in the same manner as the adult who is the subject of ordinary atrophic cirrhosis. I well remember that these cases used to be pointed out to the students as illustrating the extreme vulnerability of the liver in youth to the action of alcohol, and it was to the effect of this agent that the condition was supposed to be due.

That alcohol may play its share in the production of this variety of hepatic fibrosis is quite possible; but the view which I first heard put forward by Dr. Rolleston, of St. George's Hospital, seems to me to be more in accordance with the facts. Dr. Rolleston suggests that this form of cirrhosis is really a late manifestation of congenital syphilis—not in the sense that it is a distinctly syphilitic lesion, but that the syphilitic poison when it acts upon the liver cells of the fœtus to a degree less than that which is necessary for the production of the typical syphilitic intercellular cirrhosis, damages them, and thus places the liver in an exceptionally vulnerable position. When, then, some factor arises which would be without effect upon the healthy liver, but which completes the injury commenced in intrauterine life by the syphilitic poison, the way is laid open for the occurrence of that fibrous tissue hyperplasia which ultimately characterises the hepatic condition.

The great difficulty in the way of the suggestion that has just been put forward is the fact that a syphilitic history is, in the cases we are considering, often very poor or, indeed, is quite wanting. Though we may say that this is just what we should expect, it considerably reduces the possibility of proving the point. At times, however, as in a case which I brought before the Pathological Society last year, collateral evidence is fairly strong. In any case, an explanation of the pathology of this variety of hepatic fibrosis is difficult, but on the congenital syphilis hypothesis many of the difficulties vanish.

V.—J. O. WAKELIN BARRATT, M.D.Lond., F.R.C.S.Eng.

DR. WAKELIN BARRATT said: Considerable light is thrown upon the pathology of hepatic cirrhosis by the numerous attempts which have been made of late years to produce this condition experimentally in animals. Most of these experiments—such for example as the administration of drugs by the mouth or the alteration of the animal's usual diet—have afforded results which are inconstant or are incapable of being carried to an extreme degree, and are further open to the objection that the whole of the liver is affected, and thus the general metabolism of the animal is disordered. The only means of producing hepatic cirrhosis strictly localised in extent, and gradually becoming intense in degree, is by ligature of one of the bile ducts, and this method alone possesses the character of being simple in so far that a fraction only of the liver is involved and that no general effects are produced, the functions of the liver being carried out without any recognisable impairment by the remaining portion of this organ. Only this mode of production of hepatic cirrhosis will therefore be considered here, since it alone possesses the constancy and certainty of effect on the one hand, and the definite limitation of area on the other hand, which are necessary to scientific investigation, while, finally, it exhibits the important qualities of simplicity of conception and aim.

The earliest observer who ligatured a single bile duct in the investigation of hepatic cirrhosis was Nasse[1] in 1894, who by this means succeeded in producing increase of interlobular connective tissue.

About the same time Josselin de Jong[2] performed similar experiments. When strict antiseptic precautions were used he could find no change in the liver.

In 1897 Professor Vaughan Harley and myself commenced to investigate the effect of ligature of a single bile duct.[3] We were not aware at this time that other observers had worked in the same direction. Our experiments, which were aseptic throughout, were made upon cats and dogs, and show that cirrhosis always results in the corresponding liver area when a single bile duct is ligatured. The general health of the animals is not impaired, though the cirrhosis, which is always limited in distribution, is slowly progressive in the affected area. Microscopic examination shows that in the area of the liver corresponding to the ligatured duct, there is a development of interlobular connective tissue, rich in elongated nuclei, together with marked hyperplasia of the biliary ducts, presenting in this respect an exaggerated picture of what is seen in human hepatic cirrhosis. The larger bile ducts are dilated and tortuous, and the affected hepatic lobules are much diminished in size. Sometimes multinucleated cells are seen in small collections in the interstitial tissue. There is no appearance of jaundice or ascites.

Our observations, which were continued over lengthened periods of time, furnish a complete demonstration of the fact that simple ligature of a single bile ducts produces cirrhosis in the corresponding liver area. Owing to the simple nature of the operative interference, and the good general health which the animals subsequently enjoy, many of the disturbing factors which are present in the human subject are here absent, and the problem of the mode of production of the changes in the liver is reduced to its simplest form. It is clear also that the processes which are effective in experimental cirrhosis must also under analogous circumstances be in operation in the human subject.

After ligature of a bile duct the functions of the corresponding area of the liver are not abolished. Bile continues to be secreted and is found in the bile ducts, just as in the human subject bile continues to be formed, giving rise to jaundice, after complete obstruction of the ductus communis choledochus. It would appear that this continued secretion of the bile after ligature is a most important factor in the production of cirrhosis. It is well known that fluids injected under increased pressure into the biliary passages find their way into the circulation. This is generally regarded as wholly osmotic in its nature, though it does not appear certain that the absence of rupture of some of the finer biliary passages can be altogether excluded.[4] When bile thus escapes from the blocked biliary passages it enters in the first instance the lymph spaces.[5] It then of necessity acts as a slow irritant, and it would appear that the interlobular fibrosis which takes place in the affected area must be attributed essentially to this factor. To the increased pressure of bile in the biliary passages must also be attributed the dilatation of the larger bile ducts and the hyperplasia of the smaller ones which is so striking a feature in experimental cirrhosis. The atrophy of the liver lobules in the ligatured area appears to be due to the irritation of escaped bile acting upon the cells at the periphery of the lobule; it is not readily explicable as a pressure effect.

The above is a short outline of the leading characters of experimental hepatic cirrhosis, due to the blocking of the biliary channels coming from a limited area of the liver, a cirrhosis which may truly be termed "biliary." Further experimental work is still required to determine the extent

[1] *Semaine Médicale*, 1894, p. 202.
[2] Cirrhosis Hepatis, *Inaug. Diss.*. Leyden, 1894.
[3] A preliminary account is given in the BRITISH MEDICAL JOURNAL of December 10th, 1898.
[4] Cf. Wakelin Barratt, On the Effect of Injecting Dilute Sulphuric Acid into the Common Bile Duct, *Journ. of Path. and Bacteriology*. 1898. pp. 340-347.
[5] Vaughan Harley. Leber und Galle während dauernden Verschlusses von Gallen und Brusfgang, *Archiv f. Anat. u. Physiol.*, 1893, p. 291.

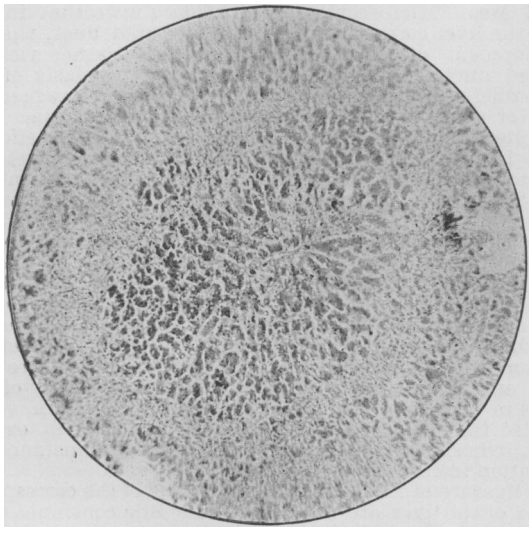
to which hepatic cirrhosis in the human subject is to be regarded as of the same nature as the extremely simple experimental form which has here been described. The study of hepatic cirrhosis is in fact reduced to its simplest conditions when a purely localised cirrhosis is produced by a lesion which involves a fraction of the liver only, leaving the rest of the liver, as well as distant organs, unaffected, and producing no recognisable change in the general condition of the animal.

VI.—THOMAS DAVID LISTER, M.D., M.R.C.P.,

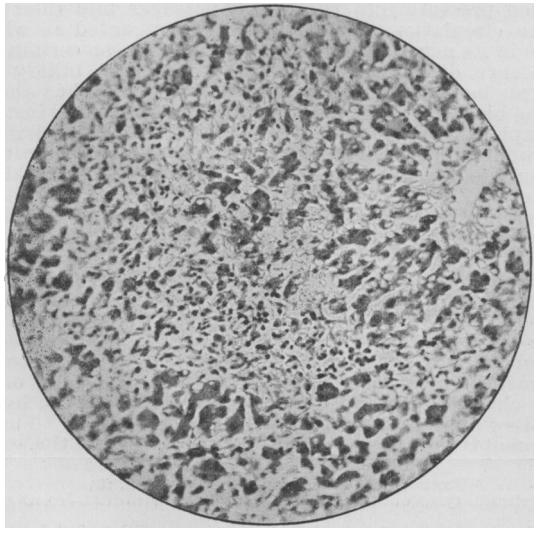
Registrar and Pathologist to the East London Hospital for Children.

DR. LISTER said: Though merely an isolated observation, the following case has an interest in relation to this subject:

The boy, a well-grown, well-developed child, aged 5, was admitted to the East London Hospital on April 11th, 1899, for vomiting and straining at stool, passing mucus and blood only, having been ill for five days. The onset was sudden, with diarrhœa, vomiting, and rigors. His previous history was unimportant, with the exception that he had had occasional



colic and diarrhœa of brief duration at intervals during the preceding ten months. He was placed under the care of Mr. Betham Robinson. On admission his temperature was 99.6°, pulse 150, small, and compressible; his extremities were cold, his respiration was quiet and easy, his abdomen was retracted, his tongue dry and brown; resonance of abdomen



normal; a doubtful tumour was thought to be present in the right iac fossa. Laparotomy was performed and the abdomen explored for intussusception without result. The operation produced no effect, either of improvement or the reverse. On April 12th (the next day) he vomited three times, and passed three stools with blood and mucus. On April 15th he passed fifteen stools; his temperature was 101.4°; the stools were brown and fluid, and very offensive, and contained much blood. On April 16th, eight stools. On April 17th, twelve stools. On April 18th, ten stools. The stools were now chiefly blood. The patient was very anæmic, pulse 140, and on April 19th he died suddenly after vomiting, being extremely blanched. The vomit had contained blood for the last four days. The wound was perfectly healed. The *post-mortem* examination showed a diffuse ulcerative colitis, intense congestion of the gastro-intestinal tract, and blood everywhefe on the mucous surface of the stomach and small and large intestine. The liver was very pale, somewhat fatty, rather firm, but with no lardaceous reaction, no irregularity or thickening of the capsule, and a normal resistance to laceration. There was nowhere any evidence of congenital syphilis, and the family history was good in this respect.

Microscopically the lobules of the liver are surrounded by a zone of small cells; some of the liver cells show vacuolation and hyaline necrosis. Some of the sections show large groups of bacilli; possibly this is a *post-mortem* invasion, as they are not associated with foci of cell deposits. There seems to me to be no doubt that this is a suggestive instance of the association of an acute interstitial hepatitis with an acute diffuse hæmorrhagic ulcerative catarrhal colitis of uncertain origin, which had caused death by hæmorrhage and exhaustion. The appearances resemble those produced experimentally by Professor Flexner and others in guinea-pigs. It is probable that the liver does not always escape scatheless from the very mixed toxins that must be passed through it in some of the intestinal infections of children, and that, as in the guinea-pig, fibroid changes may follow on acute interstitial inflammation.

VII.—THEODORE FISHER, M.D., M.R.C.P.,

Pathologist to the Bristol Royal Infirmary; Physician to Out-Patients, Bristol Hospital for Sick Children and Women.

DR. FISHER differed from the view that all cirrhoses originated as proliferation of interstitial tissue consequent upon degeneration of liver cells, and thought that some might originate in an interstitial hepatitis. He gave brief notes of four cases of acute cirrhoses of the liver present in cases of septicæmia. One was in a woman, aged 22, who died two months after an operation for appendicitis; another in a woman, aged 26, who died of chronic pyæmia; a third in broncho-pneumonia in a boy aged 4 years, and a fourth in a child who died of suppurative peritonitis and pleurisy. In the first case not only was there acute proliferation of the interstial tissue, but small-celled infiltration throughout the lobules. In the other cases also the microscopical changes were obviously acute in nature. Dr. Fisher also referred to a case of Banti's disease, which, if Dr. Banti's theory of the causation of the disease be correct, must be allied in nature to cases in which septicæmia sets up interstitial changes in the liver.

VIII.—JAMES LAIDLAW MAXWELL, JUN., M.B., B.S, London.

DR. MAXWELL pointed out the close resemblances between the sections of cirrhosis of the liver after ligature of one of the bile ducts and sections of cirrhosis of the liver in congenital atresia of the hepatic duct. In two cases of the latter condition examined by the speaker the same position of the fibrous tissue was noted with the same freedom of the unaffected masses of liver cells from any intercellular cirrhosis. Also the same resemblance in the multiplication of bile channels, many of them containing inspissated masses of bile. He also wished to question the value of Dr. Voelcker's statistics of cirrhosis of the liver in children taken from the *post-mortem* room. He urged that frequently in pericellular cirrhosis there was no change in appearance or shape of the liver, and quoted in illustration two extreme cases of peri-cellular cirrhosis of the liver in congenital syphilitic infants which he had examined, in which there appeared to be no macroscopic changes whatever. Further, that in stillborn children it was comparatively common to find advanced forms of cirrhosis without any changes in the appearances of the liver. This was not a fibrosis in the proper sense of the word but a large increase in the connective tissue cellular elements between the individual liver cells. He was inclined to believe that these cellular elements grew into the ordinary fibrous elements if the child survived its birth.

IX.—STUART MCDONALD, M.B., C.M.,
Pathologist to the General Hospital, Birmingham.

DR. MCDONALD referred to a case of cirrhosis of the liver in a girl with fatal hæmatemesis.

A girl of 15 was admitted to the General Hospital, Birmingham, suffering from severe hæmatemesis. She died a few hours after admission. The condition was thought to be due to gastric ulcer, but at the necropsy cirrhosis of the liver was discovered; the cause of the bleeding was rupture of a group of varicose veins in the stomach wall. The cirrhosis was of the coarse hobnail variety. Microscopically the condition appeared to be a mixture of polylobular and pericellular cirrhosis. On the cellular areas some of the capillaries showed emboli of micro-organisms. There was no history of either alcoholism or syphilis. The patient had had measles in infancy, but no other specific fever.

REPLY.

Dr. VOELCKER stated that he had brought forward his statistics derived from a general hospital, with the object of showing the relative occurrence of cirrhosis of the liver. He pointed out that the chief ages at which cirrhotic livers were found were either in the first two or three years of life or between 8 and 10, and then not again till after 25. From this he concluded that the severe and frequent intestinal catarrh to which children were so prone could have little if any effect in the production of cirrhosis of the liver. It was known that in enteric fever areas of necrosis of liver tissue, followed by a localised fibrosis, occurred, but he did not think that these played any part in the production of cirrhosis. In the case of children it was certainly true that the microscope revealed a degree of cirrhosis often quite unexpected from naked-eye examination. In his classification of cases of cirrhosis, increased consistence of the organ had been the requisite condition. He did not share Dr. Lazarus-Barlow's aversion to including cirrhosis as an inflammatory affection, and thought that the conditions in the liver were comparable to those in the kidney; and that, although in view of Professor Flexner's observations on the increase of elastic tissue, which certainly did not appear to be inflammatory in origin, yet the increase of connective tissue was more reasonably regarded as inflammatory than as a hyperplasia the result of an attempt to fill up the space left by the atrophy of the liver cells. With regard to the form of cirrhosis in children, he had met with both pericellular and perilobular sclerosis; and while he considered that syphilis was a frequent, he did not think it the only, cause of cirrhosis in children. The formation of new bile ducts he ventured to think was still open to doubt, but he agreed with Dr. Maxwell that in some cases of congenital obliteration of the bile duct there was seen a new formation of tubes lined apparently with altered liver cells, and containing bile in their lumen. In view of the occurrence, often quite unexpected, of cirrhosis of the liver in the *post-mortem* room, he thought it very necessary to hesitate before ascribing a causal relationship to any other factor, such as an appendicitis or remote suppurating focus present at the same time. The pathology of cirrhosis of the liver must still be the subject of investigation by experiment and observation.

THE ETIOLOGY OF TROPICAL DYSENTERY.

By SIMON FLEXNER, M.D.,
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THE imperfection of our knowledge of the nature of dysentery is not due to lack of opportunity for, or of energy in, its study. The disease in the past quarter of a century has not escaped the attention of bacteriologists, although it must be confessed that the results of somewhat extensive studies along these lines have been far less conclusive than might have been predicted. The attempt to establish a common etiological factor for all cases of dysentery has thus far failed. This failure has tended to emphasise the existence of several pathological states for which the term "dysentery" is employed merely as the collective designation. That these conclusions regarding the disease may after all not be in keeping with the facts is at least open to suspicion. When we recall the protean nature of other infectious diseases, there can be no *a priori* objection to the hypothesis that the causative agent of dysentery need not necessarily vary for each of the many types of the disease that have from time to time been distinguished.

That the lines of demarcation between the several clinical and pathological types should be inaccurate is not a matter of wonder. Both the beginning and end of any given instance may vary very widely, and the symptoms and lesions of cases arising sporadically in temperate climates may agree with those of dysentery occurring endemically in the tropics or epidemically in both localities. The terms "catarrhal," "tropical," "epidemic," and "diphtherial" are far from signifying sharp-cut entities.

As must always occur when classification of a disease proceeds upon clinical and pathological rather than etiological lines, the literature of dysentery is burdened with an interminable mass of appellations indicating the nature of the disorder or the author's conception of its pathological anatomy. Dysenteries, however, are now divided by the chief writers into several groups, depending upon the clinical history or the mode of prevalence; thus Osler writes of the acute catarrhal, tropical or amœbic, the diphtherial and the chronic dysentery. Davidson considers the subject under two headings: first, according to prevalence—epidemic, endemic, the dysentery of war and famine; secondly, upon clinical grounds—acute, fibrinous, or pseudo diphtherial, and chronic dysentery. Kartulis described endemic, epidemic, and sporadic varieties. Manson speaks of a catarrhal and ulcerating dysentery, while Delafield distinguishes in the environs of New York at least five distinct types of the disease, only one of which appears to be due to a specific agent, the amœba coli.

Bacteria have been urged by many investigators as the cause of dysentery. The earlier studies of Klebs, Prior, and Ziegler have now only a minor historical interest, although Ziegler still holds that the relation of certain bacilli to the lesions speaks for their pathogenic action. The early studies of Hlava upon the epidemic disease yielded quite inconclusive results. Chantemesse and Widal were somewhat more fortunate in that from five cases of tropical dysentery they obtained a bacillus which, when injected into the stomach or rectum of guinea-pigs, gave rise to diphtheritis, an observation, however, which Grigoriew, who believed that he had isolated the same micro-organism from 10 cases of dysentery, failed to confirm. Maggiori obtained from 11 cases of the epidemic disease B. coli communis. This investigator considered it highly probable that the disease was caused by this organism whose virulence was intensified, a conception also shared by Laveran, Arnaud, Celli, Fiocca and Escherich, who isolated the same organism from dysenteric cases.

The studies upon this bacillus by Celli and Fiocca are the most important which we possess. Their cases included examples of the sporadic, epidemic, and tropical disease occurring in Italy and Egypt. They paid special attention to the occurrence and action of the amœba coli, so that they are doubly useful. They exclude this organism as a cause of any form of the disease, and consider that a variety of the colon bacillus particularly pathogenic, which they designate B. coli dysenteriæ, is responsible for the lesions. A toxin separated from growth of the organism was found to act upon the intestines of animals in a manner similar to the bacilli. Results similar to those of Celli were obtained by Del Pino and Alessandri. The colon bacillus is also believed by Escherich to play an important part in the production of colitis contagiosa in children which in its morbid anatomy agrees with catarrhal dysentery.

The bacilli thus far enumerated, except those of Chantemesse and Widal, show no specific properties. They all represent a well-known bacterial species, constantly present normally in the situations from which they were obtained in disease, and whose only unusual properties were increased virulence when tested upon animals, and a capacity to set up enteritis when injected into the intestines of dogs and cats.

Investigation of an epidemic of dysentery which prevailed in Japan yielded different and apparently more convincing results. Ogata isolated fine bacilli, which liquefied gelatine, stain by Gram's method, and set up, in guinea-pigs and cats, intestinal ulcerations. A similar organism was later obtained in Padua by Vivaldi, since which time it appears not to have been found again. This list covers the bacillary species isolated in cases of dysentery, with the exception of an organism obtained by Shiga, who also studied the disease prevailing in Japan. This investigator's studies, which have a very direct value upon my own, are deferred for the present.

On the other hand, a causative *rôle* in the production of

dysentery has also been ascribed to the pyogenic cocci. Besides being found in association with bacilli by several of the investigators already mentioned, they have been regarded as the chief pathogenic agents by Zancarol, whose studies were carried out in Alexandria, and very recently by Ascher, who investigated cases arising in Eastern and Western Prussia. Similar observations were made by Silvestri of Turin, and by Bertrand and Baucher in France. These cocci, especially the streptococci, were capable in certain instances of setting up in cats dysentery and liver abscess. An especial variety of endemic dysentery occurring in Cochin China yielded Calmette the B. pyocyaneus. The same micro-organism was isolated from the small epidemic of the disease occurring in New York State by Lartigan; in another epidemic in children prevailing in Canada by Adami, and in certain sporadic cases by Barker in Baltimore.

Protozoa have also been brought forward as the cause of dysentery. These organisms differ from the bacteria in not existing in easily demonstrable forms or numbers in the dejecta in health, and the number of species occurring under all conditions is small. Among the protozoa the amœbæ have achieved the distinction of being connected in a causal relation with endemic dysentery. Since the studies of Kartulis, Councilman and Lafleur, and Kruse and Pasquale, so firmly has the idea of this connection taken hold of the popular medical mind that the designation "amœbic" as synonymous with "endemic" or "tropical" dysentery has been widely adopted, and yet the evidence upon which this belief is placed cannot be regarded as convincing. Until we shall have gained other means of differentiating amœbæ than we now possess, and, moreover, until we are able to control their development with at least as great perfection as in the case of bacteria, the question of the precise part played by them in dysentery cannot be satisfactorily determined. The last ten years have seen a modification of the views regarding amœbæ as causes of pathological conditions in human beings.

That these organisms exist in diseases other than dysentery was conclusively proved by the early observations (Cunningham, Lewis) upon choleraic discharges. Grassi found them in diseases so varied as typhoid fever, cholera, pellagra, and colitis secondary to tumours. He also found them in the dejecta of healthy individuals, a fact further established by Calandrucci, Massiutin, Kruse and Pasquale, Gasser and Schuberg.

It can, therefore, no longer be held that amœbæ are necessarily pathogenic when found sojourning in the intestine of man. That these organisms when combined with bacteria may cause intestinal lesions and even ulceration is now established. The experiments of Kartulis and Kruse and Pasquale with the contents of hepatic abscesses supposed to be free from bacteria are all but convincing in so far as they are supposed to prove the capacity of amœbæ alone to set up such changes. Councilman and Lafleur believed that the amœbæ alone produced the intestinal lesions. Kartulis, on the other hand, sees in the occasional diphtheritis evidence of the action of bacteria, while Kruse and Pasquale have followed the latter in their penetration into the coats of the gut, where they lie "cheek by jowl" with the amœbæ or even precede them in the invasion.

We may, I think, sum up the present knowledge of the cause of dysentery in the following way:

1. No bacterial species yet described as the cause of dysentery has an especial claim to be regarded as the chief micro-organism concerned with the disease.

2. It is improbable that any bacterial species that is constantly and normally present in the intestine or in the environs of man, except where the disease prevails in an endemic form can be regarded as a probable cause of epidemic dysentery.

3. The relations of sporadic to epidemic dysentery are so remote that it is improbable that the two diseases are produced by the same organic cause.

4. The pathogenic action of the amœba coli in many cases of tropical and in certain examples of sporadic dysentery has not been disproved by the discovery of amœbæ in the normal intestine and in diseases other than dysentery. While amœbæ are commonly present and are concerned in the production of the lesions of subacute and chronic dysentery, they have not thus far been shown to be equally connected with the acute dysenteries even in the tropics. In the former varieties bacterial association probably has much influence upon the pathogenic powers of the amœbæ.

THE DYSENTERY OF JAPAN AND THE PHILIPPINE ISLANDS.

Every year, especially in the summer and autumn, dysentery prevails in Japan. The epidemic studied by Ogata occurred in the province of Oita. Lesions in the intestine are described in one instance, death having occurred on the eleventh day of the disease. The lower segment of the small intestine was hyperæmic. The large intestine was greatly swollen, so that the lumen was almost obliterated. The mucous membrane was hyperæmic and presented a deep bluish-red colour. The mucous membrane of the transverse and descending colon showed small ulcers, which were so numerous as to give to the membrane a sieve-like appearance. The peculiar bacilli described by him were obtained from these cases.

The most recent bacteriological study of Japanese dysentery has been made by Shiga. Out of the considerable number of cases of the disease occurring in Tokyo in 1897, 36 were subjected to examination.

Shiga recognised that in endeavouring to show that an organism which is suspected of standing in etiological relation to a disease is really the causative agent, four points have to be proved; first, that organism must occur constantly; secondly, it must be a species not present normally in the diseased parts; thirdly, it must be pathogenic, and produce in experimental animals lesions similar to those from which it was obtained; fourthly, it should, in virtue of its pathogenic activity in man, show the Widal agglutination reaction with the blood sera of those who have suffered from the disease. From the series of cases examined, there was obtained from the dejecta and intestinal contents and walls, and from the mesenteric glands, a bacillus which fulfilled all these requirements, and which was regarded as the cause of at least Japanese dysentery.

Before describing this organism I wish to direct your attention to the dysentery prevailing in the Philippine Islands, specially in and around Manila. The report of the Surgeon-General of the Army for 1899 contains a tabulation of diseases observed among the American troops during the first four months of the American occupation of Manila. In it the dysenterics are included with the diarrhœal diseases. The total number of cases reported was 445, death-rate being 0.48 per cent. The comment made is that the malarial diseases exceed their prevalence in the United States in the proportion of 370 to 97, and the diarrhœal diseases in the proportion of 445 to 116 or about 4 to 1 in both instances. This compilation fails to give an adequate idea of the extent, severity and mortality of dysentery in Manila. Although the figures were not obtainable, a conviction gained during nearly three months' residence in Manila is that the enteric diseases, of which dysentery was the most frequent and important, were the chief causes of disability and mortality among the land forces of the American army.

The disease occurs in two main forms—acute and chronic. The stools and intestinal contents were scrutinised for amœbæ. These organisms were absent or very difficult to find in the acute cases. In the chronic forms of the disease, in which ulcers were present, they were commonly found, but were variable as to actual occurrence and number. Large hepatic abscesses, usually single, were encountered in a number of these cases.

The morbid anatomy of the chronic disease agrees in part only with that of the so-called amœbic dysentery. The pathological changes in the acute disease differ widely from those of the chronic cases. I shall give an illustrative example in an American soldier, death on the sixth day of the disease. The entire large intestine, from the cæcum to the rectum is dilated, and the walls of the gut are thickened. The mucous membrane is swollen, the consistence much increased, and the normal folds are thrown into elevated coarse corrugations. The general colour of the mucous membrane is deep red; there are present many brighter spots evidently due to hæmorrhage. A false membrane consisting of scattered white elevations occurs upon the surface. Distinct ulceration cannot be made out with the naked eye.

The histological changes consists in necrosis of the mucosa with exudation of fibrin and leucocytes, together with more or

less hæmorrhage. The submucosa shows considerable cellular infiltrations, in which the main new elements are Unna's plasma cells. Focal hæmorrhage is common, and fibrin exists, especially in the lower levels. Ulceration is uncommon, and the submucous infiltration may occur independently of profound alterations in the mucous membrane. Bacteria—cocci and short bacilli—are abundant in the necrotic mucous membrane.

Bacteriology of Philippine Dysentery.—In the study of the bacterial flora of the disease acute and chronic cases were utilised. Plate cultures in agar-agar were employed. The material for the cultures was obtained from the dejecta and from the intestinal contents after death. From the separated colonies slant cultures were made. Those consisting of the pyogenic cocci, which were never absent, were not studied further. Portions taken from the several bacillary colonies were tested upon various culture media, with the result that two distinct types of organisms could be distinguished, especially in the acute cases. Their properties are as follows:

Type I.—Bacillus of average size, variable in length; usually occurs singly, sometimes in pairs, but only very rarely in filaments. The ends are slightly rounded. Moderate motility. Gram's stain negative. Morphology: Colon, typhoid type.

Growth takes place upon all culture media at the room temperature, but better in the thermostat. Gelatine is not liquefied.

The colony forms resemble those of B. typhosus; after many successive transplantations upon artificial culture media, colonies and surface growths become more opaque and abundant.

Potato.—Growth takes place along the line of inoculation and spreads beyond. After some days it is a little elevated, and of a pale brown tint. On unfavourable potatoes the growth is slight, moist, and membranous, resembling that of B. typhosus when typical excepting for the greater amount of moisture.

Sugar-agar is not fermented; in glucose media a moderate acid production takes place.

Litmus Milk.—At first a very faint lilac reaction appears. It is discernible after 24 hours, but more marked at the end of 48 or 72 hours. After a lapse of 6 to 8 days alkali begins to be produced, which increases in amount until the litmus is rendered deep blue in colour. No coagulation of the milk ensues.

Indol.—This body is variable in its formation. Even in sugar-free bouillon, it may fail to appear or be produced in small quantities only.

Suitable cultures of this organism when tested for the agglutination test with the blood serum of persons suffering from dysentery, whether the host or another individual, give in many cases a positive reaction.

Type II.—Present in all instances. In the acute cases it may not predominate, being less numerous than the members of Type I. In all others it is the predominating bacterium. Its properties are variable, but agree with those of the group of B. coli communis. The main variations relate to the extent and rapidity of growth upon the several culture media as exhibited by the colour, thickness, etc., of the colonies. The sugars are broken up with the formation of gas. Litmus milk is reddened promptly, but coagulation sets in at variable intervals, sometimes after twenty-four hours, at other times not for several days or weeks. Indol is produced, but cannot be demonstrated in all cases within twenty-four hours. In morphology the bacillus resembles B. coli communis. Some examples are motile at the end of twenty-four hours; in others motility could not be demonstrated.

In agglutination tests the results varied according as the blood of the host or another individual was employed. With the host there was frequently a reaction in low dilutions; with another person the reaction was rarely and very inconstantly obtained.

Before proceeding to the assumption that this organism was concerned with the production of the intestinal lesions of dysentery occurring in Manila, its absence from the stools of healthy persons and those suffering from other diseases must be established. Strong presumptive evidence of its being an unusual inhabitant of the intestine of man may be gathered from the facts already known concerning the ordinary intestinal flora. But as such observations would not suffice for a new region and under new conditions, the organism was searched for in other persons who had been in close association with those suffering from dysentery, and also in inhabitants of other parts of the island of Luzon. The organism was not demonstrated in healthy dejecta or in the evacuations of persons (native Filipinos) suffering from beri-beri. A further argument in favour of its restricted distribution is furnished by its absence from cases of chronic dysentery or its marked reduction in numbers.

Pathogenicity.—The pathogenicity of the bacillus Type I was studied, soon after its isolation, upon mice and monkeys in Manila and upon various animals in this country with cultures brought back from the Philippines. Mice are susceptible to subcutaneous injections, but react more readily to intraperitoneal inoculations. According to the dose, death takes place in from 12 to 48 hours—more rarely after several days. The site of the puncture shows œdema, and when inoculation is made into the peritoneum, a slight turbid exudate is present. Bacilli are present in very large numbers in both situations and there is a general invasion.

Guinea-pigs react much in the same way as mice. The dose required is slightly larger, but successive inoculations quickly increase the pathogenicity. At first the organisms remain confined to the site of injection, but when the virulence has become intensified the body is invaded. Intraperitoneal injections cause a sero-purulent peritonitis, many bacilli being contained within polymorphonuclear cells. The intestines are hyperæmic; the contents are watery and the bacilli can be cultivated from the fluid portions. Swelling of Peyer's patches occurs.

Rabbits.—Subcutaneous injection gives rise to a localised swelling which is sometimes followed by death. At other times an abscess forms and perforates the skin, after which recovery may take place.

Cats and dogs are also susceptible to feeding with cultures, the first after the administration of croton oil, the second directly. In both enteritis is set up, an increased secretion of mucus takes place, hæmorrhages may occur, and bacilli are cultivatable from the dejections and intestinal contents. Ulceration does not occur.

Tests made with dead cultures upon guinea-pigs show them to be highly toxic.

An interesting if somewhat uncomfortable result of the accidental swallowing of a small quantity of a broth culture should be mentioned. While aspirating some of the culture into a tube, one of the laboratory assistants drew the fluid into his mouth. Notwithstanding the use of an antiseptic wash a severe muco-hæmorrhagic diarrhœa set in in about forty-eight hours, accompanied by tenesmus and fever. Recovery did not take place for two or three weeks. I was absent from the city at the time, and the assistant's ardour was so greatly depressed because of his discomfort that cultures were not made from the stools.

If the bacillus described is of significance in the etiology of dysentery, it must occur with regularity in the disease. Whether or not it will be found to have the distribution that is necessary in order to establish this relationship can only be determined when the study is carried on in widely different places and in all forms of the disease. That the bacillus is identical with the organism obtained by Shiga in the epidemic dysentery which prevails in Japan there can be no reasonable doubt.

I have recently been enabled to study bacteriologically and pathologically a case of chronic Puerto Rican dysentery contracted during the Spanish war. The necropsy showed the colon to be greatly thickened, especially along the sigmoid flexure. The mucous membrane presented a roughened surface without showing pronounced ulceration. The submucosa is thickened and there is considerable contraction. A very small amount of pseudo-membrane is present over the lower part of the sigmoid flexure. Bacteriological examination yielded two types of bacilli, the prevailing one agreeing with the type of the B. coli communis, the other with bacillus Type I already described.

The bacteriological studies of Egyptian dysentery published by Kruse and Pasquale contain numerous references to typhoid-like bacteria. Critical examination shows that the majority belong to the group B. coli communis. Still

other examples of bacilli similar to and possibly identical with the B. dysenteriæ have been found in dysentery, although they are not suspected of standing in any etiological relation to it. Pansini studied 4 cases of abscess of the liver, 3 of which had followed dysentery. The bacilli which were isolated resembled B. typhosus—indeed, Pansini could not distinguish between the two series. Babes also, although only in a single instance, isolated such an organism from a case of dysentery.

The question naturally arises, in what way does this organism differ from the B. typhosus? When the properties of Shiga's bacillus and that of the Eberth-Gaffky organism are compared, the criteria of difference are not numerous. The main features, however, are as follows: The former shows less marked motility when isolated and a tendency rapidly to lose motility in artificial cultivations; it displays a more uniform generation of indol; after a brief preliminary acid production in milk there follows a gradually increasing alkalinisation, it is inactive to blood serum from typhoid cases but reacts with serum from dysenteric cases to which the B. typhosus does not respond.

THE AGGLUTINATION TEST.

The tests in the case of the bacillus isolated in Manila were made at the time with blood obtained from acute and chronic cases of dysentery; and after the return to this country with blood serum from the case of the chronic Puerto Rican disease, as well as with blood obtained through the courtesy of Assistant Surgeon Craig, stationed at the Presidio at San Francisco, the last having been taken from convalescent and other soldiers suffering from chronic dysentery who had returned from the Philippines. The results were positive in the cases of acute disease in which infection with the bacilli was established. It was also positive with the blood of the Puerto Rican case of chronic dysentery, but was inconstant with blood from other chronic cases. Dr. Osler has told me of his experience. In several cases of amœbic dysentery that have come to his attention in the Johns Hopkins Hospital the blood serum has not caused agglutination of the dysenteric bacilli obtained in Manila. In a case of the Puerto Rican disease a positive reaction was obtained.

These results are, I think, suggestive of the nature of tropical dysentery. The typical acute and infectious variety is probably bacillary in origin, and the indications are that the particular bacillus which has been described is the cause of this variety of disease. On the other hand, the chronic form of the disease would appear to be dependant upon at least two sets of causes, the first represents the continuation of the acute disease, and probably is due to the same micro-organism; the second is due to a different organism, apparently the amœba coli. The first variety of the chronic disease only gives the serum reaction with the B. dysenteriæ.

Protective Inoculations and Serumtherapy.—It is not unreasonable to hope that with the discovery of the specific cause of dysentery, particularly if it be a bacterium capable of being artificially cultivated, means will be found by which protective inoculation may be carried out with effect and safety. The fundamental conditions underlying such immunisations are now fairly established, and two general methods of accomplishing such results are open to investigation. In the first place, an active immunity may be achieved through the use of cultures of a determined grade of activity; in the second, the serum of animals may be employed either as a therapeutic agent or to provide a passive immunity.

It has been found possible, through the use of cultures destroyed by heat or the addition of chemicals, to protect small animals from the effects of subsequent inoculations of the virulent bacilli. Larger animals such as the goat, when treated first with the dead and afterwards with the living cultures develop a gradually-increasing resistance to the inoculations; their blood serum assumes highly agglutinating qualities for the bacillus, and coincidentally acquires protective and healing properties. My own experiments relative to this topic have been carried out on small animals only, as no patient with acute dysentery has been seen by me since the serum from the goats has been available. Shiga has, however, been able to test the serum upon human cases in Japan.

According to Dr. Eldridge, up to November 1st, 1899, Shiga treated with the serum cases as follows: 1898, in Laboratory Hospital 65 cases, death-rate 8 per cent.; 1899, in Laboratory Hospital 91 cases, death-rate 8 per cent.; 1899, in Hirowo Hospital 110 cases, death-rate 12 per cent. During the same period of 1899 there were under ordinary treatment at Tokyo: At Honjo Hospital 166 cases, death-rate 37.9 per cent.; at Horowo Hospital 53 cases, death-rate 37.7 per cent.; at Komagome Hospital 398 cases, death-rate 34.7 per cent.; in private houses 1,119 cases, death-rate 28.5 per cent.

I should, however, expect greater benefit from a species of vaccination, especially in those exposed to the endemic or the endemo-epidemic dysentery of the tropics. The encouraging results of the injections of the dead bacilli of Asiatic cholera makes the use of a similar procedure in persons exposed to dysentery advisable. The practical details of such inoculations will of course be established only after trials preferably upon human beings who are anxious to submit to this method of treatment.

Very little remains for me to say at the present time. It is only natural to ask whether the results given in the last half of the paper justify a belief in a specific organism of dysentery. My own sense is against that belief, although it must be conceded that the varieties of the disease are fewer than the clinical and pathological-anatomical conceptions of this time would lead one to suppose. I am disposed at this time to view tropical dysentery as consisting of a bacillary and an amœbic form separable in their early and later stages by their clinical histories, their etiology and pathological anatomy. Whether epidemic dysentery may have a simpler etiology future studies will be necessary to decide. The view expressed by Shiga to the effect that the bacillus isolated by him is the cause of the epidemic disease occurring in Japan may be followed by the establishment of the same organism as the principal agent in other epidemics. My own studies lend support to the wide distribution and pathogenic activities of the bacillus, as well as its relation with a certain class of dysenterics.

In conclusion, I should add that the studies here recorded were carried out while acting on a commission with Professor L. F. Barker, sent out by the Johns Hopkins University of Baltimore, to study the disease prevalent in the Philippine Islands.

Dr. MANSON said that he had listened with very great interest to Professor Flexner's paper, more especially as it gave distinct ground for hope that he had found the germ of one form of dysentery. Such investigation, however, must not overlook the fact that the expression "dysentery" indicated merely a group of symptoms characteristic of inflammation of the colon, and that as there might be many kinds of dermatitis, each attributable to a different and specific cause, so there might be many forms of colitis, each acknowledging a different origin, each with a different clinical history, and each with a different gravity as regards prognosis. Any one with experience of the dysenterics from different parts of the world soon learned to recognise this. The dysentery of English asylums, so intractable and so deadly, was a very different disease to the dysentery of India, comparatively so curable. The dysentery of Manila was evidently a very different disease to the dysentery of the South Pacific as described by Comry—so deadly, so rapid in its progress, and so contagious. All of these were different from the relapsing or amœbic dysentery of American writers. Dr. Manson was interested to hear that Professor Flexner had, in common with other authorities in America, somewhat modified his views as to the significance of the amœba in dysentery: for, according to the original description of the disease, one was led to conclude that a dysentery associated with the amœba was almost necessarily fatal. His own experience of dysenterics and liver abscess with the amœba in the stools or pus was that they were just as amenable to treatment as non-amœbic cases, and he hesitated to accept the presence or absence of the amœba as of value in prognosis, or as an adequate mark of specific distinction. After alluding to Dr. Durham's discovery of an extremely minute bacterium in English asylum dysentery, Dr. Manson asked Professor Flexner if any intestinal lesions of a characteristic nature had been produced in his experimental animals by the administration of cultures of his bacterium.

NUTRIENT MEDIA OF "STANDARD" REACTION FOR BACTERIOLOGICAL WORK.

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THE reaction of different batches of nutrient media prepared from meat extracts or *Fleischwasser* in different laboratories varies within wide limits and is largely the result of the methods of neutralisation in vogue in this country; a state of affairs sufficiently surprising when one considers the importance attached to the reaction of their media by individual workers. I believe that I am right in stating that hardly two laboratories neutralise their media in a similar or even comparable manner, and none use media prepared to an exact "standard" reaction for ordinary laboratory work; whilst practically every English textbook in describing the preparation of media gives instructions differing in some one or more details from those of its contemporaries.

American bacteriologists, on the other hand, have recently adopted a standard reaction for their ordinary media, largely through the energy of the Laboratory Section of the American Public Health Association, and in this respect a distinct advance has been made and an example set us which I venture to hope we shall not be slow in following.

Instances of the influence exerted by the reaction of the medium upon the biological characters of various bacteria are of everyday occurrence, and are so familiar that it is unnecessary to insist further on the importance of the subject. I will therefore content myself with enunciating, as a self-evident postulate the following thesis: The standardisation of nutrient media by exact titration methods, using a really delicate indicator and accurately standardised neutralising solutions, can alone be depended upon to give consistent and comparable results.

HISTORICAL.

A large amount of more or less exact work has been carried out upon this subject of medium reaction, chiefly in German laboratories, during the last eight or ten years; and many descriptions of methods, applied to the preparation of special media for the cultivation of some one special organism are to be found scattered here and there in bacteriological literature.

From the time of the introduction of solid gelatinised media by Koch (1881), when it was considered sufficient to say that neutralisation should be effected by means of potassium carbonate, sodium carbonate, or sodic phosphate, to the present day variants of this method, the chief work in this field may be summed up as follows:

Behring, in 1888, adopted titration methods for the purpose of estimating the acidity of his media, and used rosolic acid as the indicator.

Schultz (1893) detailed a most careful study of the methods then in use, and described his method of preparing media, which consisted in the use of phenolphthalein as the indicator, and $\frac{n}{10}$NaOH, as the neutralising solution.

Dahmen, in the following year, controverted Schultz's work, declaring that phenolphthalein was useless for this purpose owing to the presence of ammonia and its salts and of carbonates in the media to be neutralised.

Timpe in 1893 published his work on the albuminous bodies present in the various ingredients of nutrient gelatine, and pointed out that they possessed both acid and basic characters, but that the former predominated—a feature that necessitated the use of an acid-sensitive indicator such as phenolphthalein, and caustic potash solutions as the neutralising agent.

Petri and Massen, about the same time, held that the amphoteric nature of the phosphates present in the meat extract was the important factor to be dealt with, and advised the use of phenolphthalein and lacmoid in the neutralisation of the original broth, but themselves used litmus tincture when neutralising the gelatine and agar prepared from such broth.

At the present time most laboratories in this country use litmus paper as the indicator, and neutralise their acid *Fleischwasser*, broth, gelatine, or agar, as the case may be, by the cautious addition of successive small quantities of a saturated solution of sodium bicarbonate to the medium in bulk. Some few use $\frac{n}{1}$NaOH. After the neutral point to litmus has been reached, a varying quantity of the alkali, equivalent to from 2 to 5 c.cm. of $\frac{n}{1}$NaOH per litre, is added by a few.

In *Procedures Recommended for the Study of Bacteria*, published in 1898 under the auspices of the Laboratory Section of the American Public Health Association, the method of preparing standard media already referred to is given in full. It is based on the work published by Fuller in the journal of the Association, and is an improved and modified Schultz's method. Briefly it consists in using phenolphthalein as the indicator, estimating the acidity of original solutions by means of $\frac{n}{20}$NaOH, neutralising by adding the requisite amount of $\frac{n}{1}$NaOH, and finally rendering the media acid to this indicator, to the extent of 1.5 per cent. by the addition of the calculated quantity of $\frac{n}{1}$HCl.

THE REACTION OF THE RAW MATERIALS.

Having summarised the steps that mark the history of the study of these "reaction" problems, it is now necessary to touch upon the factors involved in the production of standard media, and the first point that arises is the reaction of the various ingredients of such media.

Meat extract as usually prepared in the laboratory is faintly acid, or amphoteric—occasionally it is faintly alkaline—to blue litmus, but is always definitely acid when tested with phenolphthalein or rosolic acid. This reaction is due to the presence of weak organic acids and amphoteric organic compounds and salts of phosphoric acid, in which, however, the acid character predominates.

The following table shows the behaviour of some of the phosphates to various indicators, and explains in some measure how neutralisation carried out by the aid of different indicators will affect the final reaction of the finished medium.

TABLE I.

	Phenol-phthalein.	Rosolic Acid.	Litmus.	Lac-moid.	Methyl Orange.
Phosphoric acid (H_3PO_4)	+	+	+	+	+
Monobasic sodium phosphate (NaH_2PO_4) ...	+	+	+	o	o
Diabasic sodium phosphate (Na_2HPO_4) ...	o	—	—	—	—
Tribasic sodium phosphate (Na_3PO_4)	—	—	—	—	—

+ = Acid. o = Neutral. — = Alkaline.

From this table it will be seen that in neutralising media with a caustic soda solution and using litmus as the indicator, the neutral point is reached as soon as the phosphates present have been converted into the dibasic form, and as these acid phosphates react alkaline to litmus their presence will prevent the addition of sufficient free alkali to effect complete neutralisation.

In other words, as the amount of phosphate present in different samples of *Fleischwasser* necessarily varies, the final reaction of these samples, all neutral to litmus, will vary within very wide limits, and the production of a standard medium by the aid of this indicator becomes an impossibility.

Table II (p. 922) gives the reaction of each of the various ingredients of nutrient media when tested against the several indicators.

INDICATORS.

Thompson, during the years 1883-5, made some important contributions to the study of the possibilities and limitations of indicators in general, and of those derived from the azo colours in particular, and so paved the way for the intelligent selection of a suitable indicator for bacteriological work.

The indicators in general use are litmus, lacmoid, methyl orange, phenolphthalein, and rosolic acid. Of these methyl orange and lacmoid are but very slightly sensitive to organic acids and salts and are therefore practically useless as indicators for the neutralisation of media.

Litmus, rosolic acid, and phenolphthalein are sensitive to weak acid compounds in very varying degrees, as may be

gathered from a consideration of Table I, which shows their behaviour towards sodium phosphates.

TABLE II.

	Phenol-phtha-lein.	Rosolic Acid.	Litmus.	Lac-moid.	Methyl Orange.
Fleischwasser	+	+	+	+	−
Sodium chloride (0.5 per cent. solution)	o	o	o	o	o
Peptone, Witté (1 per cent. solution)	+	o	−	−	−
Gelatine, best French (10 per cent. solution) ..	+	+	+	−	−
Agar, powdered (2 per cent. solution)	+	o	o	−	−
Glucose (2 per cent. solution)	+	o	−	−	−
Sodium formate (0.5 per cent. solution)	o	−	−	−	−
Glycerine (5 per cent. solution)	o	o	o		

+ = Acid. o = Neutral. − = Alkaline.
All solutions were prepared with distilled water.

Litmus tincture, being perhaps the most generally used for all ordinary purposes, needs first consideration, and I may state at the outset that for the neutralisation of a solution whose acidity depends on weak organic and amphoteric substances with an acid leaning, litmus is not sufficiently sensitive; the acid in litmus being relatively stronger than the acids of the meat extract, this indicator is not sufficiently delicate for exact work, and we must therefore have recourse to one whose acid is relatively weaker than those present in the solution we wish to neutralise.

Further, free carbonic acid interferes very considerably with the production of the blue colour, and unless the solution is kept at the boiling point during the operation of titration, it is very easy to overstep the "end-point." The end-point, too, in the turbid and flocculent solutions with which we have to deal is by no means a sharp one when neutralisation is being effected by daylight, although it becomes more clearly defined if the titration is performed in a dark room illuminated by a yellow sodium flame, for then the acid red appears colourless, and the blue coloration gives an inky appearance to the solution. Even under these improved conditions, however, it is quite easy to overshoot the end-point to the extent of 2 per cent. when $\frac{n}{10}$NaOH is used.

Litmus Papers.—Apart from the fact that litmus itself is not sufficiently delicate for the work, there are further objections to the use of litmus papers, in that unless freshly prepared at the time of using, their sensitiveness will be found to vary immensely with age, while if purchased ready prepared their sensitiveness will vary not only with age but also with each batch, even from the same maker. For example, a brew of *Fleischwasser* which when titrated against blue litmus required the addition of 2.5 c.cm. of $\frac{n}{1}$NaOH (per cent.) to render it neutral, was found to give a faintly acid reaction in one case, amphoteric in the second, and faintly alkaline in the third, when tested with three sets of red and blue litmus papers from three different well-known manufacturers of chemical sundries.

Rosolic Acid.—Rosolic acid is soluble in 50 per cent. alcohol, and for use as an indicator is kept in 0.2 per cent. solution. It possesses a much greater degree of sensitiveness towards weak organic acids than litmus, but, like that indicator, its reliability is affected by the presence of free carbonic acid; and as the recognition of its end-point (the change being from a faint yellow to a delicate rose pink) is almost as difficult, it may lead to equally large errors.

In spite of all these disadvantages and defects, however, it was the indicator used by Washbourn and myself for many years in our attempt to prepare a medium of standard reaction for the growth of the pneumococcus, and with fairly good results.

Phenolphthalein.—Phenolphthalein is highly sensitive to the weak organic acids, such as lactic, glycocolic, etc. Like rosolic acid it is soluble in 50 per cent. alcohol, and for use is prepared in 0.5 per cent. solution.

The colour change with this indicator is from no color in acid or neutral solutions to rose pink in the presence of the faintest excess of a caustic alkali—a marked excess leading to the development of a deep purple red. The end-point even in such a turbid solution as agar is sharp and distinct, so much so that it is difficult to make a greater error than 0.5 c.cm. of $\frac{n}{1}$NaOH in neutralising a litre of medium. Practically its only disadvantage is that it is useless for the titration of solutions containing 0 03 per cent, or more of free NH_3. As, however, both the free and combined ammonia present in the media amount to certainly not more than a tenth of this quantity, this objection need not weigh with us. A more valid objection is that, like the two previously mentioned indicators, the presence of free carbonic acid interferes with its reliability, and even this drawback may be overcome by the keeping the solutions to be neutralised at or near the boiling point.

NEUTRALISING SOLUTIONS.

As the media with which we have to deal give an acid reaction, alkaline solutions must be used for the purpose of neutralisation, and either the hydrates or the carbonates of both sodium and potassium are those generally employed. Of these the hydrates are to be preferred for accuracy in titration and ease of manipulation, whilst of soda and potash the former is generally the more convenient.

An accurately standardised decinormal solution of sodic hydrate will be required for the estimation by titration of the acidity of the medium; but as the quantity of $\frac{n}{10}$ solution necessary to neutralise, say 1 litre of nutrient gelatine, might amount to 250 c.cm., it is needless to remark that the percentage amount of gelatine would be considerably diminished if this solution were used, therefore it is advisable to add a corresponding quantity of an equally carefully standardised normal solution of NaOH to the bulk of the medium.

METHOD OF EXPRESSING THE MEDIUM REACTION.

In dealing with standard solutions for neutralisation, several simple methods of expressing the medium reaction will at once suggest themselves:

1. By the number of c.cm. of $\frac{n}{1}$ alkali or acid required to neutralise each c.cm. of medium.
2. By the number of c.cm. of $\frac{n}{1}$ alkali or acid required to neutralise every 100 c.cm. of medium.
3. By the number of c.cm. of $\frac{n}{1}$ alkali or acid required to neutralise each litre of medium.

The first two of these methods may involve the use of fractions, while the last usually deal with whole numbers, and this is obviously the most handy one for use. If now the symbols + and − are used to represent acidity and alkalinity respectively, the reaction of any particular batch of medium may be easily and quickly recorded, and comparisons readily instituted between any two or more batches, independently of the time or place of manufacture. For example, nutrient gelatine 10 per cent., reaction + 10 would indicate that the reaction of a batch of 10 per cent. nutrient gelatine was such, that it still required the addition of 10 c.cm. of $\frac{n}{1}$NaOH per litre, to render it neutral to the indicator used.

OPTIMUM REACTION.

The reaction which gives the best results may be said to vary within certain limits in the same way that the optimum temperature does with each individual organism, and should, like the temperature, be carefully worked out in those cases where a new organism is being described; yet it appears that the optimum reaction for working purposes is the one corresponding to + 15 or + 10, according to the suggested method of recording reactions; indeed I will go further and say that if the end-point to be described immediately is used, that a reaction of 10 will be found to give the best results, and this is the reaction that temporarily at any rate might be adopted as a "standard."

THE PREPARATION OF A "STANDARD" MEDIA.

Having briefly indicated the factors which influence the reaction of nutrient media, and the most suitable indicator and reagent for neutralisation, I now propose to detail the technique I have adopted for the production of media of standard reaction in my own laboratory, and here I must point out that the method differs in many details from that adopted by American bacteriologists. This fact is to be

regretted, for if media are to be standardised, it would obviously be more convenient to work to a standard already in use by a large number of investigators rather than start off with a fresh method, but after attempts to produce a standard medium (intended primarily for the cultivation of the diplococcus pneumoniæ) extending over a period of at least six years, I find myself unable to accept some of the opinions upon which the American procedures are based.

First and foremost we must consider the preparation of the meat extract which forms the basis of nutrient bouillon, gelatine, and agar, and for which the highly expressive name of "*Fleischwasser*" is suggested by Mr. Pakes.

Fleischwasser.—Five hundred grams of lean beef are thoroughly minced, added to 1 litre of distilled water in a large flask, and a thermometer having a long stem placed in the interior of the flask, its bulb resting on the bottom. The flask is placed in a water bath, care being taken that it does not come into contact with the bottom of the bath. The temperature of the water bath is now gently raised, and for the first twenty minutes the temperature of the contents of the flask, which must be occasionally agitated, is not allowed to exceed 40° C.; after this time the temperature is run up to 60° C., and maintained at this point for about 10 minutes. The *Fleischwasser* is next filtered through two thicknesses of filter paper into a sterile flask, its bulk measured, and the loss from evaporation replaced by the addition of distilled water.

Nutrient Bouillon.—If bouillon is the medium required, measure out 1,000 c.cm. *Fleischwasser*, and weigh up 10 grams of Witté's peptone and 5 grams of sodium chloride. Use 20 to 30 c.cm. of hot *Fleischwasser* to mix the peptone and salt into a smooth paste, and add this to the bulk of the fluid, which is contained in a flask, and warm up again in the water bath until thorough solution is effected.

Neutralisation, or rather the production of a reaction of + 10 is performed as described below. The flask is then replaced in the water bath at 100° C. for 30 minutes, filtered into sterile test tubes, in quantities of 10 c.cm. each, and sterilised in the steam steriliser for 20 minutes on each of three successive days.

Nutrient Gelatine.—Add peptone and salt, as in preparing bouillon, then best gold label French gelatine, equivalent to from 9 to 12 per cent. (the amount of gelatine added varies, of course, with the purpose for which it is intended, and with atmospheric conditions) is introduced into the flask, and the flask replaced in the water bath (100° C.) for about 30 minutes, during which time the contents must be frequently shaken. The gelatine will now be completely dissolved, and the medium mass ready for standardising. After this has been done, the liquid is allowed to cool down to about 50° C., then the whites of two eggs (well whipped) are added, and the flask returned to the water bath, the temperature of which is gradually raised from about 40° C. to 100° C., and maintained at this latter point for a good half an hour. The nutrient gelatine is filtered through papier Chardin into sterile test tubes in quantities of 10 c.cm. each, and sterilised in the steamer for 20 minutes on each of three successive days.

Nutrient Agar.—If nutrient agar is to be prepared, 20 grams of powdered agar, 10 grams of peptone, and 5 grams of salt, are mixed into a perfectly smooth paste, with 200 c.cm. of cold distilled water. This paste is thoroughly incorporated with sufficient *Fleischwasser* to make up 1,000 c.cm., in a 2-litre flask, which is then placed in the steam steriliser and vigorously steamed for about 30 or 40 minutes. At the end of this time it is standardised, allowed to cool down to 50° C., the whipped-up whites of two eggs added, then placed in the water bath or the steam steriliser, which must be started cold, gradually raised to the boiling point, and kept there for a further period of 40 minutes, filtered through papier Chardin into tubes and sterilised in the steam steriliser for 30 minutes on each three successive days.

STANDARDISATION OF MEDIA.

In the first place, the reaction of the original medium must be estimated, and this must be done whilst the solutions are still at the boiling point in order to avoid the danger of error due to free carbonic acid present in the medium or absorbed from the air.

Still more important is the fact that as the acid properties of substances depend upon their dissociation values, and therefore weak organic acids increase in strength with each degree rise in temperature, these latter can only be effectually neutralised at the boiling point. From this a valuable practical point follows. When in titration the end-point is reached, rapid cooling of the solution will cause the characteristic but faint colour to shoot up and become more readily distinguishable, the colour again fading if the solution is once more heated.

Solutions Required.—$\frac{n}{10}$NaOH, accurately standarised. $\frac{n}{2}$NaOH, accurately standarised; 0.5 per cent. solution of phenolphthalein in 50 per cent. alcohol (in bottle with pipette holding 0.5 c.cm. through the cork).

Apparatus Required.—25 c.cm. burette graduated in tenths of a c.cm. 25 c.cm. measure or pipette. Bohemian glass flask, fitted as a washbottle, filled with distilled water and kept boiling on a tripod stand. Several 60 c.cm. Ehrlenmeyer flasks or conical beakers. Some squares of white blotting paper.

Method.—The burette is filled with $\frac{n}{10}$NaOH; 25 c.cm. of the fluid medium are measured out into one of the flasks or beakers, the measures rinsed out with a small quantity of boiling distilled water from the washbottle and added to the medium already in the flask, then half a cubic centimetre of the phenolphthalein solution run in. To this colourless fluid $\frac{n}{10}$NaOH is added cautiously from the burette until the end-point, as indicated by the development of a pinkish tinge, is reached. A control, a second or even a third may be titrated, but such is the sharpness of the end-point that after a little experience with this indicator there will not be a greater difference than 0.1 c.cm. of the $\frac{n}{10}$NaOH between the several estimations, and as a matter of fact it is almost impossible to overshoot the end-point of even the first titration by more than 0.2 c.cm. of the decinormal solution. From these estimations, the amount of $\frac{n}{2}$NaOH requisite to neutralise the remainder of the medium can be easily calculated, and from this figure is deduced the amount that is necessary to add to the remainder of the medium in order that it may still remain acid to phenolphthalein to the extent of 1 per cent.; in other words, have a reaction of + 10.

The differences in technique between this method and that recommended by the Americans are:

1. The use of 25 c.cm. of medium instead of 5 c.cm. of medium + 45 c.cm. boiling distilled water.
2. The use of $\frac{n}{10}$NaOH in the place of $\frac{n}{50}$NaOH.
3. Regarding the first appearance of a pinkish tinge as the end-point instead of producing a purple red by an excess of alkali.
4. And, as a result of (3), adopting a reaction of + 10 instead of + 15.
5. And finally, in adding only sufficient $\frac{n}{2}$NaOH to leave the medium of the desired acidity rather than adding enough to render the medium neutral to phenolphthalein, and producing the desired reaction by the subsequent addition of $\frac{n}{2}$HCl.

In the following table is given the initial reaction of a few selected batches of media when neutralised against phenolphthalein, rosolic acid and litmus respectively, the figures quoted sufficiently emphasising the value of phenolphthalein as an indicator for this class of work:

TABLE III.

	May 17th, 1900.			July 3rd, 1900.			July 11th, 1900.		
	Phenolphthalein.	Rosolic acid.	Litmus.	Phenolphthalein	Rosolic acid.	Litmus.	Phenolphthalein.	Rosolic acid.	Litmus.
Nutrient bouillon	+20	+9	+2	+19	+9	+2	+18	+8	+2
Nutrient gelatine	+38	+26	+10	+30	+16	+9	+30	+26	+7
Nutrient agar	+22	+12	+8	+21	+13	+8	+20	+10	+5

The figures indicate the number of c.cm. of $\frac{n}{2}$NaOH that would be required to render the unfinished medium neutral to the indicator used.

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Mr. ALEXANDER FOULERTON pointed out that for comparative experiments as to the acid-producing power of different bacteria, standardisation of the finished media, prepared as Dr. Eyre had suggested, would be quite useless in many cases unless the meat from which the nutrient broth was made had also been, so to speak, standardised. The amount of muscle sugar in different samples of meat varied with the length of time which had elapsed since the killing of the animal, and with the conditions under which the meat had been kept. And so one might make broths from the meat of two different animals, standardise both samples most carefully, and then after the same stock of, say, bacillus coli communis, had been incubated for twenty-four hours, the amount of acid produced in each of the two samples might be found to difer considerably. The remedy for this—if one wished to get really standardised media—was either to keep the meat in ice from the time that the animal was killed, or else to get rid of all the muscle sugar by fermentation before standardising the broth. There were great practical difficulties on the way of the absolute standardisation of media; different samples of the same brand of commercial meat extract probably were less likely to vary in their composition in this respect than different samples of meat bought under the usual conditions, but many bacteria would not grow nearly so well on media prepared from such meat extracts as they would on those prepared from fresh meat.

Professor MUIR asked whether Dr. Eyre was quite satisfied that accurate results could be obtained with comparative ease with phenolphthalein. In the case of an organic mixture such

as bouillon, the question from the chemical point of view was one of great complexity, and in his experience it was often difficult to say when the exact point of neutralisation was reached.

Dr. LAZARUS-BARLOW said that for all ordinary purposes in the laboratory he used Liebig's or some other meat extract in the preparation of the culture media. It saved much trouble and was fairly satisfactory.

Dr. EYRE, in reply, said he had found practically no difficulty in determining the end-point when using phenolphthalein, as this end-point was sharp and clear, and after having reached the point the addition of even 0.2 c.cm. of $\frac{n}{10}$NaOH produced a deep red purple colour. With reference to the use of commercial meat extract as the basis for standard media, Dr. Eyre had tried many, and found that media prepared from Wyeth's beef juice gave the best results, but even these results are inferior to those obtained by the use of media made from meat extract prepared in the laboratory.

TWO CASES OF LIPOMA OF THE KIDNEY.

By W. S. LAZARUS-BARLOW, B.A., M.D., M.R.C.P.,
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LIPOMA of the kidney is apparently a very rare condition if one may judge from the statements made about the subject in books. As a rule, it is dismissed with the bald statement that it is "very rare" in the more important textbooks, while in those of somewhat smaller size it is not even referred to at all. During the last eight months, however, I have come across two examples, one of which I show as a macroscopic specimen and the other in microscopic section.

The conditions under which these specimens were met with were curious and highly suggestive. In both instances they were removed from the kidney under the impression that they were small secondary deposits. In the one case the prime lesion was a glioma of the brain and the lipoma of the kidney was removed for histological examination as the sole discoverable metastatic deposit. In the other instance the prime lesion was an intense suppurative meningitis arising from disease of the antrum and the lipoma of the kidney was regarded at the necropsy as a metastatic pyæmic abscess in which softening was just about to commence. The obvious suggestion to be derived from these two facts is that all foci supposed to be "metastatic" should be subjected to microscopic examination because some of them may turn out to be lipomata. In other words, it is possible that lipomata of the kidney are not quite so rare as we have been led to suppose.

In any case, lipoma of the kidney is an extremely interesting tumour from the point of pathogeny, since it offers certain marked differences from ordinary lipomata in the situation which it affects. As a rule lipomata are found in places where fat is normally present, but when they affect the kidney it is not in the region of the hilum that they are found, but on the contrary, in the cortex, a part of the organ which is normally devoid of fat.

Both of the specimens which are the subject of the present communication were found in adults, the one being a man aged 70 and the other a woman aged 30. They were approximately spheroidal, were about the size of a Spanish nut, were situated in the cortex of the organ immediately beneath the capsule, to which they were not adherent, and though they could be sharply differentiated from the surrounding renal tissue by their pale yellow colour, were not surrounded by a capsule. Microscopically they were composed of fatty tissue of the ordinary kind, with fat cells which varied considerably in size and stained an intense black with osmic acid. After removing the fat, a loose connective tissue showed itself, in which the nuclei of the connective tissue corpuscles were few and shrunken. Though this fatty connective tissue could be easily distinguished from the surrounding renal tissue, the lipoma had nothing approaching to a capsule.

Lipomata of the size that have just been described are only pathological curiosities, and have no clinical importance, but occasionally, as in a case recorded by Warthin, a tumour weighing 2 lbs. may be produced which is recognised during life, and is the object of operative interference. Their interest lies, however, in theoretical considerations. It is not at all easy to explain their occurrence, and in this respect they are altogether comparable with the other new growths of the kidney. It has been suggested that they result from a localised metaplasia of the renal substance, but it is more probable they result from a fatty modification of a pre-existing mass of ordinary connective tissue. Even then a difficulty still remains, for we do not consider that a lipoma in such a situation as the subcutaneous tissue arises from a fatty modification of pre-existing fibrous tissue, but hold that its first beginning is fatty tissue, just as we hold that the first beginning of an angioma is vascular tissue. An argument that has been used to support the view that the lipoma originated in a mass of ordinary fibrous tissue is the fact that lipomata have been found in kidneys the seat of chronic fibrosis. This argument certainly does not apply in the case, aged 30, which I have brought forward, for there is no abnormality of the kidney other than the lipoma. Nevertheless, fibrous tissue of course forms an essential constituent of the renal substance, and it is not impossible that though the general bulk of the fibrous tissue of the organ is normal, the seat of the lipoma was a seat of an abnormal accumulation of fibrous tissue originally. Upon this point, however, we can only theorise, and with hardly more satisfactory results than in the case of the new growths elsewhere.

The best account of the condition I have been able to find is contained in a paper in the *Transactions* of the Pathological Society of London for the year 1900, written by Dr. Parkes Weber.

THE SIGNIFICANCE AND PATHOLOGY OF THE ARGYLL-ROBERTSON PUPIL.

By WILFRED HARRIS, B.A., M.D., M.R.C.P.,
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THE loss of the pupil reaction to light, or the Argyll-Robertson pupil, is a physical sign of the greatest value in the examination of cases of nervous disease. Of these it is by far the most commonly met with in two diseases, locomotor ataxy and general paralysis, inasmuch as these diseases are due largely, if not entirely, to previous syphilis, acquired or, in a few cases, congenital. The loss of the pupil contraction to light may be looked on as an almost certain sign of antecedent syphilis, congenital or acquired, and it is therefore to be met with not infrequently unassociated with tabes or general paralysis in syphilitic subjects showing otherwise, perhaps, no symptoms, or suffering from other syphilitic lesions. In addition to tabes and general paralysis with a history of acquired syphilis, I have met with Argyll-Robertson pupil in juvenile locomotor ataxy and general paralysis with marked evidences of congenital syphilis, in progressive muscular atrophy, in lead poisoning, aortic aneurysm, hemiplegia, syphilitic meningitis, ataxic paraplegia, nuclear ophthalmoplegia, choroiditis, and in numerous instances in patients who presented themselves for all manner of symptoms, but showing no signs of ataxy or anæsthesia, and with normal or even brisk knee-jerks, but with in almost every case a clear history of syphilis. It has also been described as occurring in poisoning by bisulphide of carbon, and in diabetes mellitus. I have never yet seen it in Friedreich's disease or in disseminated sclerosis, and in only one instance in which a history of syphilis seemed to be fairly excluded, in a man of 30, whose niece suffered from well-marked Friedreich's disease, while he himself suffered from spastic paraplegia, with simple optic atrophy, and some mental dulness, the pupils being small, and neither reacting to light or accommodation. The appearance of the pupils in which the light reaction is lost may vary considerably; both may be very small, in which case they may contract still further on convergence, but the reflex dilatation on stimulation of the skin is also usually lost (reflex iridoplegia). Both may be large, even considerably dilated, and then their power of contraction on convergence is usually lost or very slight, while further dilatation may be produced by stimulation of the skin. All intermediate stages are met with, and the pupils are frequently unequal. The very small pupils often met with cannot be explained simply as paralytic myosis, since they are smaller than is ever met with in sympathetic paralysis; nor can it be believed that thereis any continual irritative process affecting the sphincter centre in the third nucleus. Their small size is probably due

in part to a contracture of the sphincter muscle, as they dilate only partially under atropine. The loss of light reaction may be quite unilateral, as I have seen in some twenty cases, though more often the light reflex is impaired on both sides, being more marked in one than in the other. This is probably only a stage in the development of complete loss of the light reflex in both eyes.

When unilateral reflex iridoplegia is present, it is important to test the consensual reactions to light (Fig. 1), and it

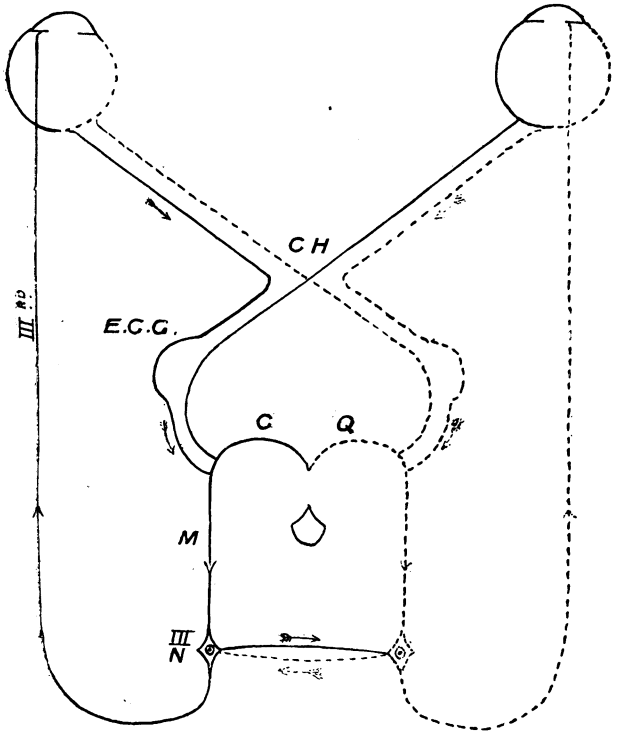

Fig. 1.—Usually accepted scheme to show the path of the reflex for the contraction of the pupil to light in man.

will be found that the sound pupil, if shaded, will contract when light is focussed on the affected pupil from any direction, as when testing for Wernicke's hemianopic pupil. This proves the afferent part of the reflex in the optic nerve to be intact, and, moreover, would disprove the possibility of a nuclear lesion in Argyll-Robertson pupil, if the usually accepted diagram of the course of the light fibres were correct. The morbid anatomy of the Argyll-Robertson pupil has never been demonstrated, though it has been variously surmised to depend on a nuclear lesion, or on sclerosis of Meynert's fibres between the anterior corpora quadrigemina and the third nucleus, or even on a lesion of the ciliary ganglion. The third nucleus, or its anterior portion, is certainly included in the reflex arc, and it is not surprising therefore to find the phenomenon of reflex iridoplegia present in cases of nuclear lesion. That is not however sufficient argument for placing the usual site of the lesion in the nucleus, inasmuch as the vast majority of cases of Argyll-Robertson pupil are unaccompanied by any other sign of nuclear lesion. Analogy, too, would rather suggest sclerosis of certain fibres, in view of its frequent association with posterior sclerosis, in which lesion of nerve cells is a rare exception (Fig. 2). The study of the pupil-reflex in birds and animals, with and without binocular vision, proves that the two third nuclei are not tied together for the light reflex, since only the pupil exposed to light contracts; moreover, in birds and lower mammals there is complete decussation of the optic nerves at the chiasma, and it therefore follows that there must be also a posterior decussation of the fibres subserving the light reflex between the optic lobes and the third nuclei. It is highly probable therefore that in man and other animals with binocular vision, in whom there is semi-decussation of the optic nerves at the chiasma, that a similar arrangement holds good between the anterior corpora quadrigemina and the third nuclei (Fig. 3), namely, that there is a semi-decus-

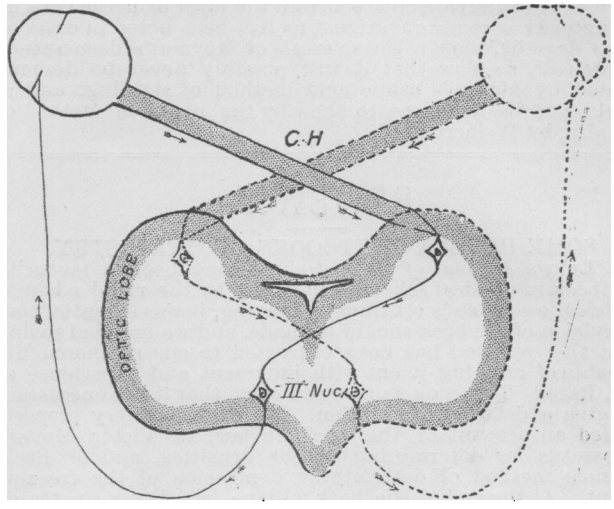

Fig. 2.—Scheme of pupil reflex fibres in birds.

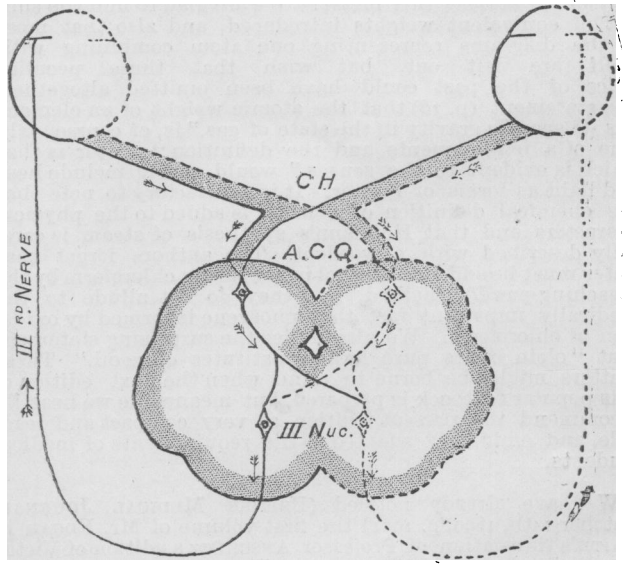

Fig. 3.—Scheme of pupil reflex fibres in man.

sation of the fibres subserving the light reflex between these two parts.

Meynert's fibres have been shown by Boyce and others to be not a complete decussation, some fibres remaining uncrossed in or close to the posterior longitudinal bundle of the same side, and it seems not improbable that these fibres have the above function. This being the case, it is no longer necessary to conceive the two third nuclei being tied together in order to explain the consensual reaction of the pupils to light, as light thrown on either pupil in any direction will thus cause afferent stimuli to reach both third nuclei independently. It seems to me much more probable then, in the absence of direct pathological evidence, that the Argyll-Robertson pupil is due to sclerosis of these fibres on one or both sides according as the loss of light reaction is unilateral or bilateral, rather

than due to any nuclear degeneration, such as has been suggested. It is interesting to note that considerable atrophy of the plexus of nerve fibres beneath the layer of nerve cells of the anterior corpora quadrigemina has been noted in cases of tabes dorsalis, though the sclerosis of Meynert's decussation is probably so slow that it will possibly never be demonstrated by Marchi's osmic acid method of staining, and it would not be sufficient to show by the negative method of staining by Weigert-Pal.

REVIEWS.

SOME RECENT TEXTBOOKS OF CHEMISTRY.

DR. LUFF'S *Manual of Chemistry* has long been a favourite textbook in medical schools, but owing to the rapid advance which the science is continually making, it was essential that a revision of the book should be made, and we are glad to find that this revision has been entrusted to one so thoroughly capable of carrying it out with judgment and experience as Mr. Page.[1] The book is so well known that it is unnecessary to give a detailed description. Mr. Page has very properly added an account of the periodic law, of Victor Meyer's apparatus for determining vapour densities, and of Beckmann's method of determining depression of the freezing point. At the end of the book will be found some notes on the preparation of salts, such as those which may have to be made by candidates at the conjoint examination. We also notice that the old woodcuts representing the preparation of zinc *per descensum* have been displaced by an engraving representing a more modern process. Mr. Page explains why ozone is held to have the triatomic formula; but why does he prepare ozone in a eudiometer containing mercury, seeing that ozone attacks this metal? We are glad to find the subject of equivalent weights introduced, and also that most of the diagrams representing one atom combining with itself are left out, but wish that these peculiar relics of the past could have been omitted altogether. The statement (p. 16) that the atomic weight of an element "is its specific gravity in the state of gas," is, of course, only true of a few elements, and the definition "matter is that which is evident to the senses," would surely include heat and light as forms of matter. It is satisfactory to note that the chemical definition of a metal is added to the physical characters, and that Hofmann's synthesis of steam is carefully described with a woodcut. The authors forget that water must be added to alcohol in preparing chloroform by the bleaching-powder method, and they do not allude to the medically important fact that phosgene is formed by oxidation of chloroform. We also notice the surprising statement that "olein in its pure form constitutes olive oil." These matters might be borne in mind when the next edition of this popular textbook is prepared, but meanwhile we heartily recommend the present edition as very compact and readable, and eminently adapted to the requirements of medical students.

We have already noticed (BRITISH MEDICAL JOURNAL, October 14th, 1899, p. 1021) the first volume of Mr. EDGAR F. SMITH'S translation of Professor ANSCHÜTZ'S edition of Victor von Richter's *Organic Chemistry*.[2] The present volume deals with organic compounds, the molecules of which contain atoms arranged in rings. These are styled "carbocyclic" compounds. There is an excellent index containing the names of between seven and eight thousand of these compounds, and this will give some idea of the immense mass of material crowded into the book. Nevertheless, the arrangement is thoroughly systematic, and although it has been found impossible to give anything like a full description of individual substances, particular attention has been paid to such reactions as throw light upon the constitutional formulæ of the compounds described. The book is to be recommended to anyone who, having a good general knowledge of organic chemistry, desires a handy and concise statement of the modes of formation, melting and boiling points, and structural formulæ of the principal derivatives of benzene, naphthalene, pyridine, quinoline, and the vegetable alkaloids. A good deal of information is also given upon various forms of nomenclature which have recently been introduced. Thus we are told that benzene may be called "cyclohexatrien." At the same time the nomenclature actually employed is fortunately that in common use. There seems, however, to be some carelessness in the printing of names of substituted compounds. Thus, "phenyl-acetic acid" is quite correct, but "Propyl Benzoic acid," without even a hyphen between "benzoic" and the prefix "propyl" is certainly a mistake, and the same may be said of "Dimethyl Aniline," which is usually printed "Dimethylaniline." The translator follows the German custom in using the prefixes "chlor-" and "brom-" instead of "chloro-" and "bromo-", but we think that the usual English form in such a word as "chlorobenzene" is preferable to "chlorbenzene." An excellent feature is the constant reference to original papers. This enables the book to be used to a great extent as a dictionary. It is interesting to note that a large proportion of these references are to recent chemical literature, and this is an indication of the enormous amount of original chemical work which is now annually published. In most cases the references are given without the authors' names; this is a pity, since the association of facts with the authors who discovered them seems to add a human interest to a subject which must at times appear somewhat dry. The names of Richter and Anschütz are guarantees that the work is accurate and thoroughly up to date.

MR. ALLEN'S *Organic Analysis* has long been recognised as a standard work, and it is to be found upon the laboratory shelves of most analytical chemists. It is published in eight parts, and we have received recently the third edition of Part II of Volume ii.[3] It contains many additions, especially as regards acetylene and as regards drugs, food preservatives, and disinfectants derived from benzene. Dr. Leffmann has added a great deal of information obtained from American sources. In the chapter on petroleum it is pointed out that there are at least three kinds of vaseline in commerce, those obtained by direct distillation of American and of Russian petroleum, and a specious mixture of solid paraffin with heavy lubricating oil. This spurious article is said to be liable to deposit crystals of paraffin on keeping, and is therefore not so suited for the preparation of ointments. We find an excellent and very complete account of the methods for detecting the admixture of alpha-naphthol with its more useful isomeride, beta-naphthol; while the account given of the phenols is particularly thorough from the practical point of view. There is also a good description of the complicated mixture known as wood-tar creosote, and of the tests by which it may be distinguished from the cresols. It is pointed out that owing to the large demand in recent years for guaiacol and its preparations much of the wood creosote now sold has been more or less deprived of its guaiacol, and methods for ascertaining whether this has been the case are discussed. The organic compounds dealt with in this volume are hydrocarbons and phenols, and we feel sure that anyone interested in these subjects will find in this book a large amount of new and useful information.

Professor WALKER states that his main object in writing *An Introduction to Physical Chemistry*[4] was to treat certain chapters of physical chemistry at some length with a constant view to their practical application to ordinary chemical phenomena. From this statement we were prepared to find the book eminently readable, and such is, indeed, the case. We are taken through a wide range of subjects, including the ordinary laws of chemical combination, the kinetic theory of gases, the phase rule, the properties of solutions, electrolysis,

[1] *A Manual of Chemistry.* By Arthur P. Luff, M.D., F.R.C.P., F.I.C., and F. J. M. Page, B.Sc., F.I.C. London: Cassell and Co. 1900. (Cr. 8vo, pp. 541, 40 engravings. 7s. 6d.)

[2] Victor von Richter's *Organic Chemistry.* Edited by Professor R. Anschütz. Translated by Edgar F. Smith. Third American edition. Vol. II. London: Kegan Paul, Trench, Trübner and Co. 1900. Demy 8vo pp. 671. 15s.)

[3] *Commercial Organic Analysis.* By A. H. Allen, F.I.C., F.C.S. Third edition, vol. ii, part ii, with revisions and additions by the Author and Henry Leffmann, M.A., M.D. London: J. and A. Churchill. 1900. (Demy 8vo, pp. 330. 14s.)

[4] *An Introduction to Physical Chemistry.* By J. Walker, D.Sc., Ph.D. London: Macmillan and Co. 1899. (Demy 8vo. pp. 335, 47 illustrations. 10s.)