origin from the central fibro-cartilage of the heart, becomes thinned out till at the opposite side it is non-existent, so that this orifice, which itself contracts and expands with the ventricle, can have no more resistant power than the muscular substance of the ventricle itself.

Obviously auscultatory percussion leaves much room for the exercise of the imagination, and any statements as to the variations in the size of the heart based on this method of examination must be rejected as absolutely untrustworthy. To ascertain the position and dimensions of the heart we must continue to employ the sober method of carefully collating the evidence afforded by palpation, percussion, and auscultation.

That a diminution in the volume of the heart may take place under the influence of saline baths and certain movements there can be no doubt, but such diminution is an occurrence which is perfectly familiar to all who are in the habit of noting the changes in the size of the heart under other methods of treatment or from various causes. In a heart dilated from over-exertion, for example, the apex beat may often be felt to come in for half an inch towards the normal situation when the patient is simply made to walk two or three times across a room.

The Schott treatment has undoubtedly potentialities of usefulness in certain forms of heart disease, and it is a matter of great interest and importance to ascertain with some degree of certainty and precision in what class of cases it is of most service. No advance can be made in this direction while it is employed indiscriminately in all forms and stages of heart disease, including cases where perfect compensation has been attained and cases where no real heart affection exists, nor while statements are made which seem to imply that it is equally efficacious under all circumstances. It must be borne in mind, too, that any treatment which is powerful for good can also when misapplied do harm; grave risk, for instance, is incurred when the Schott methods are practised in cases of aneurysm.

THE LUMLEIAN LECTURES

ON

THE SEQUELS OF DISEASES.

Delivered before the Royal College of Physicians of London, March 19th, 1896.

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LECTURE I.

[The lecturer prefaced his address with some reference to the early conditions of the lectureship, reminding his audience that the appointment used to be for life, and that Harvey had held it for a period of forty years, and then proceeded:]

I propose in this course of lectures to discuss as fully as I can the subject of the sequels of diseases. Our knowledge of this is far from anything like completeness; indeed, it may be said to be very small and most inadequate, yet it is a very large subject and it has never, so far as I am aware, been made one of systematic study. It was a saying of one of our most distinguished Fellows, the late Dr. William Baly, whose early death was the gravest loss to my own hospital, to this College, and to the whole profession in England, a saying treasured up in the writings of his colleague, Sir James Paget, that, in his opinion, one of the most useful books that might be written would be one on the diseases of convalescence. The field for observation and exact determination in the direction I now set out upon is indeed immense, so large that the experience of no one amongst us is, or ever can be, adequate for the purpose in view, and we may therefore ask at the outset, Who is sufficient for these things? I can only hope, then, to try to map out the large field before me somewhat in the fashion of an explorer in a new territory.

The first difficulty which besets the inquirer into this subject is to determine and define what constitutes a veritable sequel in the case of any disease. This difficulty grows greater

as modern research throws more light upon etiology and the intimate nature of morbid processes. What the physicians of half a century ago deemed to be sequels of disease must now be regarded by us, in not a few instances, as but later evolutionary manifestations of the primary and original *quidquid irritans*. Such consequences may occur early or very late, and yet may be certainly referred to the noxious elements which originally broke in and disturbed the health of the individual. In such instances I take it that we must regard the particular consequence as a veritable sequel, although we do not regard it from the patient's point of view as a new malady. We shall find that many of the disorders of convalescence fall into the category I have just indicated. The early physicians recognised the occurrence of some sequels of diseases, though but little is to be found bearing on the subject in their writings. It is certain, for instance, that Hippocrates was familiar with orchitis as an early and a late consequence of parotitis, since he described the condition at some length in the *Epidemics*. Aretæus noted that gout passed into dropsy and sometimes into asthma.¹ Seventy years ago the subject attracted much attention from Graves, who in his chapter on Fever described several sequels and especially the occurrence of white leg or venous thrombosis.² About the same time, Dr. Caleb Hillier Parry of Bath, a Licentiate of this College, was near to describing sequels of disease in his interesting books on the *Elements of Pathology and Therapeutics*, especially in his chapter on the Relation of Diseases by Conversion, wherein he embodies a series of careful observations made upon patients many of whose symptoms were then really inscrutable to him, although they were believed to be due to increased determination of blood, his universal doctrine, but of which some admit now of very clear interpretation. Thus we meet with accounts of "cases of pleurisy which gave way to immediate and fatal diseases of the head, of which one case was proved by the dissection to have arisen from inflammation and albuminous effusion above the pia mater." Here we have without doubt a case of tuberculous pleurisy to which tuberculous meningitis was a sequel. In another case he tells of hæmorrhage from the kidneys immediately succeeding the desquamation of measles. We can hardly doubt that this was an example of glomerular nephritis following, not measles, but scarlet fever. Amongst these observations are many remarkable instances of metastasis of gout, of which, I venture to believe, we now see fewer examples than did the physicians of the eighteenth century. To mention but one, the frequency of erysipelas in Parry's time as a precursor and a sequel of gout is certainly not recognised in these days. (James Gregory, of Edinburgh, noted the frequency of facial erysipelas in the daughters of gouty men.) Caleb Hillier Parry was a great physician, and it is not sufficiently known that he anticipated Graves in the recognition of exophthalmic goitre, and was possibly the first to describe the visual phenomena of migraine known as "trichopsia," a fact which has been fully set out in his learned work on *Hemicrania* by our present Registrar.

The ordinary conception of a sequel is the occurrence, sooner or later, after recovery from an illness is seemingly established, of new symptoms and physical signs of disease either near to, or remote from, parts which had been the seat of disturbance in the original malady. Some of these have long been recognised, and little surprise is felt when they supervene, though we may never have been able to predict their certain onset. Amongst such may be mentioned the occurrence of various palsies after diphtheria, and of rheumatism with cardiac complications after scarlet fever. However we may explain these, they are true sequels, albeit they may be inconstant, and only ensue in a proportion of cases of these disorders. Throughout our present inquiry we shall do well to bear in mind the following apophthegm of Sir William Jenner to the effect that "the invariable antecedent of any given event is not necessarily its cause. Invariable antecedent and invariable consequent are not synonymous with cause and effect." I shall endeavour to find a reply to the very pertinent inquiry which Sir James Paget has suggested, whether each disease does not leave after it has ceased certain conditions of blood or structure

¹ Περὶ αἰτίων καὶ σημείων χρόνιων πάθων. βιβλ. Β. Περὶ Ἀρθρίτιδος καὶ Ἰσχιάδος

² *Clinical Medicine*, reprint from second edition, p. 195, 1864.

which sooner or later may manifest themselves in what may be named a residual disease. He remarks that of the soon-occurring sequels of disease we know many; of the later comparatively few. We shall find that our knowledge of the later sequels has been enlarged within quite recent date, especially in regard to the large class of specific and infectious diseases. The question relating to latency of such peccant matters as may sometimes after very long intervals be roused into activity and afford characteristic signs is one of large interest and receiving some attention at the present time. We have to determine what are the limits of duration of latency, and in any given instance to prove, if possible, that these specific and toxic residues have remained latent, and have not been reintroduced from without. We have to learn what conditions of tissues and blood serum dispose to and determine latency, and, further, to ascertain in what forms, particulate or other, germs or toxins remain latent within the body. We must look almost exclusively to the pathological laboratories for replies to most of these pressing inquiries. Such investigations call for the highest skill and experience from workers widely trained in animal chemistry no less than in bacteriology, for they are beset with many pitfalls which are alone known to skilled observers. The physician who is conversant with the attested results of these researches is indeed well equipped when he comes to his work at the bedside.

We have next to consider the occurrence of new morbid conditions which appear to be determined by the previous incidence of definite disease. An example of this is perhaps afforded by the onset of the malady known as *tabes dorsalis*, which is now recognised as a not infrequent sequel in the subjects of constitutional syphilis. It is found that in the subjects of *tabes dorsalis* syphilis figures to the extent of over 80 per cent., and it is hardly possible to believe that this far-reaching infection is not answerable for a very large proportion of cases of *tabes*. We cannot assign the specific spinal and cerebral lesions of this latter malady to any definite forms of syphiloma, neither morbid histology nor therapeutics affording any proof in support of such a contention; hence we are constrained to believe that the blighting influences of the infection of lues in some way predispose the subjects of it to subsequent specific degenerations in certain tracts of the spinal marrow, and thus we have to regard *tabes dorsalis* as one of the possible sequels of syphilis. One of our present Censors, pre-eminent for minute scrutiny and little ready to be satisfied with specious arguments, has declared in respect of this very question that possibly as large a percentage of syphilis might be discoverable were it looked for amongst the unhappy subjects of broken limbs in any surgical wards. This may be the case, but I hardly see that it materially affects the proposition before us, and I think great force is added to the contention by the fact that when women, who are rarely the subjects of *tabes dorsalis*, suffer from it, they have frequently at an earlier period been the victims of constitutional syphilis. (I may add the authority of Dr. Buzzard for the latter statement.) We shall find as we proceed how certain illnesses, as it were, test the constitution of the patient and bring to light some phase or indication of his peculiar diathesis or habit of body, and this it may be for the first time in his life-history. In this way scrofulous manifestations may supervene upon enteric or upon scarlet fever, and gout or disorders of gouty nature may come out after fevers or prolonged illnesses, neither tendency having previously been suspected. Such developments may fairly be regarded as sequels of the original ailments that primarily evoked them, for they might possibly never have been manifested, or have remained dormant till otherwise called into activity later in life.

[The lecturer went on to say that the study of convalescence from acute diseases was a large one, and that he should first consider the large class of specific contagious diseases, and after a brief reference to typhus and relapsing fevers he devoted the rest of his lecture to the consideration of]

ENTERIC FEVER.

The sequels of this disease are numerous and varied. They are now commonly recognised.³ I will consider them in the order in which they most frequently occur.

Phlebitis is perhaps most often met with, and the left femoral vein is the commonest site of it. It is of more frequent occurrence in this disease than in typhus fever. Symptoms pointing to this condition may arise as early as in the third week of the fever, or in the fourth week. In such cases we are hardly justified in reckoning it as a sequel; rather it should be considered a complication. In a prolonged case under the care of my colleague, Dr. Church, phlebitis set in on the fifty-fifth day in both legs, and prevented the patient from rising till the 69th day of the illness. As a rule, the sequels of enteric fever are met with when convalescence is fairly well or apparently completely established. Phlebitis is certainly amongst the earliest sequels, and hardly gives rise to constitutional disturbance. This process may be accompanied with severe pain in the site of it or it may be painless. Pain may be also present or absent in phlebitis dependent on other conditions such as gout or anæmia. The duration of phlebitis varies, and the effects likewise. Complete recovery is the rule, but there may remain permanent obstruction of the affected vein with compensatory enlargements of adjacent ones, and some inability in the limb, with tendency to slight œdema for the remainder of life. There is sometimes reason to suspect that some of the pelvic veins are involved in this condition, though no very clear physical signs of it may be detectable. Suppurations do not result from post-enteric phlebitis, nor are instances on record, so far as I am aware, where any detached particles of clot have been embolically lodged elsewhere in the body, though the possibility of such an accident should not be forgotten. Paget regards the thrombosis as secondary to the inflammation of the coats of the vein. Bradycardia sometimes remains after convalescence.

Arterial plugging is an occasional trouble, hardly to be reckoned as a sequel, since it is rather a late complication. The femoral artery is most often affected, and gangrene rapidly ensues. The condition is that of thrombosis and not of embolism, and in most cases a fatal result ensues. Osler records a case in which the left femoral artery was blocked on the 16th day of the fever. In a case recently under the care of my colleague, Dr. Hensley, in St. Bartholomew's Hospital, there was pain in the right foot with coldness and asphyxia, and absence of pulsation in the femoral artery on the 47th day, continued fever having been present without any relapse in a young woman of 21 years. The heart sounds were clear but feeble, and the first one reduplicated.

Periostitis and perichondritis are sequels which may present themselves at periods long after convalescence is well established. Old fistulous openings may show signs of activity, and lead to areas of subjacent necrosed bone. Simple periostitis may occur without any necrosis of bone. The common site is the tibia. Both tibiae may be symmetrically affected, but this is rarely the case. The disorder may occur within a month of full convalescence. I met with three examples in five years amongst my hospital in-patients. In one case, seen in private practice, three months had elapsed before this trouble came on. In another case periostitis occurred before convalescence was complete. The femur, ulna, ribs and cartilages, and the parietal bones have been noted as liable to be affected. Nodose swellings, with heat and pain, are generally first recognised. These often subside but may break down, and dead bone is to be felt with a probe. Long periods may elapse before a necrosed lamina is expelled, and tedious suppurative discharge may be expected until this separation is effected. The trouble is generally more tedious when a rib with its cartilage is involved, and a year, or even two years, may pass before all becomes quiet. The bones are not deeply involved as a rule. This sequel may occur in persons whose constitution has been and still remains sound, and it does

³ Vide Sir J. Paget, *Clinical Lectures and Essays*, 1875, p. 395; and *Studies of Old Casebooks*, 1891, p. 98. Dr. C. Murchison, *Treatise on Continued*

Fevers, 1873, Second Edition. Dr. T. W. Shore, *Case of Muscular Atrophy and Gangrene of the Lung after Typhoid Fever*, *St. Bartholomew's Hospital Reports*, vol. xxiii, p. 109, 1887, with admirable bibliographical notes. Dr. H. Handford, *Nervous Sequelæ of Infectious Disease*, *BRITISH MEDICAL JOURNAL*, September 21st, 1895, p. 702. Dr. W. R. Gowers, *Manual of Diseases of the Nervous System*, vol. ii, 1895, p. 895, Second Edition. Dr. W. Osler, *Report on Typhoid Fever*, *Studies in Typhoid Fever*, etc.; and *Neuritis during and after Typhoid Fever*, *Johns Hopkins Hospital Reports*, vol. v, 1895.

not appear that this condition betokens any evidence of scrofula, although when a rib is involved the likeness of the disorder to ordinary scrofulous periostitis is, according to Paget, singularly close. The latter authority has described a case in which the eleventh or twelfth rib being involved, a great abscess made its way between the abdominal muscles and had to be opened in the groin. In one case which came under my care the patient, a man aged 28 years, had enteric fever in August, 1892, while serving in India. Five weeks after convalescence an abscess formed near the sternum over the cartilages of the left fifth and sixth ribs. Mr. Howard Marsh undertook the surgical treatment of the case. The general health was excellent, but the local trouble proved most tedious. An abscess was found behind the rib in front of the parietal pleura. The sinuses in connection with it, and the indurated swellings of the cartilages were long in healing, and the parts were not fully sound till after the lapse of two months. Most bone lesions occur within two years after the original attack of fever. Deep scars usually remain. Necrosis of the ribs is met with sometimes, but is less frequent here than in the tibiae. The periosteum may long remain inflamed. Paget records an instance where repeated attacks of pain and swelling occurred without suppuration for three years. Permanent thickening of the periosteum remained. In another case he met with a recurrence of periostitis after nine years of apparent soundness. Men suffer more than women from post-typhoid bone lesions, probably owing to exposure to injuries and strains. The cartilages of the larynx may become necrosed, also the arytenoid cartilages. The latter have been found thus involved and accompanied with an abscess in *post-mortem* examination, and therefore this trouble may not, perhaps, be regarded as a true sequel. They may lead to general emphysema. The larynx may be affected directly by a specific ulcer which is not infrequent on the vocal chords or on the epiglottis.⁴

Phlegmonous cellulitis of the orbit has been observed as a sequel, also orchitis followed by epididymitis, suppurative parotitis, ovaritis, salpingitis, and suppurative thyroiditis. Various affections of joints have been described as sequels. Chantemesse of Paris, who has very fully studied this subject, tells of a case of hypertrophic osteo-arthritis which ensued two and a half years after an attack of enteric fever.⁵ The small joints of the hand and feet and of the cervical spine may be affected. These cases are rarely seen in Great Britain. They must be distinguished from pyæmic arthritis, which sometimes occurs at the end of a case of enteric fever, which merges into a general pyæmia, due to other microbic invasions than those of the specific bacillus of Eberth. The cases referred to here are apparently more often encountered in the United States of America, and have been described at length by Dr. W. W. Keen, of Philadelphia.⁶ The larger joints are chiefly involved. Suppuration is rare, but ankylosis may occur. Dislocations sometimes arise—"distension luxation." Synovitis is first observed, and may arise spontaneously or occasionally from periostitis or necrosis extending into the joint. In a series of forty-three examples collected by Keen, the lower extremities were affected in thirty-nine, the upper in only seven, three of the cases involving a joint in both, for, though commonly a monarticular trouble, two large joints may be affected together. Pain is noted as but slight, but Chantemesse describes nocturnal osteocopy, analogous to that of syphilitic bone disorders as not uncommon in cases of periostitis, and pain in the affected joints as simulating that of rheumatism.

Marasmus is sometimes a sequel of enteric fever, and may occur in various degrees, the patient never regaining his former trophic level. Anæmia is occasionally seen but is commonly recovered from. I have known of several instances and heard of others in which patients have declared that they enjoyed better health than they had before they suffered from this fever.

⁴ Such cases are well described and discussed in the Toner Lectures (Lecture V, vol. xv, of *Smithsonian Miscellaneous Collections*, by W. W. Keen, M.D., of Philadelphia, February, 1876 (Washington, 1878). Vide also remarks by Dr. Church in the *St. Bartholomew's Hospital Reports*, vol. xvii, 1891, p. 104. These cases appear to be less common in Great Britain than in France and the United States.

⁵ *Société Médicale des Hôpitaux*, Juillet, 1890.

⁶ *Op. cit.*, p. 3.

Deafness has been noted as a sequel, or perhaps more correctly as a symptom, towards the end of the illness. Tinnitus aurium is not uncommon in the earlier course of the disease. Neither may be regarded as unfavourable. Mental weakness may occur, the patient becoming silly and childish after the decline of fever and remaining so for some weeks. This intellectual failure is commonly temporary.⁷

In some cases there is an extraordinary silence, an inability or disability for speech. This is apt to follow as the deafness passes off. In one instance under my care a young girl, though perfectly conscious, remained silent under all conditions and often in presence of her relatives for thirty-five days. She was naturally bright and lively. In another case under the care of my colleague, Dr. Church, a boy of 9 years old remained silent for fifty-four days. The fever was severe in both cases. Much muscular wasting occurred in mine, but perfect recovery followed. In Dr. Church's case great stupor occurred at the end of the third week, the right arm and leg were parietic, consciousness hardly returned till the fortieth day, when he could move his right limbs. The sphincters were unstable till the sixty-ninth day. A perfect recovery followed. Choreiform movements have been noted in association with disability for speech in one case.⁸ Paralysis of the vocal cords has been observed. In two cases both abductors were so involved as to necessitate tracheotomy. In another case with much muscular wasting and sensory disturbance one cord was affected. Recovery was complete. The distinction between central and peripheral palsies is often difficult, and is chiefly determined, according to Gowers, by noting the presence of pains in the limbs and the existence of tenderness in the nerves. The condition of silence just referred to is no true aphasia, but is almost certainly due to exhaustion of cortical nerve areas, to enfeebled circulation of impoverished blood, and, perchance, to direct and specific fever poison. Active mental derangement with delusions may supervene after apparent recovery, also melancholia.⁹ These conditions are generally recovered from, but evidences of cerebral and intellectual enfeeblement and defect of memory may remain for many months, or even permanently, after severe attacks of enteric fever.

Minute changes have been met with in the brain of the nature of small inflammatory foci. Recent researches plainly indicate that the spinal cord may suffer from residual disorders after infectious fevers, and especially after enteric fever. Dr. Handford has described a case of general muscular wasting in a boy aged 11 years, the limbs and trunk being especially affected. The knee-jerks were absent, but the other reflexes remained. Enteric fever occurred at the age of 5 years, and there was inability to walk for two months after convalescence had been established. The arms became enfeebled after the legs. At the age of 9 years scarlet fever occurred, and the muscular wasting made subsequent rapid progress. There were no electrical indications of any qualitative change in the muscles, and the condition was apparently one of anterior poliomyelitis. This affection is believed by Gowers to follow upon enteric fever more frequently than any other of the infectious diseases. Disseminated patches of sclerosis of the cord have been found by Ebstein. Leyden has placed the nervous sequels of this fever in three categories: 1. Paralysis of single muscles or groups of muscles supplied by one nerve, including cases resembling post-diphtheritic paralysis, facial palsy, strabismus, disturbances of accommodation and palatal palsy, atrophic paralysis, with neuralgic pain and diminished electrical reactions, paralysis of the radial and ulnar nerves, and other varieties. These are regarded by Leyden as peripheral neuritic disorders, and not of central origin. My colleague (Dr. Shore) has, however, described a very important case, in which localised muscular atrophy occurred which was proved to be due to subacute myelitis of the grey matter of the anterior cornua, involving the origins of the fifth, sixth, and seventh cervical nerves. The patient, a woman aged 26 years,

⁷ On Some of the Nervous Phenomena of Typhoid Fever, by Dr. F. W. Andrews, *St. Bartholomew's Hospital Reports*, vol. xxv, p. 127, 1889.

⁸ De la Harpe: quoted by Gowers. An interesting observation in view of the theory held by myself and others that chorea is rheumatism of the brain, specially involving the cortex. Vide *The Rheumatic Nature of Chorea*, *Lancet*, April 7th, 1894.

⁹ Osler records three cases as having occurred in 229 patients.

suffered from loss of power, first in the right and later in the left hand and arm, three weeks after leaving the hospital convalescent from enteric fever. The extensor muscles of the forearms were wasted, and there was double wrist-drop. There were no sensory symptoms. No other paralyses were discovered. Death occurred in two weeks from pulmonary gangrene and pyo-pneumothorax, and this latter complication was believed to be due to trophic disturbance arising from the spinal lesion, no other cause for it being found. 2. Paralyses of a spinal type, including paresis of the lower limbs, without atrophy and sensory symptoms; paresis with hyperæsthesia and rigidities, due to myelitis or meningo-myelitis; acute ascending paralysis (Landry); progressive muscular atrophy; and acute ataxia with affections of speech and inco-ordination. 3. Affections of a cerebral type: psychoses, mania, melancholia, hemiplegia with aphasia, and with optic atrophy.

Osler groups neuritis as an accompaniment or sequel of enteric fever under two heads; (a) local neuritis, and (b) widespread, diffuse, or multiple neuritis.¹⁰ Doubt has lately been thrown upon the nature of some of the neuritic sequels of enteric fever which so closely resemble post-diphtheritic palsies, since it has been suggested that they are not improbably due to a concurrent but unrecognised specific diphtheria. Murchison described a case in which this concurrence was met with. Palatine paralysis should perhaps be regarded as a symptom suggestive of this combination, but it may, however, occur, together with general muscular weakness, after enteric fever. According to Gowers there is never the loss of accommodation or the slow progress of palsy from one part to another that is significant of diphtheria. Gubler, however, has recorded an example which, according to Bury, is unique, where paresis of the palate occurred with nasal twang of voice and paralysis of ocular accommodation. Amongst the varieties of local neuritis tenderness of the toes has been described by Handford and Osler, the pain being severe and the weight of the bedclothes unsupportable. The ulnar nerve is particularly apt to suffer. The cranial nerves may be involved, especially the third and seventh branches. Optic neuritis is very rarely met with as a sequel. Enteric fever is probably followed by neuritis more often than any other infectious fever, with the exception probably of diphtheria and influenza. From a study of many cases Bury remarks that the resulting paralyses are usually partial in extent and degree, that the muscles affected are both wasted and weak, and that the paralysis is almost invariably preceded or accompanied by some form of sensory disturbance. The muscular tremors which occur in severe cases of enteric fever may continue and be followed by symptoms of disseminated spinal sclerosis, but not by paralysis agitans. Tetany has been met with during the fever and in convalescence after some epidemics. A condition described as "the typhoid spine" by Gibney of New York and by Osler is met with sometimes late in convalescence, which may confine the patient to bed for weeks. It is characterised by pains in the back, hips, and abdomen, shooting and paroxysmal, elicited by slight movements. It is sometimes associated with general debility, but not always. No evidence of spinal disease has been detected, though periostitis and spondylitis have been suggested as possible causes. Osler believes that the disorder is purely neurotic. In his special report¹¹ on neuritis during and after typhoid fever he mentions having met with five cases of focal neuritis amongst 390 patients. In two of these the disorder developed during the height of the fever. In the third case neuritis occurred when convalescence had been established for ten days. In the fourth case neuritis began after five weeks' illness, as the pyrexia declined. In the fifth case the disorder came on late in a tardy convalescence. In four examples of multiple neuritis, also recorded by Osler in his report, the disorder came on either late in the course of the fever or somewhat early in the convalescence.

Paraplegia of considerable severity, though not complete, has been noted, accompanied with spinal tenderness, hyperæsthesia, and sensory disturbance in the legs. It may pass off in the course of a few weeks, and is believed to be dependent on a slight degree of diffused myelitis. Increased knee-

jerk and foot-clonus existed in one case seen by Gowers some months after the fever. Symptoms of more acute and rapidly spreading paralysis may sometimes supervene and lead to a fatal issue in the course of a few days. Hemiplegia is very rarely met with, but two cases have been recorded of right-sided disorder with aphasia, and in one of them optic atrophy followed.

Pleural effusion of all varieties may occur, but are not frequent. Empyema has been met with.¹² Dr. Hale White has recorded two cases in which pyo-pneumothorax was a sequel. The fever was protracted in each case. The lung gave way in both patients while straining at stool. One of these proved fatal. The other made a good recovery.¹³ This accident may be explained by the softening of the pleura due to suppuration, or by the occurrence of rupture of a pulmonary abscess due to typhoid fever or to mixed infection.

One of the most curious sequels I have met with was linear atrophy of the skin, with extreme hyperæsthesia of adjacent parts, in a young and vigorous man. This began three months after a severe attack of enteric fever. Parallel stripes of discoloured skin were found on the outer side of the left thigh, depressed and showing perfect characters of the well-known lineæ atrophicæ or "lineæ gravidarum." This condition was evidently due to a neuritis involving both sensory and trophic fibres of a specific (typhoidal) character. Six months later I learned that the pains had much subsided and the colour of the stripes was fading, but recovery was not complete. I have found reference to several other similar cases as having been met with in this country, in France, in Germany, and in Canada.¹⁴

Typhlitis is certainly not generally recognised as a sequel of enteric fever, but Barling has recorded an instance in which the vermiform appendix was involved in ulceration leading to stenosis. He believes that this resulted from an attack of enteric fever which had occurred five years previously.¹⁵ The connection is, I think, at least doubtful, and I have never read of or met with a similar example.

Gangrene of the lung has been already mentioned as an early sequel to the remarkable case recorded by Dr. Shore. The history of that case plainly indicates that this condition was due to neurotrophic disturbance. Sir William Jenner met with two examples after typhus fever, but with none after enteric fever. Murchison considered it a rare event, but had met with one or two instances. Probably in the majority of cases this condition may be regarded as a complication rather than as a sequel. In Dr. Shore's case the occurrence was clearly an early sequel.

A crop of boils is recorded as a sequel, causing post-typhoidal pyrexia in a case under the care of Dr. Osler.¹⁶

Enuresis, even of long duration, has been known to be temporarily cured after the occurrence of enteric fever.¹⁷

It appears certain that during convalescence there may be recurrences of pyrexia which simulate, but are not truly relapses of, enteric fever. Putting aside such causes as may disturb any convalescent—such as emotion, constipation, etc.—and cause temporary pyrexia, also such recognised sequels as periostitis, necrosis of bone, suppurative arthritis, pyæmia, erysipelas, phlebitis, and suppurative otitis media, we may note, according to Osler, a continued fever, lasting two or three weeks, apparently due to the profound anæmia which follows enterica. The temperature may range from 99° to 101° F. This is one case in which normal temperature prevailed for four days after convalescence there followed a febrile period extending over sixteen days. The red globules were reduced by one-third. The fever subsided as the blood state improved, but ten weeks elapsed before the normal condition of the blood was attained. In another class of cases, two or three weeks after convalescence, a rigor may supervene and a temperature of 104° or 105° F. occur on four or five occasions daily, or with intervals of a day or two of normal temperature, or of slight continued fever, and this for a period varying from two to sixteen days. No plain indica-

¹² Weintraud, *Berl. klin. Woch.*, Jahr xxx., No. 13, p. 346.

¹³ BRITISH MEDICAL JOURNAL, February 22nd, 1895, p. 466.

¹⁴ Vide *British Journal of Dermatology*, No. 62, vol. v, where I have recorded my case at length.

¹⁵ BRITISH MEDICAL JOURNAL, May, 1895, p. 1135.

¹⁶ *Johns Hopkins Hospital Reports on Typhoid Fever*, No. 1, vol. iv, 1894.

¹⁷ Church, *St. Bartholomew's Hospital Reports*, vol. xvii, 1887, p. 107. Trousseau, *Chî. Med.*, Sydenham Society's Translations, vol. iii, p. 405.

¹⁰ *Johns Hopkins Hospital Reports*, vol. v, 1895.

¹¹ *Ibid.*, vol. v, 1895.

tions of the cause of this condition may be manifested, but it may be surmised that septic absorption has occurred from intestinal ulcers, or from a purulent focus in the spleen, or a mesenteric gland. In two of Osler's cases in this series numerous miliary abscesses were found in the kidneys, and in one of these typhoid bacilli were found and no other microbes. In other cases Eberth's bacilli were discovered in the kidneys together with other microbes, namely, the bacillus coli and the streptococcus. Sterilised cultures of the typhoid bacillus were found to produce nephritis in animals. The fact of ulceration of the bowels in enteric fever allows a ready entry into the system of specific bacilli, and Konjajoff has frequently found them in cases where albuminuria occurs in this fever. The kidneys appear to be one of the channels through which bacilli pass out of the body.

Having now considered the many and varied sequels which have been met with after enteric fever we may seek next for a rational explanation of them. If we can discover this we may fairly hope to find the clue to a settlement of the question, not only in respect of this particular fever, but of that which presses for solution in the case of all the specific infectious fevers and diseases. Modern bacteriological research leads us to regard it as highly probable, if not actually certain, that the toxins generated by the bacilli, specific in each case, are the active agents by which most of the sequels are induced in such instances. We have seen that many sequels may fairly be attributed to the extreme debility and exhaustion entailed by the acute manifestations of the disease. It suffices to examine with care the several viscera in fatal cases to be assured of the damage suffered in vital organs which is to be fairly set down to pyrexia alone. The softening of the cardiac walls, the shrinkage of the liver induced by atrophy and molecular degeneration, the condition recognised as "cloudy swelling" of this viscous witnessed on section, and the like state of the kidneys, all point to grave trophic disturbance with inadequacy of metabolic, secreting, and other functions. Although those changes are most obvious in the organs just mentioned, we may feel sure that they exist in all the textures of the body, and must during life have been potent for evil. Similar acute degenerations occur without doubt, though in lesser degree, in non-fatal cases, and we may cease to wonder at the low health, tardy recovery, and long failure to reach the normal level of health in these cases.¹⁸ That special organs or areas of tissue should suffer more in some cases than in others is probably to be explained by inherent and personal weakness, since we know that such visceral weakness and textual defects are hereditary, and we may thus account for many varieties of ailments and peculiarities met with in patients. Acute illness tests the integrity and functional adequacy of such parts, and they break down under the ordeal, revealing to us one or another failure as a sequel. We may thus speak of specific and non-specific sequels. In the former case we have to reckon with localised residues of the primal disease, manifested by invasion of parcels of toxin-generating bacilli, working out their malign effects. Actual proof of this is not far to seek. It has been shown that such definite and local invasions occur and fully account for the sequels. In the case of enteric fever we have the researches of Chantemesse and Widal¹⁹ showing the presence of bacilli in almost every tissue thus affected. These authorities affirm confidently that they have found the true bacillus of Eberth. My friend and colleague Dr. Kanthack, however, informs me that these and other observers in France had not sufficiently learned to distinguish the bacillus coli from Eberth's bacillus at the time they wrote, and that thus some doubt must still exist as to these particular researches. In Osler's case, already quoted, no such doubt can be entertained. Sultan and Burchke discovered, in one case six years after an attack of enteric fever and in another seven years after, living bacilli in abscesses of bone.²⁰ It is now

proved that these bacilli are very tenacious of life outside the body, and can exist in a potato culture for at least two years. Some of the sequels in enteric fever are not specific, but certainly due to invasion by other than the specific bacilli, to the ordinary microbes inducing suppuration, such as streptococcus, staphylococcus pyogenes aureus, and to the bacillus coli communis. These may be classed as septicæmic or pyæmic sequels, due to secondary invasion supervening, embolically or otherwise, on the specific fever, by way of venous or lymphatic channels, from purulent foci in the intestines, mesenteric glands, or spleen. Schmitzler records a case where the staphylococcus aureus had remained latent in a bone for over thirty-five years.²¹ Splenic enlargement is not always a simple matter. Rupture may occur on slight provocation, and has been known to occur even spontaneously.

THE GOULSTONIAN LECTURES

ON

THE LIFE-HISTORY OF THE MALARIA GERM OUTSIDE THE HUMAN BODY.

Delivered before the Royal College of Physicians of London, March, 1896,

By PATRICK MANSON, M.D., F.R.C.P., LL.D.,

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LECTURE III.

WHEN some time ago I had formulated in my own mind the theory I have endeavoured to explain, I saw little prospect of ever being able personally to put it to the test of further observation and experiment. I was so convinced, however, of its inherent probabilities and of its importance if established, that I ventured to publish in the BRITISH MEDICAL JOURNAL of December 8th, 1894, a *précis* of my views.

It appeared to me that as neither Laveran nor Mannaberg had connected the mosquito with the flagellum, and that as Calandruccio had failed to observe developmental changes in malarial parasites ingested by mosquitos, the logic of the situation had been missed.

For these reasons I ventured to call the attention of observers to what I could not but regard as a promising but imperfectly worked line of investigation, hoping that someone with better opportunities than I could command might take the matter up and endeavour to confute or confirm what appeared to me a very promising hypothesis.

When I wrote the short article in the BRITISH MEDICAL JOURNAL I refer to, I hardly ventured to hope that the views expressed would so soon receive the support—I hardly risk the word, confirmation—they have already done.

ROSS'S INVESTIGATIONS.

Surgeon-Major Ronald Ross, to whom I have already referred, was in England last winter, and, being favourably impressed with the mosquito hypothesis, determined to work it out on his return to India. After much discussion, we fixed on a certain line of experiment and observation which my experience in former years in filaria work seemed to indicate as being likely to lead to some definite result one way or other.

PRINCIPLES GUIDING THE INVESTIGATION.

We considered that those forms of malaria in which the crescent body was a prominent feature were the most suitable for experiment, at all events to commence with. Of all the forms of the plasmodium the crescent is the most definite, the most readily recognised in the blood, and the easiest to work with, much more so than the potential flagella-forming intra-corporal parasite of the quartan and benign tertian infections. The behaviour, therefore, of the crescent body in the mosquito was the first point to be studied. We concluded that what might be found to happen to it could be reasonably regarded as typical of what would happen to the other flagella-producing forms of plasmodium.

²¹ On Traumatic Infection: Lockwood, *Hunterian Lectures*, Royal College of Surgeons of England, 1895, p. 42.

¹⁸ According to the late Professor Aitken, of Netley, no patient having suffered severely from enteric fever is fit to resume active or laborious duties for three or four months subsequently. In many severe cases the patient has almost to be recreated anew before sound health is established, and a year not seldom elapses before this occurs, even under favourable conditions. ¹⁹ Société des Hopitaux, Mars, 1890.

²⁰ Quoted by Dr. Washbourn, *Proceedings of the Royal Medical and Chirurgical Society*, November, 1895. *Vide* also report by H. C. Parsons, of Baltimore (*Annals of Surgery*, November, 1895.)