with the artificially-fed infant, explains the greater freedom of the former from infectious diseases.

The important question of the influence of pre-existent disease in predisposing to infection has been brought nearer to a solution by recent studies of immunity. Schütze and Scheller[24] have demonstrated that, while the normal rabbit promptly regenerates the complements used up in consequence of the injection of haemolytic serum, a rabbit infected with the hog cholera bacillus has lost this capacity. My former pupil, Dr. Longcope, has kindly placed at my disposal the unpublished results of an investigation which he is making under Professor Flexner's direction at the Pennsylvania Hospital of the intermediary bodies and the complements in human blood in different diseases. Colon and typhoid bacilli are used as the tests, as, unless one accepts Bordet's doctrine of the unity of complements, it is more important for the study of problems of infection to determine bacteriolytic rather than haemolytic antibodies. One of the earliest results of the systematic bacteriological examinations which we make at all necropsies at the Johns Hopkins Hospital was the recognition of the great frequency of terminal infections, formerly often undetected by the clinician, in chronic diseases, particularly of the heart, the blood vessels, and the kidneys. Dr. Longcope finds, although not regularly, still in many cases of these diseases a marked reduction in the quantity of complements, which may amount to a total loss of the colon complements. The analysis of the cases brings out unmistakably a definite relation between this loss of complement and the predisposition to infection.

The study of a series of acute infections, chiefly of a surgical nature, shows that in the course of the infection complements are being constantly used up and regenerated, and that at any given time there may be an excess or a reduction of the bacteriolytic power of the blood. Thus far it has been found impossible in these acute infections to attach any prognostic significance to the amount of complement or of bacteriolytic power, nor could any definite relation be determined between the leucocyte count and the content of complements.

Although we have traversed, gentlemen, in this lecture a path which I fear has seemed to you a long and winding one, I am conscious that I have been able to point out the features of the prospect only imperfectly and incompletely. The extent and the richness in details have been embarrassing. I trust, however, that I have been able to indicate in some measure the great interest and importance to biology, to physiology, to pathology, to every department of medical science and art of investigations which have led to a deeper insight into certain manifestations of cellular life. What has been conquered by these investigations is simply a bit of new territory pertaining to the intimate life of the cells, and we find here, as whenever we are able to penetrate deeper into this life, that there comes a flood of new light into every department of biology. The researches on immunity, which to some of short vision once seemed to threaten the foundations of cellular pathology, have served only to strengthen them. These researches, which have already led to the saving of thousands of human lives, and will lead to the saving of untold thousands more, have been carried on by the experimental method, and can be conducted in no other way. This method is as essential for the advancement of medical science as for that of any of the natural or physical sciences. To restrict unnecessarily and unjustifiably its use is nothing short of a crime against humanity. It is an evidence of the robust vitality of English physiology and medicine that in spite of unwarrantable obstacles thrown in their path their contributions to science in recent years have been so numerous and so important. The influence of English thought and action is great with us in America. See to it, my colleagues and men of science in the British Isles, that you retain for yourselves and hand down to your successors, at least without further impairment, the means of promoting medical knowledge and thus of benefiting mankind.

[24] Schütze and Scheller, *Zeitschrift für Hygiene*, 1901, xxxvi, pp. 270 and 459.

CONCERNING SPASTIC AND SYPHILITIC SPINAL PARALYSIS.*

By Professor Dr. WILH. ERB,
Professor of Clinical Medicine at Heidelberg.

Gentlemen,—I consider it a great honour to be allowed to deliver a lecture in this important institution, which is consecrated to medical learning and practice, and before an assembly of young colleagues all eager for knowledge. I respond with joy and thankfulness to the invitation, and hope that I shall be sufficiently understood, in spite of my imperfect English, and perhaps unaccustomed and faulty pronunciation of the Latin and Greek technical terms used in our science.

As you already know, I have chosen for my paper a subject dealing with the pathology of the spinal cord, with which I have been occupied for many years, and which has, as far as I can see, arrived, after many difficulties, at a definite scientific conclusion.

It is now exactly forty years since I ended my studies and began my practical and scientific career under the eye and guidance of Nicolaus Friedreich, who just at that time was engaged in his epoch-making observations on that disease of the spinal cord which still bears his name "hereditary ataxia" (Friedreich's disease). I was, therefore, early initiated into the pathology of the spinal cord and nervous diseases generally.

Spinal Cord Pathology.

When I look back upon those days and compare the state of our knowledge of diseases of the spinal cord at that time with our perfected understanding of the present day, I must say that probably no other branch of nerve pathology has undergone such extraordinary development and has advanced to the same degree as the pathology of the spinal cord. We are, doubtless, still far from the goal even in this branch as regards an exact understanding of its pathologico-anatomical bearings, of development and causes, and of its relations to the clinical symptoms observed; nevertheless, we may justly look with pride upon the standpoint which has been reached to-day in the pathology of the spinal cord.

A glance at the handbooks and textbooks on diseases of the nervous system of those days teaches us how incomplete our knowledge of its anatomy and pathology was, and how deficient our clinical distinction between the several forms of disease. One was just beginning to define and study more closely the anatomical foundation of locomotor ataxia, and in the seventh decade of the last century men began everywhere to study clinically and anatomically the spinal cord in particular (I need only mention the names of Duchenne, Lockart Clarke, Friedreich, Leyden, Westphal, and especially that of Charcot and his school, Vulpian and others), which led to rapid strides in broadening and deepening our knowledge. On this point I cannot go into detail here.

When I began my studies one certainly knew the diseases of the coverings of the spinal cord (meningitis, affections of the vertebrae), traumata, haemorrhages, etc., somewhat more accurately, but the diseases of the cord itself very slightly. In these two main groups were recognized to both of which the name of inflammation of the spinal cord (myelitis) was given; those forms which developed clinically with rapidity, often accompanied by fever, etc., and which showed themselves anatomically as essentially processes of softening, were classed together as acute myelitis; those forms which clinically began slowly and persisted for years, leading often to incurable disease, and which showed themselves anatomically as induration, sclerosis, grey degeneration and atrophy, were included under the term chronic myelitis.

Differentiation of "Myelitis."

It was only through elaborate methods of histological investigation and more exact clinical observation and diagnostic differentiation that a more extensive distinction and recognition of different morbid conditions was arrived at. So, taking chronic myelitis as an example, this one comprehensive term became gradually split up into the following—

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tabes, hereditary ataxy, transverse myelitis, slow compression, multiple sclerosis, amyotrophic lateral sclerosis, chronic anterior poliomyelitis, progressive spinal amyotrophy, bulbar paralysis, the simple and combined system diseases, and syringomyelia.

Of special scientific interest were those forms of chronic disease which are limited to symmetrical, definitely circumscribed regions of the cord, which conduct fibres belonging functionally and developmentally together, the so-called tracts or "fibre systems," hence they were, as you know, named "system diseases," and in latter days "neuron diseases." It is about two of these special forms of chronic myelitis, which I have myself more clearly differentiated, that I wish to speak to you to-day.

Primary Spastic Paraplegia.

The first is the so-called "spastic spinal paralysis—primary spastic paraplegia." In the year 1875 I described[1] at a meeting of neurologists of South-Western Germany a symptom group which appeared to me to be sufficiently characteristic when occurring by itself to merit introduction into nosology as a special form of disease.

Only three symptoms constituted the same: A certain amount of feebleness (paresis) of the lower extremities; more or less muscular rigidity in the same region; and a marked increase of tendon reflexes. No other symptoms were present, no disturbance of sensation, of the sphincters, or of function of the generative organs, or nutrition of muscles or skin structures, no anomaly of the brain, cerebral nerves, or organs of sense.

To this "syndrome," this symptom triad, which was doubtless referable to a disturbance in the spinal cord, I gave the name of "spastic spinal paralysis," and sought, though *post-mortem* evidence was lacking, to prove, on the basis of clinical and anatomical facts which were already known at the time, and by suitable analogies, that a chronic, slowly ascending sclerosis (or grey degeneration) of the lateral columns of the cord, limited particularly, perhaps exclusively, to the crossed or lateral pyramidal tracts, would be found as the anatomical foundation of this disease. (At that time it was called "lateral sclerosis.")

Only a short time afterwards, Charcot, who had already published a series of similar or nearly related cases and facts, described the same symptom groups under the name of "tabes dorsal spasmodique," and arrived at precisely the same conclusion with regard to the probable anatomical foundation as I had done.

In a short time our observations were confirmed and corroborated from many quarters. Many similar observations were published which, however, did not in all cases fulfil the strict diagnostic requirements laid down by me.

From other sides came contradiction, especially on the part of the Berlin School, whose most distinguished representatives could not associate themselves with our views, but believed that the picture that I had described was simply a symptom group which could be found in diseases of the spinal cord and brain under the most varied conditions.

Even if this was correct, the occurrence of the symptom-triad by itself might still be supposed to depend upon a definite and typical anatomical basis. This was disputed because no *post-mortem* evidence of any sort was as yet forthcoming.

In fact, such evidence was almost completely missing for the first few years; it even happened that, in a series of cases diagnosed as spastic spinal paralysis, the necropsy revealed the most diverse anatomical conditions, which, of course, had this in common, that there was in each case a symmetrical lesion of the pyramidal tracts in some part of their extensive course, but not a symmetrical ascending degeneration of the same.

In most instances one found multiple sclerosis, in others chronic hydrocephalus, tumours in the region of the decussation of the pyramids, syringomyelia, combined system disease, symmetrical cerebral diseases, etc.

However, a critical examination of the symptom picture showed subsequently that no pure spastic spinal paralysis had been present, but that errors in diagnosis had been made in most of the cases. Those cases which without doubt presented a pure primary sclerosis of the pyramidal tracts belonged to the amyotrophic lateral sclerosis, and always showed accompanying chronic degeneration of the grey matter of the anterior columns. The positive *post-mortem* evidence, still scanty at the time, had not been considered as conclusive.

Though a logical consideration of clinical facts pointed emphatically to the correctness of our assumption, opposition gained strength by regarding the anatomical conditions found with too much scepticism.

The matter was therefore left undecided for more than twenty years; other evidence had to be waited for, which could not be collected easily when one considers that on the whole the disease is rare and extremely chronic and does not of itself lead to fatal termination.

These facts have, however, at last arrived. First, the clinical picture became better recognized in its pure state by more accurate, critical diagnosis, and mixed cases, caused by other conditions, were eliminated. One was able to follow up individual cases through a number of years, and to prove that the symptom picture remained absolutely constant, that not even a trace of any other symptom was added to the symptom-triad. (A fourth symptom has of late been recognized, namely, the so-called Babinski reflex of the sole of the foot, which bears the closest relation to exaggerated tendon reflexes, and is apparently just as constantly present as the latter.)

Family Form of the Paralysis.

I myself know of several cases which after twenty six, twenty, and eighteen years remain absolutely unchanged, so that there can be no doubt as to the individuality of the clinical picture. To these was added a group of exactly identical cases, in which spastic spinal paralysis occurred as a family disease, evidently caused by hereditary influences in the instance of several members of a family, both in children and adults.

The closest clinical analysis of these cases showed beyond doubt that the pure symptom picture of spastic spinal paralysis, and that picture alone, was present, and that other appearances never showed themselves. And just for these cases has decisive *post-mortem* evidence been lately found; each examination showed as the main and most important feature a sclerosis of the posterior lateral tracts, especially the pyramidal tracts.

As a matter of fact, we are now in possession of a whole number of *post-mortem* proofs, both for the ordinary as well as the family form of spastic spinal paralysis, leaving no room for doubt that this disease exists, and that it has a constant anatomical condition for its foundation.

Post-mortem Findings in Spastic Spinal Paralysis.

I will not dwell on the older *post-mortem* findings, though these gain importance in the light of our newer experiences: I allude to the first observation made by Charcot in the year 1865, which of course dates from a time when the methods of investigation were still imperfect; also those of Dreschfeld (quite typical, because the lesion in the anterior columns was trifling) and of Stoffella (who, however, only made a microscopic examination). But I mention only which are indisputable and will stand any criticism:

Case I.—Minkowski: Clinically, the pure picture of spastic spinal paralysis; anatomically, a nearly pure sclerosis of the crossed pyramidal tracts (with slight changes in the direct cerebellar tracts).[2]

Case II.—Von Strümpell: Man, aged 63 (Gaum) who had a brother suffering from the same disease; clinically, presenting the typical picture of spastic spinal paralysis for at least twenty years; anatomically, a typical degeneration of the pyramidal tracts from the lumbar to the cervical region; in addition, a slight degeneration of the direct cerebellar tracts, and a still more trifling degeneration of the tracts of Goll in the upper part of the spinal cord. Strümpell would, on this account, reckon the affection among the combined system diseases, but the degeneration of the pyramidal tracts is certainly the most essential lesion, and is to be regarded as primary.[3]

Case III.—Déjerine and Sottas: Clinically, a pure case of spastic spinal paralysis of twenty-five years' duration; death from pneumonia in the sixty-sixth year; anatomically, marked sclerosis of the pyramidal tracts from the lumbar to

the cervical cord; slight partial sclerosis of Goll's tracts in the cervical region, otherwise everything normal.[4]

CASE IV.—Donaggio (1897): Man, aged 61 years: clinically, for two and a quarter years the typical picture of pure spinal spastic paralysis; death from pneumonia; anatomically, pure, exclusively primary degeneration of the pyramidal tracts from the lumbar to the cervical region (a quite typical case).[5]

CASE V.—Friedmann: Male, aged 52: clinically, for two years the pure picture of a spastic spinal paralysis. (Trace of disturbed sensation present?) Apoplexy, death from pneumonia; anatomically, classical primary degeneration of pyramidal tracts only (a trace of degeneration in direct cerebellar tracts—endarteritis obliterans of the basilar artery).[6]

CASE VI.—Von Strümpell: Clinically, picture of pure spastic spinal paralysis: death after the disease had lasted thirty-five years; anatomically, quite typical moderate degeneration of the pyramidal tracts from the lumbar cord to the region of the pyramids. Direct cerebellar tracts scarcely affected; tracts of Goll very slightly above in the cervical region. Anterior columns and train completely free (belongs to the hereditary form).[7]

CASES VII and VIII.—Bischoff: Two brothers, from their 8th and 10th years, suffering from spastic rigidity of the limbs, ascending slowly from the legs to the head. Intellectual development poor, otherwise, clinically, the typical picture of spastic spinal paralysis. Death from phthisis after about twenty years' duration; anatomically, a typical degeneration of the pyramidal tracts, extending upwards beyond the medulla oblongata, not further. Direct cerebellar tracts and Gowers's bundles all but free. Goll's tracts extremely affected. In the grey matter of the anterior columns atrophy of the ganglion cells (evidently occurring towards the end of life). The author calls the change in the spinal cord primary tract-degeneration (quite analogous to the condition found by Strümpell), and holds that thereby the existence of an infantile form of hereditary spastic spinal paralysis has been proved.[8]

CASE IX.—Ida Democh, 1900. The case is clinically and anatomically somewhat complicated. Clinically, typical picture of spastic spinal paralysis, combined with signs of chronic alcoholism, pains, tremors, etc.; anatomically, primary degeneration of the pyramidal tracts, slight degeneration of tracts of Goll, congenital hydromyelus in the lumbar and dorsal cord; direct cerebellar tracts free; nevertheless, as proved by the author, this can be termed a case of primary degeneration of the pyramidal tracts in spastic spinal paralysis.[9]

CASE X.—And just in these last days another quite typical case with necropsy came on record. Dr. Kühn has described it a few months ago (*Deut. Zeit. f. Nervenh.*, xxii, p. 144), and Professor Strümpell has made the microscopical examination of the spinal cord last week; he was kind enough to allow me to speak of this case in my lecture. He found—clinically it was a quite typical case of spastic spinal paralysis—an essentially characteristic primary degeneration of the lateral columns. I was very glad to bring this last and most evident case to your knowledge.

The result of these facts may be summed up as follows: In all cases there is a pure lesion of the pyramidal tracts, and in addition, slight lesion of the direct cerebellar tracts and trifling sclerosis of the tracts of Goll.

That these latter are points of secondary importance is clear to all who understand the subject; they cause no clinical symptoms as far as we know, and occur under the most varied circumstances without our knowing anything about them. One is not, therefore, justified in estimating their importance too highly, just as we cannot be prevented from regarding tabes as a sclerosis of the posterior tracts, although in many cases of tabes changes are also found in the lateral and anterior tracts, or in the grey matter; so our estimation of the proper value of the more important changes in the pyramidal tracts is not influenced by the presence of these slighter changes in the tracts of Goll, or, besides the pyramidal tracts, in the lateral tracts. This is all the more so considering that it is generally a question of long-standing disease in elderly persons suffering from severe illness, in whom such changes are usually observed.

It therefore appears certain that in cases of pure spastic spinal paralysis, there is present as the essential change, a sclerosis of the posterior segments of the lateral spinal tracts and particularly in the pyramidal tracts, more or less uncomplicated and exclusive. I am therefore persuaded that the existence of spastic spinal paralysis, clinically as well as anatomically, has now been amply established, and that this disease must occupy a well-deserved place among the chronic system diseases of the spinal cord.

Clinical Picture of the Disease.

There is no need of a lengthy description, but only of a short, concise sketch of the disease. The complaint is on the whole a rare one, much rarer than tabes, and not as common as I and others thought at first. It usually begins slowly and insidiously, rarely in a more rapid fashion, with some sense of weight, dragging, and slight feebleness in one or the other leg, without pain, at most only pain of fatigue after prolonged exertion, without or only slight transient paraesthesia of the legs, without any other symptom except perhaps some backache. The condition progresses just as slowly as it commenced; the legs become stiffer and heavier, the gait progressively more laboured, dragging, and distinctly spastic; occasional muscular cramps, contraction of the legs may occur, nothing else. Objective examination reveals—after the disease has already existed some months or even years—the characteristic symptom-triad: a certain weakness and awkwardness of movement of the legs, very slight, so that often for a long time nothing in the way of paresis, much less paralysis, is present; no ataxy; but far more distinct and prominent is the spasm and rigidity of the muscles, ranging from slight elastic resistance during passive movement, to marked, stiff contracture, temporarily increased by energetic muscular action, necessitating forced extension of the legs, etc.; and thirdly, the well-marked exaggeration of the tendon reflexes (patellar-clonus, ankle-clonus, reflexes from periosteum and fasciae, and numerous tendons which normally scarcely yield any reflex), with involuntary clonus of the foot (spinal epilepsy) while the patient is sitting. To these must be added the pathological plantar reflex (slow dorsi-flexion of the great toe when the sole is slightly stroked—valuable evidence of organic changes in the pyramidal tracts) recently described by Babinski.

From the foregoing—weakness, muscular rigidity, exaggerated tendon reflexes—we have resulting the characteristic "spastic gait," the details of which (dragging of the rigid and closely-adducted legs, scraping the ground, tendency to walk on the toes, tilting movement of the trunk at each step) I need not describe in this meeting.

As an early sign of the gradual ascending of the process to the arms one often finds already an increase of the tendon reflexes in the arms. This is all. Otherwise there is nothing to be found—no disturbance of the sensation, no Romberg's sign, no change in the function of the bladder, bowel, or generative organs, no muscular atrophy, no change in their electrical reaction, no ataxy, no disturbance in the organs of sense, the pupils, cerebral nerves, speech, psychical functions, memory, etc. Indeed, you may not find anything of this kind, otherwise the case is not one of pure spastic paralysis.

Prognosis.

The disease progresses as slowly as it began—endlessly for years and decades. I know of a case which has already lasted for twenty-six years without undergoing any change at all, and without the patient having completely lost the power of walking.

Should the case progress more rapidly, the patient soon becomes altogether stiff and helpless; extreme contractures prevent any movements; the arms become affected, also occasionally the back, neck, and head, so that the patients are in the most miserable plight, and finally die in a marasmic condition.[10]

But, generally speaking, the disease is not directly fatal, and there is less distress and suffering—no pain, bladder disturbance, decubitus, disturbances of the mind, or psychical anomalies—than in most of the chronic progressive spinal affections. The prognosis is therefore self-evident.

The picture of the family or hereditary form of the disease, occurring in groups of several members of one and the same family, and in several generations, both in early childhood

and in adults, is essentially the same. Repetition is unnecessary. (See the cases of Bernhardt, Strümpell, Tooth, von Krafft-Ebing, Nowmark, Erb, and others).

Differential Diagnosis.

The diagnosis presents no difficulties as a rule, especially when the cases are under observation for some time, if one bears in mind that the above mentioned three or four symptoms are the only ones, and that no other is permissible. As soon as any other symptom, however insignificant, appears —(pain, paraesthesiae, bladder trouble, pupils, disturbances in the eye muscles, tremors, ataxy or the like) the diagnosis cannot be maintained. In this way the disease can as a rule be easily distinguished from chronic myelitis, compression of the spinal cord, combined system diseases, cerebral, diplegia, syringomyelia, amyotrophic lateral sclerosis and syphilitic spinal paralysis.

There is only one disease which sometimes causes much difficulty and may be recognized only after some time, and that is multiple sclerosis: in this the three symptoms, or more correctly the four, of spastic spinal paralysis, are not uncommonly present alone, but at last the other symptoms follow (nystagmus, tremors, bladder trouble, etc.). Therefore with this disease special care is necessary.

Etiology.

About the etiology of spastic spinal paralysis I can only say a little; it is really still completely in the dark: apart from the hereditary influences, the blame is thrown upon chills, overwork, psychical shock, trauma, and also syphilis, perhaps the latter more often than was at first believed; lastly, certain poisons, lathyrus, pellagra. About these nothing certain is known.

To my mind, the outcome of this study seems clear; spastic spinal paralysis exists as a form of disease definitely characterized by the oft-named four symptoms, and will not again disappear from the pathology of the spinal cord, the anatomical lesion underlying is a grey degeneration of the lateral tracts, which is not always confined to the pyramidal tracts alone, but is mainly and most strongly marked in these.

It is impossible to consider more closely the many interesting scientific questions respecting neuron diseases which arise in this connexion. I am only anxious to fix in your minds the clinical and pathological-anatomical picture; this must suffice for to-day.

Syphilitic Spinal Paralysis.

The growing experience of the last twenty years has, of course, added to our knowledge of this and other similar spinal diseases. On this account I was prompted in the year 1892 to differentiate a second clinical form of disease, which, indeed, presented a strong resemblance to spastic spinal paralysis, but differed from this in a definite and characteristic way, as also from other symptom pictures already known. It was proved that it occurred almost exclusively in individuals previously suffering from syphilis. I have called it "syphilitic spinal paralysis."[12] It often occurs relatively early, during the first two to six years after syphilitic infection, but can also develop much later, after fifteen, twenty, or more years. Briefly it is characterized by this, that besides the typical picture of spastic spinal paralysis there is always a disturbance in bladder function, and a usually slight but always demonstrable subjective and objective disturbance of sensation. The tendon reflexes are markedly increased; the rigidity of the muscles, however, is comparatively slight when contrasted with the apparently very marked spastic gait. There are no marked pains, severe disturbances of sensation, atrophy of muscles, disturbances of the brain, cerebral nerves, eyes, pupils, etc. The onset of the disease is usually quite chronic and insidious, sometimes also more rapid, improvement and long spells of standstill are possible, but death may occur after a comparatively rapid course in a few years.

My pupil, Dr. Kuh, has collected in a long paper my own and many other observations upon syphilitic spinal disease which appear to belong to this class, and has discussed them at length. It seems to me after further experience that a still finer sifting and subdivision might be possible and useful in this series.[13]

Its probable Pathology.

Since *post-mortem* evidence obtained from well-marked and typical cases was missing both to myself and to others, I drew up a few assumptions with regard to the anatomical foundation of the disease. It seemed to me to be most probable that it was not a case of complete transverse lesion, or of a combined system disease, but only of a partial, symmetrically situated lesion in both halves of the cord in the dorsal region; it seemed to be chiefly in the posterior lateral tracts, with partial involvement of the grey posterior columns and the white posterior tracts. As to the nature of this lesion, whether a specific syphilitic infiltration, a syphilitic infection of the vessels of degenerative change, I did not dare to put forward any definite opinion. In this instance, also, I had many adherents, many opponents, as was the case with spastic spinal paralysis.

Highly experienced practitioners working at institutions for the treatment of syphilis agreed and contributed whole series of similar cases; others declared that there was nothing new in the matter, but that it was simply a gummatous myelitis or syphilitic disease of the vessels, or merely the "well-known meningo-myelitis syphilitica." What astonished me most was this latter assertion in the case of patients in whom there was not even a trace of meningitis or root neuritis. Such knowledge can, of course, only ripen gradually, and time alone can yield by degrees the necessary proofs, which in the case of such a disease as this depend a good deal on chance.

I wish to emphasize, gentlemen, that still further clinical observation is needed and a more thorough sifting of individual cases, and a more exact separation of these from others which simulate them or are closely allied to them, just as was needful in the cases of spastic spinal paralysis. At the same time, gentlemen, you must always bear in mind that in syphilis (a disease presenting such an incredible number of different forms) combinations, variations and transitions are especially frequent, and are even to be expected with certainty, it is, therefore, a question of working out with precision and fixing this definite symptom group, it will then be recognized also, occasionally, in complicated cases (of spinal and cerebral syphilis).

This problem seems to me to have been already, in some measure, solved. One must admit that the symptom picture, as I am about to describe it, is subject to variations in intensity and clearness. One cannot expect, at least in syphilitic disease, that this should be always manifested in the same way and to the same degree. Nature does not deal in schemes and diagrams: every separate individual and each case has its own peculiarity, and just as we find that in locomotor ataxia the picture is not always identical and uniform—(you know how extremely variable it is)—so we cannot expect to find this in the case of syphilitic spinal paralysis. It would be essentially pedantic to lay down hard-and-fast rules here; but still I think that the picture as I drew it at the first still holds good completely.

Symptom Picture of the Disease.

Should such a patient enter your consulting-room, gentlemen, you would notice his laboured gait, with tightly-closed stiff legs, his feet sticking to the ground, scraping at each step, often walking with the aid of a stick, a picture of extreme spastic gait. On examination you find weakness, more or less well-marked paresis of the feet and legs, the muscular rigidity often only slight, compared with the change in the gait, but sometimes sufficiently strongly marked. You find, moreover, an enormous increase in the tendon reflexes, patellar clonus, ankle-clonus, and usually the Babinski reflex; on the other hand, usually only slightly marked subjective and objective disturbance of sensation, which may be discovered only on closer examination. There is more or less weakness of the bladder, especially incontinence, but also retention of urine, so that the patient cannot avoid the use of catheter and urinal; there is usually some weakness of the generative organs. In the arms there is usually nothing except slight increase in the tendon reflexes. Head and cerebral nerves, pupils, eye muscles, speech, intellect, etc., unaffected, also the vertebral column.

In a case of such picture, you may already think of syphilitic spinal paralysis; and on questioning the patient, you

also learn that he has some time ago or recently been the subject of specific infection, more or less severe, and that he has been treated more or less thoroughly, that his complaint began slowly and insidiously, usually first in the legs, with gradually increasing weakness and stiffness; that he gets tired sooner; that there is usually no pain whatever, but all kinds of paraesthesiae. In some cases, not infrequently, bladder trouble was the first, and for a long time, the only symptom; in all cases bladder weakness occurs in greater or less degree during the course of the illness. Otherwise the patients have usually nothing of importance to tell. Sometimes they give as an additional cause some injury, cold or excess, or, severe psychical shock.

Occasionally they describe the illness as having come on more rapidly, almost acutely, followed by improvement and subsequent relapse. Even in quite chronic cases a rapid, almost sudden, exacerbation sometimes occurs, leading soon to paraplegia with more marked anaesthesia, decubitus, cystitis, etc.

It is questionable whether these cases should be included here, although such a sequence of events has its analogy also in tabes, in which disease a rapid onset and rapid decline are not uncommonly seen.

Its Pathological Anatomy.

What anatomical condition corresponds to this disease? This was for a long time doubtful, but seems now to have been cleared up to a certain extent.

It has come as a surprise, that in a whole series of typical cases there was not the picture one expected to find, namely, a specific myelitis or arteritis or gummatous infiltration, but rather that of a combined system disease, that is to say, a primary grey degeneration in various fibre systems of the spinal cord, chiefly in the posterior half of the lateral tracts, the pyramidal tracts, the direct cerebellar tracts and tracts of Gowers; then in the posterior tracts, the tracts of Goll, and partly also in the postero-lateral tracts (Burdach's tracts).

This was first clearly demonstrated by Nonne, but there are earlier observations of the same kind and of equal value; let me enumerate them briefly. The oldest is an observation made by Westphal in the year 1880. A man aged 38, suffering, three years after syphilitic infection, from typical symptoms of syphilitic spinal paralysis (erroneously called spastic spinal paralysis by Westphal). Death taking place after four years through cerebral softening. There was found a pure, typical combined system disease (pyramidal tracts and direct cerebellar tracts and, to a less extent, the tracts of Goll) without any other changes in the spinal cord.[14]

Another case is that of Eberle's, which was curiously enough also described as one of spastic spinal paralysis, though it gave the typical picture of syphilitic spinal paralysis.

The disease set in at the age of 46, syphilis eighteen years previously; died after about ten years' duration.

There was found quite a typical combined system disease (pyramidal, direct cerebellar, Goll's and Burdach's tracts most marked in the lateral tracts. Nothing else.[15]

Quite analogous is a case of Nonne's, a man aged 51, who had acquired syphilis at the age of 32—quite characteristic syphilitic spinal paralysis—death after five years from carcinoma. There was found typical combined system disease (pyramidal, direct cerebellar, and Goll's tracts, the latter affected only slightly). Otherwise nothing abnormal in the spinal cord.[16]

Again, a case published in the year 1891 by Williamson, occurrence of syphilitic spinal paralysis, several months after syphilitic infection, with somewhat unusual beginning (and repeated acute attacks of paralysis)—then, however, the usual picture. Death after nine years' duration.

One found well-marked combined system disease in the pyramidal tracts throughout the spinal cord, in the direct cerebellar tracts and Goll's tracts only in the upper dorsal and cervical regions of the cord. Postero-lateral tracts completely free. Nowhere any trace of transverse myelitis or meningitis worth mentioning.[17]

Here we have already four cases of syphilitic spinal paralysis, in which an absolutely typical combined system disease was found *post mortem*.

Associated Secondary Lesions.

To these may be added several other cases in which the anatomical picture of combined system disease was not present alone, but together with more or less well-marked transverse changes in the dorsal cord, so that, especially after some time, it is difficult to determine how much in these cases is primary degeneration and how much secondary.

The clearest case is that of Nonne's. Eight years after syphilitic infection the typical picture of syphilitic spinal paralysis began slowly to develop. Death after two years from pneumonia. *Post mortem*, chronic myelitic degeneration from eighth to the eleventh dorsal segment, but in addition a combined system disease above and below, which was certainly not secondary.

Similar cases have been contributed by von Strümpell,[18] 1880; Dreschfeld,[19] Williamson,[20] and lately another by Long and Wiki,[21] which, however, is open to dispute; it would take us too far afield to describe them more accurately and critically. I will only point out that a multiple (combined) system degeneration in the lateral and posterior tracts is common to all, the secondary or primary nature of which, however, is difficult to determine or define, because there is in addition in the dorsal cord a patchy, more or less incomplete transverse lesion (in Williamson's case a gummatous infiltration in one lateral tract). But I must say that I am strongly of opinion that the main factor is the combined system disease, by the side of which the transverse lesion appears as etiologically a quite permissible complication. This point can, of course, be cleared up only by further investigation.

Neither will I insist upon mentioning here two further cases of typical lateral sclerosis which were referred by the authors to syphilis; they are those above-mentioned cases of spastic spinal paralysis described by Minkowski and Friedmann. They should be regarded as pure disease of the pyramidal tracts and as incomplete combined system disease respectively, but I do not knew whether they can be traced to syphilis with sufficient certainty.

This, of course, applies also to most of the cases above enumerated, for a certain connexion with syphilis is difficult to demonstrate, but that syphilis has gone before, that perhaps it can still be traced in some parts of the body, that no other responsible cause is present, and the frequent clinical occurrence of this combination; these points speak in its favour. There are as yet no extensive statistics as in the case of tabes, and the so-called specific changes (gummatous infiltrations, tumours, inflammations, diseases of vessels, meningitis, etc.), are not infrequently absent *post mortem*, so that for the present it can only be said that the syphilitic origin of the disease is highly probable. Beyond this we cannot at present go.

The fairly numerous cases of other kinds, which conform to our two groups of anatomical conditions without any definite border line intervening—cases in which one finds a more diffuse myelitic change, genuine transverse lesions, softenings, and more marked alterations in the vessels, and which are finally often complicated by more extensive gummatous meningitis (meningo-myelitis syphilitica—these cases certainly run their course with quite different clinical symptoms, but leave in some cases, as a final result, the picture of syphilitic spinal paralysis, but without being identical with the same. They require to be separated from syphilitic spinal paralysis (according to their mode of origin, course, and certain types of the clinical symptom picture), and I hope that this will become easier in time, as more attention is paid to it and points in the diagnosis are more carefully looked for and found.

But as far as I can see, one may already say that the great majority of cases show a definite anatomical condition—though not quite of the kind that I had anticipated—underlying the clinical symptom group which I have described, in its pure uncomplicated form, namely, the picture of a combined system disease of the lateral and posterior tracts, present either quite alone, or accompanied by a somewhat diffuse, patchy, transverse lesion in the dorsal cord. It is almost self-evident that in the case of syphilis this anatomical picture should not always be quite pure, and that there should be transition stages to other spinal diseases of syphilitic origin.

I will not discuss to-day the pathology of the several

symptoms, but hope you will allow me to say that the symptoms of spastic spinal paralysis doubtless result from disease of the lateral tracts, and that the accompanying disturbances of the bladder functions, and of sensation, may be referred to degeneration of the posterior tracts (perhaps also of the grey posterior columns); this might also explain the fact that in some cases there are indications of ataxia, and that the muscular rigidity often appears so strikingly small in comparison.

Differential Diagnosis.

The diagnosis of these forms of disease is not very difficult in most cases, and may be confidently made when the typical clinical picture has developed slowly and gradually; or also perhaps rather more acutely—after the occurrence of injuries, traumata, excesses, over-exertion, etc.—and when syphilis can be proved in the previous history. I have often been able to make a diagnosis when a history of syphilis was at first missing, and to ascertain afterwards the existence of this disease—for example, in the case of female patients by examining the husband.

It is distinguished from simple spastic spinal paralysis by the presence of disturbances of sensation and bladder function, from transverse myelitis by the absence of marked paralytic phenomena with decubitus, cystitis; from meningomyelitis by the absence of meningitic and root symptoms, with their variable intensity and complicating paraplegia.

Actual syphilitic myelitis, spinal gummata—which not uncommonly present themselves in the picture Brown-Séquard's paralysis—softenings and haemorrhages caused by syphilitic disease of vessels; these generally present clinical pictures of a different kind, even though they may be difficult to recognize individually. Other spinal affections, like multiple sclerosis, syringomyelia, amyotrophic lateral sclerosis, anterior chronic poliomyelitis, etc., will hardly ever cause any difficulty in the diagnosis.

Prognosis.

As regards the prognosis, I will only briefly say that it is not altogether unsatisfactory, as, even though recovery only very rarely occurs, and can be expected only in the earliest stages, a standstill and improvement, the power of gaining a livelihood, and considerable duration of life may be expected. Many cases, however, succumb to exacerbation of the disease, paraplegia, marasmus, decubitus, etc.

Treatment.

I must be brief, also, as regards the treatment; energetic and repeated specific treatment with mercury and potassium iodide (or iodipin) is essential. The *traitement mixte* must often be continued for years.

In addition, the usual treatment of spastic spinal paralysis—that is, of chronic grey degeneration of the spinal cord in general—must be practised. I only mention the results of hydropathy, electricity, massage, and gymnastics, of baths rich in CO_2, of arsenic, and silver nitrate, and emphasize that in the treatment of the sequelae of the disease, especially the spastic paralysis of the legs and the obstinate disorders of the bladder, I have found the use of strychnine (repeated subcutaneous injections of 0.002 to 0.01 gr.) of great benefit.

Relation of Syphilis to Spinal Cord Disease.

Gentlemen, in speaking of syphilitic spinal paralysis, I have dealt with a subject in the pathology of the spinal cord which is as important as it is difficult and complex. The effect of this deadly and insiduous disease upon the spinal cord is extremely manifold, many-sided, changeful, and erratic. But till recently one recognized as certainly the result of syphilis only specific inflammatory changes, gummatous products and infiltrations in the spinal cord and meninges, and the specific changes in the blood vessels. It is true one always found besides these apparently simple inflammations, fibrous transformations, cicatricial changes in the connective tissue parts, and simple degenerative atrophy, grey degeneration, and sclerosis in the nerve elements. But their derivation from syphilis was in many cases doubted by their observers. But by degrees we are learning to recognize that tabes, at any rate, with its typical grey degeneration of the posterior tracts, is dependent upon syphilis, is of syphilitic origin; and the knowledge is gaining ground that those apparently non-specific alterations in structure are often due to syphilis, and that other primary degenerations also, systemic or non-systemic, are of the same origin.

A short time ago, in a paper read before the Neurological Congress in Baden-Baden, I sought to prove that those simple atrophic degeneration processes, which have not at all the appearance of being specific, may be referred to syphilis with as much right as the so-called gummatous specific changes are. There is now a widespread belief that they are probably caused in somewhat different ways from gummata, apparently by the action of specific poisons, syphilo-toxins, or the like. In this way the circle of syphilitic affections of the spinal cord is gradually expanding, and I think I have shown you to-day that certain simple and combined system diseases also, particularly of the lateral tracts, can be caused by syphilis just as well as those of the posterior tracts (tabes).

It should be the aim of our investigations for the next few years to settle the matter more definitely, to define more exactly the several forms of disease, and to make more accurate diagnosis possible; further, to inquire especially why it is that syphilis attacks at one time only the posterior tracts, at another only the lateral, and at yet another several tracts and fibre systems at once; why it affects sometimes merely the vessels, the interstitial substance, the meninges, and at other times only the nerve tissues; why in some cases it produces its changes soon after infection, in others not till years or decades later. All those points are still wrapt in obscurity, and the manifold predisposing causes and influences which are doubtless at work are only known to us in very slight degree.

It would be very tempting to elaborate these near-lying thoughts still further; but I fear, gentlemen, I have already trespassed too much upon your time and patience. I must be content with having, as I hope, pointed out to-day a few positive facts from the pathology of the spinal cord, as well as the manifold gaps in our knowledge of this special subject. It is always advantageous to science when such gaps are exposed, new problems pointed out, and new questions raised; they encourage the investigator to renewed effort.

Notes and References.

1 *Berl klin. Woch.*, 1875, No. 26; *Virch. Archiv*, vol. lxx, 1877. 2 *Deut. Arch. f. klin. Med.*, xxxiv, 1884. 3 *Arch. f. Psych. u. Nervenkr.*, t, xvii, 1886. 4 *Arch. de Physiol. Norm et Path.*, 1896, p. 630. 5 *Revista Sperim. de Freniatria*, vol. xxiii, 1897. 6 *Deut. Zeit. f. Nervenh.*, vol. xvi, 1899. 7 *Neurolog. Centralbl.*, 1901, p. 630. 8 *Jahrbuch f. Psych. u. Neurol.*, vol. xxii, Wien, 1902. 9 *Arch. f. Psych. u. Nervenkr.*, vol. xxxiii, 1900. 10 Strictly the case described by Strümpell in 1894 (*Deut. Zeit. f. Nervenh.*, v, p. 225) as a primary isolated system degeneration of both pyramidal tracts, showing only slight transitions to amyotrophic lateral sclerosis, might come under this head. 11 In certain specially rapid cases—Strümpell has described some of this kind—the spastic paresis and extreme contracture attack even the arm, neck, and face muscles; but the onset of muscular atrophy and the rapidly fatal course of these cases should place them among the amyotrophic lateral scleroses. 12 *Neurolog. Centralbl.*, 1892, No. 6. 13 *Deut. Zeit. f. Nervenh.*, vol. iii, 1893. 14 Westphal, *Arch. f. Psych. u. Nervenkr.*, vol. xv, 1881. 15 *Münch. Abhandl.*, i, No. 26, 1896. 16 Westphal, *Arch. f. Psych. u. Nervenkr.*, vol. xxix, 1897. 17 *Syphilitic Dis. of Spinal Cord*, 1899, p. 86. The author proves in detail and with ability that here it is not a question of secondary degeneration, but doubtless of primary combined system disease. I do not, therefore, understand how he can finally express the idea that this combined sclerosis started from a meningo-myelitis. 18 *Arch f. Psych. u. Nervenkr.*, vol. x, 1827. 19 *Brain*, January, 1888. 20 Loc. cit., 1899. 21 *Nouv. Icon. de la Salpêtrière.*

In *Janus* of September 15th, Professor Pagel of Berlin pays a tribute to Virchow as "a historian of medicine *par excellence*." He gives a bibliography of his writings in this particular sphere of literary research which shows the all-embracing activity of the man. It includes papers on the history of medical doctrines concerning tuberculosis, abdominal affections, the occlusion of arteries, leukaemia, thrombosis, parenchymatous inflammation, the mercurial treatment of syphilis, leprosy, lupus, and many other diseases. He also wrote on Goethe as a scientific investigator in relation to Schiller; on hospitals and lazarettos; on Jews and hospitals; on the antiquity of syphilis in Eastern Asia; on the order of Knights Hospitallers of the Holy Ghost in Germany, the Jubilee of the University of Vienna; besides papers and addresses on Eustachius, Morgagni, Langenbeck, Lorenz Oken, Schonlein, Johannes Muller, Carl Mayer, and many others.