A Lecture ON THE NATURE OF TABES.

Delivered at the National Hospital for the Paralysed and Epileptic.

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GENTLEMEN,—To attempt to expound the unknown is a task from which the boldest teacher may reasonably shrink. In the strict sense of the word "unknown," if we take it as equivalent to the unproved, it is true of the pathology of locomotor ataxy. Yet we may surmise that which we cannot demonstrate. Much in medicine that we do not think of doubting is still not strictly proved. Hypothesis may rest on ground that is firm, and yet it may be only the scaffolding for future proof. It is so, I believe, with regard to tabes. If I strive, therefore, to fulfil the promise I made in the last lecture, and attempt to explain the evidence we can discern regarding the nature of the disease, I must ask you to understand that it is only evidence of that which is probable, and not to be regarded as certain truth. It is not, therefore, the less deserving of consideration. To consider and weigh circumstantial evidence in medical problems is a mental exercise of special value to every student, young or old. It is a process on which we are often compelled to rely, not only in general problems, but also in the questions presented by single cases in our daily work.

The subject of the nature of tabes has been more discussed, perhaps, than any other in present-day pathology. The attempts to explain and elucidate its numerous symptoms—some frequent, others rare, all various in character—are almost perplexing. I propose to disregard, for the present, the diverse occasional symptoms, and to see if we can perceive some landmarks sufficiently distinct to be our guides as to the nature of its chief characteristics. There will be nothing new in what I have to say; the facts I wish to emphasize are familiar, but my object is to impress upon you their weight and indication.

I should much like to know, at the outset, what opinion you already hold—or, perhaps I should say, have already learned—regarding the nature of locomotor ataxy. You may ask what I mean by the name. In reply, I would say that two symptoms of the disease may be considered as essential. These are loss of the knee-jerks and inco-ordination of the legs. Leaving aside unusual forms of the disease, these are the common, the invariable symptoms of a case that deserves the name. If inco-ordination is absent, it may be going to be locomotor ataxy, but certainly is not yet. Often there are other symptoms—pains, loss of sensation in the skin, etc.—but they are inconstant. Loss of cutaneous sensation may be trifling or even absent; so may the pains. A patient is now in the hospital who cannot even stand from pure ataxy, who has not, and never has had, the pains that are often so distressing. So we will take as essential the two symptoms just mentioned; I presume, then, that most of you will agree with me if I say that locomotor ataxy is a disease of the spinal cord.

But I should like to know whether you do agree with me. I will ask for your votes on the subject. Will those who are in favour of this opinion hold up their hands? [About half those present raised their hands in the affirmative.] Now those of the contrary opinion. [No hands were held up.] So about half of you hesitate to say "Yes," but also hesitate to say "No." Perhaps your reticence means that you suspect I have laid a trap for you. That is not quite true; and yet you are wise—wise to hesitate to express an opinion. The malady is commonly regarded as one of the spinal cord. Further, there is disease in the cord. You know that one synonym for locomotor ataxy is "posterior sclerosis"; yet it is open to question whether the disease is primarily one of the spinal cord.

What is this posterior sclerosis of the cord? It is degeneration of the tracts adjacent to the posterior median septum, the "columns of Goll," or posterior median columns. It is a secondary, upward, degeneration which occurs above any transverse lesion of the cord. It does not occur below a lesion, therefore the fibres have their vital centre below. But the same degeneration occurs if the posterior nerve roots are destroyed. That is a most significant fact. It shows that the

fibres of these columns come directly from the posterior roots—that is, these are fibres which have their vital centres in the cells of the posterior ganglia. I show you sections of two cords from the dorsal region; they each present complete degeneration of these columns quite identical in aspect. One is from a case in which the spinal cord was crushed by injury just above the lumbar enlargement; the other from a case of tabes. Since the posterior sclerosis is purely secondary—that is, of fibres which proceed from cells outside the cord, in the posterior ganglia—their change does not prove that locomotor ataxy is primarily a disease of the cord. Associated with this sclerosis we have often conspicuous degeneration of the posterior roots. These contain many other fibres, which must end in the cord near their level of entrance to subserve reflex action. Moreover, the fibres of the peripheral sensory nerves have been frequently found degenerated. These likewise depend for their vitality on the cells of the posterior ganglia. The change in them is greatest at the periphery and becomes less as we ascend the nerves towards the ganglia. The power of a fibre to resist morbid influences seems less the greater the distance from the cell on which its vitality depends. In all cases the change is to be a primary degeneration of the nerve elements. The interstitial connective tissue undergoes only slight and secondary changes. This is true also of the degeneration within the cord, but here the secondary interstitial change is more conspicuous, and gives rise to the aspect which leads the alteration to be termed "sclerosis." Thus the essential morbid change in tabes is confined to the elements of the sensory or afferent neurons, the up-bearing neurons, dependent on the posterior ganglia. The motor neurons—the motor cells and fibres—are never altered in pure tabes.

ORIGIN OF ESSENTIAL SYMPTOMS.

Let us now turn to the symptoms of the disease, and especially to those which I have termed "essential"—loss of the knee-jerk and ataxy. To these we may, indeed, add another, less easily recognized—diminution of muscular tone, "hypotonus," as it is termed, "undertone" it might be called. This is important in many ways. In health the muscles maintain a certain degree of tonic contraction in passive movements of the limb. In such movements the attachments of the muscles become nearer together or further apart, but the muscles adapt themselves to the change, preserving a certain gentle contraction. The change follows the passive movement, and therefore there is at first a slight resistance, quite perceptible, independent of the will. It changes *pari passu* with the movement, so as to seem the same in degree. This tone depends on the centres in the spinal cord; it ceases if either the anterior or posterior roots are divided. In tabes it is lessened or lost, so that the absence of the normal slight resistance to passive movement is a feature of the disease, quite distinct when carefully observed. The loss of tone is not the result of impairment of the motor nerves or centres, and it may occur without change in cutaneous sensibility. It can only, therefore, be ascribed to impairment of the afferent muscle nerves—the peripheral sensory nerves of the muscles. Of this we have further proof. Wherever there is marked ataxy, the sensitiveness of the muscles will be found to be lessened or lost. In health you may easily ascertain its existence; if you pinch your own calf, you feel pain distinctly in the muscle; the tabetic feels none. Strong tension in health causes considerable discomfort, but in tabes it is unperceived. Even more striking is the insensitiveness of the muscle to the contraction excited by the faradic current, even when it is such as to cause acute pain under normal conditions. But the sensitiveness of the skin (unless abolished by cocaine) interferes with the attempt to observe this, because it is difficult to be sure whether any pain felt is in the skin or the muscle. A simple expedient enables this to be eliminated. Pinch up the skin over the calf between two small electrodes, and pass between them a faradic current which you have found strong enough to cause cramp-like contraction. Then separate the electrodes, keeping them in contact with the skin, so that they rest on the muscle. This contracts strongly, but the patient feels no more than he did before. He is unconscious of the muscular contraction.

Here, then, we have proof of the impairment of the afferent muscle nerves, and we have seen that to this must be ascribed the loss of tone. Here, also, we have an explanation of the loss of the knee-jerk. The word "tendon reflex" has done much to prevent a clear perception of that which it designates. The tap on the tendon excites a local muscular contraction, but the local excitability of the muscle is due to its tone, aug-

mented by the gentle tension necessary for the mechanical stimulus to act on it. If a tendon is rigidly fixed, so that the tap on it does not act on the muscle, no contraction results. You can easily test this on the Achilles tendon. It is the excitability of the muscle that is reflex, and is dependent on the spinal cord; it is really identical with muscle tone. Its loss is a delicate indication of the impairment of the afferent muscle nerves, shown later by the loss of muscular sensibility.

It is important to note clearly that the muscular tone is a reflex adjustment of the muscles, dependent on afferent impulses which must chiefly come from their nerves. Other sensory impulses from the skin, as Sherrington has shown, play some part in the reflex process, but the features of tabes show that these are subordinate to the influence from the muscles. Tone is essentially a muscle-reflex process. If we need further evidence of its reality, we have only to consider the cases of opposite nature, those in which it is in excess. In these the signs of tone, such as the knee-jerk, become augmented, and the increase passes into the extreme tonicidity which occurs in "spastic paraplegia." In this we have a process and mechanism which have an effect the opposite of the undertone and loss of knee-jerk in tabes.

We cannot doubt that this reflex process must play an important part in the adjustment of muscular contractions, by determining the related state of the muscles which oppose a movement, and, by opposing, support it. The opponents must not only contract in proportionate, though less degree, but they must yield to allow the acting muscles to effect the movement. This spinal reflex process must play a subsidiary but important part in determining the relation of the contractions for the movements arranged in the cerebral centres. We cannot understand how the cerebral and spinal mechanisms work together, but could we view each in its own plane, as it were, that which seems to us complex might be perceived to be simple. However that may be, we cannot doubt the reality of the spinal mechanism, nor can we doubt that it depends chiefly on the afferent muscle nerves. It must be disordered in tabes, in which these nerves are so conspicuously impaired. Even when the impulses produced in them are merely delayed, as we so often find to be the case with the nerves of the skin, we can easily conceive the effect of such delay in causing disorder. Each impulse would arrive just too late to excite the due contraction, and just in time to disturb the action which its absence induced. In the derangement of the spinal mechanism I think we may perceive one cause of the ataxy of tabes and, perhaps, that which determines its peculiar character.

Another element in the inco-ordination of tabes is probably indicated by the degeneration of the posterior median columns, the columns of Goll, in the spinal cord. We have seen that this is a degeneration of upward fibres from the nerve roots, fibres which belong to the neurons of the posterior ganglia, of which the lower fibres are those of the peripheral nerves. The affection of these columns entails no loss of cutaneous sensibility. Many facts suggest that they belong to the muscle neurons, and conduct impulses from the muscles which pass up to the medulla, and thence, probably, to the cerebellum. There it is probable that they are co-ordinated with others, to guide the motor cortex of the brain. If these columns are damaged in the dorsal region of the cord, the result is unsteadiness, resembling that which results from disease of the cerebellum itself. Hence their degeneration in tabes may be conceived to cause a defect in the cerebellar guidance of the brain, and to add this to the failure of the spinal mechanism in co-ordination.

We can thus conceive that the ataxy of tabes and the loss of the knee-jerk—the symptoms I have termed essential—may be entirely due to the degeneration of the sensory muscle neurons, to the effect of the loss of their impulses on the spinal and cerebral processes. With these may be associated defect of the afferent impulses from the joints and tendons, but they are of less importance. As we have seen, the inco-ordination is independent of failure of cutaneous sensibility, but a defect or delay in this is very common and must be due to coincident impairment of other sensory neurons.

Since the essential changes in tabes are in the neurons, which have their vital centres in the cells of the posterior ganglia, it is natural to look for visible changes in the microscopic texture of these cells. But they have been found apparently normal in many cases in which they have been examined, even with all the aids which chemistry gives to microscopic scrutiny. Yet in some cases conspicuous changes have been found, and the value of the negative results is

lessened by two considerations. First, molecular change must attain a relatively vast degree to be visible. Changes far below visibility may cause grave impairment of function, especially of one so high as that which determines the vital resistance of the cell-processes to morbid influences. Even more important is the second consideration. We must consider each neuron as a vital unit, the cell and the fibres which extend from it and depend on it for their life. Although the nuclei on the fibre may reinforce the vital influence they cannot replace it. The greater the distance from the cell, the less the vital power of the fibre seems to be, the less is its ability to resist morbid agents. This is the lesson taught by all the facts of peripheral neuritis. All causes of degeneration produce changes which are greatest at the distal parts and lessen as we approach the centre. The neuron unit may suffer in its farthest parts long before the centre undergoes conspicuous changes. This fact should make us hesitate before allowing the frequent normal aspect of the cells of the posterior ganglia to weigh against the evidence that the failure of vitality in these neurons is the cause of the essential symptoms of tabes.

We should note, also, that other frequent symptoms of tabes are of the same class. The defect of cutaneous sensibility, especially to pain, must be referred to the degeneration of other afferent neurons, and we have already seen¹ that the pains may be ascribed to the same cause. The tabetic atrophy of the optic nerves is clearly an affection of the same class—the degeneration of a special sensory neuron. But the morbid influence which causes tabes, whatever it is, may penetrate more deeply into the nervous system and pass beyond the sensory neurons, on which its influence acts first and chiefly. It may even involve the motor centres, as those of the eyeball muscles, and even those of the limbs, in the spinal cord. Other symptoms occur, of which we do not know the precise mechanism—the visceral symptoms and the various crises. But these should not obscure the clear perception of the fact that the cause of the disease acts chiefly on the sensory neurons, and that thus its essential symptoms are produced.

PATHOLOGICAL ANALOGIES.

So we come to the second part of the problem: What is the cause of this degeneration? Note one special feature it presents. It is a selective degeneration; it involves structures that subserve a certain function; those adjacent of different function are spared. The affection of the posterior median columns illustrates this. Not less selective is the frequent affection of the sense of pain without that of touch, when cutaneous sensibility is impaired. We only know such an acquired affection, bilateral, involving nerves of the same function on the two sides, as the result of a toxic agent circulating in the blood, passing everywhere to the nutritive plasma but acting only on structures susceptible to it. What known causes can we discern which produce similar effects, especially effects which are like those of tabes? The symptoms which I have termed essential—ataxy and loss of the knee-jerk—are sometimes conspicuous effects of certain toxic agents, especially of two, arsenic and alcohol. Their common action is on the motor nerves, causing definite paralysis of the extremities, but each sometimes spares the motor nerves and causes impairment of sensibility instead of power, and occasionally the chief symptom is inco-ordination. From alcohol the resulting condition may resemble so closely that of locomotor ataxy, the knee-jerks being also lost, that it has been called "alcoholic pseudo-tabes." Indeed, so perfect is the similitude that it may be difficult to say whether a patient is suffering from this affection, from which recovery is sure, or from true tabes, with its dubious future. We may presume that the reason for this peculiar effect of the toxic influence is that some cause determines a special action on the afferent muscle nerves. These always suffer in some degree, as the distressing muscular tenderness clearly shows. But in this pseudo-tabetic form they suffer chiefly. Why, we do not know, but we may conjecture that some special alteration in the nutritive plasma fits it for the sensory rather than for the motor nerve elements, and nutrition and function is most deranged in the structures for which it is most adapted. These nutritive processes afford evidence of differences which we are otherwise quite unable to discern.

So it is with arsenic. The common effect of the slow prolonged ingestion of this poison is motor palsy, like that of alcohol, but often with more spontaneous pain. Sometimes, however, motion is unimpaired and simple ataxy results, always attended with loss of the knee-jerk. The latter may

be due to a slight influence on the motor nerves, and therefore cannot be ascribed to the impairment of the afferent muscle nerves as it can in tabes, although we may reasonably regard this as the cause of the loss of co-ordination. How close may be the resemblance of such a case to true tabes is shown by one I have published, in which the pains, ataxy, and absent knee-jerks deceived me, until I saw the demonstrative pigmentation of the skin. Why the same agent should vary so much in its special incidence we do not know, any more than we understand the varying effect of alcohol. We may conjecture that it is due to the precise combination in which it is presented to the tissues, and also to its relative amount. The fact deserves thoughtful consideration, because it presents a close analogy to the variation of the symptoms of tabes, and because it illustrates how wide may be the difference in the result of a toxic agent—a difference that depends on conditions of chemical combination so minute as to transcend perception.

Thus toxic agents, derived from without, such as arsenic and alcohol, may derange nerves of special function and give rise to symptoms precisely like those of tabes. A similar effect is produced by poisons generated within the body. The animal frame is one vast chemical laboratory, in which processes of extreme complexity, as they seem to us, are ever proceeding, and compounds are formed and decomposed, storing or releasing energy under the influence of life. A trifling difference in a process may change that which should renew the supply of ordered energy into that which deranges it—may change that which should build up into that which destroys. This occurs in the course of the chemical disorder which constitutes diabetes—a purely endogenous malady. Toxic agents may be formed that affect the peripheral nerves, which may abolish the knee-jerks, and cause degeneration of the same fibres in the spinal cord which fail so conspicuously in tabes. I show you a section of the spinal cord from a case of diabetes with such sclerosis of the posterior median column.

The most conspicuous effects of this nature are due to the organisms of specific diseases. These generate "toxins," in part directly, in part indirectly. The organisms produce poisons, and also substances which are not poisonous but which derange the formation of albuminous substances, and convert them into nerve poisons. That has been clearly discerned and surely proved by Martin in the case of diphtheria. The agents, to which this disease gives rise, have a varied effect, chiefly on the motor structures, often also on the sensory. Sometimes this influence on the sensory nerves is strangely special. I have seen anaesthesia limited to the palms and soles, as the chief sign of diphtherial palsy. In rare cases symptoms are caused which closely correspond to those of tabes. There is the same ataxy, without motor palsy, and also loss of the knee-jerks. The latter, indeed, occurs in all forms of this nerve poisoning, and often, indeed, in diphtheria when there is no consecutive palsy. It may be due to slight interference with the motor structures, but the ataxy is evidence of a special effect on the afferent muscle nerves, and brings this occasional result of the post-diphtherial toxine into close correspondence with ordinary tabes.

RELATION TO SYPHILIS.

The bearing of this on the pathological origin of tabes must be sufficiently obvious to you. I may safely assume that you are all familiar with the frequency with which tabes is found to be preceded by one specific disease, which stands almost alone in mystery and malignancy—syphilis. I may also assume that you know that tabes, though the apparent sequel of syphilis, is attended by no morbid process such as characterizes the ordinary effects of the disease. You are familiar with the peculiar tissue-formation of true specific lesions, but that which is found in tabes is a pure nerve degeneration. Hence we assume that some toxine, analogous to the nerve poison from diphtheria, is generated by the organisms of syphilis, and causes the symptoms of tabes. Thus conceived, the malady is an indirect, not a direct, consequence of the primary affection. This conclusion is confirmed by the fact that the treatment which so speedily removes the lesions of true constitutional syphilis has little or no influence on tabes. Yet this explanation of the disease is confronted by many difficulties, which must be fairly faced. The evidence is purely that of sequence. The facts are very strong, but not at first sight absolute. They must be clearly discerned, because the sequence is still the subject of controversy, although not I think in this country.

That tabes is a sequel of syphilis was first urged by Fournier

nearly thirty years ago. The evidence he adduced was soon confirmed by Erb, myself, and others. The discussion which followed Fournier's statement illustrated a fact which is instructive. Observations regarding any special point, to be of value, must be made with special reference to that point. Physicians looked up their old notes of cases of tabes and found therein little to support Fournier's assertion. But they began to make special observations; to their surprise the facts obtained were quite different, and such as to give it strong support. The most notable of those thus converted from doubt to confidence was Erb himself, who has supplied us with the strongest evidence in combined character and extent hitherto adduced.

We cannot expect to obtain proof of invariable sequence. If tabes never occurs without preceding syphilis, we cannot obtain the constant evidence. To this point I will return in a moment. Let us consider the acts Erb has obtained with special personal care. He has investigated the facts of 1,100 cases of tabes and finds a history of a primary sore in 89½ per cent. In most of the cases there had been constitutional symptoms, but these are so often absent or forgotten, even with characteristic late symptoms, that their absence has little weight. Erb's statistics are stronger than those obtained by most others, with the exception of Fournier, Déjérine, and other French observers. The facts furnished by my own personal observation are also not so strong as those of Erb; those of several hundred cases agree nearly with the last hundred consecutive cases of tabes in males seen in private; they were carefully investigated, and the percentage they afford is convenient, because it happens to avoid the fractions which come out in a larger number. Of the 100 cases, 80 gave a history of a chancre; 15 denied a sore, but had suffered from gonorrhoea, some of them more than once. Of the remaining 5, every one admitted having run risks of infection in the ordinary way. Hospital cases are far less trustworthy. We find here a history of a sore in about 77 per cent. In the lower classes the facts are often forgotten, and much depends on the observer who takes the history of the patient. A very significant illustration of this is afforded by the notes at this hospital of one series of twelve consecutive cases of tabes. A history of a chancre was recorded in only four. All these notes were taken by the same clerk, who was a foreigner.

You may deem 80 per cent. too small a proportion on which to affirm a constant sequence. But you must remember that the frequency with which characteristic symptoms of constitutional syphilis are met with in patients who give only a history of gonorrhoea is such as to lead some authorities to suspect that the specific virus may be communicated with that of the urethritis, without even an intra-urethral chancre as suspected by many. I mention this as an illustration of the frequent absence of a history of the primary affection. It is most important to know how often such a history is absent in cases of undoubted late syphilitic affections. Few facts are to be found in literature which we may compare with those of tabes. Fournier has stated that a history of the primary disease is absent in 50 per cent. of undoubted constitutional disease in women, but these are useless for comparison, on account of the notorious frequency with which the original affection in them is unknown. I am therefore greatly obliged to Dr. Pernet, of University College Hospital, for some instructive facts he has collected for me from his notebooks. Putting aside all cases in which the record is imperfect, his notes include 58 cases of undoubted late syphilitic skin diseases, and of these 13 denied all knowledge of any primary sore; there was a history of it in 45, or 77.5 per cent. Of 66 cases of early specific skin eruptions, a sore was denied in 11; it could be ascertained in 55, or 83 per cent. Taking the two classes together (124 cases), the primary disease was known in only 100, or 80 per cent., exactly the proportion that I have found in tabes. Since all Dr. Pernet's cases were males, they are accurately comparable, and it is noteworthy that in the cases of late eruptions, the time of which renders them most analogous, the percentage of early history was actually less than in tabes. It follows from these facts that if it is true that tabes only occurs in those who have had syphilis, we should have a history of the primary affection only in the proportion that we actually find. I think, moreover, that another fact is of weight. If we except members of our own profession, I have never seen a case of true tabes in a man who had never run risks of infection in the ordinary way. There is no other disease of the nervous system of which the same assertion can be made. We may, therefore, regard as justified the

assertion of Möbius that, whatever the precise relation between the two preceding, syphilis must be regarded as a *conditio sine qua non* of the occurrence of tabes. Even if the sequence is not actually invariable, it may be as important as if it were. If exceptions should be sometimes met with, they will be too rare to invalidate the general facts.

Why then, you may ask, if the sequence is so clear, is it disputed? If the evidence against it is carefully scrutinized it is found to consist of collections of cases, vitiated by the inclusion of females as well as males, in which every immediate antecedent of the symptoms is regarded as the sole cause, sufficient to make any other antecedent negligible. No attempt is made to examine this question of sequence, irrespective of other points, or to eliminate the sources of fallacy. The impression the evidence gives is that it may wisely be put on one side. The question is one of those in which we may feel sure that the truth must prevail without the help of controversy.

Another noteworthy element in the proof of the dependence of tabes on syphilis is important because it comes from another realm of life, and yet has the same clear significance. Few of you may have seen a case of "juvenile tabes," for such cases are rare. But the malady may develop during late childhood, usually between 6 and 12, with unmistakable features, and sometimes with optic nerve atrophy. In all such cases there is, or has been, evidence of inherited syphilis. Here we have no conflicting statistics; it is a simple fact, of unmistakable meaning. It is stronger than another striking illustration, of which examples are not extremely rare—tabes in both husband and wife, the husband having had syphilis before his marriage. I have seen several examples of such marital tabes, which is an emphatic illustration, rather than confirmation, of the causal sequence.

If we recognize that tabes is a sequel of syphilis, we are confronted with a problem which we must discuss though we cannot solve. We have seen that all we know of like processes and their origin compels us to regard the immediate cause of tabes as a toxin. The antecedent—syphilis—we regard as an organismal disease. Although we are ever given glimpses of supposed discoveries, the organisms are not yet surely demonstrated. We must certainly regard the disease as one capable of giving rise to a toxine and tabes as such a disease as a toxine might cause. But all other known toxines of specific disease are produced during the active stage of the malady, and their influence is exerted speedily, endures for a time, and then ceases. This sequel occurs, as a rule, years after the last manifestation of active syphilis. It develops and varies without relation to any condition to which it can be referred. Tabes behaves as if it were an absolutely random malady—unconditioned, irresponsible. Its course is so erratic that a forecast cannot be made with certainty in any individual case. Its first symptoms may remain for ever trifling, or may remain stationary for years, and then steadily increase, or they may develop from the first, and steadily reach a high degree, or a stationary period may undergo an increase so rapid as to attain, in a few days, a degree usually only reached after many months. The onset or increase of the disease bears no relation to any evidence of activity of the preceding syphilis. Although years have commonly elapsed since the last constitutional symptom, occasionally tabes develops before the constitutional malady has ceased. Then the degenerative change is found co-existing with true specific lesions. Moreover, no treatment of the primary disease, however thorough, certainly prevents the occurrence of tabes. Even that it has any influence cannot be surely affirmed. This is the less surprising, however, if the initial induration, which determines the treatment, is a sign that constitutional infection has already occurred.

PATHOGENIC CO-OPERATION.

The relation in time and course of the assumed cause and effect are so different from any known examples of the same kind, and explanation is so difficult, as almost to make us pause and look back again at our facts. Yet we can discern no escape from the sequence, no escape from the evidence that the immediate agent must be a nerve poison, in some way the result of the antecedent. We cannot explain the mystery by conceiving that an early toxine simply lessens the vital endurance of the nerve elements; the facts of rapid development or rapid increase, even after years, compel the conviction that the morbid agent is present at the time. Equally incompatible with the theory of lessened vital endurance is the remarkable degree of recovery sometimes

met with, even in characteristic cases. Hence it has been suggested that some other agent, of unknown nature, co-operates with that which syphilis produces, and Neisser has expressed this view by saying that tabes is the result of a syphilitic toxine plus x , x being the unknown intensifying influence.

On the whole, some form of this hypothesis seems to afford the best explanation of the facts. In connexion with the long interval before tabes begins, remember the manner in which the nerve poisons of diphtheria are produced. One is produced directly by the organisms in the throat; the other has a different origin; the organisms generate also a ferment-like body which acts on the albuminoses in process of formation in the spleen and elsewhere. It acts so as to modify some of them and to convert them into a poison instead of a food. A slight modification of the relative amount of the elements of an organic body and of the way they are arranged may totally change the influence of the resulting substance. If any of you have read a small volume of lectures of mine you may remember that I showed at one, two test tubes, each containing about a teaspoonful of a white powder, each powder consisting of the same chemical elements. One was quinine, almost harmless; the other was aconitia, and even that small quantity had the potentiality of death to a thousand men.

Although the action of the ferment-like product of diphtheria is transient, we have reason to think that similar influences may be enduring, that a process thus set wrong in the complex laboratory of the body may never get right again. Consider the remarkable fact of immunity, of the lifelong protection afforded by one attack of an acute specific disease such as scarlet fever. Our present knowledge enables us to explain it only in one way—by some permanent change in certain chemical processes of the body, trifling in degree, but potent in its influence in facilitating resistance to any new infection of the same kind. The transient disease must induce a lasting modification of some process in the vital laboratory. Only thus can we explain the enduring immunity which one attack produces. If it be so, we can conceive that syphilis, although it is doubtful what immunity follows an attack, may yet cause a change in chemical processes which results, after years, in the generation of a nerve poison. We can conceive that such an effect as that caused by the ferment-like product of diphtheria, may be an enduring change, minute perhaps at first, but slowly increasing. The perversion of a process may become greater by constant action. Surely Shakespeare had this self-augmentation in his mind when he said of jealousy, that "it grows by what it feeds on." All growing things do that. I think he meant "it grows by going on"; increased strength results from mere activity. So a toxine, indirectly caused, may become sufficient to produce effects only after years. It is not so with that of diphtheria; but I mention this only to aid you in conceiving that which, in some way, must be. Moreover, just as there is no relation between the severity of an attack of diphtheria and subsequent paralysis, so there is no relation between the degree of constitutional syphilis and the occurrence of tabes. Indeed we may go further, and say that, just as the amelioration of diphtheria by antitoxin has little influence on the occurrence of paralysis, so tabes follows syphilis independently of its early treatment.

Yet we cannot thus perceive an explanation of all the facts of the course of the disease. Especially the very rapid increase in the symptoms we sometimes meet with, after early symptoms have been slight and stationary for a time, seems to imply the co-operation of some other morbid influence. Susceptibility, increased by lowered general vitality, or by local over-exertion (as Edinger has urged), may facilitate the action of the morbid influence, but often cannot be traced. We are compelled to conceive that the toxic action of the cause is itself augmented, that some other abnormal process intensifies the influence of the toxine.

We may note the course of tabes, in different cases, as giving apparent support to the hypothesis. In some cases the symptoms begin almost imperceptibly, slowly increase by a steady progress, until at last a high degree is reached and maintained. Such cases suggest that, as I have said, a slight perversion of chemical processes slowly grows and increases perhaps without extraneous aid. But the cases in which a long slight degree of symptoms is followed by a rapid, sometimes very rapid, increase to a high degree—cases which suggest the co-operation of some augmenting influence—sometimes run a course which is, I think, very significant. In several cases I have seen, in which there was such a rapid development of symptoms, improvement, almost

amounting to recovery, has slowly—very slowly—occurred. I refer to cases in which a patient had quickly become almost, or quite, unable to stand from pure ataxy, and a stationary period was followed by improvement, steady but slow, until it may be only at the end of a year or two the patient was able to walk steadily, unaided, for miles. In such cases the cause of the rapid development of the disease must have been transient. It could not have persisted, or improvement would have been impossible. Such cases strongly support the hypothesis of a temporary agent augmenting the intensity of the nerve poison, but ceasing and permitting the slow regeneration of the affected nerve elements. It is remarkable that acute arsenical poisoning, which causes immediately severe gastro-intestinal symptoms, does not affect the nerves, and cause paralysis or ataxy, until after an interval of two or three weeks, and slow improvement only begins after some months. It may be that the arsenic has to form some compound with albuminous material in order to be slowly taken up by the nerves in metabolism and slowly derange their function and structure.

The neurotoxic effect of the exciting cause of tabes may depend on more than one agent co-operating with that which follows syphilis. What these may be we must strive to learn. The chief value of hypothesis is to direct our observations. Even when hypotheses prove erroneous, their disproof always involves additions to our knowledge. But for sure proof of the primary cause, the light in dark places it may afford, and the therapeutic help it may yield, we have to wait for the certain identification of the organism of syphilis. When this is surely known, the nature of its toxins may be discovered and antitoxins obtained by which its effects may be prevented. Ever and anon our hopes are raised, but we still await the certain demonstration. We watch and wait with well-grounded hope, with patience that is compulsory, and not without some wonder that we have to wait so long.

The investigation by Metchnikoff and Roux on the spirilla of Schaudinn, announced since this lecture was delivered, are of definite promise.²

REFERENCES.

- ¹ The Pains of Tabes, BRITISH MEDICAL JOURNAL, January 7th, 1905.
² Ibid., May 27th, 1905, p. 1178.

A Clinical Lecture ON A CASE OF SYRINGOMYELIA.

Delivered at the Liverpool Royal Infirmary,

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GENTLEMEN,—The case we are to consider to-day is an instance of one of the rarer forms of disease of the central nervous system, but a disease which presents symptoms so characteristic that its recognition presents little difficulty to any one who is aware of the possibility of its existence. It is worthy of notice that most of the rarer diseases present striking characteristic symptoms, which make their recognition easy, at least, in well-marked cases. Thus, in Addison's disease there is the obvious pigmentation, in myxoedema the no less obvious swelling of the body, in acromegaly the overgrowth of the bones, in myelopathic albumosuria the unique character of the urine. No doubt it is the association with these noticeable syndromes that has led to each of these diseases being recognized as a distinct and definite pathological state; and we cannot doubt that there are still not a few morbid states which escape distinctive recognition because their symptoms closely resemble those of diseases of common occurrence.

The present case clearly presents the characters of the condition known as syringomyelia, though it is exceptional in departing in some of its features from the commonly-accepted type of the disease. Here I think it will be best for me to put before you briefly what is known of the morbid anatomy and pathology of this interesting affection. Cavities of various kinds are met with in the spinal cord as in other parts of the central nervous system. Thus a hæmorrhage, instead of becoming absorbed, may remain as a cyst or hæmatoma, and

there may be a dilatation of the central canal of the cord as there may be of the ventricles of the brain, constituting a hydromyelia. The nature of the cavities in syringomyelia is not thoroughly determined, but the trend of opinion is towards the view that they originate in a gliomatosis, or overgrowth of the neuroglia, which undergoes liquefaction in its central parts, so as to form one or more cavities with smooth walls, and containing a clear or turbid fluid. The cavities are formed in the grey matter in the neighbourhood of the central canal, with which they sometimes communicate, and they spread in various directions in the deeper parts of the cord, which may, in extreme cases, be converted throughout part of its length into an elongated cyst, so much of the nervous tissue as survives being crushed together in its walls. The change generally begins and is most advanced in the cervical region, but in exceptional cases, of which the present appears to be one, the brunt of the disease falls upon the lumbar enlargement.

The essential facts in the case of the patient I now show you are as follows:

J. B., a labourer, 54 years of age, began to suffer fifteen years ago from trouble about the feet which made walking difficult. Attacks of this kind recurred from time to time until they became continuous. The toes became strongly and permanently flexed and otherwise deformed, and six years ago some of the smaller ones on the right foot were amputated by a surgeon, but without any material benefit to the patient.

At the present time his condition is as follows: The general appearance is that of health, and the thoracic and abdominal organs are sound. The limbs, however, present several important departures from the normal.

Motor.—There is complete paralysis, with wasting, of the anterior tibial muscles, resulting foot-drop and flexion of the toes. A characteristic difficulty in walking results, the feet being raised too high and kept wide apart to enable the toes to clear the ground. The defect in walking is increased by the existence of extreme flexion at the first interphalangeal joint of the smaller toes, apparently due to shortening of the flexors. In the hands there is no obvious paralysis, but there is a similar deformity of the fingers due apparently to shortening of the flexor profundus digitorum.

Reflex.—There is complete absence of the patellar and plantar reflexes.

Trophic.—As already stated, certain muscles are wasted. There is also marked change in the nutrition of the skin. When first admitted to hospital there were numerous small ulcers, apparently painless, on the lower part of the legs and the feet and a purpuric eruption on the feet. These have healed to a considerable extent, but can still be recognized. A corn on one of the toes has ulcerated since he has been in bed in hospital.

Sensory.—Here the most characteristic changes are observed. In the region corresponding to the fourth and fifth lumbar and first sacral segments, that is, approximately, the whole of the legs below the knees, the sense of pain is almost gone. The prick of a pin causes little or no pain; but the slightest touch is felt and correctly located. Throughout the same region the ability to distinguish heat and cold is quite lost, a test tube containing iced water touching the skin cannot be distinguished from one containing warm water. In the hands the only alteration of sensibility is some confusion of hot and cold sensations in the right middle and ring fingers.

The sphincters are normal.

The paralytic and other symptoms are somewhat more marked on the left than on the right side.

It will be noticed that the clinical picture, while pointing to some profound change in the nervous system, does not conform to that of any of the commoner affections. It bears some resemblance to multiple neuritis and to locomotor ataxy, but differs from both in certain essential points. In neuritis the progress would be more rapid and the disease would not last so long, there would be tenderness of the nerve trunks and muscles, and above all there would be no dissociated anaesthesia. Anaesthesia there might be, but all forms of sensibility would be pretty equally affected.

From locomotor ataxy the case is distinguished sharply by the presence of paralysis and wasting of muscles, a distinction which is confirmed by the absence of inco-ordination, of pain, of visceral symptoms, and of tachycardia. In this connexion I should like to draw attention to what I consider the extreme importance of permanent acceleration of the pulse in the diagnosis of early cases of locomotor ataxy. I have at present five cases of locomotor ataxy, in various stages of development, in my wards, and in all of them the pulse is persistently accelerated, being generally about 100 per minute, sometimes considerably higher. In the present case the pulse is usually between 60 and 70.

We will now consider the grounds on which is based the opinion that the case is one of syringomyelia.

Authorities are agreed that the characteristic indication of syringomyelia is the presence of a complexus