ON PERIPHERAL NEURITIS.¹

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THE subject which I have the honour of introducing for discussion to-day, namely, peripheral neuritis, has only engaged the attention of our profession in recent years. The symptoms produced by the disease have long been known, and Graves even suggested, in a very pointed manner, that they had their origin in disease of the peripheral nerves; but it was only in 1864 that definite proof was given by Duménil that such a pathological condition was the cause of the symptoms in the disease now named peripheral neuritis.

As might be expected when a new field like this was opened up, a very large number of conditions, previously not understood, were attributed to this cause; and it can scarcely be doubted that the list of diseases at present referred to inflammation of the peripheral nerves will have to be curtailed. The subject, indeed, is still in its infancy, and many conditions which are supposed to be due to peripheral neuritis have not yet been proved to be so. Any member of this Association, therefore, who can afford fresh proofs of the existence of neuritis in disease will make a welcome addition to our pathological knowledge. It would be well to consider, too, whether we have not been trying to draw too sharp a line between the peripheral and the central nervous system; whether we have not been too anxious to limit the pathology of many of these diseases to the nerves, while the various agents which produce them cause alteration in the centres as well. Such poisons as alcohol and lead, the poisons of acute specific diseases such as influenza, and a good many others, too, are certainly productive of widespread central changes at the same time that they specially affect the peripheral parts of the nervous system.

One of the most important points for discussion is, in my opinion, the legitimate use of the term "peripheral neuritis." What anatomical changes do we consider as proof of inflammation? Are we justified in speaking of a change in nerves as inflammatory in the absence of those vascular phenomena which are usually looked upon as a proof of inflammation? In reading the reports of cases of peripheral neuritis it will constantly be noticed that the pathological condition found *post mortem* was segmentation and breaking up of the medullary sheath, and nothing more. This is called "parenchymatous neuritis." In other cases nothing at all is found to prove what the nature of the case was; but it is argued from the presence of some of the symptoms that occur in undoubted neuritis that the disease is neuritis. Would it be more correct to speak of peripheral nerve intoxication, where the *post-mortem* find is negative, as in rapidly fatal cases of Landry's disease, for example; of peripheral nerve degeneration where the only change is breaking up of the white sheath of Schwann; and of peripheral neuritis when the vascular phenomena of inflammation are present as well? The granular degeneration of muscles, whether fatty or albuminous, and of many cells in the body, such as those of the liver, is not the result of inflammation only. Why, then, should breaking up of the medullary sheath into droplets be called neuritis? It may or may not be true (and this is a question with regard to which we might hope to elicit some fresh information) that we cannot separate clinically the cases where the medullary sheath is broken up from those in which an inflammation of the fibrous sheath of the nerve is evident as well. Still, it may be possible to do so some day. If this distinction between nerve degeneration and nerve inflammation were made, many cases now termed neuritis would receive a more reasonable explanation as cases of degeneration. Such cases, for instance, as are now sometimes classed as "dyscrasic peripheral neuritis," being found in cases of anæmia, cancer, senile conditions, etc.

While we are considering the propriety of separating cases of nerve degeneration from cases of nerve inflammation, a very important question suggests itself. Have the changes

which the peripheral nerves undergo after death been carefully investigated? Are they not principally changes in the medullary sheath, and changes resembling those attributed now to parenchymatous neuritis? One reads of cases where parenchymatous neuritis has been observed *post mortem*, though there was no clinical evidence of disease of nerves during life. In such cases the suspicion naturally arises in the reader's mind that *post-mortem* changes may have been mistaken for pathological conditions. Any pathologists who can contribute definite information as to the changes which occur after death in the peripheral nerves, and particularly as to the rapidity with which they occur, will have made a very important contribution to this discussion.

It is a somewhat remarkable thing that in multiple neuritis the terminal portions of the nerves are nearly always first affected. Why is this? May it be partly that they are so delicate in structure, partly because in their peripheral ramifications they cover a much larger area than they do when collected into bundles and so are more exposed to the poison circulating in the capillaries; partly, perhaps, because they are farthest removed from the nerve cells, on the energy radiating from which their health certainly depends?

Another very interesting point is the special affinity which certain poisons seem to have for certain nerves. It is true that in cases of intense or prolonged poisoning the effects on the nervous system may be very widespread. Yet it is none the less true that in alcoholic neuritis the extensor muscles of the limbs, and especially of the legs, almost invariably first fall a prey to the poison; in lead, the extensors of the fingers and wrists; in diphtheria, the muscles of the throat and internal muscles of the eye.

Still more remarkable is it that the selective power of these toxic agents may exert itself on the motor filaments or on the sensory almost exclusively. In lead poisoning, for instance, sensory alterations are hardly complained of at all, and the same is often true of diphtheria; whereas, in cases of alcoholic neuritis, a stage of the most acute sensory disturbance may long precede the advent of paralysis. Indeed, there is some ground for supposing that even the trophic and vasomotor nerves may be specially picked out in some cases. The pathology of Raynaud's disease is not yet satisfactorily established; but there are certainly grounds for supposing that the remarkable vascular and trophic changes which characterise this affection are the result of disease specially affecting the vascular and trophic nerve filaments or the centres from which they radiate. Can anyone throw light upon the meaning of these interesting phenomena?

The electrical reactions of nerves and muscle are frequently altered in the diseases under consideration, but it cannot be said that we yet know as much as we might about the value of the so-called reaction of degeneration. The alterations which occur are very variable, sometimes being but slight, sometimes profound. In the latter case they indicate, no doubt, a very marked disorganisation of nerve and muscle. But what do the slighter changes indicate, or even their absence, as regards the pathological changes in the nerves? Can they be utilised for the purpose of distinguishing between nerve intoxication, nerve degeneration, and nerve inflammation?

The discovery of neuritis as a definite pathological condition has led to our removal of many paralytic affections from the category of spinal cord diseases. We now place these under the heading "peripheral neuritis." For the diagnosis of these affections we have relied largely on the simultaneous involvement of motor and sensory functions as proving that a disease which produces such symptoms cannot be due to an affection of the anterior cornua of the cord only. But now that it has been shown that these atrophic paralyses can result from disease of the peripheral nerves, when the motor filaments are specially picked out, the question must be asked, Have we any means at present at our disposal enabling us to distinguish between anterior cornual disease and peripheral nerve disease?

Again, cases of paraplegia due to an extensive affection of the spinal cord, in which nevertheless there is no alteration in sensation, are not uncommon; and similar affections of the spinal cord and its surroundings may result in paraplegia

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with pain and sensory disturbances. How can we distinguish such diseases of the spinal cord from peripheral neuritis? We have generally relied upon the presence of an affection of the sphincters in the former and its absence in the latter. This, however, is not a safe criterion. I have myself lately had a case of painful paraplegia under my care in which the sphincters were involved, and in which nothing was discovered at the *post-mortem* examination. On microscopic investigation of the nerves proceeding from the pelvis an intense neuritis was found. We have, therefore, to consider how we can advance the diagnosis of these conditions in order to put it on a level with our present knowledge of the pathological changes which lie at the root of them.

Another question which needs discussion is that of the cause of the peripheral neuritis and muscular atrophy which occur in association with joint disease. This has not yet received a satisfactory explanation. Is it due to some reflex effect on the cells in the nerve centres which preside over the nutrition of these muscles? or is it a secondary local effect of the inflammation of joint? or do both the neuro-muscular and joint changes own a common cause?

The significance of the absence of the knee-jerk which occurs in many cases of diabetes, together with the occasional presence of other symptoms suggestive of alteration in the peripheral nerves, is worthy of further consideration. Are these phenomena due to nerve intoxication produced by some poison manufactured in the body by disease? Are they the result of a simple degeneration of nerves and breaking up of the medullary sheath, or do they owe their origin to genuine peripheral neuritis?

Again, can anyone produce further evidence of the cause of Raynaud's disease? The fact that tetany has also been attributed by some to peripheral neuritis suggests another question. Does peripheral neuritis give rise to spasmodic affections? As a rule, it certainly does not; but the cramps, muscular twitchings, tremors, etc., of the earlier stages of alcoholic neuritis suggest that spasm may possibly sometimes result from peripheral changes in the nerves. I would ask, however, whether a prolonged tonic spasm is not more likely to be caused by changes in nerve centres than by changes in nerves? We might hope to have this question answered by pathological anatomy, but it is far from improbable that a nerve intoxication may be the cause of tetany, and may leave no alterations in the neuro-muscular apparatus which are capable of demonstration by our modern methods of examination.

Up to the present time most of the observations and investigations which have been carried out for the elucidation of the subject of peripheral neuritis have dealt with disease of the cerebro-spinal nerves. The vagus is not infrequently diseased and gives rise to marked and even fatal cardiac disturbance. A few observations have shown that the terminal distributions of nerves in the substance of the heart are liable to alterations which probably play an important part in some cases of serious cardiac disease. But if it has been shown that few, if any, of the cerebro-spinal nerves are exempt from pathological alterations resulting in sensory and motor disturbance, is it not probable that the sympathetic nerves may be equally vulnerable? May not many of the so-called functional disturbances of the viscera with their neuralgias and disorders of secretion and metabolism owe their existence to temporary nerve intoxications, to nerve degeneration, or to nerve inflammation? Here is a wide field indeed for investigation, and communications on this point would be welcomed by all pathologists and physicians.

In the short space of time which has been allotted to me for the introduction of this debate, I have called attention to a few points upon which I, at any rate, would like to hear the views of others. But the disease "neuritis" suggests a far larger number of questions of interest than have been touched upon, and questions too which may appear of greater importance to those who have a special knowledge of this subject. No one can desire that the contributions made by members to this discussion should be limited to the few points raised by the individual who introduces it. All additions to our knowledge, all criticisms of current theories, to whatever points they may be directed, will, I feel sure, be warmly appreciated by those who have honoured this Section by their presence.

DISCUSSION.

Dr. ORD said: For several years I have been led to observe a remarkable combination of symptoms of pericarditis and endocarditis in persons suffering from symptoms of gastric ulcer, particularly where hæmatemesis had occurred. The inflammations of the heart could not be referred in the group of cases under consideration to acute rheumatism or other malady likely to cause affection of the heart, and there was no pyrexia. I ventured to argue that the heart affection and the stomach affection were causally related to one another, either by way of reflex dystrophic influence propagated from the stomach to the heart, or by way of a common dystrophic influence exerted by the vagus on both organs as a result of nutritional changes in the vagus determined by anæmia. In a paper read a few years ago before the Medical Society of London I presented these views, but could only support them by clinical observation. Since then my colleagues, Dr. Hector Mackenzie and Dr. Turney, have each observed in *post-mortem* examinations of persons dying from perforating ulcer distinct pathological evidence of inflammation of the endocardium. Although I have no proof of the existence of neuritis in these cases I submit that they are suggestive of it, and come under the category of cases in which future investigators may be led to make examination of the vagus as well as of the stomach and the heart.

Dr. MOTT wished to call attention to the fact that in many cases of neuritis it was possible to explain the symptoms in accordance with the theory of the cause of peripheral changes in the nerves in locomotor ataxy by Marie. The nutrition of a nerve depended upon the nutrition of the nerve cell of which it was an outgrowth, and it was reasonable to believe that a toxic agent circulating in the blood would be absorbed by the dendrons of the nerve cell; but the effects would be shown by changes in the most remote portions of the cell, namely, the neuron and its peripheral termination. This hypothesis would explain the frequency with which the nerves of the apex of the limb most remote from their seat of nutrition are affected. Dr. Mott did not deny that any toxic agent which produced the clinical symptoms of peripheral neuritis did not act directly upon the terminals of the nerves. The primary local symptoms of diphtheritic paralysis showed that the poison could produce effects at the seat of absorption. The argument advanced that inflammatory changes in the nerves showed that the poison acted directly upon them, was strong; but it might be said that pathologists were not in agreement as to whether the fibro-vascular changes so often seen in degenerated nerves might not be secondary to the atrophy of the nerve fibres. In conclusion, Dr. Mott wished to point out the desirability of a more careful examination of the condition of the nerve centres in cases of peripheral neuritis. In diphtheritic paralysis it was occasionally found that the anterior horn cells had undergone destruction, but present methods did not permit of determining with reliable certainty changes in the protoplasmic processes of the cell, and, until they had such, the hypothesis he had advanced of primary or simultaneous affection of nerve cell and fibre was not proved.

Dr. G. MARINESCO (Paris) said: The question of peripheral neuritis considered from the point of view of its pathogeny is of special interest because of the tendency of a certain number of authors of great authority to attribute lesions of peripheral neuritis to an alteration in the trophic centres; this opinion has lately been maintained by M. Pierre Marie. It is extremely probable, to my mind, that peripheral neuritis is often associated with lesions of the nerve centres. The forms of generalised polyneuritis, without disturbances of the trophic centres, at least such as have a progressive course, must be considered rare. I have found with M. Souques, in a case diagnosed by Charcot as polyneuritis, besides very extensive degenerations of the peripheral nerves, a lesion of the posterior columns which I attribute to a disturbance of the trophic centre. As regards the pathogeny of polyneuritis, it is due almost always to infections or else to intoxications.

Dr. ORMERON made some remarks suggesting the probability that in peripheral neuritis neither the nerve fibre nor the nerve cell was affected alone, but that both were affected simultaneously, and that the fact that peripheral fibres were affected rather than nerve trunks was due to their small size;

in consequence of which they offered a large superficial area to the blood current and to the injurious substances circulating therein.

Professor Sir T. GRAINGER STEWART said it was necessary to select certain points for remarks, inasmuch as they were so numerous, and he should desire to speak rather of the clinical than of the purely pathological aspects of the subject. He remembered that apart from such local conditions of Bell's paralysis, as regards one great group of cases of the kind, namely, the alcoholic, he was indebted for his first definite acquaintance with the subject to the writings of the President of the Section, Dr. Wilks. He went on to refer to the clinical features of the first series of cases which he published about fourteen years ago—motor paralysis, loss of sensibility, and trophic changes, beginning at the fingers and toes and spreading upwards. He had three such cases in his clinic about the same time. Two gradually recovered, one took pneumonia and died, and *post-mortem* examination revealed definite changes in the nerves of the affected parts with no lesion of the cord or brain. He then spoke briefly of a series of points which had influenced him, namely (1) The remarkable tendency to recovery when the disease does not involve nerves of vital organs. (2) That this condition at once indicated the explanation of the temporary paralyses which occur in the early stages of locomotor ataxia. (3) That further experience had proved that not infrequently vital nerves were affected, and that death resulted. He gave some details of illustrative cases. (4) The strange way in which one found in some cases particular groups of fibres in an individual nerve, sometimes in a strand, as in optic neuritis, sometimes affecting the motor fibres, sometimes the sensory fibres alone; and, further, he thought that his experience justified what Dr. Sharkey had suggested, namely, that the vasomotor and trophic fibres are occasionally selected. (5) He begged to offer his testimony as to the great variety of toxins which might induce these changes, alcohol and diphtheria, influenza, and others. (6) That he had found remarkably good results from the subcutaneous use of strychnine after the first acuteness of the case was once passed.

Professor D. J. HAMILTON took up the question whether the term "neuritis" is really applicable to the disease in question. There existed until lately, and even yet the matter was not quite cleared up, much dubiety as to what affections of the central and peripheral nervous systems are and what are not inflammatory. Some years since the speaker had made some experimental observations on the spinal cord with the object of eliciting what the changes are which occur in the organ when it is inflamed artificially. These changes were found to be twofold, namely, those affecting the blood vessels and interstitial tissue, and those having their seat in the nerve cells and tubes. Those affecting the former were found to be identical with what are found in inflamed vascular parts elsewhere. The reaction of the nerve tubes, however, were quite peculiar and consisted chiefly in a contraction, moniliform swelling, and final segmentation of the axis cylinders. Fatty alterations were in abeyance. Similar lesions occur in syphilitic inflammations of the brain in man. In peripheral neuritis, however, it often happens that the interstitial tissue of the nerve remains unaltered while the nerve fibres are extensively degenerated. The degeneration, moreover, is not alike with that seen in myelitis or neuritis artificially induced. There is much greater evidence of disintegration of the nerve fibres followed soon afterwards by fatty degeneration. The conclusion which the speaker had arrived at was that widespread peripheral neuritis so-called is in most cases not inflammatory, but in reality a degeneration due to the action of a poison. The action of this poison is probably like that of phosphorus upon other tissues. In reply to remarks made by Drs. Saundby and Sharkey, he maintained that any reactive phenomena noticed in the interstitial tissue of the nerve might quite possibly be secondary to those found in the nerve fibres. Cases occurred over and over again, as in that recorded by Sir T. Grainger Stewart, where the nerves were profoundly degenerated without the slightest reaction in the surroundings. On the other hand, every one knew that secondary degenerations of the spinal cord from trophic causes were often followed by thickening of the neuroglia.

Dr. ELIZA WALKER DUNBAR (Bristol) said the widespread

influence of the toxin of influenza had brought the question of neuritis and pathology of the nervous system generally before every medical practitioner. She had been struck by the absence in peripheral neuritis of the signs of swelling, which they had learned to associate with inflammation, and, in some cases, by the fugitive nature of the symptoms. The toxin of influenza, for instance, might call forth in the course of half an hour in the same individual an intense hunger due to excitation of some of the nerves of the stomach, giving way to severe pain in the extremities, going on to producing restlessness due to irritation of the nerves of the muscles and passing deafness and blindness. She believed that in very many cases of so-called peripheral neuritis the pathological change was a chemical one.

Dr. GOODHART wished to ask the question, What is inflammation in nervous tissue? Is it necessarily represented by similar changes in other organs? May it not be special, and therefore may it not be quite possible that the changes in the myelium and that such degeneration may in reality be inflammation? He made this remark in opposition to his own feelings and from the drift of opinion in the discussion. From the clinical side he had certainly come to the conclusion that many cases could not be neuritis in any ordinary sense; the positive course they run, and other facts seemed to him to make it clear that the disease in many cases is of the nature of a toxic degeneration, and although it is always a dangerous line of argument to draw conclusions upon pathological change from the action of medicine, yet he could not but see it in this way, and in support of Sir Grainger Stewart's contention that the action of strychnine injected subcutaneously is of very great value, he felt quite as strongly as regards the value of strychnine administered in this way, and he thought that its sometimes rapid action in the betterment of the patient tended to show that the change was a mere nervous hebetude or degeneration; and it is probable that the action of strychnine does also tend to confirm the observations referred to by Dr. Mott and supported by Dr. Ormerod, that in many cases the nerve cells suffered either alone or in conjunction with the nerve fibre.

Dr. SAUNDBY had arrived in the meeting too late to hear much of the debate, and would not have spoken but for the proposition of Professor Hamilton that these conditions are not inflammatory. Speaking from his own experience, he had seen not only the segmental neuritis described by Professor Hamilton as present in artificially inflamed nerves, but also interstitial neuritis, and observers in every civilised country have abundantly attested their occurrence in these cases. Secondly, the tenderness over the nerve trunks affords clinical support to the theory of the presence of inflammation.

NOTES ON THE INFLUENCE OF HEREDITY IN DISEASE.¹

By WILLIAM SEDGWICK, M.R.C.S.

It seems to have been very generally admitted by those who have directed special attention to the subject, that much progress has been made of late years in the study of the laws on which both hereditary transmission and hereditary development depend; for, on referring to the well-known work by the late Mr. Darwin on the *Origin of Species*, which was published in 1859, we find it stated that "the laws governing inheritance are quite unknown." Although this statement was to some extent qualified by subsequent remarks, yet it was not till after an interval of some years, during which our knowledge of the subject had been greatly increased by a more complete investigation of the family history in cases of heredity, that he was enabled to state in his subsequent work on the *Variation of Animals and Plants under Domestication*, which appeared in 1868, that finally, "though much remains obscure with respect to inheritance, we may look at the following (five) laws as fairly well established." It is not, however, proposed on the present occasion to do more than offer some remarks on the influence of three of

¹ Read in the Section of Medicine at the Annual Meeting of the British Medical Association held in London, July-August, 1895.