Critical Review.

THE PATHOGENESIS OF TABES DORSALIS.

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IN a paper admirable alike for its thoroughness and lucidity, Richter¹ has recently made a communication which marks an epoch in the history of his subject. After reading it one feels that the hitherto impenetrable fog engendered by hazy notions of meta-syphilis, elective degenerations, hypothetical toxins, and all the other unknowns which have been invoked to explain the obscure has at last been dispelled; for this author has described a lesion in tabes which is primary, essential, and *constant*, a lesion in which the spirochæte is demonstrable and one which represents a *direct* and *local* reaction to the virus of syphilis.

This tabetic process is an inflammation of the sheath of the nerve-roots, which begins at that point above the sensory root ganglion where the dorsal and ventral spinal roots converge to form the radicular nerve of Nageotte. The reaction in this situation to the presence of the spirochæte—the tabetic granulation—presents peculiar histological characters. It is mainly fibroblastic, and arises by proliferation of the endothelial cells of the lymph channels and the fixed connective-tissue cells of the nerve-sheath. Infiltrative cells of hæmatogenous origin, lymphocytes, plasma-cells, etc., are almost entirely absent, and diffuse and perivascular infiltrations such as occur in syphilitic lesions of other parts are foreign to the tabetic lesion. Beginning in the lymph and tissue spaces of the common sheath formed by the fusion of the dura and arachnoid, the inflammation spreads inwards along the septa between the nerve bundles, and as sclerosis occurs the nervous elements themselves are damaged, and the fibres degenerate proximally. The degenerations in the posterior columns are entirely secondary, and are the natural outcome of the root lesion. The anterior roots suffer least, because they usually pierce the common sheath and leave the subarachnoid space before they reach the point at which the tabetic process begins. Meningitis in the usual sense, i.e., inflammation of the pia mater, is a frequent complication of tabes, but plays no part in its production. The lesion in the cranial nerves is an interstitial inflammation which attacks them in the proximal portion of their extracerebral course. In all with the structure of peripheral nerves the same tabetic

granulation is found. The olfactory and optic nerves, however, differ from the others in that they possess a pial sheath and contain supporting tissue of ectodermal origin. In these, therefore, the inflammation is the same as that seen in the pia mater and glia in other parts, and perivascular infiltrations with plasma-cells and lymphocytes are prominent.

This short summary is enough to show that Richter's views differ materially from any that have hitherto been propounded. They are based on a thorough examination of twenty-four cases—twelve of pure tabes, ten of tabo-paresis and two of tabes, complicated by cerebrospinal syphilis. The nerve-roots were examined in serial section, and from these alone, apart from sections of the cord, ganglia, and cranial nerves, some ten thousand finished preparations were made.

If his findings are confirmed, no one will deny that the epithet 'epoch-making' is applicable to them, for they put an end for ever to the already discredited conception of metasymphylis, and they terminate the age-long dispute between the adherents of the toxic and meningeal theories by showing that the truth lies in neither.

Richter himself is very modest in his claims to priority. He states that his discoveries confirm in the main those of Nageotte,^{2,3} and considers that the part of his work which has most claim to originality is that dealing with the histology of the tabetic granulation. But a perusal of Nageotte's papers leaves the impression that this writer was never quite sure of his ground. In an early paper he emphasized the lesion in the radicular nerve, and stated clearly that meningitis was not constant. He spoke of an *infiltration embryonnaire* in the roots—undoubtedly the *Granulation* of Richter—and did not mention perivascular and infiltrative lesions. Later, however, in his book on the pathogenesis of tabes, he describes a lesion in the roots identical with meningitis, and looks upon the tabetic process as a spread to the roots from the inflamed meninges—no tabes without meningitis. For him the degeneration in the posterior columns is the initial nervous lesion. It is an *atrophie lente* which, though dependent on a lesion of the radicular nerve, appears first in the intramedullary portion of the root fibres. This degeneration is at once radicular and systematic (*à la fois radiculaire et systématique*), and the motor roots suffer least because among other reasons they are more resistant to the syphilitic toxin. His *périnévríte radiculaire*, therefore, on his own showing is not the primary and adequate lesion in tabes, but is merely one factor in its causation. Having slain the monster which had impeded progress so long, he allowed it to raise its hydra heads—electivity, systematic degenerations, unequal susceptibilities to toxins, meningitis, and so on—and his theory gained but qualified acceptance.

In contrast to Nageotte's latest conception, Richter holds that meningitis is an inconstant accompaniment of the lesion in the radicular nerve, that the primary nervous lesion appears at the site of the tabetic granulation, whence degeneration extends to the posterior columns, that the distribution of the early degenerations in the various zones of the posterior columns can be explained without recourse to any theory of systematic degeneration, and that the relative escape of the anterior roots is explicable on purely anatomical grounds. In spite of these minor differences, however, both writers agree on one fundamental point, the importance of the lesion in the radicular nerve, and as it is almost certain that a modification of Nageotte's original theory will soon gain general acceptance, it is of interest at this point to consider some of the causes which have delayed the recognition of extramedullary root lesions as the prime factor in the pathogenesis of tabes.

One of these causes is found in the work of Obersteiner and Redlich,⁴ who published the results of their important studies a few months before Nageotte's first paper appeared. These observers drew attention to a constriction of the posterior root at the point where it pierces the pia mater and loses its neurilemmal sheath. This part of the root, they said, is a *locus minoris resistentiæ* which is damaged mechanically by inflammation in the meninges and by the pressure of sclerosed pial blood-vessels. From this point the fibres degenerate, first in their intramedullary and later in their extramedullary portion. This purely mechanical theory was not accepted in its entirety, as it was soon shown that in many cases changes in the meninges could not be demonstrated, and that when meningitis was found its severity bore no relation to the intensity of the nerve lesions. The anatomical peculiarities of the root at the point they described, however, were generally accepted as of great importance, and this part of their work has influenced the writings of almost every investigator in this field. Their strongest argument against those who postulated a lesion in the ganglia or in the extramedullary portion of the nerve-roots was that the degenerations in early cases appear first in the intramedullary part of the sensory fibres. This argument, which is probably based on a false assumption, has gone unchallenged up to the present day, and is constantly used by those who support the notion that the lesion in tabes is a primary degeneration of the sensory fibres in the posterior columns.

To overcome the difficulties presented by the incongruities of the purely mechanical theory, it was assumed that, with or without meningitis, a toxin might damage the nerve-roots at the vulnerable point described by Obersteiner and Redlich, and in this modified form the theory has survived.

We cannot illustrate more clearly the most unsatisfactory feature of the meningeal theory—its multiplicity of factors—than by quoting some of the conclusions of a writer who describes himself as a supporter thereof. *Tabes*, Schaller⁵ says, is due to a degeneration of the posterior roots. Subacute syphilitic inflammatory changes in the subarachnoid space (posterior leptomeningitis, meningeal and neural involvement of the radicular nerve) are in etiological relationship with the degeneration of the posterior roots. The manner in which this subacute inflammatory meningitis produces degeneration is as yet uncertain; it may act by direct extension of the meningeal lesions to the nerve-roots, causing a meningo-radculitis; or by pressure constriction from sclerosed meninges; by toxic products engendered by this inflammation; or even by increase of the fluid pressure, as in the case of posterior spinal root degeneration in brain tumour. These causes may act together or independently. It is hardly necessary to say that, if Richter's conclusions are correct, this list of surmises which masquerades as a theory must also be abandoned, for neither meningitis nor imaginary toxins play any part in his account of the production of the disease.

The theory of the elective systematic distribution of the degenerations in *tabes* next demands consideration, for its protagonists still hold out against those who have favoured an extramedullary origin for the disease.

It is founded on the fact that in early cases the degenerations appear with unequal intensity in different parts of the posterior columns, so that certain regions are more or less sharply delimited. Strümpell, the founder of this theory, considered that each of these regions contained groups or systems of fibres, each with biological peculiarities and different degrees of vulnerability. He held that the noxious agent in *tabes* was a general toxin with a special affinity for the intramedullary portion of the sensory root fibres, and that this toxin destroyed the different systems of fibres in the order of their vulnerability. Flechsig's researches on myelinization seemed to lend strong support to this theory, for they showed that in certain stages of this process regions similar to those seen in *tabes* were marked off, and especially that the changes were always most intense in the middle root zone. He saw herein a parallel between the march of the process of myelin formation and the degenerations in *tabes*, and concluded with Strümpell that both were systematic, and that the various systems contained independent systems of fibres of which in *tabes* the most vulnerable perished first.

This, the so-called toxic-elective theory, has always had many supporters, because it provides an explanation on many points where the meningeal theory fails. The posterior columns are affected whilst

other parts are spared because the all-pervading toxin has a special affinity for the intramedullary portion of the exogenous sensory fibres; the middle root zone shows the most intense changes because it contains a system of fibres to which the toxin is particularly obnoxious; and so on. But it cannot be said that an explanation such as this gives much intellectual satisfaction. It reminds us of Molière's student who, when asked why opium produced sleep, replied that the drug possessed a dormitive virtue whose nature it was to allay the senses, an answer which satisfied his learned examiners. Serious students are referred to Richter's paper for a closely-reasoned statement of his belief that both the apparent preponderance of the degenerations in the intramedullary portion of the sensory fibres and the apparent systematic nature of the degenerations, especially the early changes in the middle root zone, are explicable in terms of anatomy and histopathology. He has our sympathy when he states that his guiding principle in this part of his exposition has been that the principle of electivity, both in myelinization and in tabes, should not be accepted until all other possible explanations have been exhausted.

One of the most influential supporters of the primary elective theory is Professor Schaffer,^{6,7} whose article on tabes in Lewandowsky's *Handbuch* has become a classic. It was at his instigation that Richter's research was undertaken, and his discussion of the bearing of this work on his own long-held views makes interesting reading. He considers that Richter's work justifies the following conclusions: that in tabes the radicular nerve of Nageotte is the constant seat of a purely proliferative process, at first peri-, later endo-fasicular, which is characterized by proliferation of the endothelial cells of the lymph channels and the fixed connective-tissue cells of the nerve-sheath; that in uncomplicated cases of tabes infiltrative cells of hæmatogenous origin are absent, but that in taboparesis lymphocytes and plasma-cells may be found in the nerve-roots as well as the tabetic granulation cells; that the tabetic granulation is quite independent of alterations in the meninges, meningitis being a frequent but inconstant accompaniment of tabes. Tabes, therefore, is not a result of the action of a syphilitic toxin; it is not a primary toxic-degenerative form of cerebrospinal syphilis, but is the natural outcome of the local action of the spirochæte in the nerve-root; the degeneration in the posterior columns is secondary to the affection of the roots, so that one should no longer speak of a primary elective disease.

Schaffer thus adds the weight of his great authority to Richter's work; but after making these handsome admissions, he proceeds to review Kaufmann's⁸ article on the myelinization of the posterior

columns, and succeeds in finding reasons therein for believing that the degenerations in tabes are partly elective after all. Whilst admitting our great need for a single cause, he considers that in the present state of our knowledge a dual conception of the lesions in tabes is still necessary. His final standpoint is that the attack of the spirochæte on the spinal sensory protoneurones leads to the formation of multiple local lesions which, though damaging the fibres haphazard, produce degenerations which are only explicable on the assumption that the roots contain systems of fibres of which the more vulnerable degenerate first. With all due deference we consider that Schaffer's conclusions are unfortunate, not because the point at issue is a very important one, but because of the principle involved—that of explaining obscure points by pure surmises, when provable explanations have not been exhausted. He bases his conclusions on the early and intense changes in the middle root zone, that great Serbonian bog where whole armies of writers on this subject have sunk; but it is highly probable that both the early myelin formation and the early tabetic degenerations in this zone depend on the fact that it is one through which all the root fibres pass before they spread to their several destinations, and is therefore just the place where the alterations in both instances must be most obvious.

Be this as it may, the original toxic theory has given ground on every important point, and Richter's modification of Nageotte's hypothesis bids fair to win the day.

As a milestone from which progress in recent years can be measured, we may choose Redlich's statement of the problems still awaiting solution in the year 1897. He presented them in the form of two questions: Is the degeneration in uncomplicated cases of tabes confined to parts of the posterior columns connected directly with posterior roots? If so, is it confined to certain fibres of the roots—in other words, is it a systematic degeneration as Strümpell and Flechsig held, or a degeneration of all the fibres of the root? To the first question an almost unanimous answer has been given in the sense that it is the exogenous sensory fibres, and these alone, which degenerate in cases of pure tabes. The qualification regarding unanimity is necessary, because Schröder,⁹ and more recently Hassin,¹⁰ Thorne,¹¹ and others, have described scattered interstitial lesions in the spinal cord as characteristic of tabes. But this evidence, if accepted, would render the root theory untenable, for it is unlikely that degenerations following lesions of this nature would be confined to the exogenous sensory fibres. It is now well known that tertiary syphilitic lesions are common in the brains of paretics, and it is not surprising that similar changes should be found in the cords of tabetics. The fact that the material on which these discrepant observations

are made is often obtained from asylums is not without significance. Hassin's cases, for example, were said to have suffered from taboparesis and tabetic psychoses. The latter were considered to be pure cases of tabes so far as the histological changes were concerned, but nothing is more probable than that their psychoses were really a part of general paralysis or of cerebrospinal syphilis. Observations such as these served a useful purpose when evidence was needed in support of the contention that the so-called metasyphilitic diseases were direct results of syphilis, but it would be unfortunate if they were thought to support any theory of tabes so reactionary as to place the primary lesion within the substance of the cord.

When Redlich formulated his second question, it was thought that a decisive answer thereto would settle the differences between the toxic-elective and the various extramedullary root theories. In a sense the answer to this question has been given, for it is hardly likely that anyone will now maintain that tabes results from the action of a toxin which has a special affinity for the intramedullary portion of the sensory fibres; but, as we have seen, one at least of the adherents of the elective theory, by shifting the point at which electivity acts from the posterior columns to the posterior root, and by substituting the direct action of the spirochæte for the action of a toxin, is able to reconcile a lesion in the root with the principle of electivity, so that a final answer to Redlich's second question has not yet been given.

Nevertheless great progress has been made in the last thirty years, if only because the tabes question has been freed at last from the mystic epithet 'metasyphilitic'.

It is hoped that this short review will draw attention to Richter's work. It merits, indeed demands, the serious attention of everyone who is interested in the pathogenesis of tabes dorsalis.

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