On tabes dorsalis : the Lumleian lectures delivered before the Royal College of Physicians, London, March, 1906.

ON

TABES DORSALIS

The Lumleian Lectures

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS, LONDON,

MARCH, 1906

BY

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TO

SIR RICHARD DOUGLAS POWELL, BART.

K.C.V.O., M.D.,

PRESIDENT OF THE ROYAL COLLEGE OF PHYSICIANS, LONDON

THESE LECTURES

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THE LUMLEIAN LECTURES

ON

TABES DORSALIS.

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Lecture I.

Mr. President and Gentlemen. — The choice of a subject must always, I imagine, be a matter of difficulty to the one who has the honour of being appointed to deliver the Lumleian Lectures. Having been invited to open a discussion on tabes at the forthcoming International Medical Congress, it appeared to me that I might with advantage to myself, and I hope not without profit to you, take as the basis of my lectures some questions relating to the nature and pathology of this affection.

Tabes seems to be of perennial interest. Nor is this much to be wondered at, considering the vast field which it covers, and the variety of questions which it raises.

The literature of tabes is enormous, and the treatises and memoirs relating to it literally count by thousands. It will be my endeavour in these lectures to present to you as succinctly as I can

the evolution of our knowledge of tabes, its nature and causes, and to indicate the problems as yet unsolved and on which we need further light.

Tabes dorsalis, in the modern acceptation of the term (and in reference to this I would remark at the outset that but for their consecration by custom, I should like to discard the term dorsalis altogether, and the still more barbarous adjective tabetic, in favour of *tabes* and *tabid*) is a very different thing from the tabes dorsalis or dorsualis—*φθίσις νωτιάς*—of the Hippocratic writers. This was essentially a condition of neurasthenia associated with spermatorrhœa, and attributed to sexual vice or excess. It was supposed to be due to wasting of the spinal cord, but on what evidence this was based there is nothing to show. That true tabes ever existed in Europe before the introduction of syphilis in the fifteenth century is more than doubtful. The retention of the name tabes dorsalis (or dorsualis) by the older German writers for the disease as we now understand it, though strictly correct according to modern pathology, tended largely to create confusion and excite prejudice against its unfortunate victims. Though cases of what we now know must have been tabes had been described by various observers, such as Ollivier (1824), Hutin (1827), and Cruveilhier (1835-42), (who figures the *post-mortem* appearances in his atlas), in France; and by Horn (1827), Jacoby (1842), Steinthal (1844), &c., in Germany; and though in this country Todd (1847) had drawn a clear distinction between paralysis and

inco-ordination,* and was the first to connect inco-ordination with disease of the posterior columns of the spinal cord, yet there is no doubt that the first systematic account of the etiology, symptomatology, diagnosis, prognosis, and treatment of tabes was given by Romberg (1840 to 1857). In his *Lehrbuch der Nerven-Krankheiten* he describes the characteristic gait; the pathognomonic symptom now called by his name; the increase of the ataxic disorders on shutting the eyes; the shooting pains, anæsthesiæ and parasthesiæ; the bladder troubles; the affections of vision, and the striking myosis and fixity of the pupils.

He mentions the relative infrequency of tabes in women; and as to prognosis, he utters the gloomy verdict: "To none affected by this malady is there any hope of recovery; *über alle ist der Stab gebrochen.*"

Of the morbid anatomy, he says that, notwithstanding considerable differences, the *post-mortem* examination shows for the most part partial atrophy of the spinal cord, mainly in the lower part of the lumbar enlargement and onwards, and in the nerves issuing from it. The diminution of volume amounts

* Todd (*Cyclopædia*, vol. iii., p. 621) says two kinds of paralysis may be observed in the lower extremities—"the one consisting simply in the impairment or loss of voluntary motion, the other distinguished by a diminution or total loss of the power of co-ordinating movements." In two cases of the latter affection he predicted disease of the posterior columns of the spinal cord, to which he attributed the faculty of harmonising the movements of the limbs with each other.

to the half or two-thirds of a normal cord, affects the grey and white substance, or only one of these. The atrophy of the nerves in the leash of the cauda equina is often so pronounced that only the empty neurilemma-sheaths remain. Also the roots of higher inserted nerves participate in the atrophy; and what is of particular interest, the posterior roots are sometimes alone affected, at other times along with the posterior columns of the cord, while the anterior roots appear normal.

Romberg, however, did not clearly differentiate the basis of ataxy from that of muscular paresis or paralysis, and he describes as equally belonging to tabes leathery induration of the white substance and, more frequently, softening of the grey matter.

There was no notable addition to the literature of tabes until Duchenne in 1858 published his researches on "ataxie locomotrice." These were the starting-point of the extraordinary amount of attention that the subject has attracted since his time. Duchenne, purposely endeavouring to divest himself of all preconceived notions, and pursuing his investigations in the limbo of so-called general spinal paralysis and unclassified forms of chronic myelitis, discovered what to him was a new disease, which, from its most striking symptom, he termed "ataxie locomotrice," adding the further term "progressive" on account of its habitual tendency to advance rather than recede. He clearly differentiated the affection from muscular paralysis or paresis, and described with a masterly hand its

most characteristic manifestations. Trosseau, in his brilliant clinical lectures, largely spread abroad the knowledge of this affection, but he did scant justice to previous writers in calling it Duchenne's disease. For, though practically a discovery on Duchenne's part, it was no discovery in the true sense of the term, as the malady was undoubtedly the same as had been known under the name of tabes dorsalis. And though Duchenne differentiated the affection more precisely than had been done before him, yet he contributed nothing to the pathological anatomy of the disease, and was inclined to attribute it to some affection of the cerebellum rather than that of the spinal cord.

Trousseau went so far as to look upon the malady as a pure neurosis, and considered such changes as had been observed by others in the spinal cord and posterior roots as probably only the secondary result of the functional disturbances created by some obscure general condition. This view was maintained by others of his school, notably by Isnard who regarded tabes as a neurosis of the muscular sense.

The connection between the symptoms of tabes or locomotor ataxy and degeneration of the posterior columns, first termed grey degeneration by Cruveilhier, had, however, been satisfactorily established by many observers, among others by Todd and Gull in this country.

The minute anatomy of the morbid changes began with the microscopical investigations of Virchow

(1855) and Rokitansky (1857). Rokitansky described it as a proliferation of the structureless, ependyma-like connective tissue and stroma of the nerve centres, which caused destruction of the nerve elements proper, and resulted in induration or sclerosis of the affected parts (*schwielige Degeneration*).

The process was not inflammatory, however, as there was no exudation; and Rokitansky included in the same term the end-results of various other forms of lesion of the nerve centres.

But the first important microscopical investigations, specially in reference to the now well-defined symptom-complex of locomotor ataxy, were made by Bourdon and Luys (1861).

They defined the condition as sclerosis of the posterior roots, the end-result of a chronic inflammatory process; and similar views as to the inflammatory origin of the degeneration were held by Charcot, Vulpian, Gull, and others. v. Leyden, however, in his celebrated monograph, *Die graue Degeneration der hinteren Rückenmarks-stränge* (1863), combated the inflammatory origin of the degeneration, and maintained that it had more the characters of a simple atrophy, and that such indications as there might be of chronic inflammation in the membranes and vessels were only secondary or accidental. He regarded the process as a peculiar degeneration of the sensory tracts of the spinal cord, ascending generally from below upwards.

At this time, however, he did not, as he has done in later times, causally connect the degeneration of the posterior columns of the cord with that of the posterior roots or sensory nerves, though he specially noted their almost constant coincident affection. In fact, in commenting on a case reported by Gull, to whom it seemed as if the degeneration of the posterior roots caused by inflammation of the pia mater had propagated itself to the posterior columns, he says explicitly: "But the view that the atrophy of the posterior roots caused by inflammation of the pia mater leads to a similar degeneration of the posterior columns is very unlikely. Moreover, the disease of the posterior columns progresses more from the posterior periphery and middle line, rather than follows the distribution of the roots."

The next great advance in the pathology of tabes was made by Pierret (1871), who in the course of his investigations observed that the primary lesions of tabes consisted, not in a degeneration of the posterior columns as a whole, but "in two symmetrical islets of small extent, situated in a special region of the posterior columns."

"This region," he says, "which I propose to call *les rubans externes* of the posterior columns, appears on transverse section in the form of two narrow bands skirting the internal aspect of the posterior horns. It appears to contain two orders of fibres—commissural and internal radicular. The sclerosed areas do not actually touch the posterior

cornua, but are separated from them by tracts of healthy white substance, though they are connected by fibrous bands. The sclerosis, beginning in the middle of the *ruban externe*, tends to spread inwards towards the median column, and outwards towards the posterior cornu" (see fig. 1).

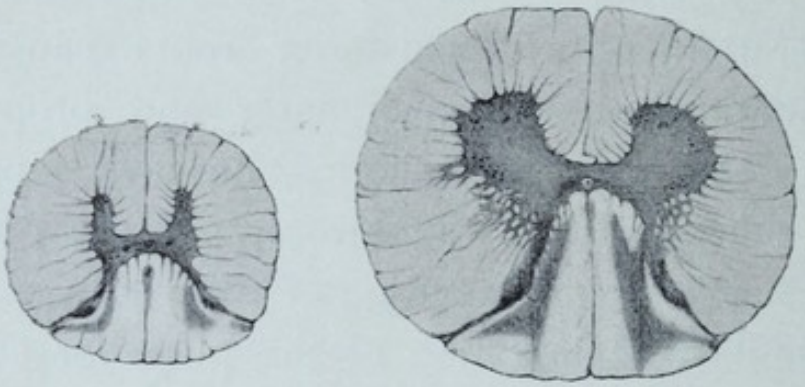


FIG. 1.—Transverse sections of spinal cord in lower dorsal and cervical regions from a case of tabes (Pierret, *Archives de Physiologie*, 1871). In lower dorsal region, note sclerosis in *bandelettes externes*, also a small area of degenerations in Goll's columns. In cervical region the bandelettes are much sclerosed; Goll's columns much less so.

Tabes then came for a time to be considered a system disease or sclerosis of the *rubans* or *bandelettes externes* of the columns of Burdach. But at this epoch nothing was known as to the relation of the *bandelettes externes* to the posterior roots. Vulpian, however (1879), saw the difficulty of connecting the supposed primary disease of the *bandelettes externes* with the atrophy of the posterior roots. A primary degeneration of the posterior columns could scarcely, he maintained, lead to atrophy of the posterior roots whose trophic centre was in the spinal ganglia. This would be a retrograde degeneration and opposed to the

Wallerian law. He therefore regarded the atrophy of the roots as undoubtedly of primary origin.

FIG. 2.

Ascending degeneration of a lumbar root in man, on right side. (Collier & Buzzard.)

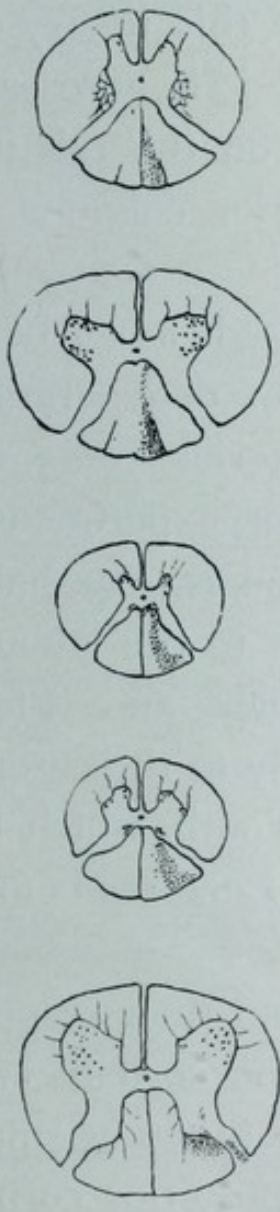


FIG. 3.

Ascending degeneration following section of the posterior roots in the monkey from L. 3 to D. 12 on left side. (Tooth, Gulstonian Lectures, 1889.)

That of the *bandelettes externes* might perhaps be so also, but only in so far as they contained

fibres not directly continuous with the posterior roots themselves.

He proposed to substitute for the formula "sclerosis of the posterior columns," "sclerosis of the posterior roots," as the primary basis of tabes. He thus inaugurated the radicular or root theory of tabes, which is now entertained in one form or another by the majority of neuro-pathologists.

In order to follow the bearing of this theory on the pathological anatomy of tabes, it is necessary to make some preliminary remarks on the relation of the posterior roots to the posterior columns of the spinal cord.

The facts on which this is based have been established mainly on the results of degeneration consequent on lesions of the posterior roots by disease in man (see fig. 2), and of experimental section of the posterior roots in animals, especially in monkeys. These we owe in part to the labours of Schiefferdecker, Schultze, Kahler and Pick, Singer and Munzer, &c.; and notably to the careful experiments and investigations of Tooth, which he made the subject of his Gulstonian Lectures before this College in 1889 (see fig. 3).

The posterior roots emerging from their respective ganglia (see fig. 4) penetrate the cord in two divisions—an external, consisting of fibres of small calibre which enter the apex of the posterior cornu, or zone of Lissauer, and distribute themselves here; and secondly, an internal division, formed of fibres of large calibre which alone take part in the forma-

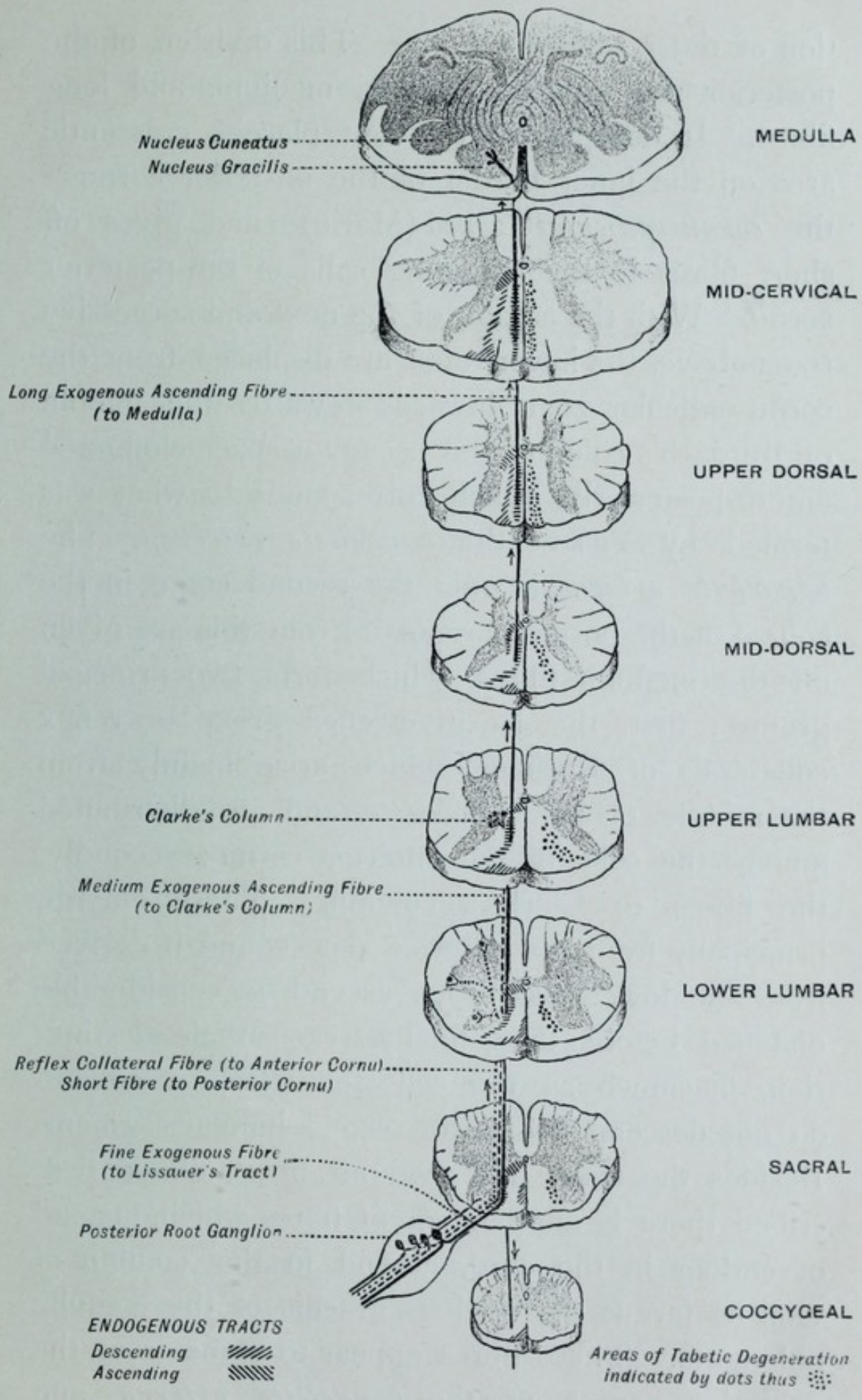

Nucleus Cuneatus
Nucleus Gracilis
MEDULLA
MID-CERVICAL
Long Exogenous Ascending Fibre
(to Medulla)
UPPER DORSAL
MID-DORSAL
Clarke's Column
UPPER LUMBAR
Medium Exogenous Ascending Fibre
(to Clarke's Column)
LOWER LUMBAR
Reflex Collateral Fibre (to Anterior Cornu)
Short Fibre (to Posterior Cornu)
Fine Exogenous Fibre
(to Lissauer's Tract)
SACRAL
Posterior Root Ganglion
COCCYGEAL
ENDOGENOUS TRACTS
Descending
Ascending
Areas of Tabetic Degeneration
indicated by dots thus

FIG. 4.

tion of the posterior column. This division of the posterior root gives off short, medium, and long fibres. It occupies in the first place a crescentic area on the inner border of the posterior cornu—the *cornu-radicular zone* (Marie)—and gives off short fibres to the adjoining cells of the posterior cornu. With the advent of the next and successive roots above, the lower roots are displaced from the cornu-radicular zone inwards towards the middle of Burdach's column, and occupy a space elongated antero-posteriorly, which corresponds to what was termed by Pierret the *bandelette externe*. The *bandelette externe* is only the second stage in the course of the posterior roots. From this are given off the medium fibres, which form two principal groups: first, the sensitivo-reflex group or reflex collaterals of Kolliker, which arise mainly from the middle of the *bandelette*, and are distributed among the cells of the anterior cornu; secondly, the fibres to Clarke's column. These emerge principally from the anterior aspect, and if derived from the lowermost roots, ascend a considerable distance before they finally reach their destination, inasmuch as the cells of Clarke's column do not descend below the second lumbar segment. Besides the short and medium fibres above described there is another set of fibres which, instead of ending in the cord, ascend in the column of Goll as far as the nucleus gracilis of the medulla oblongata. These fibres appear to come from the posterior aspect of the *bandelette externe* and

postero-lateral zone, and gradually pass inwards, and ultimately reach the mesial septum. The lowest fibres are those which are nearest the middle line.

Only the long fibres from the lumbo-sacral and lower dorsal roots ascend in the column of Goll. Those from the upper dorsal and the cervical roots ascend in the column of Burdach, the lowermost being nearest the column of Goll, and end in the nucleus cuneatus.

The columns of Goll, therefore, are formed by the long fibres of the lumbo-sacral and lower dorsal roots, and belong to the root system of the cord—the *exogenous* or extrinsic system (Marie). All these degenerate upwards on transverse section of the spinal cord at any part.

But, in addition to the exogenous, or root fibres, the posterior columns of the cord contain tracts which are probably commissural in function between different segments and different levels of the spinal grey matter. These tracts constitute the *endogenous* system of the spinal cord (Marie), and form two divisions, the ascending and descending. They only degenerate on destruction of the grey matter, and remain intact after all the exogenous fibres consequent on destruction of the posterior roots have undergone degeneration.

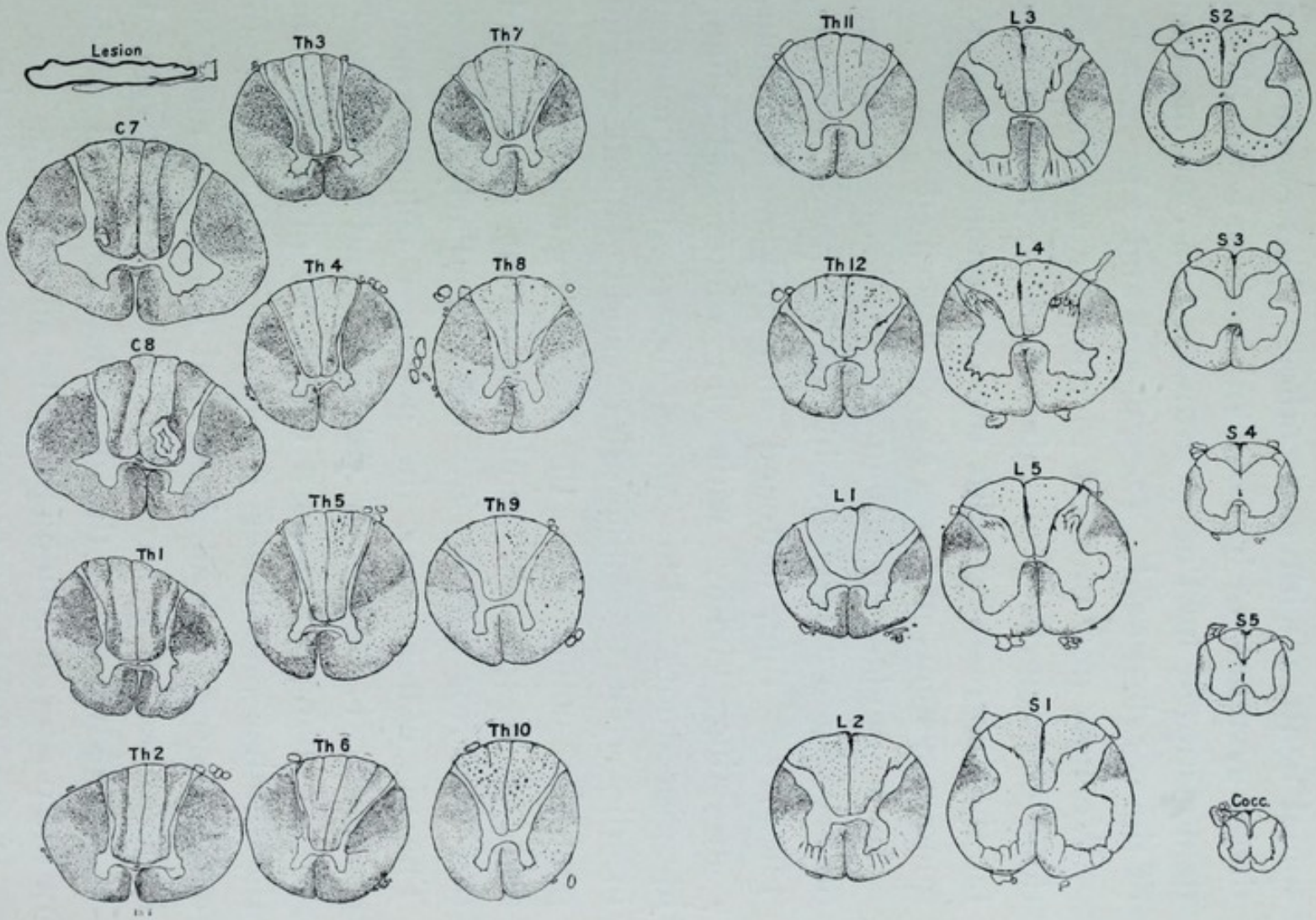
The ascending fibres occupy the *cornu commissural* zone, or ventral field of the posterior columns, lying posterior to the grey commissure, and extending some distance along the inner aspect of the

posterior cornua. These vary in size according to that of the horns of the lumbar, dorsal and cervical regions, and degenerate *above* lesions of the grey matter.

The descending system of fibres degenerates, on the contrary, *below* a transverse lesion of the grey matter. This system of fibres was first described by Schultze (1883), and is known in the cervical and dorsal regions as the "comma" tract. It occupies a position in the column of Burdach, running obliquely in an antero-posterior direction parallel to, but at some distance from, the internal border of the posterior cornu. Schultze described it as not reaching either the grey commissure or the posterior surface of the cord, but the Marchi method has shown that this is not quite correct.

This comma tract was supposed by him to consist only of descending root fibres, but the researches of various pathologists, especially those of Gombault and Philippe, have shown that this comma tract is continuous from above downwards with other tracts which have been differently named according to their appearance in different parts of the cord—namely, the *septo-marginal* tract of Bruce and Muir in the lower dorsal region, the *oval field* of Flechsig on each side of the mesial septum in the lumbar region, and the *median triangle* of Gombault and Philippe in the sacral region.

These variously-named tracts thus constitute one continuous system of descending commissural fibres,



FIGS. 5 and 6.—Descending degenerations after lesion in cervical region (Purves Stewart, *Brain*, 1901).

receiving and giving off fibres at different levels of the grey matter, and connecting together the various segments, as well as the upper and lower spinal centres, with each other. The continuity of these systems with each other has been clearly demonstrated by Purves Stewart in a case of crush of the cervical cord. (See figs. 5 and 6.)

We may now proceed to consider the degenerations characteristic of tabes, and to inquire how far they correspond with the exogenous and endogenous systems of fibres above described.

In a moderately-advanced case of tabes one observes a notable atrophy of the posterior roots. These are thin, flattened and greyish in colour, contrasting vividly with the white and plump anterior roots. This appearance is most marked in the roots forming the cauda equina. The posterior columns of the cord are also thinned, and of a greyish, semi-transparent aspect, and the posterior cornua are often similarly affected. The pia mater, over the posterior columns more especially, is frequently thickened and adherent.

The changes are, as a rule, most pronounced in the lumbar and lower dorsal region, but may in certain cases—so-called cervical tabes—be more or less limited to the cervical region. In advanced cases the whole of the posterior roots and whole of the posterior columns may be affected.

If one examines a transverse section of the lower dorsal or upper lumbar cord in an early case (see fig. 7), one observes an area of degeneration,

occupying the middle third of the posterior column, extending from the posterior cornu forwards and inwards towards the posterior commissure. This area constitutes Pierret's *bandelette externe*, and varies in breadth according to the number of posterior roots involved. The two *bandelettes*, not always symmetrical, may meet almost in the middle line. They correspond to the middle stage of the traject of the posterior roots. From this part of the

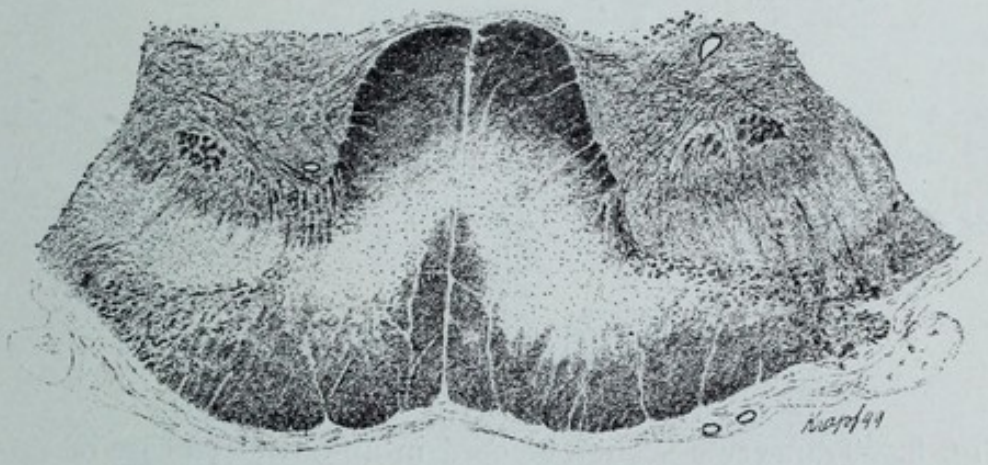


FIG. 7.—Transverse section in upper lumbar region from a case of early tabes, showing degeneration in *bandelettes externes* (Schmaus and Sacki).

course, as we have seen, are given off the reflex collaterals to the anterior cornua, and the fibres to the vesicular columns, or columns of Clarke. These are the fibres first and specially affected in tabes.

For a considerable time after the degeneration has appeared in the *bandelette externe*, comparatively little degeneration may be visible in the cornu-radicular or root-entry zone, in the long fibres occupying the postero-external zones, and

still less in the cornu-commissural zone and oval fields bordering the posterior medium septum. In more advanced cases, all the posterior columns are degenerated except the cornu-commissural zone and the oval fields of Flechsig (see fig. 8). These form, as already remarked, the endogenous systems of the cord, and only degenerate in very advanced cases in which the upper regions of the cord are invaded.

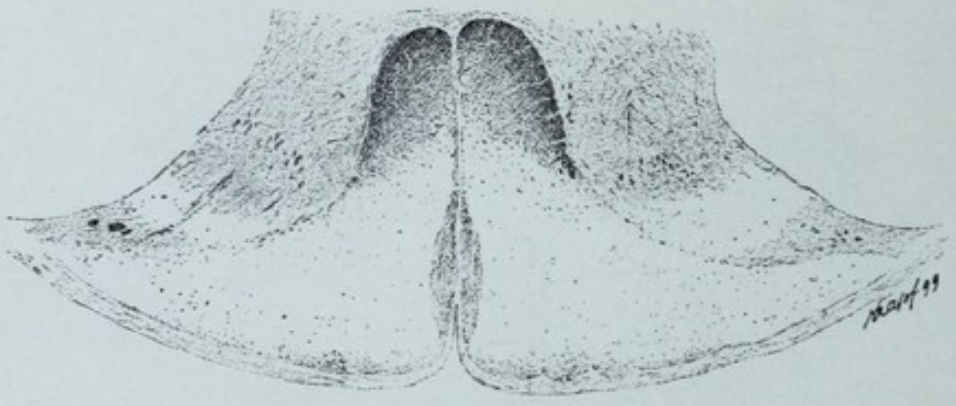


FIG. 8.—Transverse section of cord in an advanced case of tabes, showing degeneration of the whole of the posterior columns, with the exception of the endogenous tracts (Schmaus and Sacki).

The appearance of sections of the cord higher up will vary according as the degeneration of the posterior roots is confined to the lumbo-sacral region, or also implicates the dorsal.

In the first case the only degeneration visible is in the posterior median columns, which contain the long fibres from the lumbo-sacral region in their course up to the nuclei gracilis of the medulla oblongata, all the short and median fibres having by this time found their primary termination in the cells of the posterior and anterior cornua and in

the columns of Clarke. The appearance presented will be seen in fig. 9.

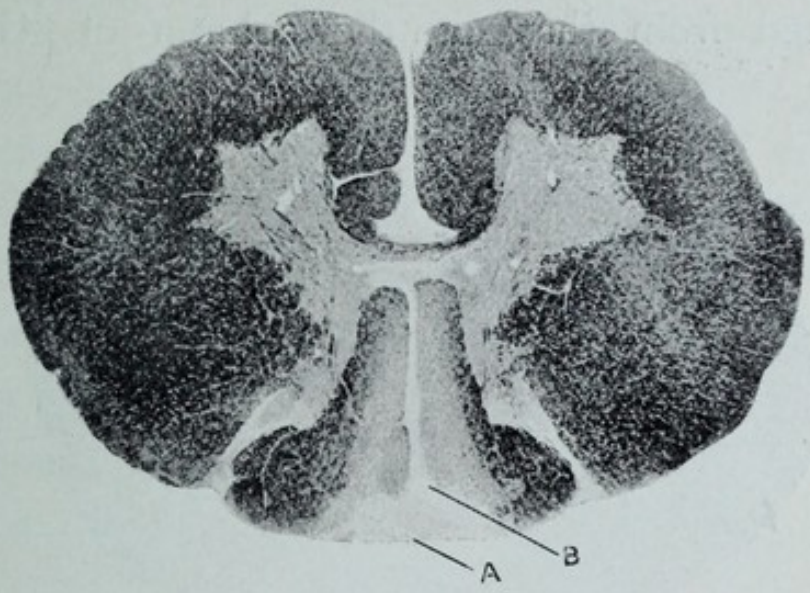


FIG. 9.—Third cervical segment of cord from a case of tabes (Leyden and Goldscheider, after Marinesco). A, degenerated fibres from sacro-lumbar roots ; B, degenerated fibres from dorsal and lower cervical roots.

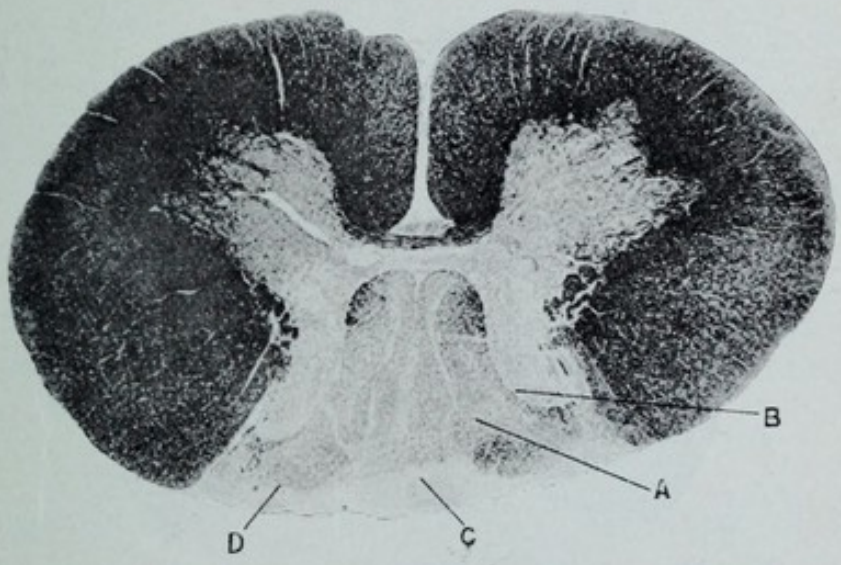


FIG. 10.—Fifth cervical segment from the same case. A, degeneration of middle root zone ; B, degeneration of fibres to posterior horn (collaterals) ; C, degeneration of Goll's column (lumbo-sacral) ; D, degeneration of posterior root-zone fibres, newly entered.

If, on the other hand, the dorsal roots are also affected, we get, in addition, degeneration in the columns of Burdach, varying in extent according

to the number of roots involved; and we may have a degenerated zone in Burdach's column separated from that of the column of Goll by

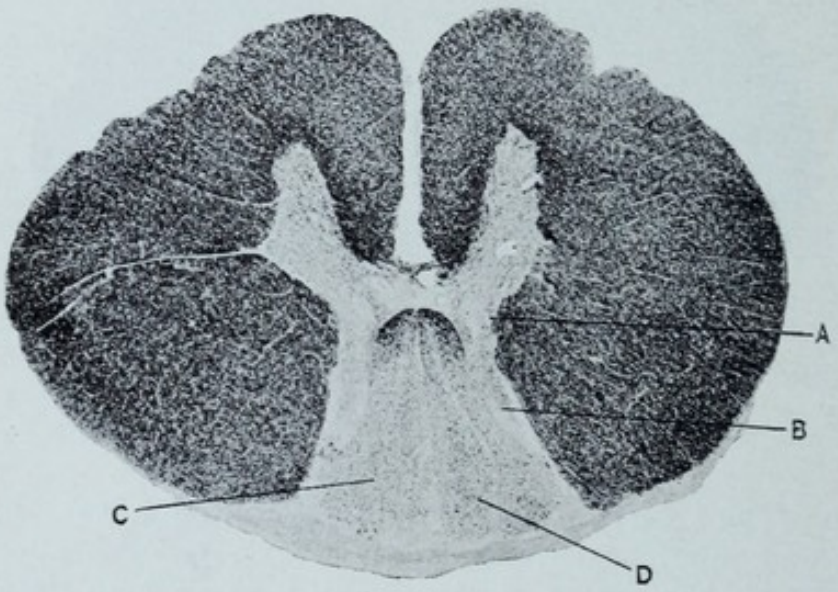


FIG. 11.—Section of mid-dorsal region.

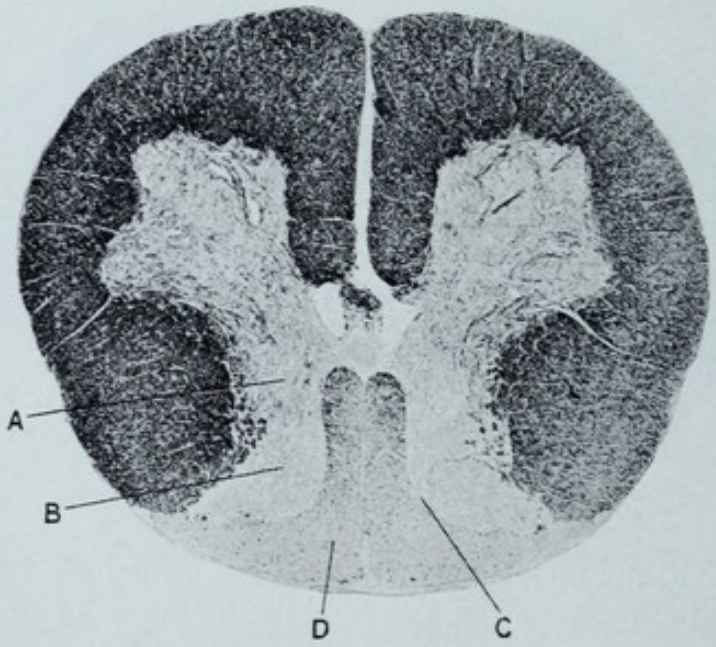


FIG. 12.—Section of mid-lumbar region. A, atrophy of Clark's column; B, atrophy of posterior horn fibres; C, middle root zone; D, ascending degeneration. (From same case as Figs. 9 and 10).

healthy tracts corresponding to healthy roots entering at a lower level (see fig. 13).

In the cervical cord, if only the lower dorsal and lumbo-sacral roots are affected, the degeneration will be confined to Goll's columns, as these are composed exclusively of the long fibres passing up from these regions. If the upper dorsal is affected, degeneration of Burdach's column will be found immediately adjoining that of the column of Goll; and if the cervical roots are also implicated, the degeneration will occupy the columns of Burdach, varying in extent with the amount

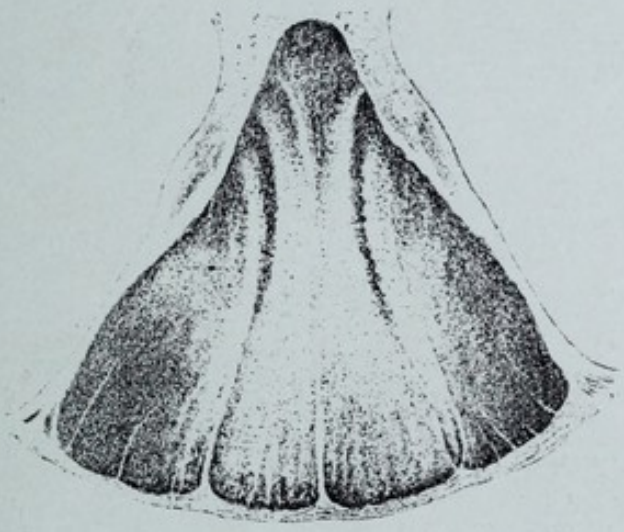


FIG. 13.—Section of upper dorsal region showing tabetic degeneration in the columns of Goll, separated by healthy areas from degenerations in Burdach's columns (Schmaus and Sacki).

of degeneration of the roots. In cases of cervical tabes there is no degeneration in the columns of Goll (figs. 12 and 13). The degeneration is confined exclusively to the columns of Burdach, and the long fibres of these roots end in the nuclei cuneati.

It is only in the most advanced stages of tabes that all the posterior columns, exogenous as well as endogenous tracts, are alike degenerated. Of

the exogenous system we have seen that they are not all equally affected at the same time. The first incidence of the degenerative process is on the medium fibres, namely, the reflex collaterals and

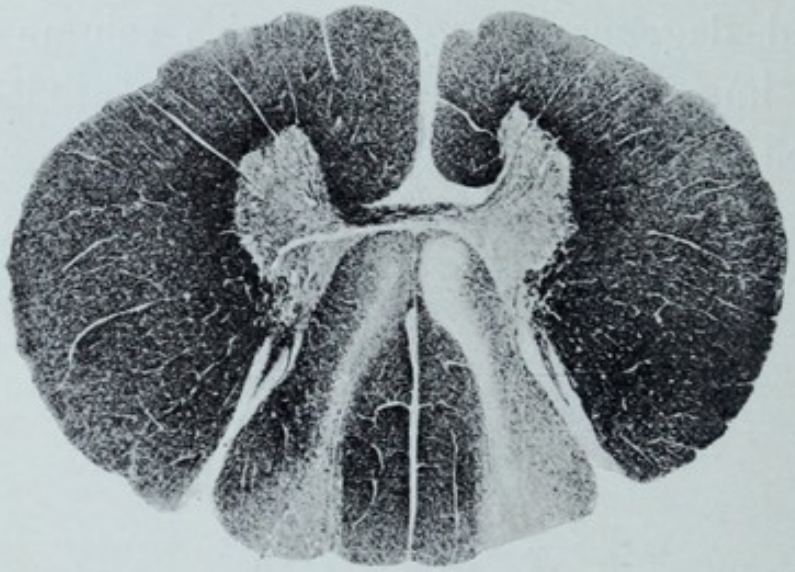


FIG. 14.—Cervical tabes—third cervical segment (Leyden and Goldscheider).

FIG. 15.—Cervical tabes—fifth cervical segment (Leyden and Goldscheider).

those to Clarke's columns (fig. 16). The long fibres which, in large measure at least, constitute the postero-external root zones are more resistant, and

often exhibit scarcely any degeneration when the bandelettes externes are completely sclerosed. There is some doubt, however, whether the postero-external root zones are composed only of long fibres. There are grounds for believing that they contain also endogenous fibres which are

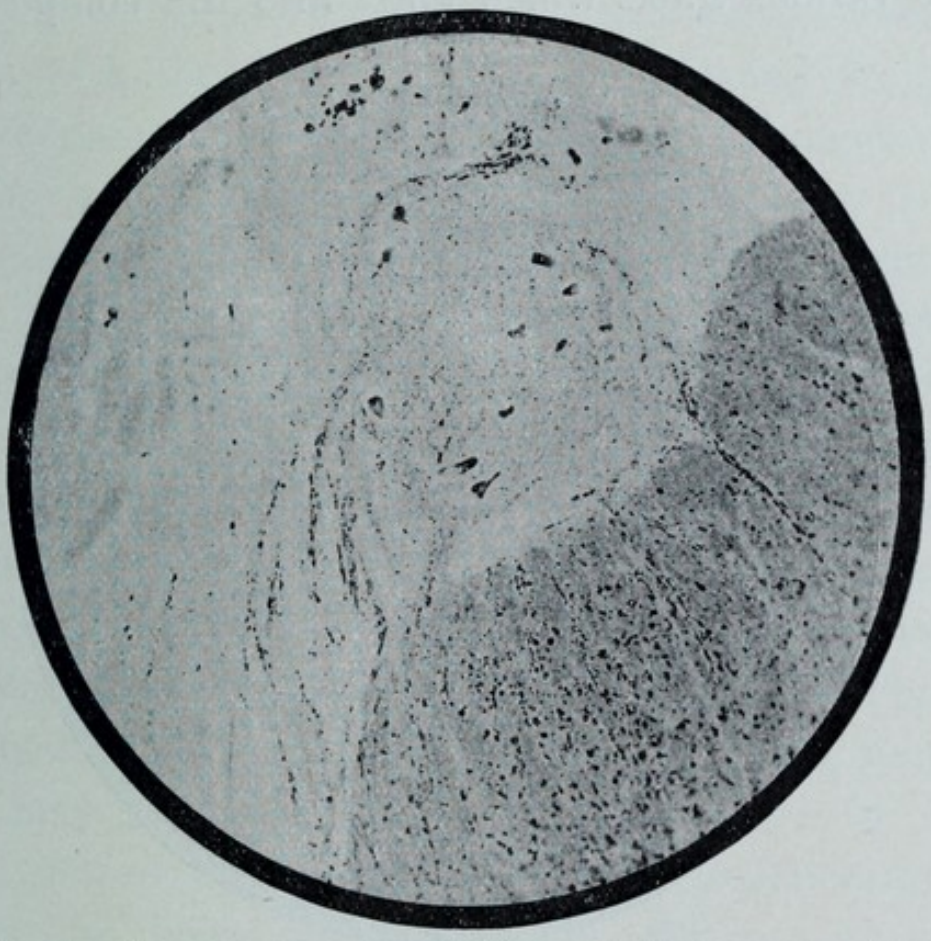


FIG. 16.—Degeneration of posterior root fibres passing towards Clarke's column (Orr and Rows, *Brain*, 1904).

relatively more resistant to degenerative change (Schmaus and Sacki).

Similarly, the fine fibres of the posterior root which enter the zone of Lissauer often escape degeneration when it is already well marked in the medium fibres of the column of Burdach (fig. 17).

The tabetic degeneration would therefore appear

to be selective in character, unlike the Wallerian, which affects all indiscriminately, attacking in succession fibres and tracts of perhaps different functional significance. In this aspect it has been attempted to establish a relation between the tabetic degeneration and the fœtal differentiation of the various tracts which enter into the composition

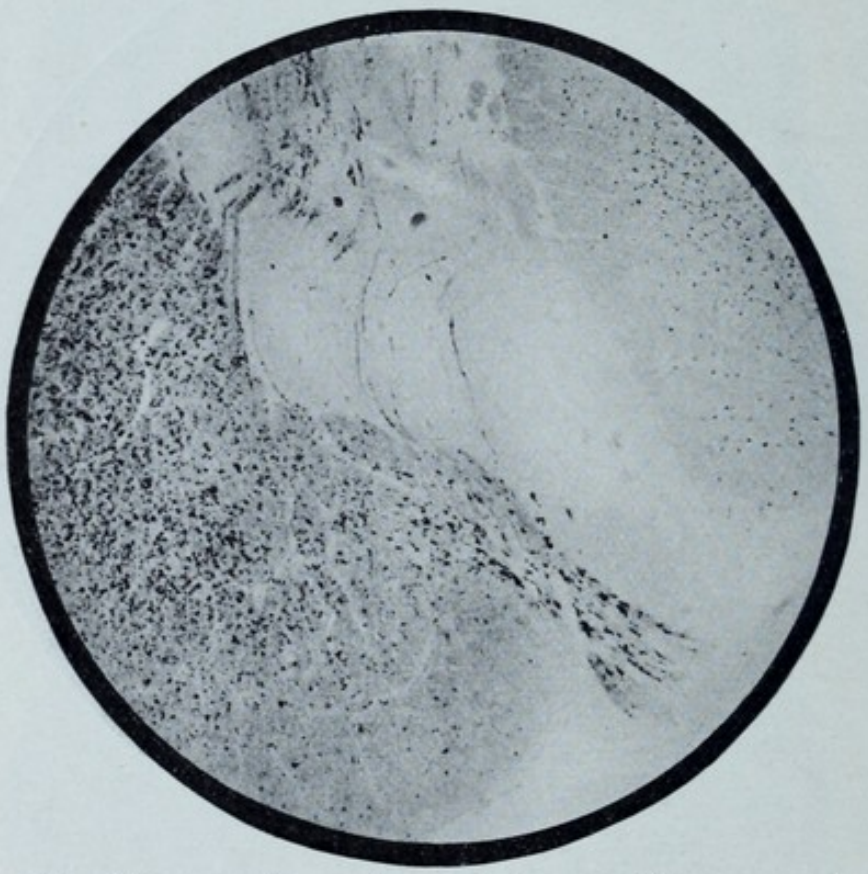


FIG. 17.—Degeneration of posterior root-fibres passing into posterior cornu. Lissauer's tract unaffacted (Orr and Rows).

of the posterior columns, as determined by the stage of development at which they respectively receive their myelin sheaths. Flechsig, by the myelinisation method, has divided the posterior columns into six main divisions, which receive their myelin sheaths at four successive stages of fœtal development. He thus divides the posterior columns into

an anterior, middle and posterior root zone; this, again, into a medial and a lateral. Added to these are Goll's column, and a mesial tract bounding the posterior median fissure. The first tract of fibres to myelinate—his anterior root-zone—corresponds with the cornu-commissural zone of Marie; the last to myelinate—his postero-lateral zone—corresponds with the zone of Lissauer. These various tracts constitute, according to Flechsig, elementary systems, and it has been assumed that they are composed of fibres of common functional significance. The researches of Trepinski, however, on the same subject, differ in many important respects from those of Flechsig; and there are many discrepancies between both and the results of secondary degeneration. Nor has it as yet been satisfactorily shown that the tabetic degeneration coincides precisely with any of the fœtal systems described by these authors. Further research, however, may clear up many doubtful points, for it is not improbable that the tabetic degeneration follows the lines of functionally different fibres, which myelinate at different stages of fœtal development.

The tabetic degeneration, so evident in the posterior columns and posterior roots, appears to stop short at the spinal ganglia. The sensory nerves distal to the ganglia have a normal appearance and normal structure. But not infrequently, as has been shown by Westphal, Pierret, Dejerine and others, the finer peripheral ramifications in the

skin, muscle, &c., undergo atrophy similar to that in the intramedullary terminations. Nor is the process limited to the spinal cord and the spinal nerves. The optic nerve is frequently affected, and occasionally, also, other cranial nerves. Degenerative changes have also been demonstrated in the ciliary ganglia and in the sympathetic nervous system, particularly in the cardiac plexus. These will be considered more in detail in connection with the physiological pathology of some of the more prominent symptoms of tabes.

If we now turn from the more gross anatomy of tabes and consider the intimate nature of the process, we find, according to the most modern research, that its essential character is a progressive dystrophy, or demyelinisation and ultimate destruction of the nerve fibres. The myelin sheath, as shown by the Marchi method, breaks up, becomes granular, and finally disappears (figs. 16 and 17). The appearances vary somewhat according to the acuteness of the process, but in general a proliferation of the neuroglia network occurs only in a proportion to the atrophy of the nerve tissue proper. There is no active hyperplasia of the neuroglia, and no vascular changes such as can be considered as the primary starting point of a sclerosis leading secondarily to atrophy of the nerve fibres. The Marchi method in the early stages of the process reveals the degeneration of the myelin long before proliferation of the neuroglia has occurred, and such sclerosis as ulti-

mately ensues is only what may be seen in any organ consecutive to degeneration of its true parenchyma.

The obvious relationship of the exogenous tracts of the spinal cord to the spinal ganglia—being, as it were, the central prolongations to the sensory neurons of which they are composed—naturally suggests that the cause of the progressive dystrophy of the posterior roots and their intramedullary terminations may be found in some morbid alteration of the cells of the spinal ganglia, the trophic centres of the fibres in question. For, as Marie remarks, it is difficult to believe that the branches of a neuron, whether central or peripheral, and performing the functions only of conductors, can undergo degeneration apart from that of the cell body which is their trophic centre. Therefore, in every case of degeneration of a nerve fibre, whether central or peripheral, the point first to investigate is the *cellule malade*.

Much research has been spent on this point, but the conclusions reached as to morbid changes in the spinal ganglia, or their constituent cells, have been far from harmonious. Gross changes, such as were described by Bourdon and Luys, are uniformly absent.

As regards the cells, Marie himself found in one case that they appeared less numerous than normal ; that some of them seemed to show signs of degeneration, and that there was distinct atrophy of a considerable number of the nerve fibres

traversing the ganglia. Some support has been given to Marie's view by the investigations of Wollenberg, Oppenheim and Siemerling, Stroebe,

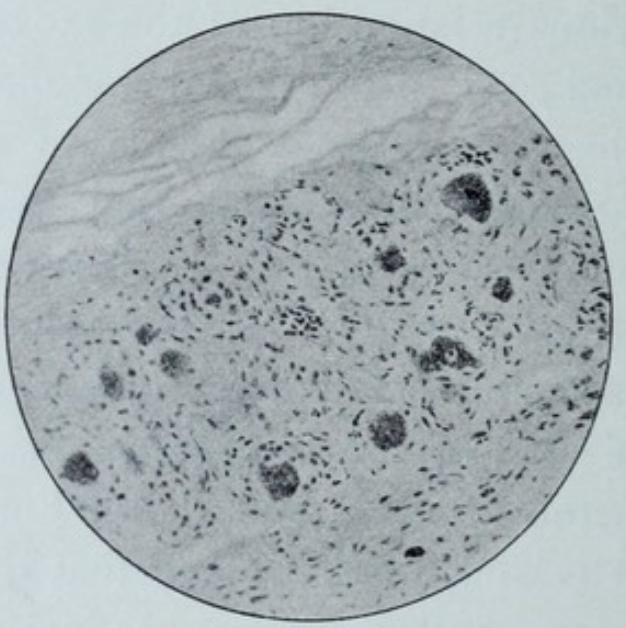


FIG. 18.

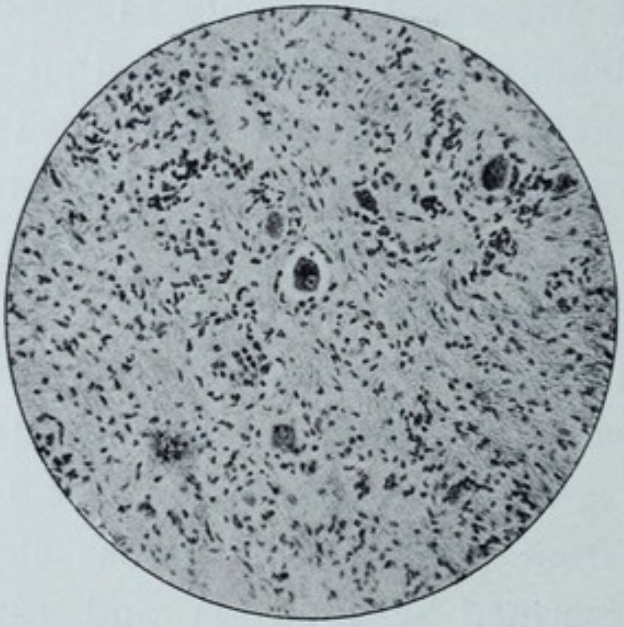


FIG. 19

FIGS. 18 and 19.—Sections of Spinal Ganglia in advanced cases of Tabes (Köster).

Redlich, Marinesco, Thomas and Hauser, &c.; but on the other hand, Schäffer, Juliusberger, Meyer, Mott and many others have found them practically normal.

The alterations which have been described by Wollenberg, Marinesco, and others who have obtained positive results, consist mainly in chromatolysis, pigmentation or fatty changes in the cells, occasional deformity or diminution in numbers, and increase of the connective-tissue elements. Köster, the most recent investigator on this subject, states that in the early stages of tabes he has observed appearances similar to those described by Wollenberg; but that in more advanced cases there are marked changes, such as chromatolysis, pigmentation, abnormalities in the nucleus, and distortion of the cells (figs. 18 and 19). They were similar to those resulting in course of time from experimental section of the posterior roots in animals (figs. 20 and 21).

It is therefore doubtful whether such changes as have been discovered in the spinal ganglia afford a sufficient anatomical substratum for the amount of degeneration, more particularly in the posterior roots and in their intramedullary terminals. And it is considered (Schmaus) a powerful argument against the spinal ganglion being regarded as the primary origin of the dystrophy, that the peripheral process, as it emerges from the distal pole of the ganglion, practically shows no abnormality (with the exception, perhaps, of some of its cutaneous terminals); while the central process, the posterior root, may be degenerated right into the ganglion itself. Whether these and other arguments are altogether valid against the primary ganglionic

origin of the tabetic process will be considered later, but it must be admitted that the anatomical changes hitherto actually demonstrated in the

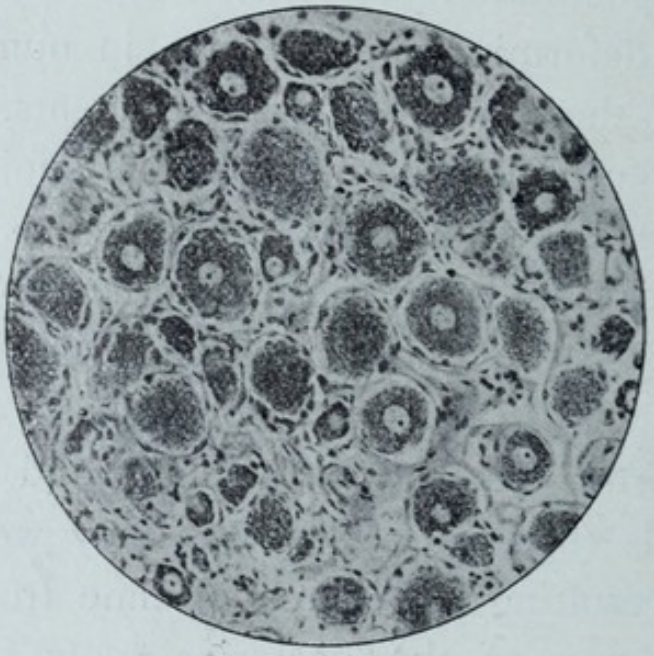


FIG. 20.—Section of normal Spinal Ganglion in Cat (Köster).

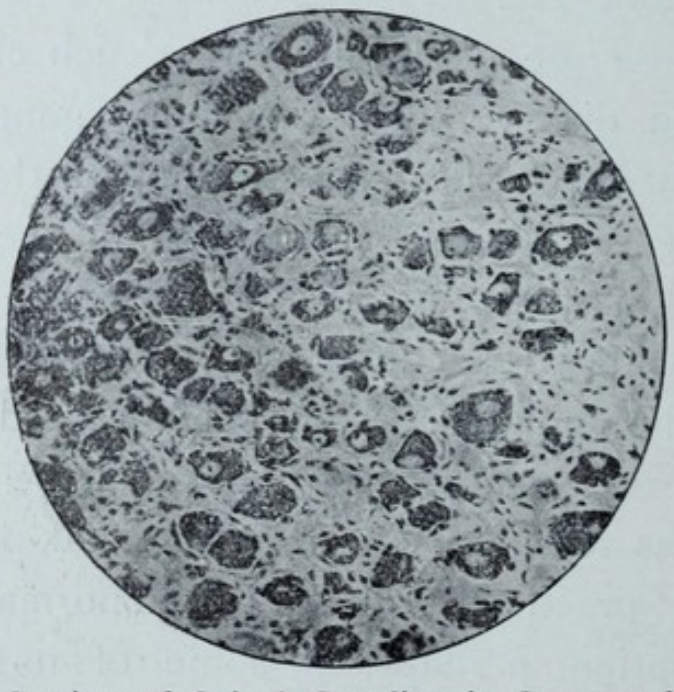


FIG. 21.—Section of Spinal Ganglion in Cat, one hundred and twenty days after division of posterior root (Köster).

ganglion cells are altogether incommensurate with the degree of degeneration of the processes (central

and peripheral) as compared with that observable in other forms of cell degeneration, such, for instance, as in the multipolar cells of the anterior cornua in atrophic spinal paralysis.

Instead of regarding the spinal ganglia as the primary origin of the degeneration of the posterior roots and exogenous medullary tracts, v. Leyden and Goldscheider are inclined to look upon the peripheral nerve endings, which not infrequently exhibit dystrophic or neuritic changes, and are naturally more exposed to traumatic influences, as more probably the starting-point of the process. It is known that after amputations and section of nerves, atrophy occurs in the posterior horns, posterior columns, and also in the anterior horns of the spinal cord. This is the form of degeneration termed retrograde, and is probably due to the cessation of the normal influences which serve to excite and maintain their functional activity. And it has been shown by Lugaro, Cassirer, and more recently by Warrington, that marked chromatolytic changes occur in the cells of the spinal ganglia on section of the sensory nerves, and of certain cells in particular, according to the kind of afferent nerve—muscular or cutaneous—which is divided. It is assumed, therefore, by the supporters of the peripheral origin of tabes, that changes, organic or functional, in the spinal ganglion cells may be induced by neuritic or other processes in the peripheral nerve endings, and thus secondarily lead to degeneration of the posterior

roots and posterior columns. It has not, however, been demonstrated that degeneration of the peripheral nerves always precedes that in the cord, nor has it been shown that such peripheral degeneration is a constant feature of the morbid anatomy of tabes, which it ought to be if the theory is at all well founded. Nor does it seem likely that neuritic or other degeneration, ascending from the periphery, can induce such dynamical or organic impairment of the ganglion cells as the theory postulates, without making itself evident at the point where the sensory nerves enter the ganglia. The peripheral theory of the pathogeny of the tabetic degeneration of the spinal cord has therefore to overcome many serious objections before it can be accepted as at all a satisfactory one.

Other pathologists are of opinion that they have discovered the origin of the tabetic process in inflammatory conditions of the meninges affecting the posterior roots. The theories of Nageotte, and of Redlich and Obersteiner, are the most important in this relation.

Nageotte, whose views have received a large amount of support, especially in France, has called attention to an anatomical disposition of the posterior roots which renders them peculiarly liable to noxious influences. Nageotte holds that in tabes there is a diffuse chronic meningitis which has all the characters of syphilitic origin—namely, infiltration with lymphocytes and plasma cells,

especially round the veins, a meningo-myelitic affection of the periphery of the cord, medulla, and even the cortex cerebri.

This general meningitis induces the degeneration characteristic of tabes by implicating the spinal roots at the point of their emergence from the dural sac. The anterior and posterior roots (fig. 22) after leaving the spinal cord traverse the

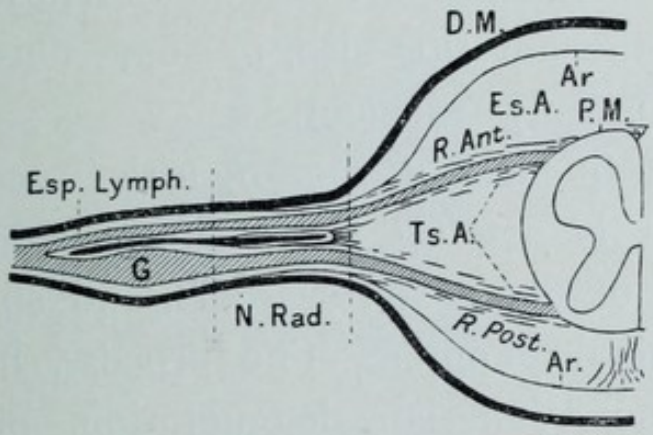


FIG. 22.—Diagram of Emergence of a Spinal Root from the Dural Sac (Nageotte). Ar. = arachnoid; D.M. = dura mater; Es.A. = sub-arachnoid space; Esp. Lymph. = lymphatic space; G. = spinal ganglion; N.Rad. = radicular nerve; P.M. = pia mater; R.Ant. = anterior root; R. Post = posterior root; Ts.A. = arachnoid tissue.

sub-arachnoid space, and at the point of exit from the dural sac receive a sheath both from the dura and arachnoid, which constitutes the peri-fascicular sheath of the roots, and beyond the ganglion the two roots unite to form the mixed nerve. The portion which lies between the ganglion and the dural sac, which varies in length in different regions, he terms the radicular nerve. The peri-fascicular sheath, derived from the dura and the arachnoid, divides the radicles into compartments, and the intra-fascicular tissue is continuous with

the pia mater. The lymphatic spaces of the radicles communicate with the subarachnoid space, and constitute a narrow and complicated channel between the great lymphatic sac and the efferent vessels. Owing to this disposition the radicles are specially liable to injury by meningeal inflammation and by toxins circulating in the cerebro-spinal fluid. Hence is developed a transverse interstitial neuritis, which specially affects the posterior radicles, and the anterior also, to some extent, which, however, is only transient.

In consequence of this neuritis, secondary degeneration is set up in the intramedullary continuations of the posterior roots, and spreads back to the spinal ganglia. The process, however, is not a true Wallerian degeneration, but a mere dystrophy, or lowered vitality, which affects more particularly the short and medium fibres of the posterior roots. In support of his views, he adduces the lymphocytosis of the cerebro-spinal fluid which occurs in tabes, to which I will call your attention presently. But in the meantime Nageotte's theory appears to offer such a simple explanation of the tabetic degeneration that it seems almost a pity to subject it to destructive criticism.

But it is open to the same objections as can be urged against the theory of Redlich and Obersteiner, in that the meningitis, which it postulates, is not a constant phenomenon, and is perhaps more frequently absent than present, and when it

exists is more often of the character of a secondary thickening than an inflammatory process. And further, it has been found in the early stages of tabes that the intramedullary degeneration is often well marked when the posterior roots exhibit no appreciable change and no indications of a local neuritis. The practical escape of the anterior roots is, I think, a fatal objection to Nageotte's

FIG. 23.—Points of entry of the posterior roots into the spinal cord (Redlich).

theory. That the neuritis which he also finds in the anterior radicle should be evanescent, while that of the posterior radicle leads to such profound intramedullary degeneration, is unintelligible; and is, moreover, opposed to the usual relatively greater affection of the motor than of the sensory fibres when neuritis attacks mixed nerves.

Redlich and Obersteiner maintain that at the

point where the posterior roots penetrate the pia mater there is a constriction which constitutes a *locus minoris resistentiae* (fig. 23), and that in consequence of meningeal inflammation and retraction of cicatrisation, as well as by thickening of the closely-adherent blood-vessels, the posterior roots become, as it were, strangled. Hence ensues degeneration in the intramedullary exogenous tracts, followed at a later stage by that of the posterior roots in a retrograde manner.

Redlich and Obersteiner's view has the merit of harmonising better with the more common starting-point of the tabetic degeneration than that of Nageotte, but, as has been remarked, the meningitis basis on which it rests is not very substantial. It is not universally present, nor is meningitis, syphilitic or otherwise, when it does occur, a common cause of intraspinal degeneration by implication of the posterior roots. That such a result is possible, and perhaps actually occurs in some cases, may be admitted, but it is extremely rare. The symmetrical and segmental character of the tabetic degenerations, which it would be difficult to correlate with any, so to speak, brutal meningeal inflammation, and the occurrence of degenerations elsewhere, such as in the optic nerve, ciliary ganglion, and sympathetic system, are all formidable arguments against the meningitic origin of tabes, whether at the point maintained by Nageotte or that of Redlich and Obersteiner.

But that the so-called "ring of Obersteiner" is a *locus minoris resistentiae*, or specially vulnerable point, in the course of the posterior root fibres, has been argued with much force by Orr and Rows in their memoir on the system lesions of the posterior columns in General Paralysis.

At this point the extramedullary fibres of the posterior roots lose their neurilemma sheath,

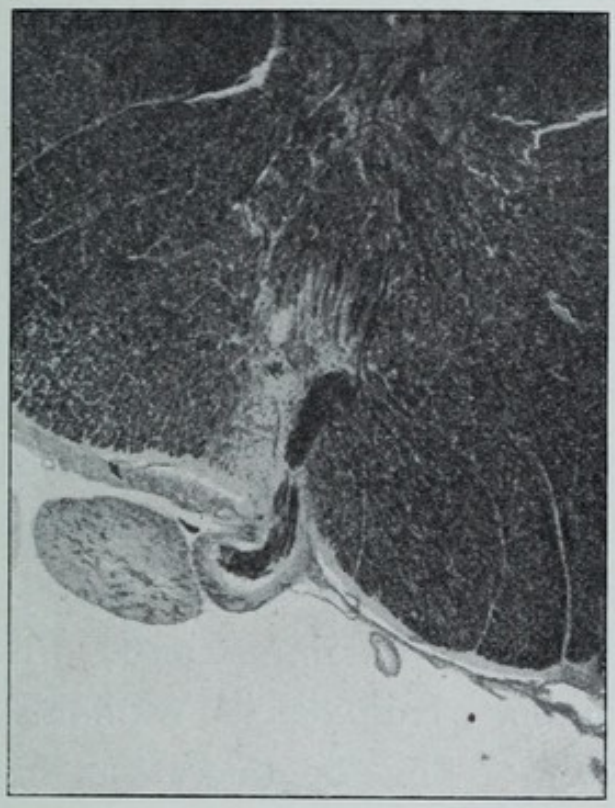


FIG. 24.—Entrance of posterior root into the cord, showing ring of Obersteiner (white band crossing posterior root). (After Orr and Rows.)

and the myeline sheath is also much thinned. That the absence of the neurilemma sheath renders the nerve more vulnerable is probable from the researches of Kennedy, Bethe, Ballance and Purves Stewart, which have demonstrated the importance of the neurilemma and its cells in the

nutrition and regeneration of nerves. These show that even in the distal segment of a divided nerve regeneration of the axis-cylinders and medullary sheaths take place, although the full maturity of the new nerve fibres is not attained until union of the proximal and distal segments occurs, and the fibres become functionally continuous with each other. This regeneration is dependent on the cells of the neurilemma sheath. Where these are absent, as in the intraspinal fibres, regeneration does not occur; and it is probable, therefore, that the absence of the neurilemma cells is the cause of the greater proclivity to degeneration of the intramedullary terminals than of the other branches of the sensory protoneurone in the tabetic dystrophy.

It has been shown also that degeneration of the intramedullary root fibres, similar to those of tabes, may occur in the course of cerebral tumours, diabetes, anæmia, and other cachetic states (Homén, Nageotte, Williamson, Bruce, Erbsloh, &c.). The degeneration extends from Obersteiner's ring into the reflex collaterals and fibres passing into Clarke's columns. Whether it begins first in the terminal fibres, and gradually extends backwards, or *vice versâ*, is the subject of some difference of opinion. Orr and Rows hold that it commences at Obersteiner's ring and extends inwards; while Nageotte considers that the terminal fibres of the reflex collaterals and those of Clarke's columns are first affected. The

more recent investigations of Spielmeyer, by means of Cajal's new axis-cylinder stain, are in favour of the view that the terminal fibres which arboresce around the cells of Clarke's columns, as well as those of the posterior column nuclei, first show signs of degeneration. This is followed by glia proliferation in proportion to the destruction of the nerve filaments.

Whether we regard the intramedullary degeneration as centripetal or centrifugal, or more probably simultaneous, it is clear that this portion of the posterior root is more liable to show signs of impaired nutrition at an early stage than either the extramedullary portion or the cells of the spinal ganglia. Some conditions probably exist favouring the incidence of noxious influences on this portion of the sensory protoneurone. In this connection Marie and Guillain have laid great stress on the peculiarities of the lymph circulation in the posterior columns of the spinal cord. They maintain that in the pia mater of the posterior columns, between the outer and inner layer, there exists a lymphatic system, the spaces of which communicate with those of the posterior columns, but are independent of those of the antero-lateral columns. In this system the current of lymph is upwards and towards the central canal. In tabes they have found this system dilated, and (by the Marchi method) black granules in the cells of the ependyma in cases where the central canal is permeable. They

attribute the tabetic degeneration to a syphilitic affection of the posterior lymphatics, and derive the lymphocytosis of cerebrospinal fluid from the elements of this system.

That noxious substances or toxins originating in the periphery ascend to the spinal cord more readily by the posterior than by the anterior roots has been shown by Homén, and also by Orr and Rows; and that in this way, or by peculiarities in the lymphatic circulation in the cord, the posterior roots and posterior columns are specially exposed to injury is extremely probable. But that there is in tabes a posterior meningitis of a syphilitic character, as maintained by Marie and Guillain, is not generally admitted. It is not supported by the results of anti-specific treatment, nor can the lymphocytosis of the cerebro-spinal fluid be adduced as a conclusive argument in its favour.

Lecture II.

In health the centrifugalized deposit from the cerebro-spinal fluid contains scarcely any cellular elements beyond an occasional endothelial cell and perhaps one to three lymphocytes in a field, with a magnification of 400 diameters (fig. 25).

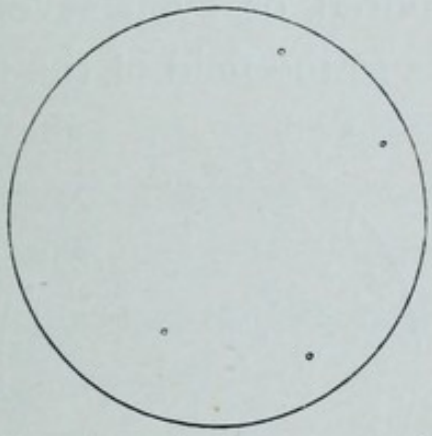


Fig. 25. — Centrifuge deposit from normal cerebro-spinal fluid (Purves Stewart).

In certain diseases the cellular elements are present in excess. In acute microbic affections of the cerebro-spinal meninges, as by staphylococcus, pneumococcus, and diplococcus intracellularis, a leucocytosis occurs, in which the leucocytes are of the polynuclear type. On the other hand, in certain chronic affections of the meninges, syphilitic, tuberculous, &c., an excess of leucocytes also occurs. These are of the mononuclear type ; in other words there is a lymphocytosis. It has been shown by Widal, Sicard, Ravaut, and others—and their observations have been confirmed by my own and

Purves Stewart's investigations—that in tabes, as well as in general paralysis of the insane, from the earliest to the latest stages there is a marked lymphocytosis of the cerebro-spinal fluid. I have in several instances relied on this lymphocytosis as establishing the diagnosis of general paralysis before there were any abnormalities of the pupils or other physical signs characteristic of the disease. In a case of tabes or general paralysis, instead of two or three, as in the normal state, one may count a hundred, or even several hundred (fig. 26) lymphocytes in the field of the microscope. At

FIG. 26.—Centrifuge deposit from cerebro-spinal fluid in tabes (Purves Stewart).

first sight this lymphocytosis would seem to confirm the views of those who ascribe the disease to a syphilitic affection of the meninges, either generally, or of Nageotte's meningeal root sheath, or of the posterior lymphatic system of the spinal cord, as maintained by Marie and Guillain. But lymphocytosis occurs in other affections in which meningitis, syphilitic or otherwise, plays no part. Thus it has been found in Landry's paralysis, in the subacute

combined degeneration of pernicious anæmia (Purves Stewart), and in herpes zoster (Sicard). Lymphocytosis cannot, therefore, be regarded as pathognomonic of meningeal inflammation, though no doubt meningeal inflammation would accentuate it. But the most powerful argument against the syphilomeningeal origin of the lymphocytosis in tabes and general paralysis, is the fact that it does not yield in the slightest degree to the most energetic antisyphilitic treatment (Milian, Purves Stewart). In active syphilitic lesions of the nervous system, however, the lymphocytosis that may be present tends to disappear in the course of treatment. Thus in a case of syphilitic paraplegia, under the care of Purves Stewart, the lymphocytes after a month's antispecific treatment had decreased from 52·6 to 16·1 per field, and the symptoms had become greatly ameliorated (figs. 27 and 28).

Having thus passed in review the different theories which have been advanced in reference to the pathogeny of the tabetic degeneration, we have seen that there is not one which is not open to several more or less serious objections.

Instead of attempting to be more precise than the facts permit, I am inclined to adopt the hypothesis of Thomas and Hauser, that the essential lesion of tabes is a dystrophy, similar to that induced by certain toxic agents, affecting the sensory protoneurone as a whole, and manifesting itself in degeneration of the peripheral and central terminations, of which the intramedullary are the more

vulnerable, and are usually the earliest to exhibit anatomical change. The process, however, is not confined to the spinal protoneurone, but may affect among others the optic, the sympathetic, and certain motor neurones.

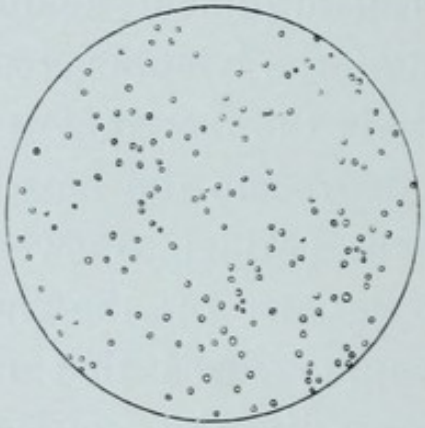


FIG. 27.—Deposit from cerebro-spinal fluid in a case of syphilitic paraplegia (Purves Stewart).

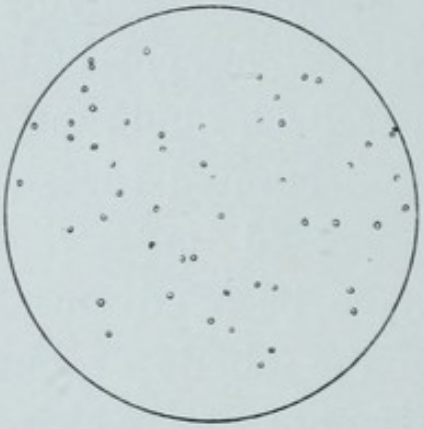


FIG. 28.—The same case as fig. 27, after three weeks anti-syphilitic treatment.

And here I would express, in concurrence with Fournier, Mott, and many other neuro-pathologists of the present day, my belief in the essential pathological identity of tabes and general paralysis. They are, in my opinion, merely different aspects of the same polymorphic disease. One cannot say that they are the same disease so far as their

clinical manifestations and course are concerned, any more than one would say that tuberculous meningitis and pulmonary consumption are the same. But the morbid process underlying both is identical.

Both are tabetic or wasting affections—of the sensory protoneurone in the one case, and of the cortical neurones in the other. The essential etiological factor is, as we shall see, the same, and the date of development of the two affections after the primary infection corresponds. No blind or crude primary meningeal inflammation could selectively attack only such regions—the fronto-parietal by preference—as exhibit the atrophic cortex and adherent lepto-meninges characteristic of general paralysis.

The primary lesion in general paralysis, as in tabes, is a dystrophy of the neurones and their connections; the sclerosis, thickening of the membranes and walls of the blood-vessels, being only a secondary result of the parenchymatous degeneration.

Not infrequently tabes and general paralysis are combined, or succeed each other, in the same individual. Clinically, some of the characteristic signs, notably the Argyll-Robertson pupil, are common to both, and in both there is the same cerebro-spinal lymphocytosis.

It would, in my opinion, conduce to a truer conception of the pathology of these affections if we were to call them both by the generic name

"tabes," classifying them specifically as Cerebral Tabes (general paralysis), Spinal Tabes (tabes dorsalis, locomotor ataxy), and Cerebro-spinal Tabes (so-called tabo-paralysis), according as the disease affects the brain, or spinal cord, or both conjointly.

Etiology of Tabes.

Up to 1876, when Fournier first pointed out the great frequency of antecedent syphilitic infection in tabes and indicated their probable causal relationship, tabes was most commonly attributed to sexual excess, or to the complex of injurious influences associated with exposure to cold. The supposed causal relationship between sexual excess and tabes was probably only a *damnosa hereditas* from the tabes dorsalis or sexual neurasthenia of the Hippocratic writers.

Sexual excess, like all other debilitating influences, may be placed among the exciting causes, and many tabetics have probably exhausted themselves in this way; but the influence of sexual excess in the causation of tabes has been greatly over-estimated, and if that were the only cause, the disease would certainly be much more common than it is.

Similarly as regards cold or damp cold, which Romberg thought, and which is still regarded by v. Leyden as one of the principle causes of tabes, this view is probably founded more on the patient's belief that his tabetic pains are rheumatic in character, and that he must have caught a chill,

slept in a damp bed, or the like, than on any more substantial basis. When we consider how often, when our etiology is at fault—not only in respect of the diseases of the nervous system, but many others—it has been the custom to fall back upon exposure to cold as the probable cause, afterwards proved insufficient, we may, without undue depreciation, call it the last refuge of destitute etiology. Like sexual excess, exposure to cold and damp would, without doubt, have an injurious influence, and probably excite or intensify tabetic symptoms already incipient, so that the patient might have some grounds for ascribing his malady to this cause. But that exposure to cold by itself is a sufficient cause of tabes is, in my opinion, a mere vague assertion, supported by no accurate data, and at variance with one's daily clinical experience. A history of exposure to cold is not found more frequently in tabes than in many other affections of the nervous system.

Fournier's views as to the causal relationship between syphilis and tabes were at first received with scepticism, not to say strong opposition, in many quarters; and the frequency of antecedent syphilitic infection in the personal history of the tabetic was not regarded as more than might be found in other forms of disease of the nervous system. But Fournier's views soon gained powerful support, among the first by Gowers in this country and by Erb in Germany; and Erb, who at one time (1878) was a strenuous opponent, is now

perhaps the most eminent advocate of the syphilitic origin of tabes. It is now so generally admitted by neuro-pathologists, with some few notable exceptions, such as v. Leyden, that syphilis is the principle cause of tabes, that it seems unnecessary to quote the data on which this opinion is based. But as the elimination of cause and effect depends for the present mainly on the statistical method, and as this is liable to many fallacies depending on the personal equation of the observers and the material dealt with, it will be sufficient to state the results obtained by Erb, whose probably unequalled experience and laborious inquiries, carried out with systematic uniformity, invest his inductions with exceptional value.

In the most recent of his numerous contributions on this question, Erb states that among 1,100 cases of tabes occurring in his own practice among men of the better class, and therefore better witnesses than those living among poor and squalid surroundings, 89·45 per cent., or practically 90 per cent., had had chancre or syphilis; and only 10·54 per cent., or practically 10 per cent., had not been ostensibly infected. But of these, in only 3 per cent. was it impossible to find any ground for suspecting an antecedent syphilitic infection.

Now contrast these statistics, obtained from 1,100 tabetics, with those of 10,000 cases, also of men of the better class, of all varieties of disease, excluding tabes. Of these, only 21·5 per cent. had had syphilis, as against 89·5 per cent. among the

tabetics, that is, that syphilis was found 4·5 times more frequently among tabetics than among other patients. Similar investigations among 138 tabetic men of the lower orders give a somewhat lower percentage of antecedent syphilis, namely, 77·2 per cent.; but among 1,300 non-tabetics only 6·54 had had syphilis, as against 93·46 non-infected.

Among women, who are less liable to tabes than men, and those of the better class less so than those of the lower orders, it is, for various reasons, much more difficult to determine the question of syphilitic infection. But Erb found that among 15 tabetic women of the better class, at least 86·7 per cent., and probably 93·3 per cent., had been infected. Among 16 women of the lower orders, however, syphilis was probable in only 68·7 per cent., and unproved in 31·3 per cent.

Taken altogether, a statistical inquiry among 1,321 cases—namely, 1,100 men of the better class, gives 89·5 infected; among 158 men of the lower class, 77·2 per cent.; and among 63 women, 80 per cent. as probably infected. Essentially the same is true of general paralysis.

So far for mere statistics, the general result being that in about 10 per cent. of the cases syphilis is unproved. These 10 per cent., however, constitute the pivot round which the essential question turns, whether tabes, like diphtheria or tuberculosis, is always due to a specific infection, or whether it may result from some other cause. This is not a mere academic question, but one of far-reaching practical

importance. Can we, in the present state of our knowledge, give a definite, or approximately definite, answer to it?

We may, perhaps, do so by taking other facts into consideration besides mere percentages.

It has been established, and is generally recognized, that tabes frequently follows syphilitic infection of a mild type, and therefore more likely to escape notice, particularly among those in whom personal cleanliness is not a cardinal virtue. And syphilis ignota or occulta is familiar to syphilologists and dermatologists.

Some noteworthy investigations on this point have been made by Hirschl, the results of which are worth quoting. He found that, of 63 patients suffering from gummatous affections of indubitable syphilitic origin, in only 54 per cent. was there a certain history of syphilis; in 9·5 per cent. it was probable; while in 36·6 per cent. no evidence, other than the patient's actual state,-was forthcoming of syphilis, hereditary or acquired. Practically the same results were obtained by him in reference to general paralysis.

Similar statistics to those obtained by him in reference to syphilis and tabes have been quoted by Gowers as having been arrived at by Dr. Pernet of University College Hospital in reference to syphilitic affections of the skin. Syphilis could only be proved in 80 per cent. of the cases.

One may therefore say with justice that the syphilitic origin of tabes and general paralysis is

statistically just as well proved as that of gummatous affections of the skin.

Apart from juvenile tabes, which is always syphilitic, hereditary or acquired, and which affects both sexes in the same proportion, tabes occurs most commonly among men of from 30 to 40 years of age, and on the average from seven to ten years after the primary syphilitic affection. There are, however, exceptions to this rule, and I have seen it develop in a man of 70, some forty to fifty years after infection with syphilis; and there is a case on record (Berger) of a man of 74 becoming tabetic after syphilitic infection at the age of 70.

Tabes at from 30 to 40 is a significant harvest of the wild oats sown some ten years previously, and the classes who sow wild oats most freely are those who reap tabes most abundantly. Townspeople furnish more cases of tabes than those who live in the country; and great centres of population with their greater risks and temptations more than the smaller. Tabes and general paralysis are rare among priests, and of these only such as have had syphilis, or exposed themselves to it (Bouchard).

Tabes is less common among women of the better class than among those of the lower—doubtless, as Moebius has suggested, owing to the fact that men of the better class less frequently marry while still suffering from infective syphilis.

But conjugal tabes is not uncommon, and most neurologists have seen examples. Among others, Mott has given several interesting illustrations.

Almost without exception there has been syphilitic infection (90 to 96 per cent., Hudovernig) on one side or the other; usually the husband has infected the wife. Nonne has related a very remarkable family history. A child of 5 was infected with syphilis through sleeping with a syphilitic bedfellow. At 18 he became tabetic. The child infected the mother, and the mother the father. Both these became tabetic. In another family, described by Souques (quoted by Erb), the father was syphilitic and became a general paralytic; the mother became tabetic, and two young daughters also showed signs of tabes—four in one family. Many similar cases might be quoted in detail, but it is unnecessary to multiply them. Syphilis, acquired or hereditary, was the common factor in all.

And the question has been mooted (Lavalle, Moebius, Erb) whether there may not be a form of the syphilitic virus falling with special incidence on the spinal and cerebral centres, and leading in due course to tabes or general paralysis. Thus Brosius relates the remarkable history of seven glass-blowers who were infected in the mouth from the same source in 1891. All were treated for syphilis and dismissed as cured after a few weeks of anti-specific treatment. In 1902, that is, after eleven years, five of them came under his observation again. One was tabetic; the second had signs of general paralysis; the third was already a marked general paralytic; the fourth had Argyll-Robertson pupils, and indications of so-called

tabo-paralysis; while the fifth, at the time of examination, was still in good health. The other two had not been traced. The only common factor in all these cases was the syphilitic infection.

It has been shown by Krafft-Ebing that general paralytics are insusceptible to inoculation by the syphilitic virus. This is a negative fact of great significance, and of much more importance than if the converse were true, for re-infection is always a possibility. Whether the same holds in respect to tabetics has not, so far as I know, been yet demonstrated, but it is more than probable. Who has ever seen a tabetic with a primary sore, or even with secondary symptoms? A considerable number, both during life and after death, exhibit tertiary manifestations, or traces of antecedent syphilitic lesions. But these date from the infection which preceded the tabes. Yet it cannot be said that tabetics do not run the risk of re-infection, for it is notorious that in the pre-ataxic stage tabetics frequently exhibit excessive erotic propensities, and expose themselves freely to the possibility of acquiring syphilis.

Female children apart, tabetic *virgines intactæ* are *raræ aves*. They are, however, not unknown. Of two of whom I have read, the one (reported by Nonne) was a tabetic girl of twenty, infected in infancy by her mother suckling a syphilitic foster-child at the same time; the other (described by Erb), a virgin of 36, who, some time previously, had had a chancre on her lip.

One might multiply arguments in favour of the causal relation between syphilis and tabes, but they are unnecessary. For those above related, singly and collectively, leave, in my opinion, little room for doubt that tabes and general paralysis are in all cases syphilitic, and that tabes *per se* is as much a proof of syphilis as a gumma of the skin. Those who may be still unconvinced, and seek a more positive sign, will probably have to wait till in some pathological laboratory a monkey will be exhibited, inoculated with a virus of syphilitic origin (a product perhaps of the *spirochæta pallida*), showing Argyll-Robertson pupils and loss of knee-jerks; and the question of the syphilitic origin of tabes will be solved by the walk of a tabetic chimpanzee!

It has been urged by v. Leyden and Goldscheider as an argument against the syphilitic origin of tabes, that the disease is rare among prostitutes, among whom, nevertheless, syphilis is rife. But it must be remembered that tabes is less common among women than men; and one must also take into account the fact that as tabes is a late manifestation of syphilis, it is not to be expected among those who are still young enough to ply their wretched calling. This accords with the statistics of Kron, who, though he found no case of tabes among 148 young prostitutes, yet among 36 prostitutes over 25 years of age found 5—a large percentage enough.

Similarly it has been contended that in certain countries and among certain races tabes is rare,

though syphilis is common. Thus it has been asserted that in Bosnia and Herzegovina, in Japan, in Abyssinia, among the Arabs, and among negroes, tabes does not occur. But more accurate investigations have proved this assertion to be unfounded. For tabes is common enough in Japan (Nose); it is not unknown in Bosnia and Herzegovina; it is as common in Abyssinia as in Vienna (v. Halban); and it certainly occurs among negroes (Collins, Hecht).

It may not be so common among primitive races as among those more advanced in civilisation and all that this connotes, but this is not the point. The fact that tabes only occurs where infection with syphilis is possible, is the essential point in this relation.

If tabes can be shown to exist, or to have existed, in any land or people among whom syphilis has never entered, and who have never had communication with any outside syphilised world, the exclusively syphilitic origin of tabes will have to be abandoned, but not till then.

The relative infrequency of tabes among those who have suffered from syphilis—it has been variously calculated at from 1 to 5 per cent. of the whole—is no argument against the syphilitic origin of tabes. For there are many affections due to syphilis, such as aortitis, hepatitis and orchitis, which are relatively rare. And as Erb remarks, the fact that perhaps only 1 in 10,000 of those infected with tubercle suffers from Addison's disease

does not disprove the tuberculous nature of the affection of the suprarenal capsules. But the smallness of the percentage, as well as other considerations, suggest that, in addition to syphilis, there may be some predisposing or other co-operating causes determining the incidence of the syphilitic virus on the nervous system, and the development of tabes either of the brain or spinal cord, or both.

Heredity, as such, plays no part in the etiology of tabes, though, as we have seen, juvenile tabes indicates a syphilitic inheritance.

Mention has already been made of sexual excess and cold, to which great, but as we have seen undue, prominence has been assigned by certain pathologists. The same may be said of neuropathic inheritance, to which great importance was attached by Charcot. It is not more frequent in tabes than in other forms of nervous disease. Some facts, however, suggest that certain families are specially prone to develop tabes ; and several instances might be quoted of more than one member of the same family becoming the subject either of tabes or of general paralysis, after acquiring syphilis.

Certain malformations, or developmental anomalies, such as heteropia spinalis, have been recorded by several observers (Mott, Orr and Rows, Rebizzi) in the spinal cord of those affected by tabes or general paralysis. All these have, no doubt, their significance, but they are by no means constant nor are they even common.

The view that the substratum of tabes lies in some defect of development, or vice of inheritance, which predisposes to premature decay of the essential elements of a highly specialised tissue, and reversion to those of a lower type, so that certain individuals are, as it were, predestined to tabes, reaches its culmination in Benedikt's burlesque, *Tabicus nascitur : non fit !* No one who has had experience of tabes in all ranks, and has seen among its victims numbers of men of the most healthy stock and vigorous physique, can regard it otherwise than a gross libel to speak of tabetics in general as being "connective-tissue individuals" (Bindegewebs-individuen) or "degenerates" in any true sense of the term.

Among other exciting causes of tabes, injuries have been blamed, and many cases of so-called traumatic tabes have been put on record. There is no doubt that in certain instances—perhaps 5 per cent.—tabetic symptoms have first made themselves manifest after injuries of the spine or other parts of the body, and the limb injured has not infrequently been the primary, or principal, seat of the characteristic pains; but a critical examination of such cases by Hitzig and others has failed to substantiate the efficacy of trauma as a cause of tabes independently of antecedent syphilitic affection.

Of greater importance, perhaps, than any of the above-mentioned exciting or co-operating causes of the tabetic degeneration is the influence of over-

strain, or of over-exertion in debilitated states of the system. The principle underlying these degenerations is that the normal equilibrium between waste and repair which characterises health is disturbed, and that in consequence of the process of waste exceeding that of repair the neurons, especially those most engaged, tend to break down and show dystrophic change. Edinger and Helbing found that in rats artificially rendered anæmic, which had been compelled to work in a treadmill, or, by other device, to engage in long-continued muscular exertion, the posterior roots and posterior columns of the spinal cord exhibited degenerations similar to those of tabes.

These facts are suggestive, and appear to harmonise well with the views of those who regard fatigue and over-exertion as the most important causes of tabes. As co-operative causes certainly, but not apart from syphilis; for the same degree of fatigue and over-exertion which may excite tabes in one in whom the soil is already prepared by syphilis, may be borne by thousands of others without material damage.

Edinger's "compensation theory" (Ersatztheorie) seems also to afford a plausible explanation of the incidence of the affection in the parts most subjected to continuous strain, the most common being the sensory apparatus concerned in co-ordinated locomotion and maintenance of equilibrium. Occasionally, however, as in cervical tabes, the arms, for similar reasons, are more especially

affected; and the pupils and optic nerves would in like manner probably suffer more readily than any of the other organs of special sense.

So also muscular atrophies would be more prone to occur in the muscles which are most taxed, similar to the occupation-muscular atrophies of blacksmiths, railway porters, and the like. Probably the same principle may serve to explain the incidence of the tabetic degeneration in one case on the brain, and in another on the spinal cord. Raymond has related an interesting narrative of two brothers, similarly constituted by inheritance, who both became infected by syphilis about the same age. The one who lived a fast life and indulged in sexual excess became a tabetic; the other who exhausted his brain in the struggle for existence, became a general paralytic. Facts like these are of eloquent significance.

The sensory neurones and posterior columns of the spinal cord appear to be specially vulnerable to certain toxic agents. Whether this can be explained on evolutional or developmental principles; or more mechanically by peculiarities in the lymph circulation in the posterior roots and posterior columns; or by an elective affinity of certain poisons for special structures, such as nicotine for the cells of the sympathetic ganglia, is a question for the future. But degenerations similar to those of tabes have been shown to occur from poisons introduced from without or generated within, as well as in the course of cerebral tumours, in some more obscure manner.

In the great epidemic of ergotism which occurred in Hesse in 1880, Tuczek observed many cases of so-called ergotin tabes, in which, following the preliminary acute gastric and other constitutional disturbances, paræsthesiæ and ataxic symptoms set in, sometimes several months after the ingestion of the poison. Occasionally there was a tendency to relapse, even when no further use was made of the poisonous grain in the dietary. These ataxic and sensory symptoms were found to coincide with degenerative changes in the posterior roots and posterior columns similar to those of tabes, differing only in their acute course and in the absence of sclerotic shrinkage. Lissauer's zones, however, remained intact, and there were no pupillary symptoms.

Somewhat similar degenerations, but less strictly confined to the posterior columns, have been observed in pellagra, endemic in certain districts, especially in Northern Italy, and due to the consumption of poisonous maize. The degenerations in this case affect not only the posterior columns, particularly that of Goll, but also the antero-lateral and pyramidal tracts. The exact nature and localisation of these degenerations are, however, not as yet precisely determined.

So also in lathyrism, caused by the seeds of the *lathyrus sativus*, degenerations occur in the spinal cord; and a large number of inorganic poisons, which specially cause peripheral neuritis, also occasionally lead to degeneration of the posterior roots

and posterior columns, such as alcohol, lead, arsenic, and some others.

Many of the organisms which are the cause of certain epidemic and endemic diseases, such as those of diphtheria, beri-beri, and lepra, generate toxins which not only induce multiple neuritis, but also in some instances degeneration in the posterior roots and in their intra-medullary processes and collaterals. Whether these degenerations are primary or secondary to the peripheral neuritic processes, or whether the two are simultaneous, is a question on which it is impossible at present to pronounce definitely. Further—and perhaps of greater significance—in reference to the pathogeny of tabes, it has been shown that in certain cachectic states of the system such as pernicious anæmia (Lichtheim, Minnich, &c.), and diabetes (Fischer, Williamson), probably by the autochthonous development of toxins, degenerations occur in the spinal cord, especially in the intramedullary processes of the posterior roots, and tabetic-like symptoms ensue in the form of paræsthesiæ, pains, and ataxic disorders; but however much these toxic affections resemble tabes, they are in reality only pseudo-tabetic, and none of them conforms in its clinical history, course, and termination to tabes properly so-called. Though weeks, or even months, may elapse before the poisons introduced into the system, or engendered in it by the specific organisms, produce their deleterious effect on the nerves and nerve centres, and though relapses may occur, there

is a direct continuity between the introduction of the poison and the development of the symptoms, which run their course, and cease when the virus is exhausted. In none of them do years elapse between the original infection and the commencement of the symptoms, and none has the progressive character of true tabes. In none of them do the children suffer like the juvenile tabetics, "who have their teeth set on edge because their fathers have eaten the sour grapes" of syphilis.

The similarity, however, between the degenerations caused by these poisons and those of tabes, strongly support the hypothesis, originally advanced by Strümpell, that the tabetic degeneration is due to the action of a toxin of syphilitic origin. The tabetic degeneration is, as we have seen, a parenchymatous dystrophy, and has none of the features usually considered characteristic of tertiary syphilitic lesions. There are no cellular infiltrations; no specific vascular or gummatous changes; and it does not yield to the usual antispecific remedies. Hence it has been customary to term the lesions of tabes parasyphilitic (Fournier) or metasyphilitic (Moebius) manifestations. It may be said, however, that this is a mere *petitio principii* and that we have no certain criterion of what constitutes a syphilitic lesion. The *spirochaeta pallida* has not yet been shown to be present in tertiary syphilis. But, in any case, it would be incorrect to term a state of abiotrophy (Gowers), or defective nutrition, a positive lesion. For this reason Lesser's term, quartary

syphilis, however appropriate to certain late manifestations of syphilis in the liver and other organs, is not strictly applicable to a condition in which parenchymatous dystrophy precedes the development of the sclerotic process.

The most probable pathogeny of the tabetic degeneration, therefore, is that it is the result of a toxin generated or conditioned by the syphilitic virus. But this is at present a pure hypothesis, and one which has to surmount great difficulties. Even if, like the diphtherial neurotoxin, it may be the product of the action of the specific organism on the proteids of the body, or set free in the elaboration of protective antitoxins, that it should take so long to develop, or lie dormant for so many years before exhibiting any signs of activity, is unlike anything that we know of organismal toxins. There is no parasyphilitic or metasyphilitic cerebro-spinal lymphocytosis as such, apart from the commencement of the tabetic process, and this is a fact of great importance. Purves Stewart, who has made investigations for me on this point in a series of 12 cases, found that the average number of lymphocytes in the centrifuge deposit of the cerebrospinal fluid in secondary syphilis was 2·7, while in tertiary syphilis it was 0·9, or not more than the normal. The tertiary cases with active cutaneous lesions in progress had more lymphocytes than the others, but even these were less than the average of the secondary cases. The lowest count in tabes, however, was 45. Most were between 80 and 100

while the highest was 316 in the same relative field.

Even if we were to consider it possible that there might be long years of apparently normal health, in spite of the presence of some malignant toxin in the system, we have to reckon with the fact that the tabetic process, once begun, is essentially of a progressive nature, and postulates a more or less continuous generation of the poison.

In this relation mention may be made of the researches of Ford Robertson, McRae, and Shennan. These observers found a bacillus, closely resembling the Klebs-Loeffler bacillus of diphtheria, in cultures from the walls of the respiratory, gastro-intestinal, and genito-urinary tracts of patients dying from general paralysis, and from the genito-urinary tracts of general paralytics and tabetics during life. Rats fed on broth cultures of this diphtheroid bacillus became ill after some weeks, and when killed, showed in addition to signs of gastro-enteritis, acute degenerative changes in the cortex cerebri resembling to some extent those of general paralysis, as well as degenerative changes in the cells of the spinal cord. These observations are of much interest, but a definite causal relationship between this bacillus and tabes, or general paralysis is far from being established. For the same bacillus was found by them in the genito-urinary tract in ten out of fourteen patients suffering from forms of insanity other than general paralysis.

I had written the above before Dr. Ford Robertson had delivered his Morisonian Lectures on The Pathology of General Paralysis, now in course of publication, and I am indebted to him for allowing me to read the MS. of those as yet unpublished, and to examine some of his microscopical preparations. He holds that general paralysis is the result of a bacterial toxic infection from the respiratory and alimentary tracts, owing to the impairment of the resisting power of the organism by syphilis, alcoholism, or the excessive use of nitrogenous foods. The bacillus has the cultural and morphological features, and reaction to Neisser's stain, of the Klebs-Loeffler bacillus, of which it is an attenuated or more probably a special form, to which he gives the name—*bacillus paralyticans*. The bacillus is polymorphic, and among other characters which distinguish it from the xerosis bacillus and Hoffmann's bacillus, is its power of forming acid when cultivated in glucose broth.

The leucocytes of the blood of the general paralytic, he maintains, have a greater dissolving power over those bacilli than those of normal blood, and the serum is also more lysogenic.

These diphtheroid baciili, more or less altered by lysogenic action, have been found by him and his colleagues in the catarrhal pneumonic foci of general paralytics, in the adventitial spaces of the cerebral vessels, and in the meshes of the pia arachnoid. They have also been found in the blood, in the centrifuge of the cerebro-spinal fluid,

and in the urine of the general paralytics, especially during congestive attacks. From these fluids cultures of the bacilli have been obtained, when sufficient time has been allowed to destroy the phagocytic or lysogenic action of the blood. Rats infected or fed with cultures of these bacilli showed changes in the cerebral cortex suggestive of those of general paralysis, and similar appearances were also found in a goat which had ingested them.

Robertson considers that in general paralysis there is a life and death struggle between the leucocytes and the diphtheroid bacilli, in which the leucocytes succumb. There is a bacillary invasion. Most of those which reach the blood are digested, but many escape from the circulation, either through the capillaries of the kidneys, or through the walls of the cerebral blood-vessels into the adventitial lymph channels. The further disintegration of the bacilli in these lymph channels gives rise to a local toxic action in addition to the general toxæmia. The special cause of the cord lesion in tabes is probably the absorption of toxins from some peripheral septic focus such as the bladder.

Interesting as these views are, there are many difficulties in the way of their acceptance as a satisfactory pathogeny of tabes, cerebral or spinal. Eyre and Flashman, as the result of examination during life of the throats of large numbers of patients suffering from different forms of insanity, as well as of the tissues of a considerable number

of cases *post mortem*, could not determine any greater incidence of diphtheroid organisms in the throats of the insane than of the sane, and found no evidence that *b. diphtheriæ* is more common in the throats of general paralytics than of other insane patients. Of ten cases of general paralysis examined *post mortem*, diphtheroid organisms were found in the respiratory tract in four, and the same number in twenty-six cases of other forms of insanity. They were unable to trace any causal connection between *b. diphtheriæ* and general paralysis of the insane.

I have the authority of Dr. Bulloch, one of our eminent bacteriologists, for the following remarks :— Diphtheroid organisms are ubiquitous both in health and disease. They may be found in the intestines, in the genito-urinary passages, in the throat; in the nasal secretions, and elsewhere in perfectly normal people, as well as in catarrhal conditions of the respiratory tracts. The characters given by Dr. Ford Robertson are not sufficient to distinguish his *bacillus paralyticans* from other forms of diphtheroid organisms. The formation of acid in glucose broth is not special to the *bacillus paralyticans*, for this is possessed in different degrees by various other diphtheroids.

If diphtheroid bacilli can be found in the blood films of living general paralytics, then general paralysis must be regarded not as a toxæmia, but as a form of septicæmia, ranking with relapsing fever as regards the dissemination of the organisms.

If diphtheroid bacilli exist in the blood or cerebro-spinal fluid of general paralysis, they should be capable of cultivation at once without waiting for the cessation of any supposed bactericidal action, for no lysogenic action of the serum for bacilli of this group has been proved to exist.

Specimens of the cerebro-spinal fluid, blood, and urine of several cases of tabes and general paralysis have been cultivated for me by Dr. Emery of King's College Hospital, and by Dr. Bulloch, and have proved absolutely sterile. Dr. Ford Robertson emphasises the fact that he finds bacilli particularly after so-called congestive attacks. It is not improbable, therefore, that the bacilli which he has found so largely diffused throughout the tissues in general paralysis are only the result of a terminal invasion.

In order to establish any causal relation between the *bacillus paralyticans* and tabes, it would be necessary to show that a toxin prepared from these bacilli can produce the symptoms and *post-mortem* appearances characteristic of tabes, cerebral or spinal. Such evidence Ford Robertson has not produced. The experiments on rats related by him are not convincing, for it has been found by other bacteriologists that rats are almost immune to the most virulent form of the Klebs-Loeffler bacillus. In presence of these and other considerations, we may, therefore, say that the diphtheroid-bacillary origin of the tabetic toxin is at least not proven.

In the absence of any living organism capable

of generating the tabetic toxin, it may be that the syphilitic virus under certain conditions so affects some viscus or gland that in time it develops, and continues to elaborate, some toxic internal secretion which exerts its noxious influence on the nervous system.

In view of the brilliant therapeutic triumphs of the present day, it is not, I think, too optimistic to hope that, with the progress of bio-chemistry, we may yet discover the source of the tabetic toxin, its nature, and the means of neutralising it and staying its ravages. We cannot expect to repair damage already done, for intramedullary degeneration is irreparable, but we may at least succeed in arresting the disease. This not infrequently happens spontaneously; and the therapeutic measures last employed are apt to get the credit of the happy result. But beyond palliation, or the temporary relief of urgent symptoms, no remedy, chemical or physical, has as yet been discovered which materially influences the morbid process. Antispecific treatment may be of service against possible coincident tertiary lesions, or may even cure pseudo-tabetic syphilitic symptoms; but certainly ordinary antispecific treatment exerts no beneficial influence on true tabetic degeneration, and may, if carried to extremes, prove positively harmful. If, however, we believe, as I think we must, that the syphilitic virus is the *sine quâ non* in the etiology of tabes, it ought to be our endeavour to combat this with all the resources at our command.

The comparative mildness of the primary constitutional symptoms in those who ultimately become tabetic, would almost seem to indicate that when the syphilitic virus expends itself in severe primary and secondary manifestations there is less tendency to the subsequent development of the subtle poison which proves so disastrous to the nervous system.

This mildness of the primary symptoms without doubt leads, in many cases, to insufficient treatment. Even the most efficient antispecific treatment, however, may fail to prevent the subsequent development of tabes in certain cases. But the facts recently brought by Fournier before the Académie de Médecine in reference to the relation between general paralysis and syphilis and its treatment are worthy of careful consideration and probation.

Fournier states that of seventy-nine cases of general paralysis coming under his own observation, in which he was able to obtain precise data as to the character and duration of the treatment to which they had been subjected, only 5 per cent. had been treated with thoroughness; while in at least 80 per cent. the antispecific treatment had been carried out in a more or less perfunctory manner. It is not enough, he says, to treat constitutional syphilis for weeks or months only. Fournier contends that mercurial treatment should be administered for at least two years continuously, and intermittently for several years longer. "Treat

syphilis well, and you will have few cases of general paralysis," he says. The same would hold true of spinal tabes. These views deserve the special consideration of those who have most opportunities of treating syphilis in its earlier stages. If they are substantiated tabes, both cerebral and spinal, will become one of the rarer, instead of one of the most common, and, it is to be feared, increasing forms of organic nervous disease.

Lecture III.

Physiological Pathology of Tabes.

I must now pass from the realms of speculation as to the nature of the tabetic toxin and the therapeutic possibilities of the future to a more abstruse part of my subject—namely, to attempt to correlate the essential symptoms of tabes with their anatomical and physiological substrata. For then only can we be said to have constructed a complete pathology of a disease when we are able to refer each symptom to its organic basis. To do this, however, in the case of such a polymorphic disease as tabes is a vast undertaking, and involves a wide and deep survey of the relations of the nervous system to almost every function of the organism—somatic, visceral, and trophic. For no disease exhibits such a complex symptomatology or puts to us such a host of neuropathological problems. On many of these problems I should despair of being able to say anything worthy of your attention which has not been said, and perhaps better said, by others before me. I purpose, therefore, to limit my survey of the physiological pathology of tabes to a few only of its more prominent symptoms, in respect to which clinical and experimental research have lately been busy and more or less suggestive or fruitful in results.

Of all the symptoms of tabes, ataxy is the most characteristic. All tabetics, however, are not ataxic, for some become blind from optic atrophy, or suffer for years with excruciating lightning pains, bladder and other visceral troubles, without becoming ataxic. Some neuro-pathologists, with strange logical incoherence, regard the occurrence of optic atrophy as exerting a kind of inhibitory influence on the development of ataxic symptoms. All that is justified is that the ataxic and amaurotic forms of tabes are often more or less distinct, though not exclusive of each other. Tabes is, as we have seen, essentially an affection of the sensory spinal protoneurone, whether in its ganglionic cell, peripheral, or intramedullary process, and in this we have to seek for an explanation of its most important symptom. For all other changes, whether in the peripheral motor nerves, anterior cornua, or bulbar nuclei, molecular layer of the cerebellum (Weigert), tangential fibres of the cortex cerebri (Jendrassik), or large cells of the post-central gyrus (Campbell) and their processes, are either inconstant, or mere concomitants, if not the results of the primary sensory degeneration. The motor neurone is intact; the electrical reactions of the muscles are normal, and their dynamic strength not necessarily impaired. The paths of impulse from the cortical centres are free from degeneration; and so also are the efferent tracts from the cerebellum by way of Deiters' nucleus, as well as the quadrigemino-spinal and rubro-spinal antero-

lateral tracts from the mesencephalon. The lesion is therefore on the afferent or sensory side of the apparatus of movement. If it is possible to give a satisfactory explanation of tabetic ataxy by the demonstrable lesion of the centripetal paths to the spinal, subcortical (mesencephalic and cerebellar), and cortical centres, it would seem unnecessary, with Erb and others, to ascribe the ataxy to lesion of some hypothetical centrifugal tracts of motor co-ordination.

It is more than probable that certain ataxic, or better, astatic muscular disorders may arise from anomalies of excitation, or irregularities in the transmission, of impulses from the motor centres, such as are exemplified in multiple sclerosis, lesions of the tegmentum, and some other intracranial lesions. But these differ in all their essential features from tabetic ataxy, and therefore need not occupy our attention further in reference to the question before us.

The degeneration of the centripetal tracts in tabes manifests itself in manifold abnormalities :—perversion, retardation, diminution, or total loss of sensory conduction in the domain of epicritic (tactile proper), protopathic (algesic, thermal), and deep sensibility, including all those factors—muscular, tendinous, articular—which form the basis of the sense of pressure and the complex muscular sense (Head).

Associated with this from the commencement, and it may be throughout the whole course of the

malady, and dependent on some subtle bio-chemical or bio-physical processes into the arcana of which we have not yet been able to penetrate, are those repeated and violent storms, somatic and visceral, which torture and rack the unhappy patient. Whether these lightning pains and crises depend on changes in the peripheral nerves, as some observers (Gowers, &c.), are inclined to believe, or have their basis in the central processes of the spinal ganglion, is uncertain and difficult to determine; but the fact that many of the subjective paræsthesiæ (such as the girdle sensation) and the objective signs of sensory impairment are to a large extent of a segmental or root distribution is, *inter alia*, in favour rather of the root origin of the tabetic neuralgia. And the fact that peripheral neuritis is relatively much less common in tabes than the lightning pains points in the same direction.

The impairment of cutaneous sensibility—epicritic or protopathic—varies enormously in frequency, degree, and range, and there is no constant relation between the ataxic symptoms and the extent to which cutaneous sensibility is affected. It may even happen that there is no obvious affection of cutaneous sensibility to the most delicate tests. This is a valid argument against the sensory theory of ataxy as first propounded by v. Leyden, who at one time put too much stress on the impairment of cutaneous sensation. The impairment of cutaneous sensibility is more marked in its protopathic (algesic) than in its epicritic (tactile) form, and is

most common below the knees. Roughly speaking, the incidence of tactile (hyp-) anæsthesia corresponds with that of (hyp-) analgesia, though the percentage of the latter is much greater than that of the former.*

It is quite otherwise, however, in respect to the relations between ataxy and impairment of the deep sensibility, which, as has been shown by Sherrington and Head, is dependent on the nerves which run with the motor nerves and originate in Pacini-like organs (muscle-spindles, Golgi organs, &c.), and are specially adapted to be influenced by pressure, muscular contraction, and change of position. A third to a half of the nerves which are distributed to muscles are of this afferent type (Sherrington).

Affections of this system of nerves reveal themselves subjectively in various ways, such as by insensibility to passive movements of the joints, inability to determine the exact position of the limbs or their segments, and defective sense of muscular contraction; these are individually affected with great diversity in different cases.

Frenkel holds that in every case of ataxy careful investigation, by precise methods calculated to eliminate all active muscular movements on the part of the patient, never fails to reveal a more or less extensive impairment of the sense of passive

* I am making these general statements on the basis of a careful investigation of the affections of sensibility in fifty cases of tabes by Dr. Golla at the National Hospital for Paralysed and Epileptic, who has kindly placed his results at my disposal.

movements of the articulations; and that this is more pronounced and more widespread in the more ataxic limb, when, as is not infrequently the case, they are unequally affected. The loss of the sense of passive movements is, according to Friedländer, always manifested first in the toe-joints, and tends to spread upwards to the higher joints with the increase of the ataxy. But the results of Golla's investigations at the National Hospital would lead me to question the accuracy of Frenkel's statements; for in a considerable percentage of cases of obvious ataxy he was unable to obtain any evidence of impairment of the sense of passive movements. And though it is the rule that this sense is more impaired in the more ataxic limb in the same individual, the rule is by no means absolute (Friedländer). And it is a remarkable fact that the ataxic disorders vary enormously in different patients in whom, to all appearances, the affections of superficial and deep sensibility are alike.

The muscles of the ataxic limbs are often tolerant of the severest pressure without discomfort. Closely related to this is the fact to which my attention has been called by Golla, and which I have frequently verified—namely, that the sense of tonic or tetanic muscular contraction induced by the faradic current is greatly diminished or totally lost, while the sense of minimal or rapid contraction is well preserved. This is at once capable of demonstration in cases in which there is already complete cutaneous anæsthesia, and can in others

be shown after preliminary kataphoresis of cocaine into the skin.

Not infrequently both forms of musculo-contractile sensibility are diminished or lost, but the two stand in no constant relation to each other; the sense of tonic contraction being by far the most frequently affected.*

Golla has luminously suggested that the loss of the sense of tonic contraction is the sensory side

* Dr. Golla has furnished me with the following statement: In two cases there was no obvious ataxy of the arms or hypotonia, while the legs were markedly hypotonic, and completely anæsthetic and algesic, with nearly complete loss of the sense of position. In both these cases there was only very slight difference in the acuity of the sense of rapid muscular contraction; while both cases had lost the sense of tonic contraction of the legs, and preserved it little, if at all, affected in the arms. I regard these two cases as of cardinal importance, as we were able to compare limbs deeply affected with limbs hardly at all affected, either as regards ataxy or any other form of sensation or hypotonia. In seven other cases there was in all more or less marked depression of the sense of tonic contraction in the less affected limbs, and complete absence of that sense in the limbs in which hypotonia and ataxy were well marked. In none of these cases was there any affection of the sense of rapid muscular contraction with the exception of two, where all forms of muscular sensation were completely lost. That the sense of rapid contraction of the muscle does not depend on the cutaneous sensibility is shown in three cases, where it was preserved with complete cutaneous anæsthesia. That the absence of the sense of tonic contraction is not a cause of loss of sense of position, but rather a specific phenomenon of tabes associated with the loss of the reflex tonus and depression of the spinal reflexes, is suggested by two cases of ataxy following neuritis, where it was preserved, though there was complete absence of the sense of position and of passive movement. In these cases tonicity had returned to the affected limbs.

of the loss of reflex tonus which seems the leading feature of tabes, while the sense of quick contraction may be the sensory analogue of the quickly contracting elements of the muscle.

This latter suggestion would be in harmony with the contractile nature of the muscle spindles, which, as Sherrington has suggested, may function in signalling active rather than passive movements.

Another form of sensibility which is frequently impaired or lost in tabes is the sense of vibration (pallæsthesia) of a tuning-fork, first described by Egger (1899), and attributed by him to the bones or periosteum. But it can be perceived in parts where there are no bones (Rydel and Seiffer), and the continuity of bone is not necessary to its propagation (Minor). It is probably dependent principally on the deep sensibility which forms the basis of the perception of passive movements and the position of the limbs, but it does not vary exactly with this (Dejerine, Marinesco, self) and its influence in respect to motor co-ordination is still *sub judice.**

Of greater constancy, and therefore of greater fundamental importance in the pathology of ataxy, is the impairment or total loss of those centripetal impressions which, arising chiefly in the muscles themselves and acting on the spinal and subcortical

* Dr. Head informs me that, in his opinion, it may be partly due to the rapidly-repeated single shocks acting on the epicritic nervous system, and therefore akin to the appreciation of simultaneous compass points.

(cerebellar) centres, are the basis of reflex muscular tone. This is shown in the loss of the so-called, but falsely so-called, tendon reflexes, of which the best known (since Westphal first called attention to it in 1875) and most commonly tested is the knee-jerk ; though the Achilles-jerk is of equal or even greater importance. Others also, usually obtainable in normal conditions, disappear as ataxy becomes more general. Associated with this is that remarkable condition of the muscles to which Frenkel has given the appropriate name *hypotonia*. This condition, so general in ataxy, had not altogether escaped the notice of v. Leyden, but it is to Frenkel that we owe a more precise knowledge of its characters and significance. The muscles are not necessarily flaccid to palpation, but they permit an undue mobility of the limbs and trunk, and do not develop resistance as antagonists when put on the strain like normal muscles. To this condition many of the characteristic attitudes of the ataxic, recumbent or erect, and the brusque overaction of the prime movers of the limbs in walking, are largely due. Better than verbal description of this condition are the accompanying illustrations (figs. 29 to 36).

This condition is due, as we have said, mainly to the loss of the tonic action of the spinal centres, but it may in part also be dependent on failure of the similar tonic influence which Luciani in animals, and Holmes and Grainger Stewart in man, have shown to be exercised by the

cerebellum. The loss of cerebellar tone, however, is not associated with loss of the tendon-jerks, and may exist when these are normal, or even increased. The non-correspondence between

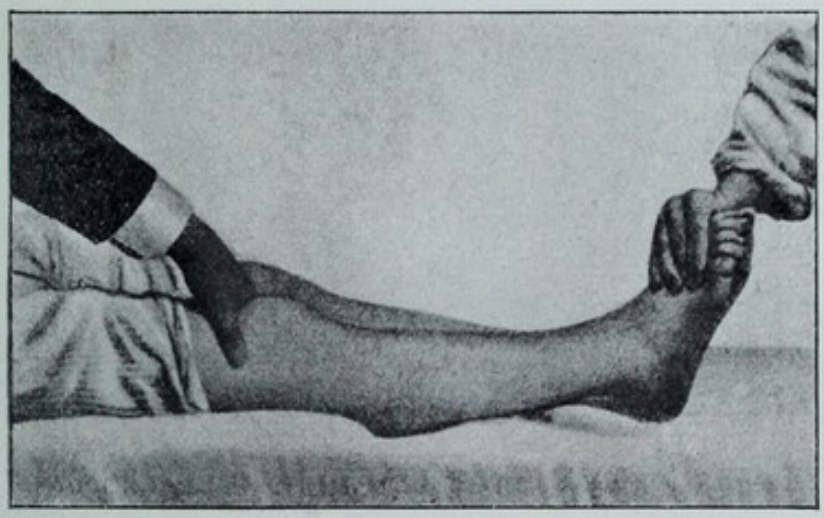


FIG. 29.—Maximal passive extension of knee in a normal individual (Frenkel).

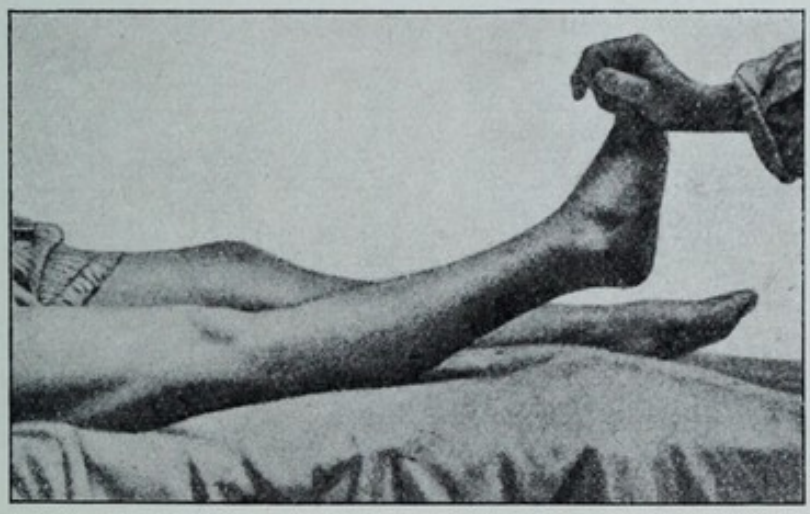


FIG. 30.—Hypotonia of popliteal muscles in tabes (Frenkel).

the state of the knee-jerks after lesions of the cerebellum and spinal lesions with loss of tone, made me at one time question the existence of Luciani's cerebellar atonia. I do not, however,

doubt the reality of a condition to which perhaps the term is not altogether inappropriate.

The basis of this loss of tone, and of the normal antagonistic counter-tension to active and passive

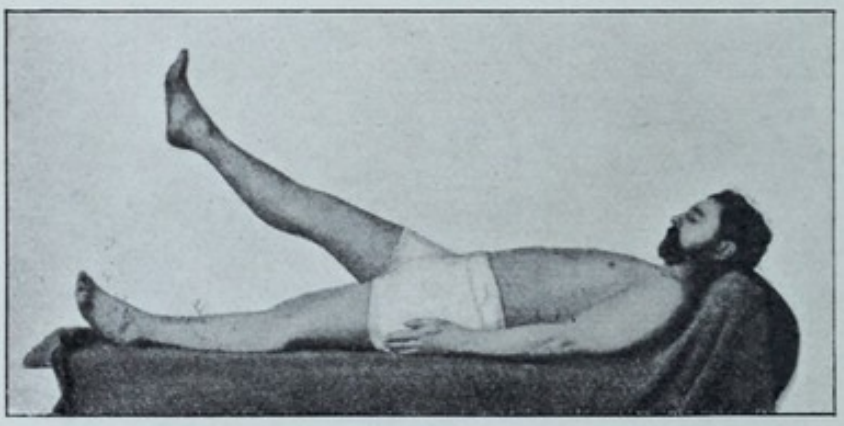


FIG. 31.—Maximal flexion of hip with extended knee, in a normal individual (Frenkel).

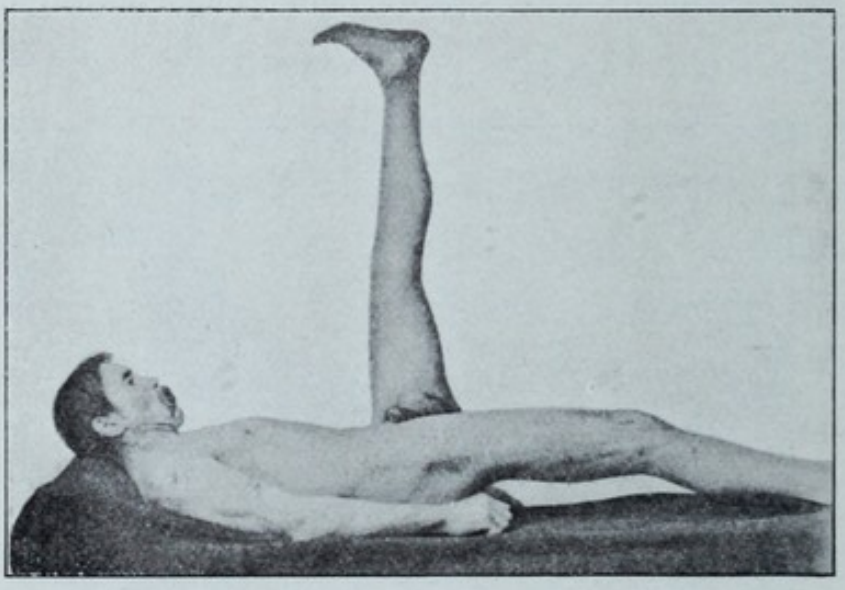


FIG. 32.—Moderate hypotonia of hamstring muscles in tabes (Frenkel).

movements, is the degeneration of the reflex collaterals of the posterior roots to the anterior cornua, and those to Clarke's columns, and thence indirectly to the cerebellum by way of the direct

cerebellar tract. By the long fibres of the posterior columns in some measure, and by other paths, the position of which in the spinal cord is still the subject of considerable diversity of opinion, and on which the last word has not yet been said, all the

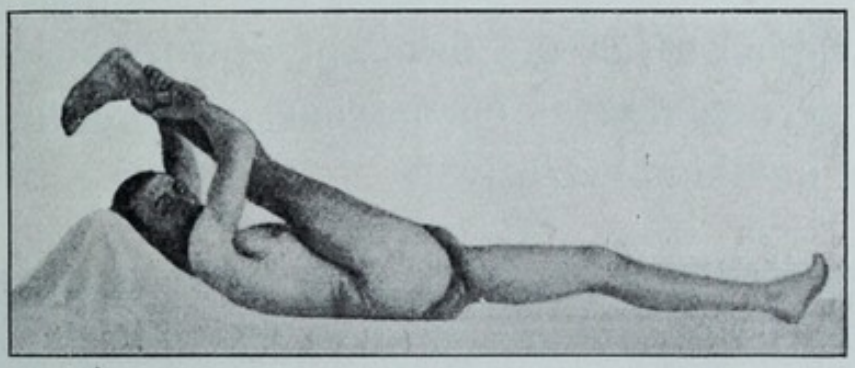


FIG. 33.—Maximal hypotonia of hamstring muscles in tabes (Frenkel).

FIG. 34.—Hypotonia of adductors in tabes (Purves Stewart).

conscious impressions, or sensations proper, derived from the skin, muscles, and deep structures are conveyed to the cerebral centres or centres of perception. To discuss these, however, at greater length, would be beyond the scope of the subject

in hand. And it is not as yet possible to say for certain how much of the sensory loss in tabes is due to the affection of the posterior roots themselves, and how much to that of the intraspinal paths, or how much to both combined.

Tabetic ataxy is probably the complex result of blocking of all the forms of sensory impression, conscious as well as unconscious, more or less, and not of one kind exclusively.

FIG. 35.—Hypotonia of gluteal and hamstring muscles (Purves Stewart).

Ataxy may result from lesion of the sensory nerves alone, apart from any implication of the spinal tracts. This is well exemplified in the pseudo-tabes or *neuro-tabes peripherica* (Dejerine), which is not an uncommon result of the toxic action of alcohol, diphtheria and other peripheral nerve poisons.

So far as the ataxic symptoms are concerned, these cases are not distinguishable from those of

true tabes. The abnormalities of superficial and deep sensibility are similar; Romberg's symptom and inco-ordination of the limbs, intensified by shutting the eyes, are alike; the knee-jerks are absent, and though there are symptoms and signs which enable a differential diagnosis to be made, yet the two affections resemble each other so closely that they can be readily mistaken for each other.

FIG. 36.—General hypotonia (Purves Stewart).

As to the effects on movement of experimental section of the posterior roots, which means cutting off centripetal impressions of all kinds, conscious and unconscious, there has been some controversy of late. In the first instance, at least, as has been known since Bell's classical experiment of section of the fifth nerve, and illustrated by Mott and Sherrington in their experiments on the

posterior roots of the brachial plexus in monkeys, there is an indirect paralysis—termed *centripetal paralysis* by Hering—in the related parts. This, however, as one might *a priori* expect from clinical observation in man, should only continue so long as the sensations from the anæsthetic limb had not been replaced or compensated by the eye. And in reality, as Munk, who has repeated Mott and Sherrington's experiments, has shown, even in monkeys the paralysis is only temporary, and in course of time the animals learn to use the anæsthetic limb again. But, and this is the cardinal point, the movements of the limb are never normal, but remain "brusque, excessive, and awkward" (*brusk, übermässig, ungeschickt*). This, though somewhat wanting in precision, is a fair description of an ataxic limb.

And Bickel and Ewald found, after similar experiments on dogs, that the ataxic movements of the limbs, which tended in course of time to diminish, were reinduced when the animals were blindfolded or placed in a dark room :—their limbs being rendered visible by luminous paint. The resemblance of these symptoms to those of ataxy in man is remarkable.

The spinal paths of afferent impressions include not only the reflex collaterals to the anterior cornua and Clarke's columns, but also those of sensation proper to the cortex cerebri. It would seem almost impossible to dissociate these from each other, but yet such a thing apparently occurred in one case

which has been put on record (Schüppel) so long ago as 1874. This was a case probably of syringomyelia, and though the symptoms and *post-mortem* appearances have not been recorded with such fulness as we should consider necessary at the present day, yet it is one of great importance as showing that total interruption of the spinal paths of conscious sensation does not of itself cause ataxy proper. The case was that of a man who became completely anæsthetic to tactile, thermal, and painful stimuli; lost all sense of pressure, and had no sense of active or passive movements of his limbs or joints, and yet, under the guidance of vision, could stand, walk, and execute all voluntary movements in a fairly normal manner. The cord lesion was a cavity occupying chiefly the grey matter, especially the posterior cornua and grey commissure. The anterior cornua were intact. Whether in this case the reflex collaterals were spared we cannot from the description say positively, but it is not improbable.

If we ascend higher towards the cerebrum we have no evidence of organic lesion strictly limited to the paths of sensation apart from those of motion, either in the mesencephalon, internal capsule and optic thalamus, or higher. And though in such cases certain so-called hemiataxic disorders of movement may be observed, probably, in part at least, dependent on impaired transmission of sensory stimuli, they are in many respects quite unlike tabetic ataxy. The only conditions which

enable us to eliminate the influence of true perception on the co-ordination of movements are, *inter alia*, cases of functional anæsthesia. These are usually hysterical and mostly unilateral, and the symptoms are so equivocal and contradictory of each other that they do not afford a safe basis on which to build. It is sufficient to say that in functional cerebral anæsthesia, notwithstanding the apparent total loss of all kinds of sensation, cutaneous and deep, co-ordinated movements of great complexity may still be effected under the guidance of vision, actual or ideal. That clear consciousness of kinæsthetic impressions is unessential is proved by the phenomena of sleep-walking and other states in which the functions of the highest centres are for the time in abeyance.

The general result of this analysis is, that tabetic ataxy depends on impairment or loss of centripetal impressions of all kinds, conscious as well as unconscious, and, of these, those from the deeper structures (muscles, tendons, joints) are more important than the superficial; and if one may single out one class as more essential than the others of the complex, I would specify those to the spinal, subcortical and cerebellar centres.

Vision can more or less completely compensate for loss of kinæsthetic sensation; and largely also, but to a much less extent, for the loss of the purely afferent impressions to the spinal and cerebellar centres. In the absence of vision, all the disorders of co-ordination, static and dynamic, are greatly

intensified, and this is the pathognomonic feature of tabetic ataxy.

The constitution and connections of the spinal and subcortical centres provide for the combined action of the various muscles (prime-movers, synergics, antagonists, and collaterals) concerned in simple and co-ordinated acts—for example, the synergic extension of the wrist in closure of the fist; and the combined flexion of the thigh, leg, and dorsiflexion of the foot of the swinging leg in walking.

This is proved by the perfectly co-ordinated movements which occur in decapitated animals in response to various external and internal stimuli, and by the similar phenomena that can be elicited by stimulation of the posterior roots after transection of the cord in monkeys (Page May).

"The afferent path evokes discharge only of harmoniously related muscular groups. If it be stimulated strongly the number of motor groups excited may be extensive, and their situation involve the whole length of the spinal axis; but the groups excited contemporaneously are always harmoniously acting groups—for example, flexors of hip with flexors of knee, and not groups mutually subversive of each other's action. Each individual muscle of each group, so far as analysed, seems in its action balanced and subordinated as in a "natural movement" (Sherrington).

The conscious accompaniments of muscular action, both in the process of learning and through-

out life, play a more important *rôle* in human actions in all their manifold diversity than in the more simple activities of the lower animals, and their removal—potential or real—exercises a greater disturbance of the whole mechanism; but the mechanism is not formed by conscious activity—it already exists.

It has been said by Förster that in the newborn infant the synergic extension of the wrist on reflex closure of the fist does not occur, and that it only becomes developed as the result of cerebral selection. I should seriously question the accuracy of this statement, for though it is difficult, as I have found, to be certain of the simultaneous action of the extensors of the wrist in the reflexly-excited closure of the fist in newborn infants, I have occasionally observed it, and Dr. Beevor informs me he has done the same; and it would be difficult to explain the extraordinary power of grip possessed by newborn infants without assuming that the extensors of the wrist were acting synergically at the same time; for infants only a few hours old, as Louis Robinson has shown ("Darwinism in the Nursery," *Nineteenth Century*, November, 1891), can hang on to the finger or a small stick, and sustain their whole weight for several seconds—a power which increases for several weeks after birth. Certainly the synergic extension of the wrist becomes manifest long before the child can have developed it by conscious selection.

In volition, or action conditioned by conscious

discrimination, the cortical centres act through the spinal, but in the cortex there is greater differentiation and power of dissociation than in the spinal cord, so that individual movements, if not individual muscles, can be isolated from their usual synergists. Thus we can voluntarily flex the fingers without extending the wrist. But our powers in this respect are limited, and we can only eliminate such synergists and collaterals as we are clearly conscious of; while others, to which our attention has not been specially called, co-operate as usual, and their action comes to us almost as a revelation when it is pointed out.

How the cortical motor centres act on those of the spinal cord, whether directly through the pyramidal tracts, or indirectly through association cells (Gad, v. Monakow, Beevor), or through the same channels as the reflex collaterals (Schäfer), is at present a matter only of speculation. But if, as Schäfer contends, the fibres of the pyramidal tracts arboresce not around the cells of the anterior cornua but around those of Clarke's columns, and at the base of the posterior cornua, then the hypothesis that the cortical centres act through the same channels as the reflex collaterals would be the most probable. For the phenomena of ataxy and pseudo-ataxy clearly demonstrate the necessity of kinæsthetic impressions to secure the due co-operation of the synergic, antagonistic, and collateral muscles with the prime movers in any given movement.

It would appear from the researches of Sherrington and Hering that the innervation of a given muscle *ipso facto* inhibits its true antagonist—so-called *reciprocal innervation.* This is well exemplified in the case of paralysis of the internal rectus of the one eye—say the left. On innervation of the lateral conjugate movement to the right the divergent strabismus of the left eye diminishes, and the eyeball swings up to the middle line, owing to inhibition of the tone of the unantagonized external rectus.

The simultaneous removal of all obstruction to the unfettered action of a muscle, implied in the law of reciprocal innervation, may be regarded as a useful provision; but it is a law subject to being overruled by the varying necessities of the case and the effects desired. Thus in sudden extension of the forearm the flexors are inhibited; but in extension of the forearm against gravity the flexors are obviously in action as well as the extensors. And as Duchenne, Richer, Demeny, and others have demonstrated, the action of the true antagonists is in manifold ways brought into play to moderate and steady that of the prime movers.

The essence of ataxy, in all its manifestations, is the loss of, or impaired transmission of the kinæsthetic impressions to the spinal, subcortical, and cerebral centres, on which the graduated and harmonious co-operation of all the muscles concerned in our various actions depends.

To analyse these in detail, however, would take

a volume. Nothing could be more admirable in this respect than the masterly analysis of tabetic disorders given by Förster in his work on the physiology and pathology of co-ordination.

One of the most characteristic features of tabetic ataxy is the overaction of the prime movers. This is manifested in almost every form of voluntary movement. It is most marked when there is also impairment of conscious sensation in the limbs. It is, no doubt, largely due, and has been attributed almost exclusively, to the defective sense of movement achieved, so that the patient has no guide to the inhibition of further motor innervation. Hence, especially when his eyes are shut, he continues the action beyond what is required, and is himself astonished when he sees how far he has overshot the mark. But this is not all, nor is it the most important factor in the sudden and immoderate character of the prime movements of the ataxic. This consists in the hypotonia and default of the afferent impressions which normally secure the development of the reflex resistance of the antagonists. The recumbent ataxic, therefore, when told to lift his foot from the bed does so with abnormal energy and brusqueness, because the extensors of the thigh fail to develop the resistance necessary to moderate the action of the flexors. So also the collateral muscles fail to steady the limb, so that it swerves from the direct line, or oscillates in various directions about the mark aimed at. The default of the centripetal spinal and sub-

cortical impressions is exemplified in many other ways. Even in the recumbent attitude the limbs of the ataxic exhibit abnormalities of position. The legs are rotated outwards or inwards, from defective reflex tone of the inward or outward rotators of the thigh; and in particular the foot assumes the equinus or equino-varus position from defective tone of the dorsiflexors.

When the leg is used as an instrument of progression, the "impulsive association," as Duchenne expresses it, or the synergetic combination of the flexors of the thigh, flexors of the leg and dorsiflexors of the foot, is dissociated, so that the dorsiflexion of the foot fails to occur, and the toe tends to drag on the floor. This defect is corrected under the guidance of the eye, but it is generally overdone. So also when the foot is again planted on the floor it not uncommonly becomes inverted or everted, from failure, as Förster points out, of the reflex tone either of the peroneus brevis or tibialis posticus, by the joint action of which the sole of the foot is kept in the normal middle position.

Similarly when ataxy invades the arms, we see dissociation of the synergic extension of the wrist from the flexors of the fingers, so that the wrist bends, and the grip is thereby rendered feeble and ineffective.

When the patient stands up he has difficulty in maintaining his balance, owing to the failure of the centripetal impressions which are necessary to

excite the muscular adjustments innervated by the cerebellum.

Here the loss of conscious sensation when present adds greatly to the difficulty; for blunting of the sensibility of the soles of the feet even by itself, as has been proved experimentally by Vierordt and Heyd, renders the maintenance of equilibrium very unsteady. So long as vision is unimpeded, and the vestibulo-cerebellar centripetal impressions operative, standing is possible on a wide base; it is more difficult as the base of support is narrowed, and is altogether impossible when the eyes are shut.

When the patient sits down, instead of doing so gently with graduated flexion of his trunk, thighs and legs, he bumps down on his seat, owing to defective reflex antagonistic tone of his quadriceps extensor muscles.

When he endeavours to maintain his equilibrium, and also to walk, he assumes attitudes, and makes compensatory movements which are almost pathognomonic. Thus, if alone and unsupported, he will walk with a constrained gait, his legs over-extended and knees recurved (so as to prevent the sudden giving way of the legs so well described by Buzzard), his body bent forward, and with his eyes steadfastly watching his feet.

But his actions vary with the conditions under which he is placed. For the same patient, if supported on both sides, and thus saved from the necessity of attending to his equilibrium, will throw out his legs and dorsiflex his feet with excessive

energy, and set them down again with equal brusqueness, stamping his heels on the floor.

Throughout all the same purpose runs. It is the attempt, clumsy at best, by conscious effort to make up for the failure of a self-adjusting mechanism which, under normal conditions, works better without conscious interference. Clumsy though it be, however, the best treatment that has been hitherto devised for the palliation of ataxy is the assiduous cultivation and judicious direction of these conscious efforts at compensation in accordance with the rules laid down by Frenkel and Förster.

The Tabetic Pupil.

One of the most important signs of tabes is the condition of the pupil, first described by Argyll-Robertson in 1869, and known universally after his name. It is scarcely necessary to say that this consists in the loss of the reflex contraction of the pupils to light, while that on convergence and accommodation remains. The frequency of the Argyll-Robertson pupil in tabes was first noted by Erb, as well as the usually associated loss of the reflex dilatation to sensory or psycho-sensory stimulation.

Reflex iridoplegia is not always present, nor is it always absolute, there being frequently only sluggish reaction, instead of total absence of contraction to light. But it is so frequent—in general about three-quarters of the cases—and so characteristic that the other symptoms of tabes must, in its

absence, be well marked to allow of a definite diagnosis of tabes to be made.

Sometimes it is unilateral, or more marked in one eye than the other. It is, in a large proportion of cases, associated with myosis, so that a peculiar appearance is given to the eye of almost a pathognomonic character.

But myosis is by no means universal ; sometimes the pupils are of medium size, or even larger than normal, and they may be unequal. The essential and characteristic feature of tabes is the reflex iridoplegia. This rarely passes into absolute iridoplegia. This, however, sometimes occurs unilaterally, but it is then more probably due to a local syphilitic affection. Absolute iridoplegia, however, occasionally gives way to reflex iridoplegia.

The outline of the pupil, also, generally undergoes change, and this not infrequently precedes the loss of light reflex. The tabetic pupil is rarely quite circular, and it is often eccentric in position.

What has been said of the pupils of tabes is true also of those of general paralysis, but here they are more often unequal in size. Reflex iridoplegia once complete is incurable ; but occasionally when incomplete the reaction may return. It may exist for many years (Erb) without any other obvious symptoms either of tabes or general paralysis. Usually it is associated with lymphocytosis of the cerebro-spinal fluid, but, as I have found, this is not invariable.

But one may say with Bumke that a permanent

isolated reflex iridoplegia occurs only in tabes, general paralysis, and as a consequence of congenital or acquired syphilis; while the cases in which, as a residuum of absolute iridoplegia, a condition remains which is not distinguishable from the Argyll-Robertson pupil, are so rare that they may be practically neglected. The general result, therefore, if we consider the syphilitic origin of tabes and general paralysis as proven, is that reflex iridoplegia is always a result of syphilis.

The pathology of the Argyll-Robertson pupil is a subject of great difficulty, for we are still far from possessing a complete knowledge of the mechanism of pupillary variations. The pupil varies in size not merely under conditions of illumination and accommodation, but with the intraocular tension and fulness of the vessels of the iris; it contracts with the orbicularis oculi, dilates under the influence of sensation and emotion, and varies with psychical activity in a manner extremely difficult to analyse. We do not yet know for certain whether the retinal elements which subserve light sensation are the same as those which excite the reflex pupillary contraction. There are conditions of the retina in which vision may be affected and the light reflex continue, and *vice versâ;* and Schirmer concludes from pathological conditions that the parareticular or amakrine cells of the inner granular layer are the special centripetal organs of the light reflex. Whether this is well founded or not is a question, but both anatomical and clinical facts point to a

differentiation in the optic nerve between the fibres conveying light impressions and those which excite pupillary reflex. In man, as in all animals with semidecussation of the optic nerves, the centripetal reflex pupillary fibres undergo also partial decussation. Hence lesion of the optic tract, as in Wernicke's well-known hemiopic test, not only causes contralateral homonymous hemianopsy, but also loss of the light reflex from the corresponding retinal halves.

In front of or in the immediate neighbourhood of the corpus geniculatum externum, the centripetal pupillary tracts separate from those which form the optic radiations, and pursue their course towards the oculo-motor centres. But what this course precisely is, is still a vexed question.

That the pupillary and other oculo-motor reflex centripetal paths do not pass through the vault or tectum of the corpora quadrigemina, is evident from the results of experimental lesions of these ganglia in monkeys, as described by Aldren Turner and myself. After such lesions the reaction of the pupils was intact ; and many cases have been related of tumours invading the corpora quadrigemina without affecting the pupillary reflex.

It has been held by some that the fibres of Meynert's *fasciculus retroflexus* (fig. 37), which courses, internal to the red nucleus, from the ganglion habenulæ towards the base, is the centripetal reflex pupillary path, and that therefore a lesion of this tract would cause reflex iridoplegia.

But no such lesion has ever been demonstrated in the reflex iridoplegia of tabes; and von Monakow has observed destruction of Meynert's fasciculus retroflexus without any affection of the

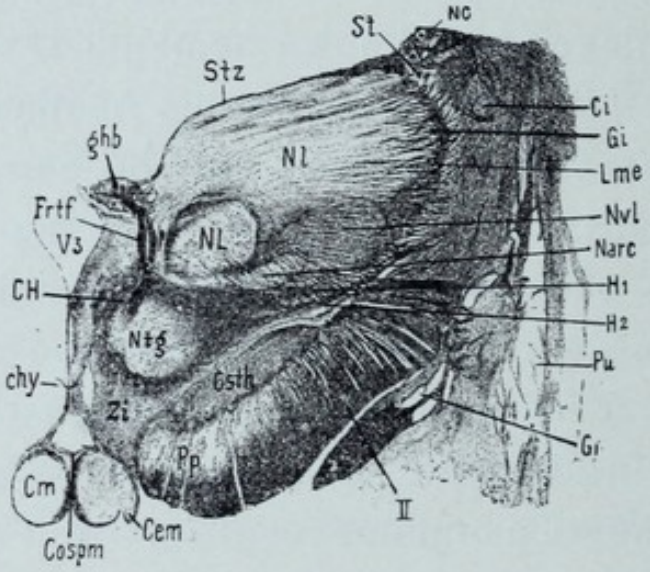


FIG. 37.— Frontal section through lenticular nucleus, showing the *fasciculus retroflexus*. Cem = corpus mamillare externum; CH = central tegmental tract; chy = commissura hypothalamica; Ci = capsula interna; Cm = corpus mamillare; Cospm = commissura supra-mamillaris; Csth = corpus sub-thalamicum; Frtf = fasciculus retroflexus; ghb = ganglion habenulæ; Gi = latticed layer of thalamus; Gp = globus pallidus; H1, H2 = Forel's bundle from the red nucleus; Lme = lamina medullaris externa; Narc = nucleus arcuatus thalami; Nc = nucleus caudatus; Nl = nucleus lateralis thalami; NL = nucleus of Luys; Ntg = red nucleus of tegmentum; Nvl = nucleus ventralis lateralis thalami; Pu = putamen; Pp = Pes pedunculi; St = Stria terminalis; Stz = Stratum zonale thalami; V3 = third ventricle; Zi = zona incerta; II = optic tract (Obersteiner).

pupillary reflex. Moreover, after extirpation of both eyeballs this tract remains free from degeneration.

The probability is that there is no direct connection between the centripetal optic paths and

the oculo-motor centres, but that the connection is indirect, through intercalary or association cells, which again form synapses with the oculo-motor nuclei. But these and their respective relations to the centripetal reflex paths from each eye are matters more of hypothesis than of actual demonstration.

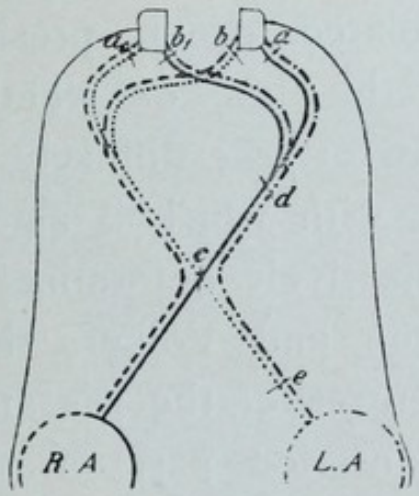


FIG. 38.—Diagram of relation of the optic tracts to the oculo-motor centres (Bumke). *a*, *b*, or *a1*, *b1*, position of lesion causing unilateral reflex iridoplegia, together causing double reflex iridoplegia; *c*, optic chiasma; *d*, position of lesion causing Wernicke's hemiopic reaction; *e*, optic nerve; *R.A*, *L.A*, right and left eyeball respectively.

In order to account for the various disorders that may be observed in reflex pupillary innervation the accompanying diagram (fig. 38) on the screen has been suggested by Bumke. This shows how hemiopic, as well as unilateral or double reflex iridoplegia, may occur according to the position of the lesion.

But it has been said, the only verified basis of this scheme is Wernicke's hemiopic pupillary reaction from lesion of the optic tract. No lesion

in the central grey matter of the aqueduct of Sylvius has been established in connection with the tabetic pupil, though Moeli has reported a case of tumour compressing the hinder wall of the third ventricle in which reflex iridoplegia was said to have been present.

Whether in the conglomeration of nerve cells which constitute the nucleus of the third nerve there is an isolated group presiding over the movements of the iris, or whether the iris is represented more or less diffusely along with the various muscles with which it acts in association, is not as yet positively determined. The experiments of Henson and Volkers, however, are in favour of the centres of the iris and ciliary muscle being in the anterior part of the oculo-motor nucleus, and their nerves in the most anterior roots of the third nerve.

Bernheimer maintains, mainly on the results of experiments on monkeys, that the centres for the sphincters of the pupils are situated in the paired small-celled nucleus termed the Edinger-Westphal nucleus (fig. 39).

He states that the cells of the corresponding nucleus show degenerative changes after enucleation of the eye-ball; that unilateral destruction causes reflex iridoplegia in the corresponding eye; and that electrical irritation of this nucleus causes contraction of the pupil of the same side. Bernheimer's experiments have been subjected to searching and destructive criticism by Bach, and

they certainly appear to me far from convincing. They are opposed to many recorded and carefully investigated clinical cases. Thus von Monakow has observed cases of total ophthalmoplegia, external and internal, in which there was complete degeneration of all the cell-groups of the oculo-motor nerve, with the exception of the

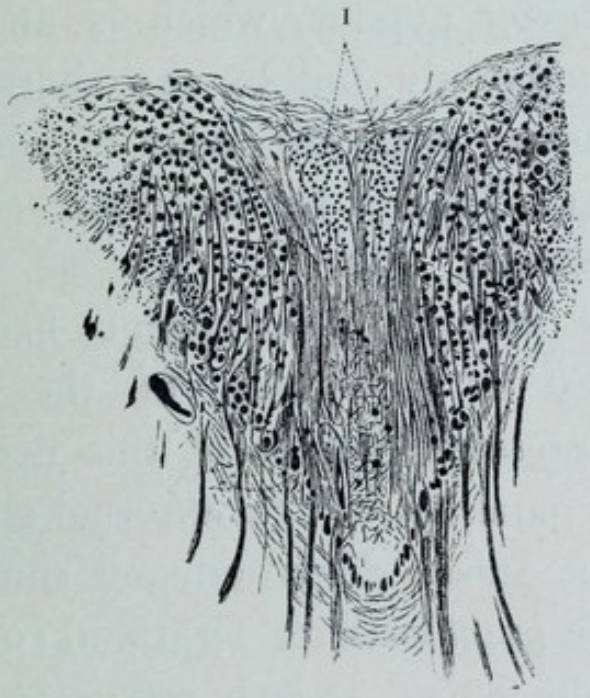


FIG. 39.—Frontal section through oculo-motor nuclei. 1, Small-celled paired Edinger-Westphal nucleus (after Bernheimer).

Edinger-Westphal nucleus. And conversely, the Edinger-Westphal nucleus has been found destroyed without impairment of the pupillary reaction (v. Rad's case quoted by v. Monakow). As against the localisation of a definite circumscribed centre for the sphincter pupillæ, is also the fact that the action of the pupil is usually unimpaired in ophthalmoplegia dependent on acute lesion of the oculo-motor nuclei (polioencephalitis superior).

A strictly limited lesion of one particular cell-group of the oculo-motor nucleus has never been demonstrated in man in relation with reflex iridoplegia or ophthalmoplegia interna. Marina, who has investigated many cases of reflex iridoplegia in tabes, has uniformly found the Edinger-Westphal nucleus normal.

The pupillary fibres of the third nerve pass to the sphincter pupillæ, which is an involuntary muscle, not directly but by the short root of the ciliary ganglion, with the cells of which it forms synapses, and thence by the short ciliary nerves to the sphincter.

In reflex iridoplegia no lesion has ever been demonstrated in the trunk of the third nerve. Complete transverse lesion of this nerve, in addition to the paralysis of the external muscles which it innervates, causes dilatation and complete immobility of the pupil both to light and convergence—absolute iridoplegia. It is, however, to be observed that a less complete lesion of the third nerve may produce external ophthalmoplegia without affecting the pupil. Many such cases are on record. Cushing has reported three cases of accidental injury to the third nerve during the operation for excision of the Gasserian ganglion, in which there was temporary total paralysis of the external ocular muscles, while the pupil remained unaffected, reacting normally to light and accommodation.

From this brief review of our knowledge respecting the reflex pupillary arc, it is evident that there

is still great obscurity as to its precise constitution, and that though, theoretically, reflex iridoplegia may be explained by interruption of certain hypothetical centripetal paths of the light reflex, no actual pathological changes have as yet been demonstrated in the reflex iridoplegia of tabes.

The frequent association of reflex iridoplegia with degeneration of the cervical region of the cord, has led several observers—notably Rieger and Förster—to place the centre for the light reflex in this region. But it is obvious that in tabes the loss of the light reflex and degeneration of the posterior columns need not be causally related to each other. And the medulla has been found normal in two cases of general paralysis with iridoplegia (Marina), and in a case of congenital Argyll-Robertson pupils by Reichart.

Degenerations of the posterior columns, other than tabetic, have also been found by various observers with normal reaction of the pupils. This is notably the case in Friedreich's disease, in which there is no abnormality of the pupillary reactions.

Bach, however, who at first was inclined to place the centre of the light reflex in the cervical cord just below the medulla oblongata, in his more recent work relates various experiments made in conjunction with Meyer, which lead him to believe that at the spinal end of the medulla oblongata, near the respiratory centre, there is an inhibitory centre of the light reflex, to which the reflex centre of the corpora quadrigemina is subordinate; and,

in addition, in close proximity, another centre inhibitory of the reflex dilatation of the pupil.*

That such a complicated mechanism—which reminds one of the cycles and epicycles of the Ptolemaic astronomy—is needed to explain the facts, is in the highest degree improbable, and that the reflex iridoplegia of tabes, often of years' duration, can be explained by persistent irritation of these hypothetical inhibitory centres of pupillary action has little in its favour.

Of all the investigations on the pathology of the

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* The facts on which Bach bases his hypothesis are as follows: (1) Total division of the cord several millimetres caudally from the fourth ventricle causes no change in the pupillary reaction. At the moment of section there is a temporary dilatation of the pupils, after which the light reflex can be elicited as before. (2) Bilateral section of the medulla at the spinal end of the fourth ventricle at a definite level causes immediate immobility of both pupils to light. (3) Unilateral division of the medulla at the same level on the right side produces not a right-sided but a left-sided reflex iridoplegia. (4) Exposure of the medulla, with its mechanical and other irritation, generally suffices to cause the disappearance of the light reflex or absolute iridoplegia. With this there is marked myosis and often inequality of the pupils. This fixity of the pupils, even after persisting from a quarter of an hour to one hour, at once disappears, and is replaced by prompt reaction of the pupils when a section is made through the middle of the fourth ventricle or at higher levels. This reaction lasted in one case for a whole hour. (5) Unilateral division of the medulla at the middle of the fourth ventricle and brainwards therefrom, renders the previously sluggish or absent light reflex again evident. The persisting inhibition can be counteracted by cocaine or by the action of ether.

tabetic pupil in recent years, those of Marina appear to me the most suggestive.

Marina has investigated, by the most approved modern histological methods, thirteen cases of general paralysis with normal pupils, twenty-three cases with Argyll-Robertson, five cases of tabes, and twenty-nine other cases with normal or abnormal pupils. In all the cases of tabes and general paralysis with the characteristic pupils he

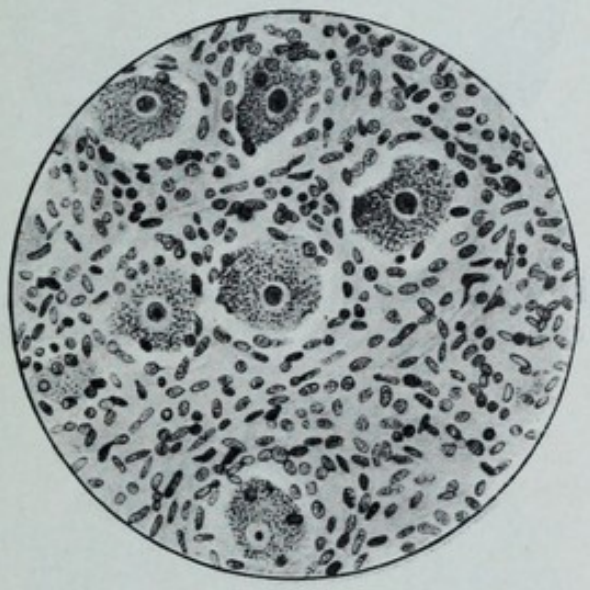

FIG. 40.—Ciliary ganglion—normal (Marina).

found signs of degeneration in the ciliary ganglia and short ciliary nerves. If the pupils were normal the ciliary ganglia were also free from degeneration. In one case of unilateral Argyll-Robertson pupil, the ciliary ganglion of the affected eye was profoundly altered, while that of the other eye was practically normal. The changes in the ciliary ganglion in tabes are of a chronic character, and consist in a gradual wasting of the nerve cells, with

chromatolysis and distortion of the nuclei (figs. 40, 41 and 42).

Degeneration of the short ciliary nerves was constantly found, and apparently secondary to that

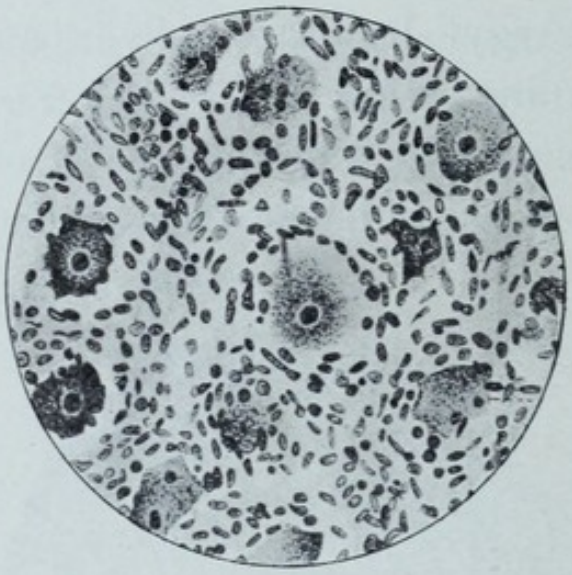

FIG. 41.—Ciliary ganglion from a case of General Paralysis with Argyll-Robertson pupils, showing deformity of the cells (Marina).

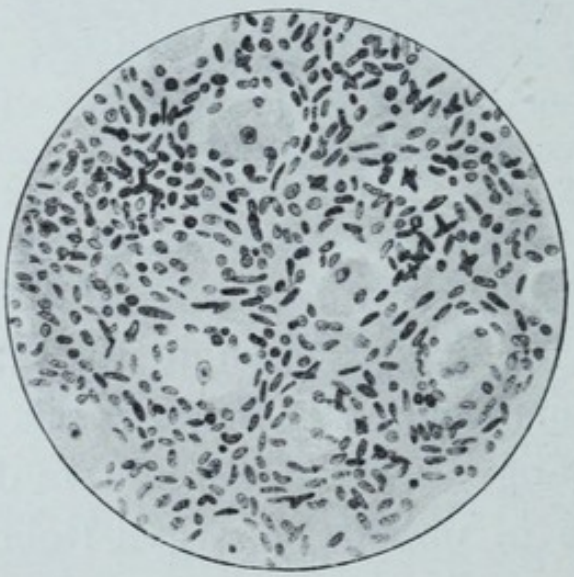

FIG. 42.—Ciliary ganglion from a case of Tabes with Argyll-Robertson pupils, showing profound chromatolysis (Marina).

of the ganglion cells. The roots of the ganglion were always found normal ; so also, with one exception, were the oculo-motor nerves, the oculo-motor

nuclei, the Edinger - Westphal nucleus, that of Darkschewitch, as well as the grey matter surrounding the aqueduct of Sylvius.

Besides the ciliary ganglion, the Gasserian ganglion showed degenerative changes in three out of

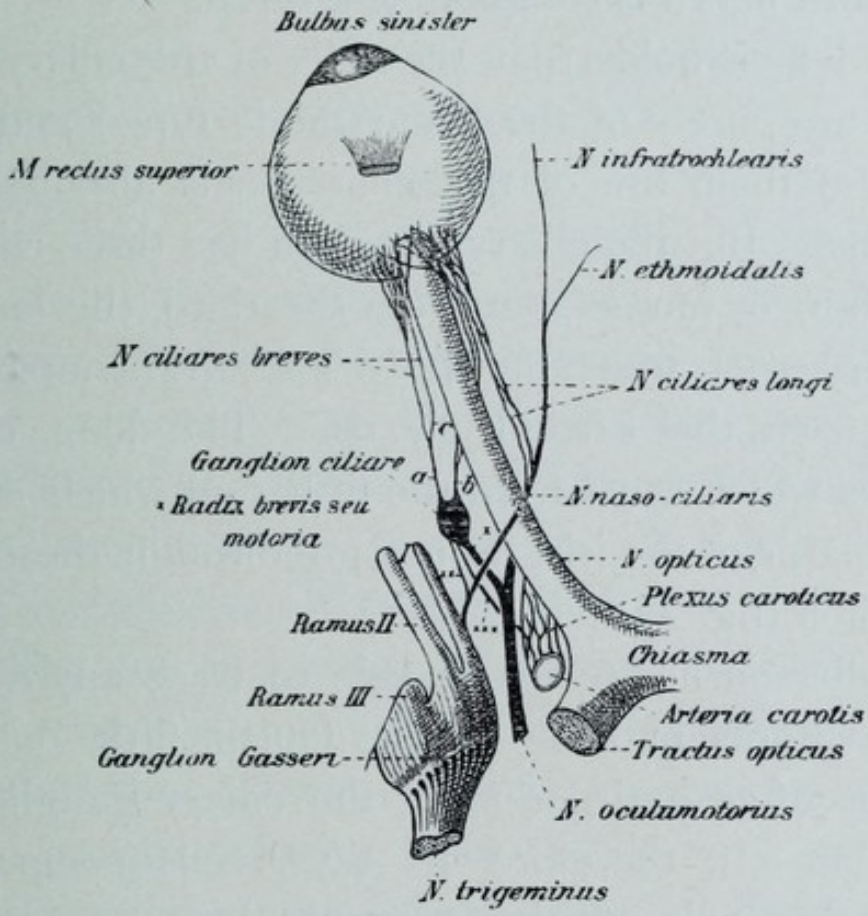

FIG. 43.—Anatomy of the ciliary ganglion in the dog (Piltz).

sixteen cases of general paralysis, and in three out of four of tabes. The superior cervical ganglion also showed degenerative changes in two out of four cases of tabes ; while in general paralysis one-third only exhibited degeneration, the other two-thirds being doubtful or normal.

The results obtained by Marina are evidently of

the utmost importance in reference to the pathology of the tabetic pupil.

The physiology of the ciliary ganglion is still very imperfectly understood. That it is not an independent centre for the pupillary reflex is evident from the fact that the pupil is quite immobile when the third nerve is completely severed.

Anderson holds that the cells of the ciliary ganglion are purely of the sympathetic type; and that most of them are of this character is also held by Marina. But the ciliary ganglion has three roots—the short or motor root from the third, the long or sensory root from the fifth, and the sympathetic root from the carotid plexus. The long ciliary nerves which come from the fifth, and which supply the dilator of the iris, do not go through the ciliary ganglion (fig. 43).

Anderson has not been able to trace any degenerated fibres in oculo-motor, fourth, fifth, or sixth nerves after extirpation of the ciliary ganglion in the cat. If, therefore, he says, cells comparable with the cells of the posterior root ganglia are present in the ciliary ganglion, they must belong to a type of cell not yet demonstrated, and send non-medullated processes to the central nervous system.

On the other hand, Marina has observed degeneration in some of the cells of the ciliary ganglion, probably of a sensory type, after lesions of the cornea. And Bumm finds that the number of cells which remain intact after section of the short ciliary

nerves, is again reduced by extirpation of the superior cervical ganglion. A considerable number, however, still remain, some of which, at least, appear to be connected with the fifth. The ciliary ganglion would therefore, if these observations are correct, appear to be a complex structure. That some of the sympathetic fibres which supply the dilator of the pupil pass into the ciliary ganglion by way of the sympathetic root from the carotid plexus, instead of all going by the long ciliary nerves as is commonly held, is, I think, probable. For though division of the ophthalmic branch of the fifth, as Turner and I have demonstrated in monkeys, causes contraction of the pupil from paralysis of the dilator, this effect is only of temporary duration, lasting usually only a week or so. And in man, as I have ascertained, after extirpation of the Gasserian ganglion for inveterate trigeminal neuralgia, the pupil does not remain permanently affected, but contracts and dilates as under normal conditions. This is very different from the state of the pupil after division of the dilator fibres as they emerge from the upper dorsal roots. Even years after this lesion the pupil remains smaller, and the eyeball sunk, as compared with the other. Nor does cocaine cause dilatation, as in the normal pupil, except in relatively very large doses. There must, therefore, be some other path for the dilator fibres of the iris than the long ciliary nerves, and it is probable that they go through the ciliary ganglion by the sympathetic root of the carotid plexus.

The ciliary ganglion, as Langley and Anderson have shown, is, like sympathetic ganglia in general, capable of being paralysed by nicotine; so that impulses to the sphincter pupillæ are blocked and ineffective, while direct irritation of the short ciliary nerves causes contraction.

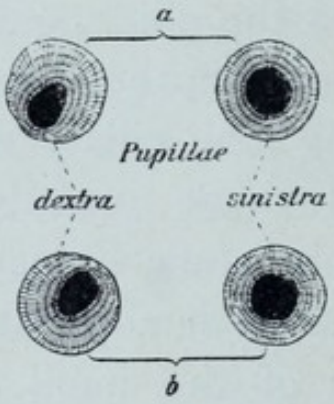

FIG. 44.—Excentric position of the pupils in general paralysis (Piltz).

The question is whether the degeneration found by Marina in the ciliary ganglia in tabes, taken in conjunction with what we know of the physiology of these structures, throws any light on the pathology of the tabetic pupil. In this relation the researches of Piltz appear to me to be of great significance. Piltz calls special attention to the fact, to which I have previously alluded, that the pupils in general paralysis and tabes commonly exhibit irregularities of outline, being angular, jagged, or otherwise misshapen, and not infrequently eccentrically situated, instead of having the smooth, circular contour and central position of health (fig. 44).

This condition often precedes the development

of the Argyll-Robertson pupil, and Joffroy and Schrameck maintain that every alteration in the form of the pupils — congenital anomalies and synechiæ excepted—even though the light reflex be retained, signifies that we have to deal with

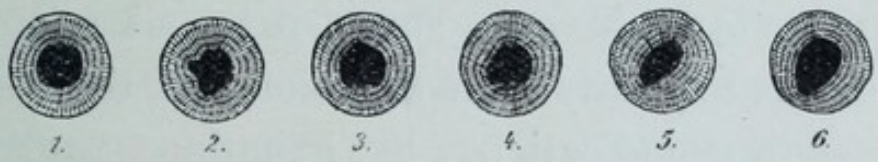

FIG. 45.—Varieties of irregularity of the pupils in different forms of organic nervous and mental diseases (Piltz).

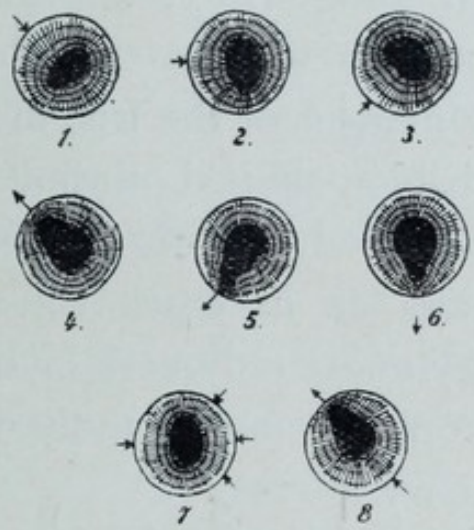

FIG. 46.—Varieties of irregularity of the pupil produced experimentally by stimulation of different twigs of the long and short ciliary nerves (Piltz).

general paralysis, tabes, or syphilis, and that the semeiological value of irregularity of the pupil is not less than that of the Argyll-Robertson phenomenon itself, which it often precedes (fig. 45). This is also the opinion of Babinski, Piltz, and others.

After complete exposure of the ciliary ganglion

and ciliary nerves in the dog, and irritation of various twigs of the short and long ciliary nerves, Piltz produced irregularities in the outline of the pupil and in its position, such as are indicated in the accompanying figure (fig. 46).

The similarity of these appearances to those of the pupils in tabes and general paralysis is obvious, and seems to justify the conclusion that these abnormalities are indications of irritation, paresis, or paralysis of different portions of the iris, due to pathological changes in the long or short ciliary nerves or their ganglia. It has also been shown by Dupuy-Dutemps that in the Argyll-Robertson pupil the inner margin of the iris, instead of having the normal cushion-shaped outline on section, is extremely attenuated. This atrophy of the iris may be general, or in cases where the pupil is irregular it may affect only certain segments of the iris. This atrophy is undoubtedly due to affection of the short ciliary nerves.

It is difficult to conceive how such irregularities of the pupil could be produced by any central lesion ; and seeing that they so often precede the reflex iridoplegia of tabes, the presumption is strong that both phenomena have essentially the same anatomical basis, namely, degeneration of the ciliary ganglia and short ciliary nerves.

Piltz's experiments enable us to understand the irregularities in the outline of the pupils, but how can we explain the loss of the light reflex, with the retention of the contraction or accommodation ?

We can, I think, cite analogous facts. We know that different nerve fibres in the same trunk may be differently affected by destructive or toxic agencies. The extensor muscles are principally affected in the peripheral neuritis of alcohol, lead and arsenic; and pressure on the recurrent laryngeal first affects the abductor nerves of the larynx. Langley and Anderson have shown that nicotine paralyses the sphincter of the pupil and ciliary muscle long before causing paralysis of the external ocular muscles; and we know that the toxin of diphtheria may affect the ciliary muscle alone, leaving the actions of the pupil and the external ocular muscles intact. It has also been mentioned that partial lesions of the trunk of the third nerve may cause ophthalmoplegia externa without impairing the action of the pupil. And total ophthalmoplegia interna due to syphilis may under antispecific treatment give way to a condition merely of reflex iridoplegia.

There is therefore nothing improbable in the assumption that in tabes the ciliary ganglion and ciliary nerves are so affected that, though they cannot transmit the reflex impulse of light to the sphincter pupillæ, they can readily allow the more powerful stimulus associated with accommodation to pass through. It is also probable that the myosis, which is so commonly associated with the reflex iridoplegia in the tabetic pupil, is due to degenerative changes of an irritative character which are going on in the sphincter.

In a similar manner may be explained the absence of the dilatation which normally results from sensory or emotional stimuli.

The dilatation of the pupil which occurs under such conditions is practically independent of the cervical sympathetic, and may be observed, though to a less extent, when this nerve is divided. This was first noted by Vulpian, and has been verified by Bumke as well as by myself in cases of lesion of the dilator roots of the cervical sympathetic.

And in tabes the dilator of the pupil is not paralysed, for under the influence of cocaine the pupil enlarges as in the normal state, and all the irregularities of its contour become accentuated.

Psycho-reflex dilatation is due, according to Braunstein, to inhibition of the oculo-motor nucleus acting through the third nerve, and therefore through the ciliary ganglion, for it does not occur in oculo-motor paralysis. Therefore, though the exact mechanism may require further elucidation, the probability is that the condition which blocks the path of reflex pupillary constriction blocks also that of psycho-reflex dilatation; and that in the degeneration of the ciliary ganglion we have the explanation of the tabetic pupil.

If time had permitted, I might have offered some considerations on the pathology of the disorders of innervation of the bladder, visceral crises, arthropathies, muscular atrophies, and other notable symptoms of tabes; but I found, as I filled page after page on the questions to which I have devoted

these lectures, that it would be impossible for me to deal effectively with them all, and it seemed to me better to discuss a few points with some fulness of detail, than range cursorily over the whole field. Such as I have chosen I might have treated at much greater length, but I shall be glad if I have succeeded in showing that in such a well-worn subject as tabes there are still many problems of surpassing interest, and worthy of further diligent study and research.

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