In the case reported by Mackay, in *Brain*, Part 84, the peripheral nerves appear to have been examined more extensively and carefully than in previous reported cases, and were all found extremely degenerated, yet clinically it was noted that there was no anaesthesia. In referring to this point he says: "The fact, moreover, frequently recorded, that the patient's sensibility to touch, pain, and temperature remains unimpaired throughout, suggests that it is the afferent nerves from muscles that chiefly suffer. This agrees with Guizetti's conclusions, who was of opinion that, in his own case, there existed a systematic atrophy of sensory fibres." But if this were so, we should expect to find in every case clinical evidence of the loss of sense of posture, or loss of muscular sense; but this has often been proved not to be the case. In some cases the spinal ganglia have been examined, and in all there was evidence of degeneration in the nerve cells, with hyperplasia of the connective tissue. Further complete investigation, both clinical and pathological, of cases of this disease are needed before we can explain the apparent discrepancy between the clinical signs and *post-mortem* findings.

Secondly, in the majority of cases there is no sphincter trouble; and even when such does exist, it is no more than some little delay in beginning the act of micturition. Sphincter trouble may arise either from motor or sensory disturbance. In tabes, for example, when there is affection of the sphincters, it will be found that there is some anaesthesia of the urethra, bladder, or rectum. In disseminated sclerosis, on the other hand, where there is, as a rule, no sensory disturbance, the sphincter trouble depends upon some derangement of the motor innervation of those parts. The absence of sphincter trouble in Friedreich's ataxia is probably due to the absence of anaesthesia of the excretory passages.

Thirdly, I would call attention to the condition of muscular hypotonia which is present in most cases of this disease to a greater or less extent; and this in spite of the contractures of the leg muscles which produce the deformity of the foot. The occurrence of this condition in Friedreich's ataxia is interesting, since it is now a well-recognised feature in tabes, and appears to be associated in some way or other with the degeneration of the posterior roots. It is probable that the absence of all the so-called "deep reflexes" is, in part at any rate, to be ascribed to this condition of the muscles.

A CONTRIBUTION TO THE STUDY OF THE POSTERIOR COLUMNS OF THE SPINAL CORD.*

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THE structure of the posterior columns of the spinal cord is as yet so dubious that the following result of an investigation of a case of tabes dorsalis will be of interest. In this research Pal's modification of Weigert's hæmatoxylin method was used.

I am aware of the possibility that nerve fibres may be present in patches of sclerosis and yet not be picked up by hæmatoxylin, and that Marchi's method would have been a better one upon which to base the conclusions I have come to in this case. Before I got hold of the cord and nerves, however, they had had the Muller's fluid washed out of them, and had been placed in alcohol, thus precluding the possibility of a reliable Marchi's stain. But I think I may safely claim that by having stained and examined some five hundred sections from all levels of the cord, I have obviated any error that was possible as the result of using the above-mentioned method.

As the nutritional condition of the posterior roots between their trophic centres in the posterior spinal ganglia and the cord—that is, the root trunk according to P. Marie—is an important factor in this case, because they are so largely

concerned in the structure of the posterior columns and grey matter they may be described at once.

In all root trunks below the first lumbar there is total atrophy of nerve fibres. In the first lumbar root trunks a few attenuated nerve fibres are present. Above the latter point to the upper part of the thoracic region the root trunks acquire a slightly increased number of nerve fibres. In the upper two segments of the thoracic region and in all levels of the cervical cord the fibres are numerous; many of them, however, are in a state of chronic wasting, and there is little doubt that a number of them have disappeared.

These facts were determined by examination of all the lumbo-sacral root fibres, and every second thoracic and cervical at three different parts, namely, close to the cord, close to the ganglia of origin, and midway between these parts.

Accepting in a limited sense the Wallerian orthodoxy of degeneration, it is to be expected, first, that that part of the posterior columns traversed by the central continuations of those posterior root fibres shown to be degenerated will be in a state of fibrosis; and, secondly, that all fibres not direct continuations of the roots but derived from the grey matter (that is, endogenous fibres of the comma tract, Marie's cornu-commissural zone, Fleschig's median triangle and posterior internal root zone, or, as it is named by Marie, to prevent any association of it with the afferent root fibres, the postero-internal zone; and, lastly, Gombault and Philippe's endogenous fibres of the sacral region) will be intact unless the grey matter can be shown to be unsound.

The first expectation is justified by the present state of the posterior columns. Not so, however, is the second, for there is an anomalous state of affairs in the endogenously-derived tracts, one having almost wholly disappeared while the other three or four have persisted. This anomaly may, I think, be explained by a certain degeneration of the grey matter, which is probably the seat of origin of the affected endogenous fibres.

First of all those parts of the posterior columns now widely recognised to be composed of the centripetal continuations of the afferent roots will be disposed of. I find that the posterior columns in all planes are marked by a somewhat triangular area of absolute sclerosis roughly corresponding to the track of the lumbar and sacro-coccygeal root fibres of the normal cord. Throughout the whole length of the posterior columns this area of scar tissue contains no sign of nerve fibres whatever, except a few fibres of the lumbar region in the position of the median triangle (Figs. 1 to 4).

Thus the path of the lower thoracic, lumbo-sacral, and coccygeal fibres in the columns of Goll coincides with the state of the same fibres exterior to the cord. If the claim that Goll's columns are amplified in their whole upward extent by fibres originating in successive levels of the grey matter is allowed, this total fibrosis will appear strange. Still it is a fact, and seems to dispose of such a contention.

It may, however, be urged in favour of the above-mentioned claim, first, that the trophic centres from which the supposed endogenous fibres take origin are atrophied and along with them their extensions into the postero-median columns; or, secondly, that the pressure exerted by the scar tissue which has replaced the wasted exogenous fibres was cause enough to set up a retrogressive atrophy in the endogenous feeders of the columns as far forward as the antero-lateral limit of the scar tissue, or even to the grey matter itself.

The second contention, however, is effectually disposed of by reference to the lumbar posterior columns. In this region (see Fig. 5 a) there is to be seen a small group of fibres in the middle third of the posterior columns in and about the position of the median triangle. This is one of the tracts of intracordal origin, and will be referred to more fully later on. If this tract, whose fibres beyond a doubt come from the grey matter, can persist in a plane of the cord, whose posterior columns are densely fibrosed, and whose posterior horns show the greatest wasting of grey matter (see Fig. 1 a), it would not be too much to expect a like persistence of endogenously derived fibres in higher related parts of Goll's columns the associated grey matter of which, except Clarke's columns, is almost normal.

The first claim—namely, that the trophic centres of the fibres of endogenous origin are atrophied, and along with

* Towards this research the Scientific Grants Committee of the British Medical Association made a grant of £30.

them their extensions into Goll's column, is not so easily disposed of. On the whole the posterior grey matter of the lumbo-sacral metameres is deeply sclerosed, especially the heads of the posterior horns, as may be seen in Fig. 1 *a*. But this ceases rather abruptly in the lower thoracic segment, and from thence upward is, generally speaking, sound. It is slightly "rarefied" along the tracks of those afferent root fibres which penetrate and enter into its composition, and also in the intermediate part where the pyramidal fibres of the lateral columns pass forwards to their destination in the ventral horns. But most of the cells appear healthy, except those of Clarke's columns. So there is little warrant for supposing that in the general health of the thoracic grey matter only the cells of those parts which pass to Goll's columns are destroyed. It is possible that the supposed amplifiers of Goll's columns may spring from an isolated group of cells, and that this group is atrophied in the upper levels of the cord where a general affection of the grey matter has ceased.

But I have observed only one such group in each half of the grey matter in extreme degeneration, namely, Clarke's cylinders of cells both large and small. Fibres from some of these may, of course, pass, as was suggested by Tooth, to the median columns, as I intend to point out they probably do to the comma tract.

Taking all points into consideration, however, it appears more probable, as Déjerine and others have shown in cases of total degeneration of this same part without involvement of Clarke's cylinders, that, the median columns, having once been formed in the higher lumbar region, are in the rest of their upward extent given over to the conveyance of representative fasciculi of root fibres to the bulb, and that any fibres which pass between them and the grey matter are probably collaterals from the ascending root fibres themselves.

Now to a consideration of those fasciculi of fibres of the posterior columns whose genetic point is held to be intracordal. First, the cornu-commissural zone of Marie (Figs. 1, 2, 3, 4 *b*). I find in all levels between the upper sacral and first lumbar, where, as I have stated, there is total obliteration of all extracordal feeders of the posterior columns, that there is nevertheless a considerable number of fibres in various phases of degeneration lying in the apices of the columns closely apposed to the posterior grey commissure and median margins of the necks of the dorsal horns. In no level do they extend further posteriorly than the posterior extension of the healthy grey elements. Above the level of the second lumbar segment they begin to blend with a few vertical fibres of the cornual portion of the cornu-radicular zone, which at this plane put in their first appearance.

The fact that the above-mentioned zones are extant where they cannot possibly be considered to be continuous with root fibres, seeing that at the level of their first appearance these are absent; that they bear a relation by their position to the healthy grey elements of the dorsal horns; that they predominate in number and health on the left side corresponding to a like state of affairs in the posterior grey commissure and grey matter, all tend to prove that this collection of fibres in the position of the cornu-commissural zone is in the main of intracordal origin. And it may be reasonably assumed that throughout the rest of the posterior columns a part of the fibres in the same relative position are of similar derivation.

Next the median triangle of Flechsig which has already been alluded to (see Fig. 5 *a*). This is stated to lie in the middle and lower lumbar plane in apposition to the postero-median septum, and to extend backwards, it is claimed by some observers, to the periphery of the cord. The figure shown is of a section from the lower lumbar region. It exhibits a cluster of discreetly-laid attenuated fibres in about the position of the median triangle. Below the last lumbar and above the third lumbar segments it is not observable. Keeping in mind the abolition of all fibres from the posterior roots of this and adjacent upper and lower levels, it seems proved without further remark that this small aggregation is of intracordal origin. But the following additional facts also militate in favour of such a conclusion, and perhaps suggest the path by which they come and go:

1. They preponderate on the left side, corresponding to a like preponderance of fibres in the left half of the posterior grey commissure.

2. Some of the fibres fringing the median septum between the median triangle and grey commissure cut obliquely in accurate transverse sections. This appears to indicate that fibres from the median triangle are taking a dorsal slanting direction to reach their destination in the triangle, or that they are taking a ventral path from the triangle to the commissure.

3. The fibres stretching between the commissure and the triangle disappear at the level of the cord immediately above the level of disappearance of the triangle itself from the posterior columns. At the level of the triangle a fibre or two may be seen passing dorsally from the grey commissure towards the triangle. Although these fibres could not be traced the whole way to the median triangle, I am convinced from examination of a series of sections that they do reach and enter into it. For in such sections portions of fibres may be observed taking the same horizontal or slightly oblique direction parallel to the posterior median septum, and one or two of these actually enter the tract. By the aid of these consecutive sections a complete fibre may be synthetically built up, and apparently passes between the posterior grey commissure and the median triangle.

5. In further evidence it is to be observed that the isthmus of fibres which extends between the commissure and the tract contains all that can possibly have any association with the latter. For in all but its ventral aspect, where this isthmus is, the tract is encompassed by a dense fibrosis containing no nerve fibres whatever.

These evidences certainly support the contention that the median triangle of the normal cord is of almost purely intracordal origin, and that its fibres reach it by way of the grey commissure.

That it is not wholly of endogenous origin seems likely in view of the discrete arrangement of its fibres in this cord and the pervasion of it by sclerotic tissue, a condition due in all probability to the absolute atrophy of those fibres intermixed with it which were of extra-medullary derivation.

The aggregation of fibres shown in Figs. 3 and 4 *a* is in the position of the postero-internal zone. Marie claims that these fibres are of intracordal rather than extracordal origin. But the evidence in favour of this is not so positive as in the case of the other endogenous tracts. The research on this cord does not clear up the doubt in regard to their origin, but suggests that they are mostly endogenous fibres, and that they do not extend downwards below about the tenth thoracic segment.

Here, again, it will have to be kept in mind that below the first lumbar metamere the afferent root trunks are bared of proper fibres. And to this statement may be added that the fibres present in the first lumbar root trunk are few in number and in a very unsound state. None of them appear to proceed to the median columns, but towards the median margins of the posterior grey matter or through the substantia gelatinosa. It will be remembered that the lower five or six thoracic root trunks contain a scanty number only of root fibres.

Therefore, the rather abrupt appearance of a large mass of fibres in the posterior part of Burdach's column, that is, in the parts corresponding to the location of the postero-internal zones of the normal cord, calls for some remarks.

It appears to indicate, in view of the above-mentioned status of the root trunks, that the great majority of the said fibres are derived in a large measure from sources other than extracordal, that is, from the grey matter.

The following observations strengthen this claim:

1. The postero-internal zones are not present in the lumbar region where proper grey elements of the posterior horns are almost exclusively confined to the necks of the latter, nor do they appear until at least three levels above the first appearance of proper fibres in the afferent roots.

2. Above the lumbar region the proper grey elements begin to appear normal. Soon after there is the first evidence of fibres in the postero-internal zones.

3. The number of fibres in the zones in the level where they are first observable are out of all proportion to the number of proper fibres observable in the root trunks. And further, there are not enough fibres in the posterior columns in any level of the cord above the first appearance of the zones to warrant an assumption that the fibres of these zones are root fibres on their way to the medulla.

Fig. 1.—Lower lumbar region. Cornu-commissural zone of Marie at *b*. Degeneration of posterior horns at *a*.

Fig. 2.—Lower thoracic region. Cornu-commissural zone at *b*. Degenerated comma tracts at *c*. Clarke's column may be seen heavily sclerosed: also area corresponding with lumbar and sacrococcygeal fibres.

Figs. 3 and 4.—Thoracic and cervical regions. Postero-internal zone at *a*. Degenerated comma tracts at *c*. Cornu-commissural zone at *b*.

Fig. 5.—Lower lumbar region. Mass of fibres in position of cornu-commissural zone. Remnant of Flechsig's median triangle at *a*.

Fig. 6.—Degeneration in Clarke's vesicular cylinders at *b*. The lines have been carried through Clarke's columns.

Thus it seems probable that the majority of all postero-internal zone fibres take origin in the grey matter. And when it is remembered that the fibres do not put in an appearance until the sclerosis of the heads of the horns is in a large measure replaced by proper grey elements, it does not seem improbable that they take origin in the most dorsal portion of the grey matter.

This disposes of three of the tracts of the posterior column whose fibres are by most investigators thought to be of endogenous origin, and which persist in all lesions exclusively confined to afferent root fibres, but which are the earliest to succumb to any morbid process which primarily affects the grey matter.

The fourth and remaining one is Schultze's descending comma tract. In the normal cord, like others of intracordal origin, this tract is of mixed composition, containing fibres that degenerate when the posterior roots are severed, and others that atrophy only when the grey matter is diseased. But it is generally believed that fibres which depend for their nutritional activity on the cells situated in the grey matter largely preponderate over those whose trophic centres are in the cells of the posterior spinal ganglia.

In view of the fact that three tracts of acknowledged intramedullary origin have persisted even in the presence of considerable chronic poliomyelitis, there arises a natural desire for an explanation of the presence of degeneration in this tract (see Figs. 2, 3, and 4 c) whose main origin is similar. For, as already intimated, the comma tract is in a state of almost absolute fibrosis from its usually assigned upper to its lower limits. (See Figs. 2, 3, and 4 c).

An explanation which has presented itself is that being of more mixed origin than the other endogenous tracts it has suffered doubly as a result of a chronic degeneration its centres in the cord and in the posterior root fibres.

Yet I have not been able to convince myself into accepting so easy an explanation. It seems to me that there must be some specific reason for this contradictory degeneration, that there must be some special groups of cells whose fibres enter into the posterior external columns and congregate as the descending comma tracts, and which in this case have been so severely affected by the atrophic process at work as to cause abolition of these fasciculi of fibres.

The only groups of cells, however, which show extreme degeneration are Clarke's (see Fig. 6 a). Is it possible that cells of the vesicular cylinders, besides being the authors of the direct cerebellar tracts, also give origin either directly from some of the cells themselves, or as collaterals from the cerebellar fibres to the descending comma tracts?

In a normal cord fibres may be seen passing from the grey matter mesial to Clarke's columns, where they exist, into the postero-external columns to about the position of the comma tracts. Fibres corresponding to these cannot be observed in this cord; and that these fibres, Clarke's cells both large and small, and the comma tracts are all degenerated, appears to be above coincidence, and to point to some anatomical association.

Again we know almost precisely the vertical extent of the vesicular cylinders. Day-by-day evidence is being adduced which tends to prove that the descending comma tracts are of about the same vertical extent as the cylinders, and it seems probable that before inquiry stops it will be determined that there is an exactness in the range of both structures.

It appears unlikely, in view of what we know of cell associations, that an almost continuous column of cells of the extent of Clarke's are unassociated by commissural fibres; and taking into consideration the nearness and apparent association of the vesicular cylinders with the fibres leading from their neighbourhood to the vicinity of the comma tracts, and the likeness in vertical extent of both the cylinders of cells and fasciculi of fibres, it does not appear improbable that the latter function between upper and lower levels of the former. If such an anatomical connection exists, there is at once found an explanation of the persistence of fibres in three tracts of intracordal origin and the abolition of the greater part of the fibres from others of like origin.

NOTE.—Since the above was read at the 1897 meeting of the British Medical Association, Dr. Bruce has published an interesting case showing the connection of Flechsig's median

triangle and Gombault and Phillip's sacral fibres which together he has named the septo-marginal tract. This case is certainly strong negative evidence in favour of Bruce's contention regarding the extent of the septo-marginal tract. The disappearance of the lower and more peripheral portion of the latter in this case, which corresponds to Gombault and Phillip's fibres, while the upper portion corresponding to Flechsig's triangle persists, is no doubt due to the greater degeneration in the grey matter of the sacral posterior horns.

THE CROONIAN LECTURES

ON

SOME POINTS CONNECTED WITH SLEEP, SLEEPLESSNESS, AND HYPNOTICS.

Delivered before the Royal College of Physicians of London.

By JOHN BUCKLEY BRADBURY, M.D. CANTAB.,

Fellow of the College; Downing Professor of Medicine in the University of Cambridge; and Senior Physician to Addenbrooke's Hospital.

LECTURE IV.

I CONCLUDED my last lecture by stating that attempts had been made to find a less dangerous and equally effective substitute for morphine. To two such compounds I now wish to draw your attention.

In 1890, Stockman, in conjunction with Dott,¹ published experiments made on some derivatives of morphine. They introduced into the morphine molecule various alkyl and acid radicles and chlorine, and also modified it by the addition of methyl chloride. Morphine contains two hydroxyl groups, and the hydrogen of one of these, probably united to an aromatic nucleus, is more easily replaced than the other. When this is replaced by methyl, ethyl, or amyl, the morphine action still remains, but the compounds thus produced are more toxic, their narcotic power is less, their tetanising power greater, and they have a greater effect upon the motor nerves. On the whole, their experiments do not seem to give much support to Schröder's law, as they say: "Theoretically, there is possibly a difference in the actions of the three substances, but it must be entirely quantitative, not qualitative, and our methods of investigation were not sufficiently fine to detect it (if it really exists)." Von Mering's recent observations are even more convincing. From clinical observation he found propyl-morphine, isobutyl-morphine, and amyl-morphine distinctly feebler than methyl- and ethyl-morphines.² When acetyl and benzoyl radicles were introduced, and acetyl-morphine, di-acetyl-morphine, benzoyl-morphine, and di-benzoyl-morphine were thus produced, a similar effect was obtained. The narcotic effect, however, was present after small doses (1 mg.— $\frac{1}{2}$ gr.—of acetyl morphine in the case of rabbits), but it did not appear to increase with increase of the dose, tetanic symptoms developing instead. "The depressant action of small doses on the cord, and especially on the respiratory centre," Stockman and Dott say, "is very much greater than that of morphine." From this statement we should not expect any of these to be of value as substitutes for morphine. But the case is otherwise regarding codeine, as they say that, compared with codeine, "they (the acid derivatives) induce an equal narcotic effect with about one-tenth of the dose, while a dose about three times as large is necessary to cause tetanus. Their depressing action on motor nerves is about the same; the nausea and diarrhoea occurring in dogs is quite as great as after codeine." Thus as a substitute for codeine we might expect one of these substances to be of value. Quite recently Dreser,³ from researches mainly on the respiration, has introduced diacetyl morphine, under the name of "heroin," into therapeutics. According to him it is more powerfully sedative, and correspondingly less toxic than codeine; it lengthens the time of inspiration, increases the gaseous exchange, and does not affect the sensibility except in diminishing any tendency to over-extension of the lungs. So far the clinical results have supported Dreser's experiments, but as yet they have been too few to decide the position this drug will hold in therapeutics.

But von Mering has found that monoacetyl-morphine—in which the acetyl replaces the hydrogen of the alcoholic