OBSERVATIONS ON THE ANATOMY OF THE SPINO-CEREBELLAR FIBRES IN MAN

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CHAPTER I

INTRODUCTION.

This thesis is concerned with the origin, course and termination of the spino-cerebellar fibres in man. In addition to this study, which forms the major part of the thesis, two relevant subsidiary pieces of work are included. These are: (a) Certain original observations on degeneration in the central nervous system, and on their demonstration, in particular by the Marchi method; and (b) Presentation of a simple method of charting the cerebellum.

The studies reported here were made in the Neurological Unit of the Medical Research Council, National Hospital for Nervous Diseases, Queen Square, London W.C.1. They represent one part of an investigation into the functional anatomy of the human spinal cord.

The investigation was designed so as to make use of the operation of ventro-lateral cordotomy, performed for the relief of pain. Patients with incurable cancer, not involving the spinal cord, giving rise to intractable pain, and with an expectation of limited survival, have the pain-relieving operation of ventro-lateral cordotomy. In most cases the operation is performed by Mr. Wylie McKissock. Detailed clinical observations are made before and after the operation by Dr. P.W. Nathan. After death, histological studies of the brain, spinal cord and peripheral nerves are made by the writer. This material is particularly suitable for studying the degeneration in tracts, resulting from limited lesions. In every case part of the cerebellar tracts are cut at operation, for it is impossible to divide the spino-thalamic fibres associated with the modality of pain, without damaging the spino-cerebellar fibres also.

When one traces the history of the acquisition of knowledge of the anatomy of the central nervous system, one notes that the first observations were made on human pathological material, and to a lesser extent, on normal human material and embryos. To add to this picture workers undertook experimental and embryological investigations on laboratory animals. It was implied that these investigations should serve as models to guide later studies on man. But, as will be seen from the review of the literature given here, these later investigations have rarely been carried out. Instead, it has tacitly been assumed that the findings from laboratory animals are fully applicable to man. This assumption may or may not be justified. In any case, as doctors we are all interested finally in man. Hence it is particularly the anatomy of man which requires investigation.

Although it is almost eighty years since the spino-cerebellar tracts were first described there still remain large gaps in our knowledge of the tracts. The object of this investigation, which forms the material of this thesis, has been to work out the anatomy of the spino-cerebellar fibres in man.

CHAPTER II

HISTORICAL REVIEW.

Preliminary note on terminology.

The nomenclature of the long ascending tracts of the lateral columns is confused; often the same term is used by different workers to designate different tracts. The term "Gower's tract" is varyingly applied to the spino-thalamic tract only, to the ventral spino-cerebellar tract only, both of these together or to the whole complex of ascending tracts in the ventro-lateral quadrant. The spino-cerebellar tracts are respectively termed the direct and indirect, uncrossed and crossed, postero-lateral and antero-lateral, Flechsig's and Gowers', or dorsal and ventral tracts. In this thesis, for the sake of clarity, the terms "dorsal spino-cerebellar tract", "ventral spino-cerebellar tract" and "spino-thalamic tract" will be used whenever possible, and they will be substituted for the terminology employed by the author quoted where this is necessary.

The nucleus dorsalis, or dorsal nucleus of the spinal cord is so commonly known as "Clarke's column", and the cognominal terminology is so free from ambiguous application in this case, that either term will be used.

The earliest recognition of the existence of a tract in the lateral column of the spinal cord was by Foville; in 1844 he distinguished a peripheral tract on account of its myelination at an earlier stage than the adjacent tracts.

A few years later Clarke (1851, 1859, 1863) published his observations on certain cells in the cords of a series of lower animals, and of man. He described a column of vesicular cells at the base of the dorsal horn, extending throughout the length of the cord. He thought these cells had some intrinsic relation with the dorsal roots without forming any apparent connection with them, and that they had processes, some of which extended into the lateral columns. In his later papers Clarke accepted the view of Stilling (1859) that some scattered cells in the situation of this column, in the cervical and sacral regions, might in fact form separate nuclei; these are usually called the "cervical" and "sacral" nuclei of Stilling. In 1853 Türck, examining unstained sections of material from a case of compression of the spinal cord, described the continuation of one centripetal path from the lateral column through the restiform body into the cerebellum. Bouchard (1866) and Bastian (1867) made similar observations in cases of lesions of the spinal cord. Flechsig (1876), from myelination studies on foetal cords, deduced a connection between the cells of Clarke's column and an ascending tract in the dorso-lateral part of the cord, which he traced into the restiform body and hence into the cerebellum. This tract myelinated before neighbouring tracts. He observed that it had two rather distinct parts in the cord. This dorso-laterally situated spino-cerebellar tract has, although he was not the first to observe it, always borne his name.

Westphal (1880) published an account of a case of cord degeneration following involvement of the upper thoracic segments in tumour. He traced degenerating fibres into the restiform body, and also noted a second small bundle between the olive and the descending root of the fifth cranial nerve. All these degenerating fibres were referred to as spino-cerebellar.

A big advance in knowledge of the long ascending tracts in the cord was made by Löwenthal (1884, 1885), working on the dog. After making spinal lesions he traced two ascending bundles cranially. He described this spino-cerebellar system as extending from the ventral extremity of the substantia gelatinosa to the level of the ventro-lateral nucleus. One part, the dorsal, he found moved dorsally in the medulla to take part in the formation of the restiform body; it eventually terminated in the superior vermis. The other part, which Löwenthal referred to as the ventral portion of the cerebellar tract, lay on the ventro-lateral periphery of the medulla. He described its course in the lateral part of the pons, lying dorso-medial to the fibres of the brachium pontis, and ventral to the fifth nerve nucleus, and then dorso-lateral to the inferior colliculus. In the region of the brachium conjunctivum the tract made a half circle, lying dorsal and lateral to the brachium. This relationship was maintained as the brachium entered the cerebellum. The termination of the tract was not determined. When the lesion in the cord was confined to the dorsal half of the lateral column, there were degenerating fibres in the restiform body only.

von Monakow (1883) produced further evidence for the existence of a long ascending tract in the ventro-lateral column. He made lesions in the cords of new-born rabbits and examined them six months later; the degenerated tracts were then atrophied. He followed the dorsal spino-cerebellar tract into the restiform body and a second tract up to the level of the facial nucleus. von Bechterev (1885A, 1885B) made a significant contribution, from his studies on myelination, from his observations on degeneration in rabbits and dogs after experimental lesions, and on man after pathological lesions. He recognised the existence of three ascending bundles in the lateral column. He identified one of these as the dorsal spino-cerebellar tract, another peripheral bundle lying ventral to this tract was identified as distinct from a third, more medial bundle. He found that many of the fibres of these ventral bundles ended in the formatio reticularis; he could not trace the remaining fibres higher than the pons.

Up to 1875 there was uncertainty as to

whether the fibres associated with the modality of pain travel in the white or the grey substance. A most important contribution to knowledge came from Woroschiloff, who, in 1875, reported the results of his experiments on a large series of rabbits. He made a variety of carefully controlled lesions in the spinal cord, and observed the altered reactions to stimuli. He concluded that sensory fibres ran in the lateral column, being most abundant in the middle third, and that most of the fibres are in the lateral column of the side opposite to the part of the body stimulated. He pointed out that some of the stimuli he used would undoubtedly be painful in man, although in the rabbit one could not prove that they caused pain. Ott and Smith (1879), employing Woroschiloff's technique, made a series of lesions in the cords of dogs, and tested the sensory and motor functions. They concluded that sensory and motor fibres in the cervical cord lay exclusively in the lateral columns.

In 1877 Gowers read a most important paper reporting his findings in the case of a Parsee student, who fired a bullet through his mouth, thus causing an injury of the spinal cord between the first and second cervical segments. The sensibility to pain was very distinctly diminished on the side opposite the lesion, whereas tactile sensibility was retained. The cord showed a limited lesion in the ventral part of the lateral column opposite the side of the analgesia. From this case Gowers deduced that in man fibres associated with the modality of pain run in the ventro-lateral column of the cord.

In 1880 and 1886 Gowers produced further evidence for the existence of an ascending tract associated with the modality of pain in the ventro-lateral column of man. He described this tract as extending across the lateral column about two thirds of the distance from the surface to the intermediate grey substance, from the angle between the pyramidal and direct cerebellar tracts almost to the anterior median fissure.

By 1885 then, we seethat three long ascending tracts had been described in the lateral column; and one of these - the dorsal spino-cerebellar tract - had been clearly separated from the others.

The tract which Gowers had described was a deeply lying tract subserving the modality of pain. We are now in a position to conclude that this is the spino-thalamic tract. The clear separation of three tracts, dorsal and ventral spino-cerebellar tracts and spino-thalamic tracts, was not always clear to the original workers, nor to their contemporaries. The confusion in the literature lingers on today; this is due to the failure to distinguish these three tracts, and to Continental workers naming ascending tracts in the ventro-lateral column, Gowers' tract. It is unfortunate that the name of Gowers' tract is still used, as it is rarely made clear which ascending tract is meant, and it is to be noted that it is not often used as a name for the spino-thalamic tract, the tract which Gowers actually described.

The next worker who made basic contributions to knowledge of the course and termination of the long ascending tracts in the lateral column was Mott (1888, 1890, 1892, 1895). From his work on the monkey, he was led to believe that the dorsal spino-cerebellar tract did not reach the surface of the cord until about the seventh thoracic segment.

In a further series of experiments he mapped out ascending degeneration in monkeys after cord lesions. In the lateral columns he recognised two ascending spino-cerebellar systems, for which he suggested the names dorsal and ventral ascending cerebellar tracts. He stated in his papers that he had divided only the ventro-lateral part of the cord on one side, but it is not clear from his account if he ever found degeneration confined to the ventral tract. The dorsal tract he traced to the dorsal portion of the superior vermis, and the ventral tract to the ventral portion of the superior vermis. A few fibres of the ventral tract were traced to the anterior quadrigeminal body of the same side. Mott thought that the origin of the dorsal tract was Clarke's column cells, and of the ventral tract, medium-sized, intermedio-lateral and solitary cells of the dorsal horn. He did not describe the detailed distribution of these cells, and may have included all the larger dorsal and intermediate cells. Mott denied that fibres of the ventral column were associated with pain, as he considered that complete division of the tract did not produce analgesia.

Edinger (1889), working mostly on fish and amphibia, had determined that some fibres which he thought were concerned mainly with sensation, enter the cord in the dorsal root, and synapse with cells in the dorsal horn. Fibres from these cells then cross and ascend in the ventro-lateral column, some going as high as the thalamus. Edinger found that few fibres entered the grey matter at the level of their entrance into the cord, and that most of them did so at some distance more cranially. Mott confirmed some of Edinger's observations. He cut the dorsal roots of the lower lumbar segments in two monkeys and a month later examined their cords; from this material he concluded that fibres from these roots passed into Clarke's column as high as the seventh thoracic segment. Later, in 1897, Marguliés repeated the experiment and came to the same conclusion.

Gaskell (1886) had suggested, without clear evidence, that fine efferent fibres to the viscera arose from Clarke's column cells. Mott refuted this suggestion, and confirmed that the upward prolongation of these cells formed the spino-cerebellar tract. Mott had also made most important observations on the comparative distribution of cells in Clarke's column in three species, man, monkey and dog (1888). He showed that the column is better developed in the upper dorsal region in the dog and monkey than in man. This important finding does not seem to have been adequately considered by later workers, as this and similar variations in different species render observations made on one animal not generally applicable. Mott also showed that from the eighth thoracic to the second lumbar segment in man Clarke's column is well developed. In higher and lower segments there are few cells, or none at all. Ample evidence that the dorsal spino-cerebellar tract arose from the cells of Clarke's column had been produced by a number of workers, but up to this time no irrefutable evidence for the cells of origin of the ventral spino-cerebellar tract had been produced. Singer, in 1887 suggested that the ventral spino-cerebellar tract arose from cells of the ventral horn, for he found that after compression of the aorta for varying times in dogs, ventral horn cells disappeared, and there was also degeneration of the ventral spino-cerebellar tracts.

Most workers considered the dorsal and ventral fibres to form two distinct tracts. Hadden and Sherrington, in 1889, appeared to hold the view that the dorsal and ventral fibres are part of one and the same system. They studied a case of locomotor ataxy, and concluded that the ventral spino-cerebellar tract passed to the cerebellum via the restiform body, having the same course in the medulla as the dorsal spino-cerebellar tract. But in the following year (1890), Sherrington produced evidence which appears to contradict this view, and made no comment on the contradiction. He wrote: "In fully grown dogs, in the monkey, and to a less extent, in the Human adult, a small septum, more marked than any of the neighbouring, projects into the lateral column at the level of the ventral extremity of the area of the crossed pyramidal tract... That the septum is of real morphological significance, I believe from the fact that it divides from one another two masses of nerve fibres which offer a strong contrast in their appearance. On the dorsal aspect of the septum lie coarse fibres of fairly equable size (cerebellar), on the ventral axits an admixture composed largely of fine fibres (ascending ventro-lateral)...." He also noted that in the monkey there was a portion of the pyramidal tract which lay lateral to the dorso-spinocerebellar tract, along the surface of the lateral column. No other worker has confirmed this last observation, although Sherrington had already observed it in 1889. In 1895, describing the pattern of ascending degeneration in the monkey, Sherrington observed that the longest fibres tended to be peripheral in both the dorso-lateral and the ventro-lateral columns. Later, with Laslett (1903), he demonstrated this latero-medial lamination in the dorsal spino-cerebellar tract in dogs.

A number of workers recorded their findings in tracing degeneration in the lateral ascending tracts to varying levels. Tooth (1885, 1887, 1889) traced a degenerating ventral tract to the lower medulla, in man, and later (1892), he followed the dorsal and ventral tracts to the restiform body and to the upper pons, in monkeys. Testut (1893) traced the two tracts into the vermis superior in man; Bruns (1893), in a man with a traumatic lesion of the cord, traced the dorsal and ventral tracts in the cord, and Patrick (1893) followed the degeneration in this same case to the restiform body and to the level of the brachium conjunctivum. At this level he found degeneration in the lateral lemniscus and in the angle between the lateral lemniscus and the brachium conjunctivum. Schaffer (1895), in a patient with a lumbar lesion, found degenerating fibres in the ventral column, but only as high as the second cervical segment.

Auerbach (1890), after destroying the dorsal ~~posterior~~ part of one half of the cord in cats and dogs, described three spino-cerebellar tracts. The dorsal tract ended in the dorsal part of the superior vermis, the ventral part in the ventral part of the superior vermis; a third small tract, which lay between the dorsal and ventral tracts in the cord, and continued with the ventral tract up to the level of the exit of the fifth cranial nerve, entered the restiform body, and passed towards the dentate nucleus. Pellizi (1897) also identified a third spino-cerebellar tract in dogs; it was smaller than the dorsal and ventral tracts, and consisted of large fibres. He found that this tract accompanied the ventral tract to the level of the exit of the eighth cranial nerve and then entered the cerebellum by the middle peduncle and passed towards the ventral superior part of the superior vermis. The dorsal tract crossed and radiated towards the superior ventral and inferior part of the superior vermis. The ventral tract gave off a large ipsilateral bundle to the superior portion of the superior vermis, and then gradually crossed and radiated into the folia of the ventral and inferior part of the superior vermis. He thought the ventral tract arose from Clarke's column cells or their homologues.

Other workers traced the dorsal and ventral tracts to varying levels. Patrick (1896) reviewed the literature, and also made original observations on three cats, some of which he illustrated clearly in drawings. He described the ventral tract as lying along the periphery of the cord immediately ventral to the dorsal fibres, and extending almost to the most lateral ventral nerve root. He considered that the fibres of the ventral tract were about the same calibre as those of the dorsal tract. He found the tracts distinct from each other in the medulla, but difficult to distinguish in the cerebellum. He emphasised that the ventral tract did not pass further cranially than the aqueduct of Sylvius. The terminations he ascribed to the systems are not quite clear. The dorsal tract was said to end in the "dorsal and proximo-ventral portions" of the vermis, and the ventral tract in the "ventral and distal dorsal portion" of the vermis, as well as in the lateral lobe. In the cerebellum, the majority of the ventral fibres appeared to decussate, whereas the majority of the dorsal fibres did not. In 1896, Hoche published a detailed paper in which he described the degeneration of the spino-cerebellar tracts in man. His two cases consisted of total transverse lesions of the cord, one in the mid-thoracic, the other in the upper thoracic region of the cord. He distinguished clearly between dorsal and ventral spino-cerebellar fibres, and traced the ventral fibres into the cerebellum; he concluded that they crossed in the root of the fourth ventricle and ended, mainly, in the superior vermis.

André-Thomas (1897), in a period when illustrations to papers tended to be poor, or non-existent, described and illustrated beautifully ascending degeneration in a case of Pott's disease, with softening of the third thoracic segment. He did not trace the ascending fibres into the cerebellum, and, confirming what most workers had found, stated...."il est moins aise de poursuivre sa terminaison dans le cervelet chez l'homme, chez l'animal, au contraire, on a pu suivre ses fibres dans le cervelet". In drawings of the cerebellum of the cat, Thomas showed the dorsal fibres terminating in the ventral vermis, the majority contralaterally but some ipsilaterally. The fibres of the ventral tract were shown in the contralateral hemisphere in the ventral part of the superior vermis, ventral to those of the dorsal tract.

In 1897 an important advance was made by von Solder. He studied the cord of a thirteen year old girl who had tuberculous meningitis affecting the cervical cord for six months before death. He described four long ascending tracts in the lateral column, the two well-known ones to the cerebellum, and another two going to the thalamus. Quensel (1898) gave some confirmation of von Solder's observations, tracing a tract from the lower thoracic region to the thalamus. This tract had already been seen in fish and amphibia by Edinger (1889). It was also observed by Van Wallenberg (1900) in rabbits, Probst (1900) in dogs, and Rothmann(1900) in dogs.

There was still little evidence of the terminations of the spino-cerebellar tracts in man. Bruce (1898) wrote a particularly important paper illustrated by drawings. He gave a detailed description of the course of the ascending lateral column fibres, in a case of compression of the cervical cord. In agreement with the descriptions given in animals, Bruce found that the dorsal tract occupied the dorso-lateral column in the cord, and the region immediately ventral to the spinal nucleus of the fifth cranial nerve in the lower medulla. The ventral tract lay ventral to the dorsal tract both in the cord and in the lower medulla, where it occupied the region just dorsal to the olive. The dorsal tract fibres entered the cerebellum by way of the restiform body, and the ventral by way of the brachium conjunctivum. Bruce found that the dorsal tract ended in the lobulus centralis, the culmen (monticulus), and to a slight extent in the lingula, the majority on the same side, with a considerable number on the opposite side. A small number of fibres were traced also to the nodulus and uvula; they were too few, however, for him to be able to determine if any of them crossed: Bruce found no evidence that any fibres terminated in the nuclei of the middle lobe, and was certain that none entered the nucleus dentatus or the cortex of the cerebellar hemispheres. The ventral tract he found to end in the lingula, almost all on the same side.

Risien Russell (1898) studied degeneration in the spinal cord of man, following various lesions. Two points of particular interest were contributed by him. A lesion of the third and fourth lumbar segments led to degeneration in the ventro-lateral column, but not in the dorso-lateral column. The ascending degeneration in this cord lay deep to the surface, about mid-way between the periphery and the grey matter of the ventral horn. In another case in which there was a transverse myelitis at the sixth and seventh cervical segments the ascending degenerating tract occupied the same region. It must be accepted that Risien Russell showed, as Gowers did earlier, the existence of a ventro-medial ascending tract. In view of the evidence of all other workers both at this time, and later, of a ventro-lateral ascending tract also, it is difficult to see why it was not degenerated in this case. As the extent of the lesion was not shown, although said to be a complete transection, and in view of the evidence consisting of one section only stained by the Weigert Pal method, it is impossible in retrospect to re-assess the findings.

Rossolimo (1898) described in a girl of 12, the ascending degeneration in the ventro-lateral region of the cord, which resulted from sarcomatous deposits in the lower thoracic and lumbar region. He found a few fibres leaving the main bundle of degenerating fibres to enter the cerebellum by way of the restiform body. He denied that any fibres entered the cerebellum by way of the brachium conjunctivum or by the velum medullare.

A number of workers, tracing ascending degeneration from the ventro-lateral column of the cord, had found fibres continuing further cranially than the brachium conjunctivum. Edinger (1889); Mott, (1892); von Solder, (1897); Quensel, (1898);

Tschermak, (1898); Rossolimo, (1898).). There was considerable variation in the termination of fibres in the brain stem, cranial to the brachium conjunctivum, as found by different workers. As these fibres are obviously not part of the cerebellar system they will be considered only where they are germane to our present problem. But it is necessary to recognise the possibility of their existence, for in regions caudal to the brachium they are intermingled with spino-cerebellar fibres.

The first author who seems to have recognised definitely that the so-called "Gowers'" tract contained a number of different long tracts was Barker (1901). He suggested that "Gowers' tract" might contain the following seven sets of fibres:-

1. Spino-cerebellare ventro-laterale conjunctivale.
2. Spino-quadrigeminale superius (Mott).
3. Spino-thalamicum (Mott).
4. Spino-cerebellare ventro-laterale restiformale (Rossolimo).
5. Spino-quadrigeminale inferius (Tschermak).
6. Spino-pedunculare ad substantiam nigram (Tschermak).
7. Spino-lentiformale (Tschermak).

Of the seven tracts recognised by Barker, only two are essentially relevant to the present study: 1. the spino-cerebellare ventro-laterale conjunctivale, and 4. the spino-cerebellare ventro-laterale restiformale. Only the first of these two tracts has been generally recognised by later workers. The evidence for the existence of a spino-cerebellare ventro-laterale restiformale tract has been almost completely disregarded. In this respect it may be noted that the evidence of Pellizi and of Kohnstamm, for a third, intermediate spino-cerebellar tract, has likewise never been generally accepted.

Thus, by the end of the nineteenth century two spino-cerebellar tracts were recognised by the majority of workers: the dorsal spino-cerebellar tract, and a ventral spino-cerebellar tract. These two tracts were considered to be distinct from each other, except for their contiguity, in the cord and in the medulla. The dorsal spino-cerebellar tract was described as entering the cerebellum by way of the restiform body, and the ventral tract by way of the brachium conjunctivum. This became the generally accepted view and appears in all text books.

Both tracts were thought by most workers to end in the superior vermis, but there was considerable variation in the views held on the exact distribution of the fibres, and on the degree of crossing of the fibres in the cerebellum. Abundant evidence had been produced showing that the dorsal tract arose from the cells of Clarke's column. Evidence for the cells of origin of the ventral spino-cerebellar fibres was less convincing. Cells of the dorsal horn and of the intermediate grey matter, cells of the ventral horn, and cells of Clarke's column had all been suggested as giving rise to the ventral spino-cerebellar tract.

In the ventral quadrant of the cord there is considerable overlap between the various tracts. The cells of origin and the terminations of fibres made to degenerate by experimental surgical lesions can be ascertained. But it remained a matter of conjecture and personal interpretation which fibres arose from which cells and had which termination.

Although the conception of the ventral spino-cerebellar tract as completely distinct from the dorsal spino-cerebellar tract is the one universally held, several workers have produced evidence showing that a few, or many, fibres pass from the ventral spino-cerebellar tract into the restiform body. Some have shown that some fibres pass from the ventro-lateral to the dorso-lateral column during their ascent in the cord.

In 1889 Hadden and Sherrington made some observations on the course of the spino-cerebellar tract in man. They reported that some fibres of the ventral tract entered the cerebellum by way of the restiform body. Barbacci (1891), and Rossolimo (1898), made similar observations in man. Tschermak (1898) recorded similar findings in the cat, and Kohnstamm (1900) in the rabbit. All these workers found that a certain proportion of the fibres of the ventral spino-cerebellar tract entered the restiform body, while the remainder reached the cerebellum via the brachium conjunctivum. Schäfer (1899, 1908), Ninian Bruce (1910) and Schäfer and Ninian Bruce working together (1907) not only supported these findings; they came to the conclusion that the dorsal and the ventral spino-cerebellar tracts are merely components of one common tract. Their views are particularly important, and are most relevant to the findings presented in this thesis.

In the spinal cord of monkeys Schäfer and Ninian Bruce (1907), found that there was an important transference of fibres from the ventral to the dorsal tract. They stated that this dorsal movement of the fibres of the ventral spino-cerebellar tract occurs both in the spinal cord and in the medulla. All these fibres enter the restiform body. In 1910 Ninian Bruce noted, further, that the most marked transference of fibres from the ventral to the dorsal tract occurred after lesions in the lower thoracic level, and was less marked after higher lesions. The peripheral fibres of the ventral tract appeared to Bruce to be the same size as those of the dorsal tract.

Schäfer had earlier (1899) made experiments in monkeys in order to show which tracts arose from Clarke's column cells. He found that there was an equal degree of atrophy of the cells of Clarke's column after hemisection of the cord and after section of the spino-cerebellar tracts only. Further, he found that section of the dorsal spino-cerebellar tract alone led to changes in fewer cells than when both spino-cerebellar tracts were destroyed. Thus he concluded that the cells of Clarke's column gave origin to both of these tracts. In the eleventh edition of Quain's Anatomy published in 1908 Schäfer stated that: "The dorsal and ventral tracts perhaps have a common origin, possibly from cells of Clarke's column, but also from other cells in the grey matter of the same and possibly of the opposite side". His own earlier work would appear to be adequate enough to justify a more positive statement.

In 1910 Ninian Bruce concluded, from experimental lesions on the monkey, that the cells of Clarke's column of the more caudal segments of the cord give rise to the ventral spino-cerebellar fibres, whereas the cells of Clarke's column of the more rostral segments of the cord give rise to the dorsal spino-cerebellar fibres.

Thus, as has been mentioned, these two workers believed that the dorsal and ventral spino-cerebellar fibres should be considered as part of the same tract, having the same cells of origin; they thought that the majority of fibres enter the cerebellum by the restiform body, and a majority by the brachium conjunctivum. Despite their evidence it will be seen that most later workers have maintained the view that there are two separate systems, and that all the ventral spino-cerebellar fibres enter the cerebellum by way of the brachium conjunctivum.

Throughout this time, observations on the degeneration of the spino-cerebellar tracts in man were made by Laslett and Warrington (1899), Purves Stewart (1901) and Goldstein (1910). These papers will not be reviewed here, as their authors added nothing new to the subject under discussion.

The observations of other workers who provided further evidence about the spino-cerebellar tracts will now be considered.

In 1901 Thiele and Horsley in a case of crush injury of the lower cord, determined that the dorsal spino-cerebellar tract ends in the superior vermis, and in diminishing numbers in the rest of the cortex, many terminating contralaterally. They found some fibres also going to the flocculus. The ventral tract went to the anterior part of the vermis, mixed with the fibres of the dorsal tract. They distinguished between coarse external fibres of the ventral spino-cerebellar tract going to the cerebellum, and fine internal fibres going to the tectum and thalamus. Collier and Buzzard (1903), from their work on ascending and descending degeneration in a series of twenty patients, described degenerating fibres from the dorsal tract to the superior vermis, the inferior vermis, the dentate nucleus and the lateral lobe of the hemispheres, and from the ventral tract to the superior vermis and the flocculus. They made no mention of the crossing of the tracts, and unfortunately gave no illustrations of the terminal parts of the tracts.

Von Dydynski (1903) who also worked on man observed that some fibres of the ventral spino-cerebellar tract entered the cerebellum by way of the middle cerebellar peduncle. This was also noted by Collier and Buzzard (1903) and Van Gehuchten (1906).

Page May (1906), in an excellent review of the literature referred to the great deal of uncertainty which existed regarding not only the origin but also the precise termination of the main bundles of the ventral (and dorsal) spino-cerebellar tracts. He attributed this to the difficulty of limiting exactly a lesion to fibres of a tract which are almost inextricably mixed with those of other tracts, and thus an absolutely pure degeneration of "Gowers'" (meaning the ventral spino-cerebellar) tract had rarely, if ever, been produced. He stated that in his own Marchi preparations showing degeneration of the spino-cerebellar tract, no further light on terminations could be shown because of this difficulty.

Bing (1907) published a most important monograph on the spino-cerebellar system, which included a comprehensive review of the literature. He emphasised the need to distinguish between the evidence obtained from man, and that obtained from animals. The material for his observations on man was a case of poliomyelitis affecting mainly the second lumbar to the first sacral segments. Cells of the ventral horn and of Clarke's column were affected. From this material Bing deduced that the dorsal tract arose from Clarke's column cells, and the ventral tract from lateral cells in the ventral horn, on both the ipsilateral and the contralateral sides. From this case Bing thought that the dorsal tract arose about the second to third lumbar segments, and the ventral tract at least one segment lower. Owing to the difficulty of impregnation in the Marchi method, Bing did not consider human material of any value in following degenerating fibres in the cerebellum, so in this part of his work he used dogs. In this animal he found that the dorsal tract ended in the anterior superior part of the upper vermis, and the ventral in the anterior inferior. These fibres were, at least partially, but probably totally, crossed.

The majority of the papers we have been considering concern the topography of the long tracts, rather than their function. But deductions as to the site of the tracts in the cord may be made also from physiological observations. In the 1870s, as has been seen in this review, several workers had concluded that fibres associated with pain run in the ventro-lateral column of the cord. This view had been fairly widely accepted, but not by all workers. Several skilled observers found no loss of pain sensation after section of the ventro-lateral column in monkeys (Mott, Schäfer, and Bruce). Spiller in 1905 wrote two papers concerning the fibres associated with the modality of pain. He considered a case which he described to be most important, as it provided definite evidence for the site of the fibres subserving the modality of pain; for, in his opinion, such evidence had hitherto been scanty. This was a case of tuberculosis; there were tubercles in the ventro-lateral funiculus of the cord, causing loss or impairment of pain and no impairment of touch. Spiller later suggested to Cadwalader and Sweet that confirmation of the association between pain and ventro-lateral fibres should be obtained experimentally. These workers produced contralateral analgesia after division of the ventro-lateral column in dogs (1912).

Schüller in 1910 considered the advantage of dividing the dorsal columns or the ventro-lateral columns, in order to relieve tabetic crises. But he does not appear to have actually performed the operation of cutting the ventral columns. In 1912 Spiller and Martin reported their first case of ventro-lateral cordotomy for the relief of pain; and in 1913 Foerster performed the same operation, apparently independently.

This development in neurosurgery could be used to provide more material on man and this material was infinitely more valuable than that for animals, as the relevant functional aspects of the anatomy could be adequately studied during the patient's life. It should be noted, however, that the account of the ascending tracts of the lateral column given in textbooks of anatomy and neurology is based on the earlier work, and has not taken cognisance of this more important work on man.

Very numerous papers on the subject of cordotomies have been published, but in only a few has any histological examination been carried out. Owing to their close association in the cord, division of the spino-thalamic fibres involves cutting some spino-cerebellar fibres also. This has often been ignored, and degenerating tracts in the region of the operation have been interpreted as being spino-thalamic only; any reference to spino-cerebellar fibres has been made only en passant.

Foerster (1927) and Foerster and Gagel together (1932), were particularly interested in analysing cordotomy material. Most important is their joint paper published in 1932, in which they made a detailed study of twenty-nine patients who had the operation of ventro-lateral cordotomy, including post-mortem examinations in nine of them. No other workers have made such a careful clinico-anatomical study in similar material. These workers found fibres of the ventral tract migrating dorsally in the cord, and called these fibres an aberrant tract. They thought that these aberrant fibres arose from dorsal horn cells, and noted that they could not tell if these fibres continued to the cerebellum or not.

A most original approach in cordotomies is that utilised by Kuru (1938). He reported the clinical and histological results of two cordotomies. He made his operative lesion so that the knife entered the cord through the dorso-lateral column, and cut through the fibres in the middle zone of the ventro-lateral column, sparing the peripheral fibres in this region. As his lesion transected fibres of the dorsal spino-cerebellar and the spino-thalamic tracts, but not fibres of the ventral spino-cerebellar tract, he hoped to be able to deduce which cell groups caudal to the lesion gave rise to the degenerating fibres. By correlating the distribution of the sensory changes after the operation, with the distribution of the cells showing degeneration changes he deduced that the spino-thalamic tract arises from the apical cells of the dorsal horn. As the basal cells were the least affected he thought that they probably gave rise to the ventral spino-cerebellar tract. This is a very good report of an original and careful work. But nevertheless, all the deductions made by Kuru can not be taken as final. He presented the percentage of cells showing axonal reactions to normal ones, in each cell group, in different segments of the cord. As he did not state whether he had examined every section of the segments concerned, and in view of the difficulty other workers have experienced in determining the proportion of cells showing definite changes, it is questionable if such detailed deductions are justified.

In 1940 Walker reported two cases dying after the operation of cordotomy. In one of the cases the distribution of ascending degenerating fibres was mapped out, with special reference to the spino-thalamic tract. The degeneration was indicated in a series of sections of the cord, medulla and pons by stippling in the distribution of the degenerating fibres. All the degeneration was described as spinothalamic, except for a few fibres of the ventral spino-cerebellar tract. The degenerating fibres were described as occupying the region between the inferior olive and restiform body in the medulla, and as lying in the extreme lateral portion of the medial lemniscus. A few of the ventral spino-cerebellar fibres went to the dorsal surface of the brachium conjunctivum. The pseudo-Marchi staining in the second case was too bad to do more than "confirm" the findings in the first case. The very poor histological preparations which illustrate this paper render it valueless as definite evidence, although the discussion is of considerable interest. Rasmussen and Peyton, in the following year (1941) illustrated very clearly by numerous drawings, and one photograph of a Marchi preparation, the course of the spino-thalamic tract, and associated fibres, from the fourth thoracic segment to the thalamus. Little alteration in position of the ascending fibres at different cord levels was observed. The operation appeared to involve the ventral part of the dorsal spino-cerebellar tract. A few fibres only were shown to enter the restiform body.

In 1941 Brodal and Jansen studied a case of cordotomy. They established the extent of the lesion, and determined the distribution of fibres in the cerebellum. In their case, death had supervened seventeen days after the operation. At the operation the dorsal and ventral spino-cerebellar tracts had been cut almost completely on both sides of the cord. They found that the largest number of spino-cerebellar fibres terminated in the lobus anterior, (lobulus 1 and lingula) not only in the vermis, but also for about $1\frac{1}{2}$ cms. lateral to the mid-line. Some fibres also went to the lobulus C1 (pyramis), and a few to lobulus B (uvula), lobulus C2 (declive folium and tuber), and lobulus A (nodulus). They illustrated their paper by small drawings. As the operation was bilateral, no conclusions could be drawn with respect to the degree of crossing of the fibres.

Gardner and Cuneo, (1945), traced the ascending degeneration in a man who died twenty-one days after a cordotomy. Although their interest was mainly in the spino-thalamic tract, their observation that the dorsal spino-cerebellar fibres moved dorsally in the spinal cord, during their ascent, is to be noted. These workers traced the degenerating fibres in the cord and brain stem, and confirmed the observations of others as to the distribution of the main mass of degenerating fibres. In the pons they found the degeneration to be in the lateral lemniscus. This paper is important for the authors discuss competently the questions still unanswered on the spino-thalamic and associated tracts.

The operation of intramedullary tractotomy was introduced in 1941 by Schwartz and O'Leary. Although this operation could be used to study the spino-cerebellar tract, it seems that histological studies of such material have not been carried out, other than to confirm the extent of the operative lesion only.

Studies of myelogenesis have never been used much in the study of tracts by later workers. It was therefore of great interest when Langworthy in 1930 described the medullated tracts in the brain of a seven month human foetus. Langworthy found that medullated spino-cerebellar fibres of the dorsal and ventral tracts ended in the vermis. He did not find any fibres running into the cerebellar hemispheres. In 1931 Keene and Hewer published a similar study on human embryos, being concerned with the myelin present at various stages of development. They found a few very finely myelinated fibres in the dorsal spino-cerebellar tract at sixteen weeks' development; the myelination increased slowly to twenty-eight weeks, when it was considerable in amount. At full-term the tract was found to be particularly heavily myelinated. In the ventro-lateral tract they found a very little myelination at fourteen weeks, much more marked myelination at twenty-eight weeks, but even at full-term the sheathes were found to be less heavily myelinated than those of the dorsal spino-cerebellar tract.

In 1936 Strong published some observations on the origin of the fibres entering Clarke's column. The title of this paper is misleading: 'Some observations on the course of fibres from Clarke's column in the normal human spinal cord'. This paper, in fact, is concerned only with the fibres running to Clarke's column. Strong studied these fibres in a one month old baby, using the Weigert Pal stain to show myelinated fibres. He found that most of the fibres running from the dorsal column into Clarke's column run to the ipsilateral Clarke's column cells, while a few may cross the mid-line in the ventral white commissure. He found that the fibres entering Clarke's column came from roots which had entered the cord several segments further caudally; and that most of the fibres are collaterals of ascending dorsal column fibres.

Hogg (1944) studied the development of Clarke's column in human foetuses. He found that practically all the fibres leaving the nucleus passed to the dorsal part of the lateral column of the same side. A very small number were sometimes seen to pass to the more ventral part of the lateral column.

Larsell, who has contributed greatly to knowledge of the cerebellum in different species, wrote, in 1947, a paper on the development of the cerebellum in man, in relation to its comparative anatomy. The paper is mainly concerned with the external topography of the cerebellum, but contains the useful observation that many of the dorsal spino-cerebellar fibres in embryos can be seen to decussate in the cerebellum, some of the fibres going to the anterior lobe, and some to the posterior lobe.

This is the last paper reporting contributions to the anatomy of the spino-cerebellar system in man. However, while these contributions to the understanding of human anatomy were being made, the classical method of making experimental lesions in animals continued to be employed. This work will now be briefly reviewed.

The majority of workers who used experimental animals made lesions of the white matter, and traced the degenerating fibres; in some cases the cells retrograde to the lesions were examined. The approach used by Ljubuschin (1902) was to destroy parts of the grey matter of the cords of rabbits and trace the degenerating fibres. He concluded that both crossed and uncrossed fibres of the ventro-lateral column arise from cells of the dorsal horn and the central grey matter. Similar experiments were made by Macnalty and Horsley (1909) in dogs, cats and monkeys. They made small experimental lesions in the grey matter at different levels of the cord and followed degenerating fibres from the destroyed cells into the cerebellum. In view of the importance of this study it is unfortunate that their findings are not shown in more detail and more clearly illustrated. They concluded that the origin of the ventral tract consisted of cells in the grey matter ventral to a line passing through the dorsal limit of the central canal. An important observation in this paper was that some of the spino-cerebellar fibres appeared to them to arise in the cervical cord. With respect to the crossing of the fibres within the cerebellum, they found that the ratio of crossed to uncrossed fibres was 1 to 2, and of the ventral tracts the ratio of crossed to uncrossed fibres was 1 to 4. They found that the dorsal tract terminated in the superior vermis (lobulus centralis and culmen) and in the inferior vermis (lobulus posterior and pyramis); the ventral tract terminated mainly in the central lobule, and to a lesser extent, in the culmen and declive. No degenerating fibres were found in the lingula. The distribution of the fibres was the same, regardless of the level of the lesion in the cord. Other workers employed the more usual method of making lesions in the white matter and following Wallerian degeneration.

Lewandowsky (1904) who made lesions of the cord in cats and dogs, thought that the origin of the ventral spino-cerebellar tract, as well as of the dorsal, is the cells of Clarke's column. In the cord he found that the two tracts form a single unit, and that they become distinct in the medulla, only where the dorsal tract enters the restiform body. In the cerebellum he found the dorsal tract to be distributed to the anterior vermis, and the ventral tract to the posterior vermis. Most of the fibres of both the dorsal and the ventral parts of the spino-cerebellar system appeared to him to be crossed.

Van Gehuchten, who contributed greatly to neuro-anatomical knowledge, showed in 1906 a series of drawings of lateral column degeneration in the rabbit, and also in one man. In these species he showed that the ventral spino-cerebellar fibres entered the cerebellum by way of the middle cerebellar peduncle, as well as by the brachium conjunctivum. He found that the dorsal spino-cerebellar fibres terminated in the posterior part of the superior vermis, mostly, not all, on the same side, and that the ventral spino-cerebellar fibres terminated in the anterior part of the superior vermis. He does not state if the ventral fibres crossed or not.

Edinger (1911) described the position occupied by the spino-cerebellar tracts in the cords of cats, and amphibia. He found that the dorsal spino-cerebellar tract occupies the periphery of the lateral column from the dorsal horn to the ventral nerve roots, and that the ventral spino-cerebellar tract lies ventral to this. It is to be noted that this is a much more ventral site for the ventral tract than that attributed to it by most workers.

Horrax (1915) investigated the physiological effect in dogs of lesions of the dorsal and ventral spino-cerebellar tracts in the mid-thoracic region, and later mapped out the degenerated spino-cerebellar fibres. He found that fibres of the spino-cerebellar tracts presumably supplying the lower limbs go to the caudal half of the vermis and the medial portion of the lateral hemispheres by way of the dorsal tract, and to the cephalic half of the vermis by the ventral tract. The fibres are both crossed and uncrossed in the cerebellum.

Ingvar (1918) made a most thorough study of the spino-cerebellar tracts in birds and mammals. He found that the dorsal and ventral tracts in the cat are not clearly separated into two tracts in the cervical cord, but are clearly divided in two in the medulla oblongata, also, in the cerebellum the two tractscan not always be separated. According to Ingvar the main contingent of fibres from both the dorsal and ventral tracts crosses in the cerebellum. A few fibres go to the lingula; the majority of the fibres end in the lobulus centralis, some in the anterior part of the culmen, very few to the posterior part. A very few fibres go to the lobulus simplex. From the dorsal spino-cerebellar tract some fibres go to the pyramis, a few to the uvula, and a few to the paraflocculus. A few fibres, mainly dorsal, were said to go to the tectal nuclei. Ingvar could find no evidence that any fibres entering the spino-cerebellar fibres arise from the cervical cord.

In 1927 Beck published an excellent paper on the course of the degenerating fibres in the spino-cerebellar tracts of the cat. He supported his observations with clear photographs of his actual findings in sections cut in different planes in different animals. It is unusual for such adequate evidence to be produced. Beck found the dorsal tract to be clearly established as low as the fifth lumbar segment, and the ventral as low as the second, between these two, but more closely associated with the dorsal tract, he found a thirdsmall tract which he called the fasciculus spino-cerebellaris intermedius. There appeared to be no difference in the calibre of the fibres in the different tracts. The course of the dorsal tract into the cerebellum by way of the restiform body, and the course of the ventral tract by way of the brachium conjunctivum were clearly distinct. In the cerebellum he found that the dorsal tract was uncrossed, the majority of the fibres terminated in the anterior lobe, large numbers went to the central lobule, many to the dorsal part of the culmen and the dorsal part of the declive, and a "goodly contingent" to the pyramis. A few were seen to go to the uvula, tuber and ventral part of the culmen; a very few fibres were seen in the stalk of the paraflocculus. In the anterior lobe the dorsal tract fibres lie lateral to those of the ventral tract. With respect to the ventral spino-cerebellar tract, Beck found that many, if not the greatest number, of the fibres cross in the cerebellum. No fibre of this tract was found to enter the inferior vermis or to end in any of the lobules of the hemispheres. The fibres all end in the medial part of the anterior lobe, the bulk of the fibres going to the lobulus centralis, the dorsal part of the culmen and a fairly large group to the lingula. There was degeneration in both the dorsal and the ventral tracts in all the animals but Beck considered that the two tracts appeared as separate entities until near their ultimate termination, and that there was always either a difference in staining or in compactness of the fibres.

Pass (1931, 1933) reported the results of his experiments in the cat. He made lesions of Clarke's column, and also, in some cats, in the dorsal and ventral commissures. His findings concerning the course of the fibres from the cells are dissimilar to those of most workers, as he found that practically all the fibres arising from Clarke's column crossed and ascended in the opposite dorsal spino-cerebellar tract. The fibres were found going from Clarke's column cells into the ventral spino-cerebellar tract. But in this respect it is necessary to note that he made his lesions in the third lumbar segment, and generalisations should not therefore have been made as to the standard pattern of the fibre distribution at all levels. In the course of his investigations he confirmed the observations of earlier workers, that after section of lumbar and lower sacral nerve roots, degenerating fibres entered the Clarke's column as high as six segments above the highest root sectioned.

Ferraro and Barrera (1935) drew attention to the lack of detailed correlation between physiological and anatomical observations, especially in primates. Using monkeys, they made lesions either of the dorsal spino-cerebellar tract in the mid-cervical cord, or of the restiform body. Temporary but definite symptoms of ipsilateral weakness, slight hypotonia and dysmetria occurred after all types of lesion. A most important finding was that their lesions of the dorsal spino-cerebellar tract in the cervical cord were followed by disturbances in the ipsilateral fore limb. They therefore concluded that part of the cerebellar representation of the fore limbs must be established through the dorsal spino-cerebellar tract. As there is a poverty of information regarding spino-cerebellar fibres from the fore limbs, this observation is particularly valuable. Although a number of workers made their lesions in the cervical cord, they did not record any observations of the effect of their lesion physiologically, and so deductions could not be made as to whether the degenerating spino-cerebellar fibres found cranial to the lesion were associated with the fore or hind limbs.

Schimert (1939) made very detailed observations on the origin of fibres entering Clarke's column in cats. He found that the fibres are collaterals of ascending fibres in the dorsal columns. He also found that the fibres ascend one or more segments above the level of their entrance into the cord, before entering Clarke's column.

Observations on the cells of origin of the ventral spino-cerebellar tract in monkeys were presented by Cooper and Sherrington (1940). They found that after transecting the cord, chromatolysis occurred in numerous large cells in the border zone of the ventro-lateral spinal grey matter. These cells lay in the lowest thoracic and six adjacent lumbo-sacral segments. Their fibres crossed to the opposite side. These same cells were found to remain intact after section of the motor roots. They also observed that Clarke's column cells aboral to a lesion always became chromatolytic, mostly, not entirely on the same side as the lesion. In view of this evidence and that of some previous observers, these workers concluded that fibres of the ventral spino-cerebellar system arise from these "border" cells of the ventral horn.

Anderson (1943) mapped out the cerebellar distribution of the dorsal and ventral spino-cerebellar fibres in the white rat. He made lesions at the upper cervical, upper thoracic and lower thoracic levels, and also lesions of the brachium conjunctivum. These findings were illustrated by drawings. He found that the dorsal spino-cerebellar tract terminates in all parts of the anterior lobe, the lobulus simplex and the pyramis, and a few fibres in the most medial parts of the lobulus pyramedianus and uvula. He found no fibres going to any other parts of the vermis nor to the cerebellar hemispheres. He assessed the proportion of ipsilateral to contralateral fibres as about 3 to 1. The ventral tract was distributed to the anterior lobe and the pyramis, and a few fibres to the lobus simplex. All the ventral fibres lay near the mid-line. In the medulla he found a small group of fibres leaving the dorsal tract and joining the ventral tract, being distributed with it.

Chang and Ruch (1949) showed the distribution of degenerating fibres in the cerebellum in monkeys, after cord sections at the upper caudal level. They found that the fibres ascend in the ventral spino-cerebellar tract, and enter the cerebellum in the superior cerebellar peduncle. Some fibres cross in the rostral part of the great anterior cerebellar commissure. Both crossed and uncrossed fibres go to the lingula, lobulus centralis and the anterior folia of the culmen. The most severe degeneration was in the lingula and the anterior folia of the lobulus centralis. These workers consider that this evidence supports the view that there is a projection from the caudal part of the body to the anterior cerebellum, and from the rostral part of the body to the posterior cerebellum. Chang (1951), continuing his observations on the spino-cerebellar systems, described a group of cells in the caudal segments of the spider monkey which appears to be a caudal extension of Clarke's column. Some of the cells of this nucleus chromatolyse after unilateral section of the dorsal spino-cerebellar tract, twice as many ipsilaterally as contralaterally.

Morin, Schwartz and O'Leary (1951) made an extensive experimental study of the spino-thalamic and related tracts in monkeys and cats. This paper is largely concerned with the topical arrangement of fibres of the spino-thalamic tract, but some observations are pertinent to the present enquiry. They commented on a moving dorsally of superficial fibres from the ventro-medial to the ventro-lateral position during their ascent. Retrograde cell changes were seen, mostly on the side opposite to the lesion, in the larger cells of the dorsal grey matter, and in the border cells of the ventral horn; and retrograde changes were also seen in Clarke's column cells, mostly on the same side as the lesion.

Another worker at the present time, interested in the spino-cerebellar tracts, is Yoss (1952, 1953). His papers are concerned mainly with the question of topographic localisation in the dorsal and ventral tracts in monkeys, and this part of his work is illustrated. The distribution of the degenerating fibres in the cerebellum is briefly enumerated, but not illustrated.

In the dorsal tract he found a dorso-ventral lamination of fibres arising below the cervical cord; he had no evidence whether fibres arise in the cervical cord or not. But he considers it unlikely that there is a pure segmental pattern of distribution, for when there was a lesion at the second lumbar segment he found degenerating fibres throughout the dorsal tract. He says that he found the projection of fibres to the cerebellum from the dorsal tract to be mostly to the anterior lobes, a few fibres also going to the pyramis, declive and uvula. No fibres were found to go to the lingula, nodule, tuber or folium. No intermediate spino-cerebellar tract was seen. In his study of the ventral spino-cerebellar tract, Yoss made the assumption that if no degenerating fibres could be found in the thalamus, then it could be assumed that none of the degenerating fibres closer to the lesion were spino-thalamic fibres. All workers have commented on the difficulty of tracing the terminal parts of degenerating tracts, especially by means of degenerating myelin, even when excellent staining of the more proximal parts of the fibres is obtained. Yoss's deduction is then unwarranted, and he has no evidence that the degeneration he described in the cord derived only from the ventral spino-cerebellar tract. The evidence which he presented as concerning the ventral spino-cerebellar tract alone cannot be accepted; it is possible that it may hold for the whole complex of ascending ventro-lateral fibres.

He demonstrated a segmental lamination in a dorso-lateral ventro-medial direction in the ventro-lateral column. He found that in the upper cervical cord the ventral tract shifts slightly ventrally. He denied that there is any dorsal shift of ventral fibres, as described by Ninian Bruce, and considered that Bruce was actually describing the dorsal shifting of dorsal fibres themselves, and not of ventral fibres. Voss found that the fibres of the ventral tract spino-cerebellar system terminate in the vermis in the lingula, central lobule, culmen, declive, pyramis and uvula. He did not mention the degree of crossing, if any, of the fibres in the cerebellum.

It has now been shown that many major contributions to knowledge of the anatomy of the spino-cerebellar tract in animals were made during the past 50 years. Considerable evidence has been produced on the distribution of the tracts in the cerebellum. Most workers found the main terminal to be the ventral portion of the anterior lobe, and some workers found a considerable number of fibres going also to other parts of the vermis. But there was still lack of agreement as to the distribution of each of the tracts separately, the extent to which the fibres cross in the cerebellum, and the topographical localisation, if any, in the cerebellum.

The development of electrophysiological methods of investigation during this century has resulted in another approach to these questions. All the evidence available from this source has been derived from animals only. It will now be reviewed briefly.

The evidence produced by the earlier workers supported the view that there is no topographical localisation in the cerebellum. Beck and Bikeles (1912 A and B) from their work on the dog, studied the effects of single induction shocks applied to the sciatic nerve and to nerves of the brachial plexus; they found that the regions where the responses were received were the same whether the nerves from the upper or those from the lower were stimulated. Dow (1939), working on the cat, stimulated the spino-cerebellar tracts directly. He picked up a response only from the entire anterior lobe, the lobulus simplex, the pyramis and occasionally from the lobulus paramedianus. He also found no difference in the response with relation to the site of stimulation, except that the response was of greater amplitude when the stimulus was ipsilateral. Dow's physiological and anatomical work led him to conclude (1942) that in cats the whole of the ventral spino-cerebellar tract and most of the dorsal tract end in the anterior lobe. He found that some fibres of the dorsal tract go also to the lobulus simplex, pyramis and lobulus paramedianus, mainly, not entirely, on the side of entrance to the cerebellum. He thought there was no somatotopic representation. Dow and Anderson (1943), investigated spino-cerebellar projections in the white rat, and were unable to demonstrate any topographical localisation, but they thought that the brain of the rat was too small for general conclusions to be drawn from their observation.

Definite evidence for a somatotopic localisation of spino-cerebellar fibres, on the other hand, comes from Grundfest and his co-workers. In 1942 Grundfest and Campbell found that in the cat dorsal spino-cerebellar fibres from the hind limbs are distributed to the central lobule and the adjacent folia of the culmen; these fibres are mainly ipsilateral but some overlap to the opposite side; the fibres crossing to the opposite side of the cerebellum do not extend as far laterally as do the ipsilateral fibres. In 1954 Carrea and Grundfest produced detailed evidence, in the cat, regarding the ventral spino-cerebellar tract. They considered that the lumbar component arises from ventro-marginal cells and that the ventral spino-cerebellar tract ascends mainly, if not exclusively in the ventral half of the lateral column. They found no evidence of any transference of fibres between the dorsal and ventral tracts. In the cerebellum they have definite evidence of a somatotopic localisation. They found that the lumbar component of the ventral tract terminates in the central lobule and first two folia of the culmen, supplying the vermis bilaterally and also the medial half of the ipsilateral hemisphere. The cervical component was found to terminate in the rest of the culmen, supplying the whole vermian part of this and the entire hemispheral part on the ipsilateral side.

The observations of Adrian (1943) and of Snider and Stowell (1944) are interesting, but are of limited value in respect to the spino-cerebellar tracts, as they were made largely in relation to tactile projections. These workers thought the spino-cerebellar projections were probably co-extensive with the tactile projection areas. Adrian found a somatotopic localisation in the anterior lobe comparable to that described later by Grundfest and Campbell and by Carrea and Grundfest. Snider and Stowell found a comparable, but not identical unilateral projection of fibres to the anterior lobe. These workers found that impulses from the hind limbs were received in the rostral folia of the culmen, while those from the head and fore limbs were received in the caudal folia of the culmen and adjacent folia.

They also recognised a bilateral projection in the paramedian lobule, the fibres from the head and neck going to the rostral folia, those from the fore limbs to the middle folia, and from the hind limbs to the caudal folia.

Combs (1954) produced interesting evidence in the cat of two systems of spino-cerebellar projections, the one being localised, the other unlocalised. This work is not yet complete. He tentatively suggested that the anatomical observations of others may indicate that the long spino-cerebellar fibres are the non-localised system, and other spinal cord - brain stem - cerebellar systems are the localised system. But this is unproven as yet.

Thus from the electrophysiological work we see that there is the usual lack of unanimity. Some workers definitely conclude that there is topographical localisation in the cerebellar projection of the spino-cerebellar fibres, and others conclude that there is none. Most of the work shows that the spino-cerebellar tracts run to the cerebellum ipsilaterally, although there are some fibres running contralaterally. No electrophysiological evidence regarding the exact termination of the spino-cerebellar fibres in the folia supports the view that many fibres of both the dorsal and ventral tracts appear to project to the anterior lobe. There is insufficient evidence as yet regarding the exact termination of the fibres in the folia of the anterior lobe and regarding the projection of fibres to other parts of the cerebellum, for any conclusions to be drawn.

Let us now briefly consider what then is the present state of knowledge concerning the spino-cerebellar tracts. Two long ascending tracts are usually described in man and in other mammals, a dorsal and a ventral tract. There has been ample evidence to show that the more dorsal of these two tracts is composed of fairly large fibres; it arises from the cells of Clarke's column and ascends in the dorso-lateral column of the cord to the medulla. The bulk of the evidence goes to show that the fibres run on the same side as their cells of origin, but some workers think that a few fibres also arise from cells on the opposite side; one worker found that all or nearly all the fibres arise from cells on the opposite side, in the cat. It is agreed that Clarke's column cells are found throughout the thoracic cord and in the first lumbar segment. Some workers believe that the column also extends into the eighth cervical and the second or third lumbar segments. A few workers think that Clarke's column cells or similar cells are present right up to the rostral and caudal limits of the cord, at least in some species. The bulk of the evidence on the dorsal spino-cerebellar tract is related to fibres arising in the thoracic or upper lumbar card. There is some evidence, mainly physiological, that spino-cerebellar fibres also arise in the cervical cord, but this has never been shown in man. There has been considerable evidence that the fibres of the dorsal roots which carry impulses to Clarke's column cells ascend first in the dorsal columns (of Goll and Burdach), before entering

Clarke's column; it has also been shown that fibres entering Clarke's column are mainly collaterals of long ascending fibres of the dorsal column. There are varied opinions on the lowest level at which the dorsal tract appears on the surface of the cord, but species variation may contribute to varied findings in this respect. In man, the fibres have been found as low as the second or third lumbar segment. A latero -medial lamination of fibres in the dorsal tract has been described in dogs and monkeys, the longer fibres lying most peripherally.

There is unanimous agreement that the dorsal tract occupies the region in the medulla immediately ventral to the spinal nucleus of the fifth cranial nerve, and that it enters the cerebellum by way of the restiform body. Most workers are of the opinion that most of the fibres go to the anterior lobe, but details as to the distribution vary.

In man the dorso-lateral fibres have been described as terminating: in the anterior lobe, mainly, not entirely ipsilaterally (to the side of entrance into the cerebellum), and in the nodulus and uvula; in the superior vermis, and, in diminishing numbers, in the rest of the vermis, and in the flocculus (laterality not determined); in the superior and inferior vermis and the lateral lobes of the cerebellum (laterality not determined); in the medial part of the anterior lobe, and in smaller numbers, in all the other divisions of the vermis (laterality not determined).

In monkeys the dorso-lateral fibres have been described as terminating: in the dorsal portion of the superior vermis; in the dorsal and ventral parts of the superior vermis, mostly contralaterally; in the vermis, in the superior vermis, except the lingula, and in the inferior vermis, mostly ipsilaterally; in the anterior lobe except the lingula, and a few fibres in the pyramis and uvula (laterality not determined); in the anterior lobe and lobulus simplex, ipsilaterally, and in both paramedian lobules.

In lower mammals workers have found the dorsal spino-cerebellar fibres terminating: in the proximo-ventral part of the vermis, mainly ipsilaterally; in the dorsal part of the superior vermis (laterality not determined); in the ventral part of the superior vermis (laterality not determined); in all parts of the superior vermis;

in the caudal half of the vermis and medial part of the lateral hemispheres; in the anterior lobe of the cerebellum, and a few fibres to the lobulus simplex, pyramis, uvula and paraflocculus (laterality unstated); in the anterior lobe and dorsal part of the declive and the pyramis; and a few fibres to the uvula, tuber and ventral part of the culmen, all ipsilaterally. The majority of workers have not found any fibres going to any of the cerebellar nuclei; but a few workers have mentioned a very few fibres going to the dentate, or to the roof nuclei, in man and other species.

The ventral tract in man is thought by some workers to be composed of fibres of calibre equal to those of the dorsal tract, and by others to be composed of distinctly finer fibres. There is no general agreement about the cells of origin for this ventral tract; the following have been proposed by different workers: cells of the dorsal horn and of the dorsal horn and of the intermediate grey matter; cells of the ventral horn; cells of Clarke's column. Evidence of the existence of the ventral tract in man as low as the third or fourth lumbar segment has been provided; there is no evidence what is the most cranial level at which fibres arise. A dorso-lateral ventro-medial lamination of fibres in the ventral tracts in monkeys has been described, the longest fibres lying dorso-laterally. This has not been described in man. The majority of workers believe that the ventral tract maintains its position in the ventro-lateral column throughout its ascent in the cord; but some workers have described a transference of fibres from the ventral to the dorsal tract in man and in monkeys. A third, intermediate tract between the dorsal and ventral tracts has been described in man and in other species; but this has not been generally accepted. There is general agreement that the ventral tract in the medulla lies ventral to the dorsal tract, in the region dorsal to the olive. Most workers agree that in the pons the ventral tract lies in the most lateral part of the lateral lemniscus; but the tract has been described as lying in the medial lemniscus in man. Most workers are of the opinion that the ventral tract enters the cerebellum by way of the dorsal surface of the brachium conjunctivum; a few workers believe that all, or some, of the fibres enter the cerebellum in the restiform body with the dorsal tract; and a few workers believe that some fibres enter the cerebellum by way of the middle cerebellar peduncle. These observations have been made both in man and in lower animals. In the cerebellum many workers have commented on the difficulty of distinguishing the ventral tract fibres from the dorsal tract fibres, other workers found no such difficulty. In man, the ventral fibres have been described, as terminating in: the superior vermis, contralaterally; the lingula, almost all ipsilaterally; the superior vermis and the flocculus (laterality not determined). In monkeys the ventral fibres have been described as terminating in: the ventral portion of the superior vermis (laterality not determined); the superior part of the superior vermis, ipsilaterally, and the inferior part of the superior vermis, contralaterally; in the ventral and distal dorsal part of the vermis and in the lateral lobe, contralaterally; in the ventral portion of the superior vermis, contralaterally; in the central lobule and culmen, but not the lingula, and in the declive, mostly ipsilaterally; in the lingula, central lobule and anterior part of the culmen, FIG I

STRONG, O.S., & ELWYN, A. Human Neuroanatomy (1943).

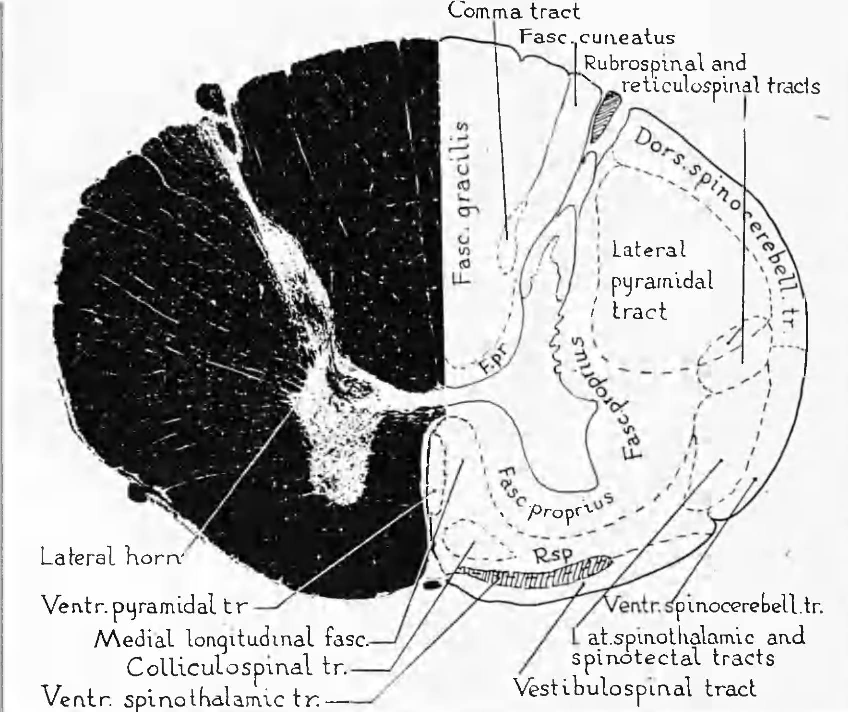


Fig. 142. Section through second thoracic segment (lower portion) of adult human spinal cord. Weigert's myelin stain. Photograph. The principal fiber tracts are indicated schematically on the right side. F.pr., fasciculus proprius; R.sp., reticulospinal fibers.

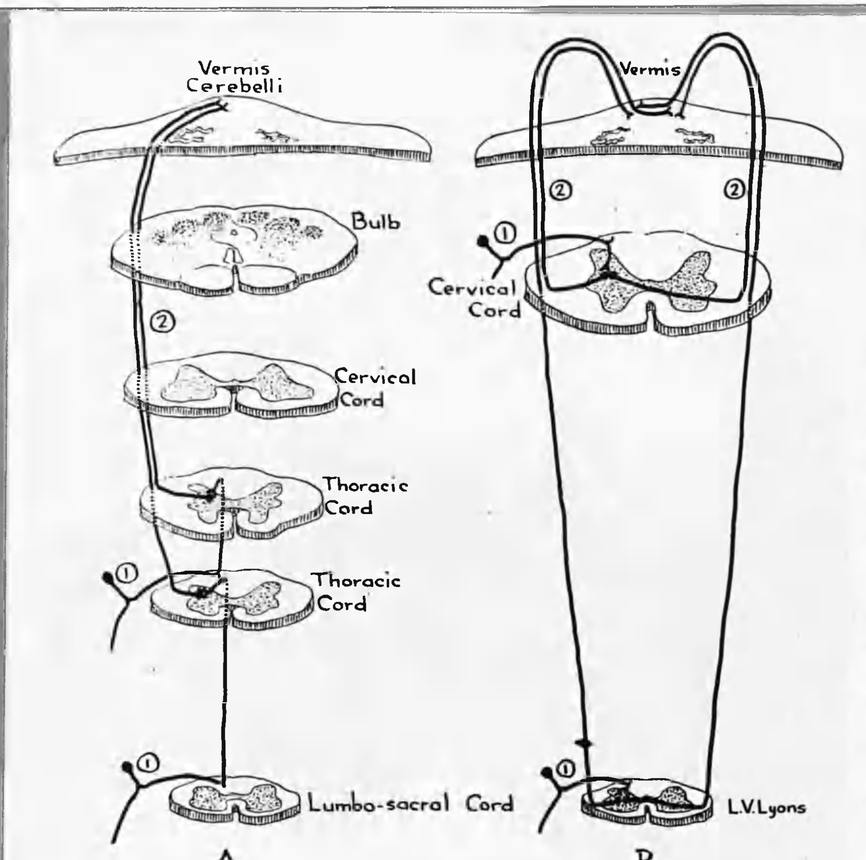


Fig. 138. Scheme of dorsal (A) and ventral (B) spinocerebellar tracts and the paths of which they are a part. (1) spinal ganglionic neurons; (2) spinocerebellar neurons.

mainly contralaterally; in the lingula, central lobule and culmen, both ipsilaterally and contralaterally; in the anterior lobe, and in the declive, pyramis and uvula (laterality unstated).

In lower mammals the ventral fibres have been found to terminate: in the superior part of the superior vermis, ipsilaterally, and in the ventral and inferior part of the superior vermis, contralaterally; in the ventral and distal dorsal portion of the vermis, and in the lateral lobes, mostly contralaterally; in the posterior vermis, contralaterally; in the lingula, central lobule and anterior part of the culmen, mostly contralaterally; in the medial part of the anterior lobe, mostly contralaterally; in the anterior lobe, mostly ipsilaterally.

Occasional mention of a few fibres going to the dentate or to the roof nuclei has been made, in respect of man and other species, but most workers have found no fibres going to any of the nuclei.

It may be useful here to refer to Figs.1 and 2. They are from Strong and Elwyn's Textbook of Human Neuroanatomy, and from Brodal and Jansen's

FIG 2

Abb. 1. Querschnitt durch das Rückenmark in der Höhe von Th. IV—V. Die Läsion der linken Seite. Zeichnung.

Abb. 2. Wie Abb. 1. Die Läsion der rechten Seite.

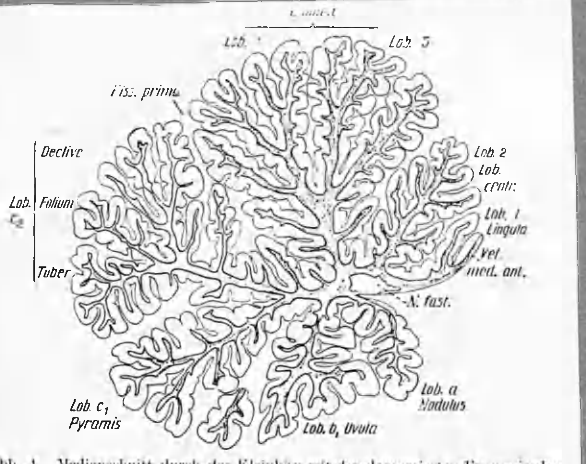


Abb. 4. Medianschnitt durch das Kleinhirn mit den degenerierten Fasern in den verschiedenen Lobuli. Zeichnung.

From: Brodal, A.,and Jansen, J.,(1941). "Beitrag Zur Kenntnis Der Spino-cerebellareu Bahnen beim Meuschen."
Anat. Auz. 91, 185.

paper "Beitrag zur Kenntnis der spino=cerebellaren Bahnen beim Menschen".

Strong and Elwyn's diagrams are shown as being a typical example of the tracts as shown in text-books of neuroanatomy. Fig.2.a and b. are the main illustrations given by Brodal and Jansen in their paper; and this paper is that which is quoted by many text-books with reference to the termination of the spino-cerebellar tracts in man.

It will be seen from this review that there remain certain large gaps in our knowledge of the spino-cerebellar tracts in man. The following questions still remain unanswered.

1. Whether the second lumbar segment is the most caudal level of origin of the dorsal spino-cerebellar tract and whether the eighth cervical is the most rostral level of origin.

2. What are the cells of origin of the ventral tract; and whether the third lumbar segment is the most caudal level of origin of the ventral spino-cerebellar tract, and what is the most rostral level of origin.

3. It is not yet agreed what relationship incoming dorsal root fibres have to Clarke's column.

Do the dorsal roots send collaterals cranially and caudally along the cord, and if so, how far in each direction at which segments? From how many dorsal roots does each group of Clarke's column cells receive fibres? Are these particular dorsal root axons destined only for Clarke's column, or are the fibres reaching Clarke's column collaterals of the axons running in the dorsal columns?

4. All the points discussed in question 3. apply also to the cells of origin of the ventral spino-cerebellar tract.

5. a) Whether the dorsal spino-cerebellar tract runs in the cord ipsilateral or contralateral to its cells of origin, or whether it has both ipsilateral and contralateral fibres.

b) Whether the ventral spino-cerebellar tract runs in the cord ipsilateral or contralateral to its cells of origin; or whether it has both ipsilateral and contralateral fibres.

6. How far is there any somatotopic arrangement of the axons of these tracts in the cord?

7. The distribution of the spino-cerebellar fibres in the cerebellum has been insufficiently explored, and there is no unanimity in the views of those who

have investigated this problem.

8. Whether the fibre spectrum is the same in the dorsal and in the ventral spino-cerebellar tracts.

9. The relationship of the two tracts to each other in the cord and medulla oblongata, both with regard to location and to transference of fibres from one to the other is not definitely known. The present way of dividing the spino-cerebellar system into two separate tracts, a dorsal and a ventral, may not be correct.

10. There is good reason to doubt whether the usual course of the fibres of the ventral spino-cerebellar tract into the cerebellum is the only course.

All these questions are not being answered in this thesis. But work on them continues.

Nothing has been added to question 3 and 4. Some evidence has been given towards answering questions 1 and 2, 5.b), 6 and 8. Questions 5.a), 7, 9 and 10 have been answered.

CHAPTER III

MATERIAL.

General remarks on human material.

There are obvious and inevitable disadvantages of investigating human anatomy by means of studying degenerations consequent on surgical lesions. The most disappointing feature of the work is that a necropsy cannot always be carried out. When it is obtained, the period of survival may be such that optimal histological techniques cannot be used. Attempts are made to overcome this difficulty by using various staining techniques; it is clear, however, that histological preparations from such material will not be so consistently useful as those made from animals which can be killed at a required time.

Remarks on present material.

The material for this investigation consists of 34 patients who had the operation of ventro-lateral cordotomy for the relief of pain. This operation consisted essentially of dividing the spino-thalamic tract, but it was varied with regard to depth and

TABLE 1.

CASES WITH UNILATERAL CORDOTOMY

Case Number	Age (Years)	Level of Cordotomy	Post-operative Survival (days)
1	40	C1	34
2	51	C2	313
3	49	C3	185
4	46	C3	5
5	42	C3	81
6	52	C3	110
7	66	C3	112
8	52	T3	112
9	34	T5	23
10	54	T5	174
11	46	T8	116
CASES WITH BILATERAL CORDOTOMY			
12	60	C5(R) C6(L)	123
13	34	T1	159
14	57	T7(R) T2(L)	170(R) 102(L)
15	50	T3	53
16	53	T3	242
17	51	T3(R) T4(L)	390
18	47	T4	66
19	44	T4(R) T5(L)	23
20	41	T5(R) T4(L)	101(R) 70(L)
21	63	T6(R) T4(L)	53(R) 118(L)
22	54	T5	24
23	57	T5	39
24	51	T5	75
25	21	T5	141
26	39	T5	154
27	61	T5(R) T6(L)	42
28	66	T6(R) T9(L)	87
29	46	T6	203
30	37	T7	23
31	49	T7	280
32	54	T8	239
33	59	T9	109
34	49	L1	91

ventro-dorsal extent, and the segment of the cord incised. After the patients' death, the brain, spinal cord and peripheral nerves were removed by Dr. P.W. Nathan and myself. The period of survival, from operation to death, varied from five days to fifteen months.

In some of these patients, the growth had involved certain peripheral nerves; in others it had replaced the body of a vertebra, and caused collapse, so that the cord was crushed; this marked the effects of the surgical lesion previously made in the cord, hence this material could not be used in full.

In order to overcome such disadvantages the work was planned so as to collect a large number of cases. This provided adequate numbers from which comparable evidence could be obtained.

Table I sets out the number of patients, the various levels of the cord incised at the operation, whether the operation was unilateral or bilateral, and the periods of survival.

To establish the reliability of the methods used, and to determine whether spontaneous degeneration in fibres occurs, representative sections from a control group consisting of patients who had cancer, but in whom no cordotomy had been done, and also some who had died from other causes, were also examined. The results of this investigation is presented in Chapter V and Table 2.

CHAPTER IV

HISTOLOGICAL METHODS.

I. Preparation of Material.

The post-mortem was done as soon after death as possible; in cases where an early post-mortem could not be obtained, 10% or 20% formol saline was injected into the cisterna magna, and simultaneously cerebro-spinal fluid was drained by lumbar puncture. This resulted in excellent fixation of the spinal cord and lower brain stem. At post-mortem the brain, cord and relevant dorsal root ganglia were exposed and removed. Care was taken to avoid pulling the nerves or pressing on nervous tissue. The cord was divided between the first and second cervical segments, the first cervical segment being fixed with the brain. The material was fixed in a container holding 4 litres of 20% formol saline. The corpus callosum was cut transversely to allow free access of formol saline into the ventricles. The brain was suspended by a string under the basilar artery. The meninges of the cord were cut along the ~~anterior~~ ventral and ~~posterior~~ dorsal aspects and divided by 3 or 4 transverse cuts on each side, to prevent distortion of the cord caused by the shrinking of the meninges. In a few cases the cord was fixed separately in a long container, so that it lay naturally, uncurled; in all other cases it was fixed in the brain pot, where it had to curve very slightly. No difference was noted in the results of these two methods.

In most cases fixation was continued for 14 days only, but in a few cases the time was fixed for periods up to 6 weeks. Spare blocks were kept in formol saline for months or years. The tissue was then washed for 24-48 hours in rapidly running water. The cord was divided into segments, and each segment was subdivided transversely into a number of slices which were again washed overnight. In the cervical cord there were usually 4 slices in each segment, in the thoracic up to 8 slices, and in the lumbo-sacral cord 1 or 2 slices in each segment. In the operation area several slices selected to include the operation cut were usually mordanted for the Marchi method; in all other segments at least one slice was also mordanted for this method. At least one slice from each segment was embedded in celloidin, and in many cases another slice from each segment was put into the Weigert Pal mordant. Whenever feasible a slice from each segment was kept, as a spare block, and in some cases used later for frozen or paraffin preparations. In cases where it was thought that cell studies would prove more interesting than fibre degenerations, fewer slices were prepared for the Marchi or the Weigert Pal method, and more for plain celloidin sections.

In a few "Marchi" blocks in the early cases frozen sections were cut from the block, which was then embedded, as was all the other tissue, in celloidin.

In most cases the brain stem was cut transversely into thin slices (3 mm.) and this horizontal plane was maintained, with a slight correction of angle, through the diencephalon. In some cases the brain stem was cut sagittally with the cerebellum. The slices of brain stem were prepared for Marchi, ordinary celloidin and a few Weigert Pal preparations. The cerebellum was cut in various planes; either horizontally, sagittally, coronally, or in an oblique plane, at right angles to the middle cerebellar peduncle. The cerebellum was mainly studied by means of the Marchi technique; a few blocks were also prepared for Weigert Pal and ordinary celloidin preparations. The proportion of the slices throughout the central nervous system prepared by the different methods varied from case to case, in accordance with the period of survival.

The Marchi and Weigert Pal sections were cut at 15-20μ, the celloidin sections at 10μ, paraffin sections at 5μ, frozen sections at 20μ, of thickness.

A few sections at least were cut from each block, and the range of stains shown below was applied to adjacent sections. In all areas of special interest complete series were cut throughout the block.

II. Staining Techniques Used

a) For cells.

(i) Neurones:

Thionin.

Haematoxylin and van Gieson's stain.

Haematoxylin and eosin.

(ii) Glial tissue:

Mallory's phosphotungstic acid haematoxylin

Holzer's stain.

Anderson's Victoria blue.

b) For fibres.

(i) Myelin:

Swank Davenport's modification of the Marchi method.

Kulchitsky's modification of the Weigert Pal method.

Loyez' method.

Scharlach R.

(ii) Axons:

Gros Bielschowsky's silver impregnation.

Holmes' silver method.

CHAPTER V

ORIGINAL OBSERVATIONS ON HISTOLOGICAL METHODS USED.

I. The Marchi Method.

Hamilton wrote in 1897: "The clearness with which the oil globules can be shown in the degenerated tracts is beyond all praise". This is indeed true. No other method shows so clearly even a few degenerating fibres. But since the introduction of the method by Marchi in 1875, the capriciousness of the stain has been a great drawback. The main disadvantages of the method are: the limited penetration of the tissue by the mordant, involving the necessity to use small blocks; the strong tendency for artefact formation; the necessity for distinguishing between artefacts (pseudo-Marchi staining) and true degenerating myelin (Marchi bodies); and the possibility that true "Marchi degeneration" may occur in normal control individuals without evidence in life of a tract lesion. These points will now be considered in some detail.

a) Lack of penetration, and small blocks.

Owing to lack of penetration by the mordant, workers have tended to use small and thin blocks. But when the blocks are too thin, there is another difficulty: the tissue is brittle and inclined to warp.

In my experience the blocks do have to be thin, but they need not be small. I have found that 3 mm. is the best thickness for large blocks and 5 mm. the best for small blocks.

In order to obtain an uninterrupted picture of a degenerated fibre and its relations, large blocks were prepared. Good results have been obtained with blocks up to 9 x 6 x 3 mms. This is larger than appears to have been used by most workers. With these blocks particular attention has been taken to ensure that they lay on a flat surface at all stages of preparation. With all blocks it was found that better penetration was achieved if they were turned over every two days, so that each side was equally exposed to the mordant. This was found more satisfactory than suspending the blocks, as some workers have done; this latter method is suitable only when there are a few blocks, and when these are small.

Care was taken to allow ample fluid for the number of blocks in a pot, e.g. about 200 ccs. to one large block, or 10 small blocks (cord), and superimposition of the blocks was carefully avoided. In some cases fresh mordant was added on the fourth day, but this did not appear to improve the preparations.

The method of using more dilute osmic acid in the mordant, as recommended by Poirier, Ayotte and Gauthier (1954) was tried in a few of the later blocks. The penetration was not so good, nor the staining so vivid, as with the ordinary Swank Davenport technique. It is possible, however, that some modification in the concentration of osmic acid used may prove satisfactory, and work is being done on this question.

b) <u>Tendency for artefact formation.</u>

A large literature exists on the subject of pseudo-Marchi artefacts. Apart from the numerous papers devoted solely to this aspect of the subject, most workers who have utilised the Marchi method have commented incidentally on these artefacts. Probably the most useful papers on this aspect of the method are those of Duncan(1930&'31) this includes an excellent comprehensive review of the literature;

of Swank and Davenport (1934 A and B; 1935 A and B); of Glees (1943); of Mettler (1932); and of Mettler and Hanada (1942).

It was found that the occurrence of various forms of pseudo-Marchi artefacts could not always be prevented; but certain precautions were found to be helpful.

Extremely careful and minimal handling of the material at all stages from post-mortem onwards is essential. Even slight tension on nerves must be avoided. Duncan found in animals that it was better to fix the peripheral nerves in situ before removing them, but better to remove the spinal cord unfixed. In our experience equally clear preparations were obtained with fixation before, or only after, removal of the cord and brain. It was the gentleness in handling the specimens which was vitally important.

The slices of tissue must never be allowed to dry at any stage of the process. (Duncan also noted this). The tissue must be washed gently but thoroughly in running water for 24-48 hours after fixation, and before mordanting, to remove all the formalin. This is absolutely essential. Minor precautions which were found helpful in preventing pseudo-Marchi formation were: to keep the tissue when in the mordant, in the dark; and to use tight-fitting non-metal tops for the containers of mordant and tissue, in order to avoid any escape of the osmic acid vapour, or reactions with the metal.

A particular feature noted has been the clear preparations, consistently free from pseudo-Marchi deposits, obtained by using frozen sections. The appearanceof such sections, compared to adjacent celloidin sections, would seem to suggest that it is the dehydration processes which are frequently factors in the production of the pseudo-Marchi artefacts. This was shown to be so by the following experiments. Frozen sections were cut from a number of blocks after mordanting, and the block was then dehydrated and embedded in celloidin as usual. The frozen sections and the celloidin sections were then compared. In many instances pseudo-Marchi artefacts were found in the celloidin sections, while the frozen ones were perfectly clear. In no frozen section was there any significant quantity of Marchi dust.

In this piece of work celloidin preparations of the Marchi material were mainly used. This was because many complete series of sections through a large number of blocks were wanted, and this is much more easily achieved in celloidin than in frozen blocks. But for any investigation in which complete series are not essential the frozen sections were found most satisfactory. The normal myelin in the frozen sections stains far more palely than in celloidin sections, and counterstaining may be helpful in some cases, to demonstrate the background more clearly. Light green has been found satisfactory for this.

To sum up: I have found that the two essential precautions in avoiding artefact formation are extremely careful handling of the tissue at all stages, and the thorough removal of formalin before mordanting. Frozen sections are far less prone to contain pseudo-Marchi artefacts than celloidin sections, or, in my limited experience, paraffin sections.

c) <u>Recognition of artefacts</u>.

Even when all precautions are taken, some artefacts may appear. It is essential to distinguish between the various forms of pseudo-Marchi artefacts and true degeneration. The appearances of these artefacts will be described and photographs of their basic forms will be given.

In this chapter of the thesis, the terms 'longitudinal section' and 'transverse section' will be used with reference to the long axis of the degenerating fibres; they do not refer to the position of tracts in the nervous system.

In transverse section, the Marchi-stained degenerating fibre appears as a black, round body of varying diameter. In longitudinal section, depending on the stage of degeneration, it appears either as an irregularly swollen thread, or as a string of spherical black bodies. Certain forms of pseudo-Marchi artefacts resemble and may be confused with the Marchi bodies seen in transverse section, and others with those seen in longitudinal section.

Probably the most important point in the identification of true Marchi degeneration is the consistency of its appearance in neighbouring blocks of tissue. This is in definite contrast to the random distribution of most of the artefacts.

The different types of artefact will be grouped as follows:-

1. Pseudo-Marchi dust.

   (i) fine

   (ii) coarse

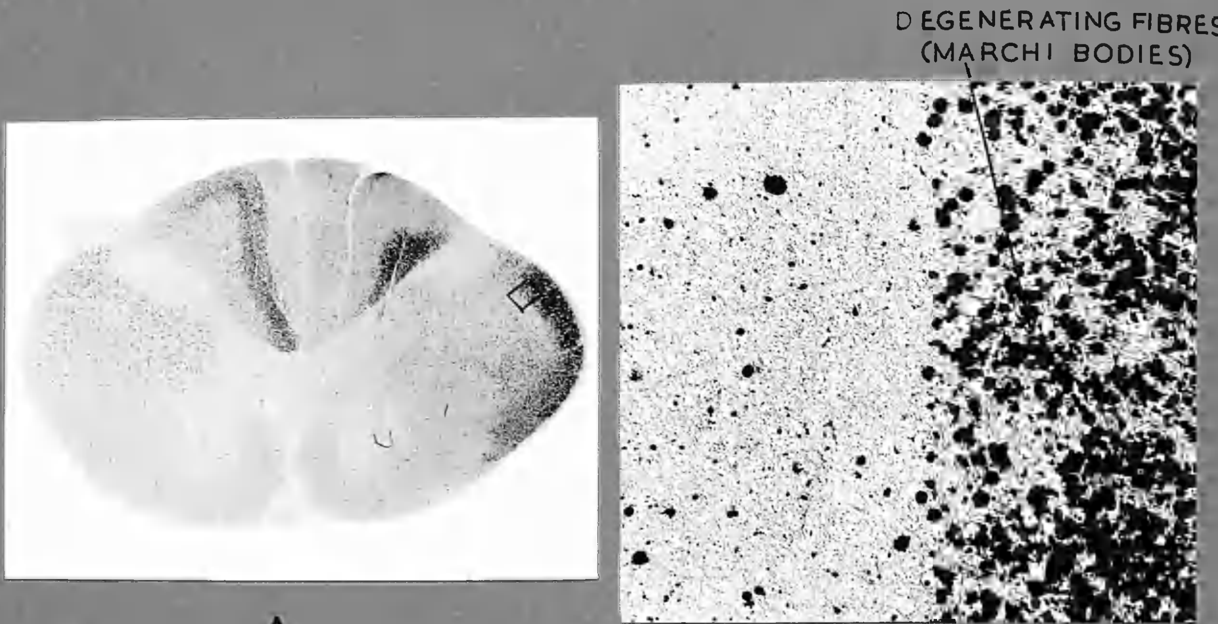
   (iii) organised network.

2. Pseudo-Marchi staining of normal fibres.

3. Massive pseudo-Marchi staining.

The terms 'pseudo-Marchi' staining, 'Marchi dust', 'Marchi granules' and 'Marchi bodies' are used by all workers in this field. Unfortunately there has been no standardisation; and so these terms need to be defined by every worker as he uses them. In this thesis, the term 'Marchi bodies' will be used to indicate true degeneration of fibres. All other terms indicate various forms of artefact.

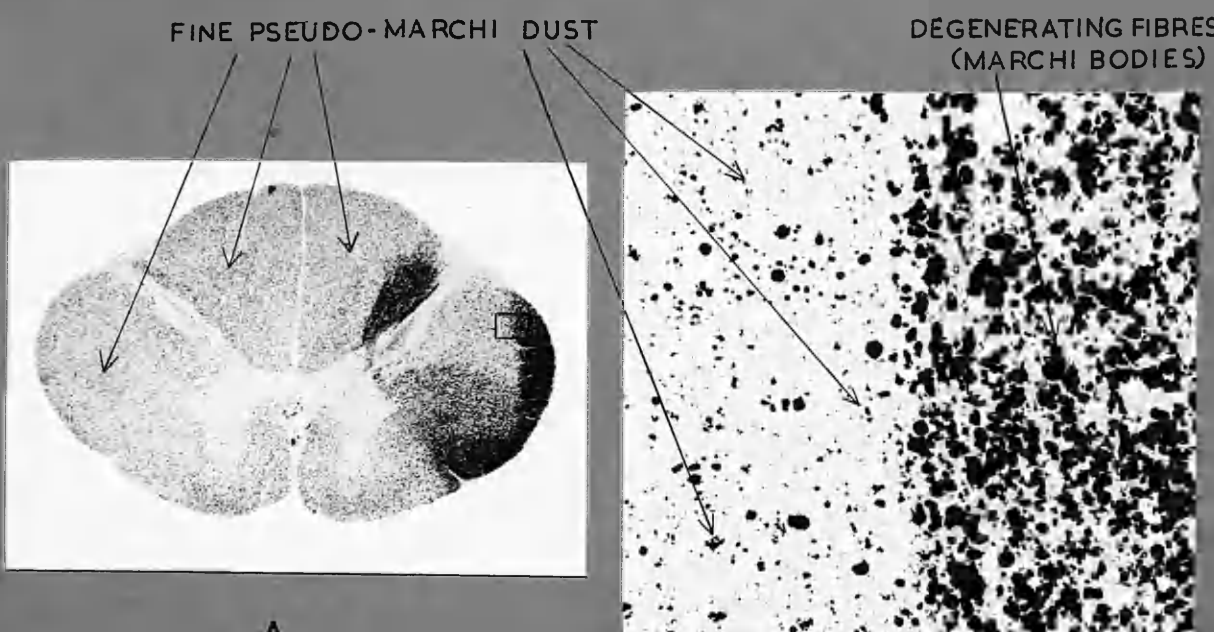
1. (i) Fine pseudo-Marchi dust: This is a common artefact. It is seen as fineblack "particles" usually scattered through the whole section, with no more concentration in the area of degeneration than elsewhere. This fine pseudo-Marchi dust is an unpleasant artefact, rather than one causing difficulties in interpretation, for it makes the preparation dirty-looking. The particles are usually too fine to be confused with Marchi bodies, and, like most other artefacts, it has a random



A

B

FIG 3



A

B

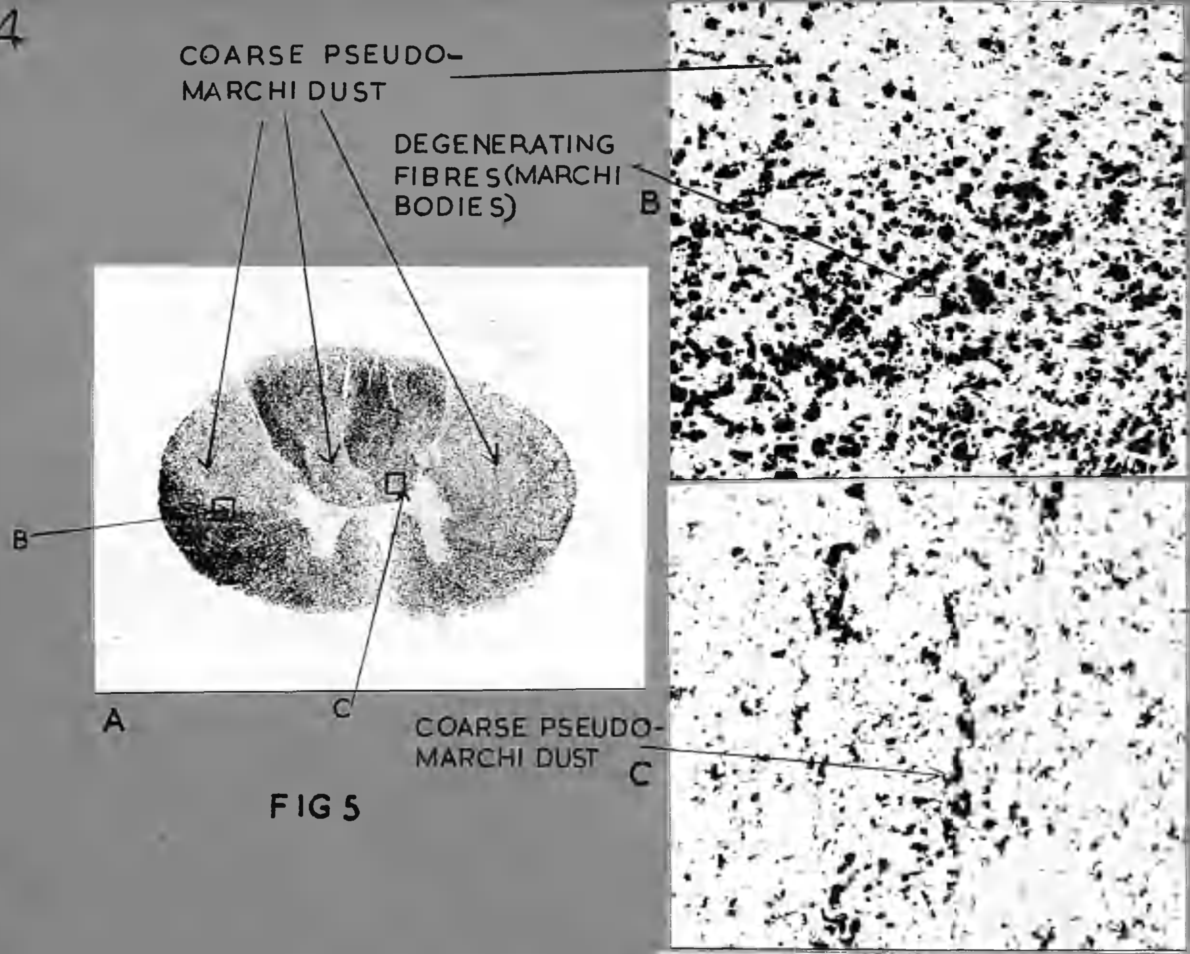
FIG 4

distribution, (Figs.3 and 4).

1. (ii) <u>Coarse pseudo-Marchi dust</u>: The pseudo-Marchi dust varies in size from being a mere peppering of fine particles to coarse granules up to 30 μ diameter. It may be that these coarse particles are aggregates of the fine particles. The appearance of coarse pseudo-Marchi dust is clearly seen in Fig.5C. These particles may confuse the picture, if the true degenerating fibres are all of narrow calibre. One of the main points of distinction from the rounded bodies of true degeneration is that some of the coarser particles have angulated outlines (Fig.5C).

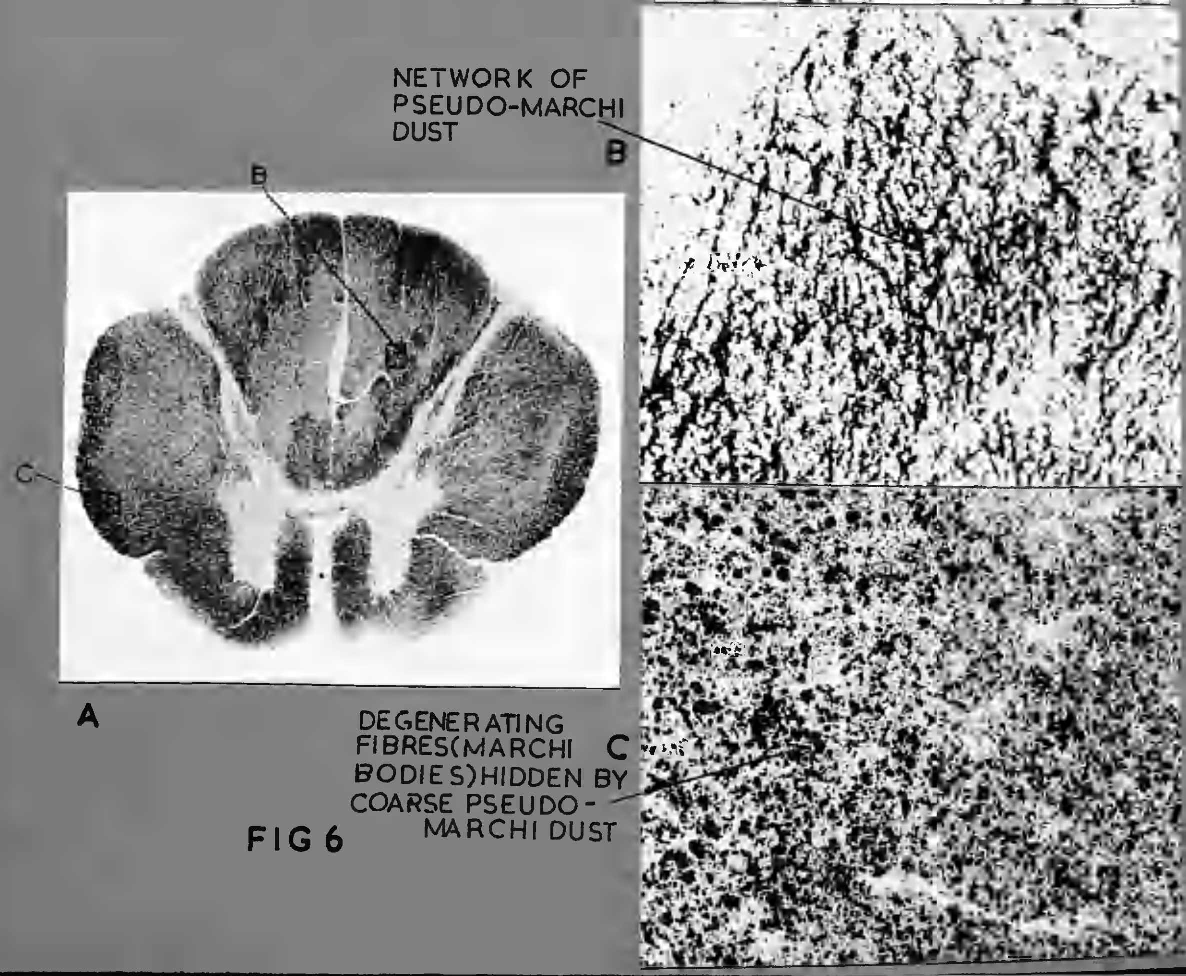
The distinction between true degeneration and pseudo-Marchi dust is best seen in Plates 3 and 4. In Fig.3 there are degenerating fibres cut in transverse section; there is a negligible amount of pseudo-Marchi dust. In Fig.4 there are degenerating fibres and also a diffuse peppering of pseudo-Marchi dust throughout the section. In the higher magnification (Fig.4B) the main mass of degenerating fibres can be clearly distinguished. The coarse pseudo-Marchi particles tend to cause confusion only on the boundaries of a zone of degeneration, and

4



COARSE PSEUDO-
MARCHI DUST
DEGENERATING
FIBRES(MARCHI
BODIES)
B
B
A
C
COARSE PSEUDO-
MARCHI DUST
C

FIG 5



NETWORK OF
PSEUDO-MARCHI
DUST
B
B
C
A
DEGENERATING
FIBRES(MARCHI
BODIES)HIDDEN BY
COARSE PSEUDO-
MARCHI DUST
C

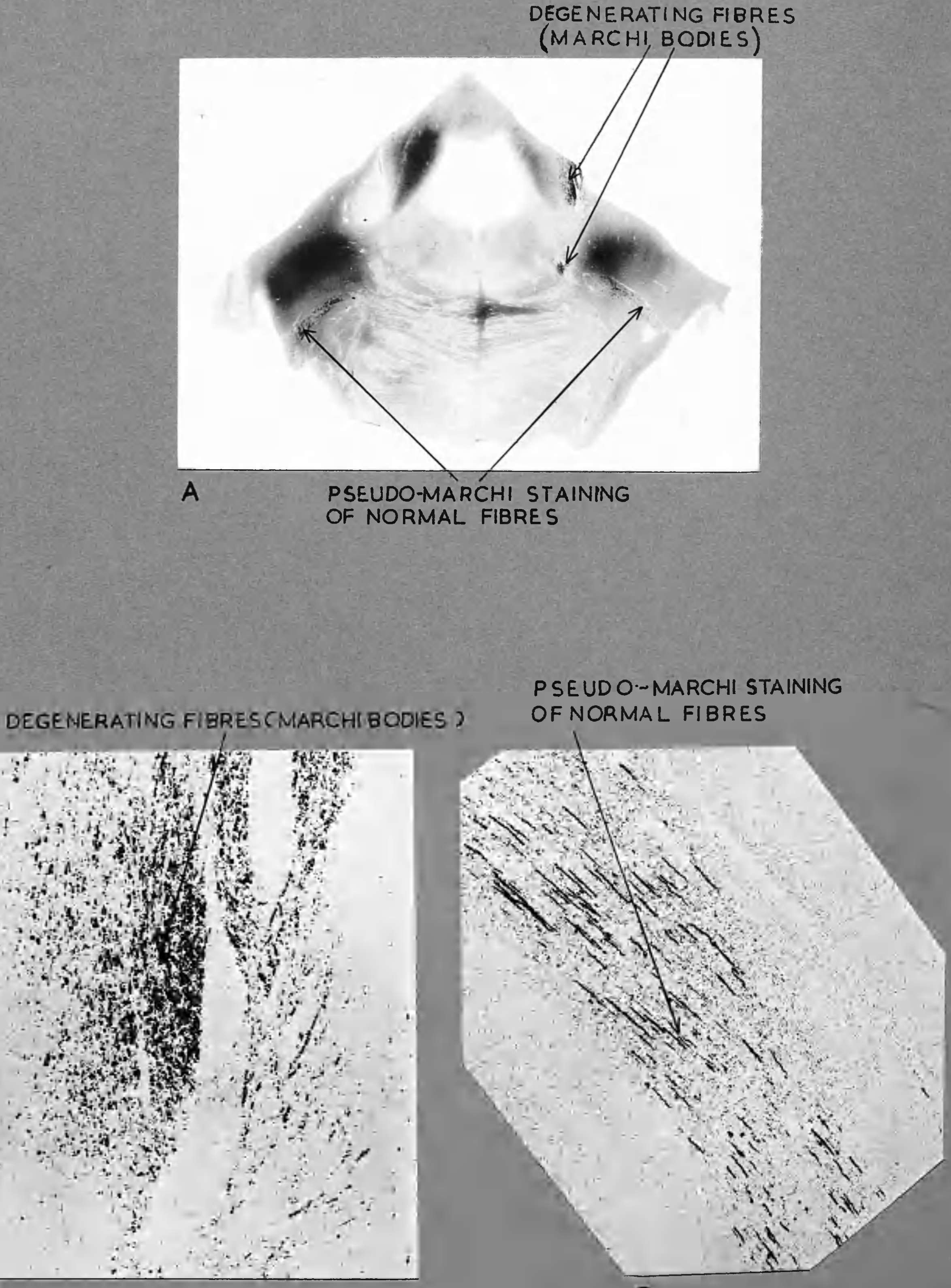
FIG 6

obscure the detail of the course of a few fibres as they quit the main mass of degenerating fibres. This is shown in Figs.4 and 5. As the larger black bodies are present only near the main mass of degenerating fibres, and as they can be traced through successive sections, they are therefore degenerating fibres. As the fine bodies are similar in appearance and number to those scattered throughout the rest of the section and throughout the whole cord, they are therefore taken to be pseudo-Marchi dust.

It can sometimes happen that the coarse pseudo-Marchi dust particles reach such numbers that they seriously obscure the true degeneration (see Fig.5A and C).

1. (iii) Organised network of pseudo-Marchi dust: This term is used to describe a type of artefact not easily confused with true Marchi staining. It is a form which can completely hide true degenerating fibres. It occurs as large, irregular black masses. An example of a particularly severe form of this (produced intentionally, by inadequately washing out the formol-saline after fixation), is shown in Fig.6B.

FIG 7


DEGENERATING FIBRES
(MARCHI BODIES)
A
PSEUDO-MARCHI STAINING
OF NORMAL FIBRES
DEGENERATING FIBRES (MARCHI BODIES)
PSEUDO-MARCHI STAINING
OF NORMAL FIBRES
B
C

2. <u>Pseudo-Marchi staining of normal fibres</u>: This form of artefact closely mimics the appearance of true degeneration, particularly when seen in longitudinal sections. It appears in certain characteristic sites, such as the larger cranial nerves, particularly the second, fifth, seventh and eighth, and also in the corpus callosum. It seems to be associated with post mortem trauma to the tissues, and probably with tension on them. These fibres which have been pulled on at post mortem become stained over a considerable length, and then they resemble fibres which were degenerating before death. They differ from the true degenerating fibres, in that the diameter of the fibre is seen to be constant throughout, and, in that lengths of the fibre remains unstained while other lengths are stained black. The true degenerating fibre, it will be remembered, has a beaded or broken up outline, and stains black throughout.

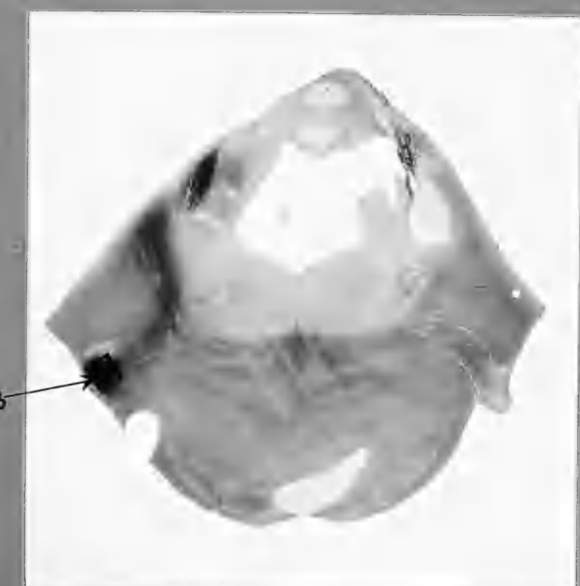
There is, however, another form of pseudo-Marchi staining of normal fibres. It can be readily understood that if at any time between death and fixation some droplets of myelin escape from the neurilemmal sheath, they may stain with the Marchi

A

DEGENERATING FIBRES(MARCHI BODIES)

B

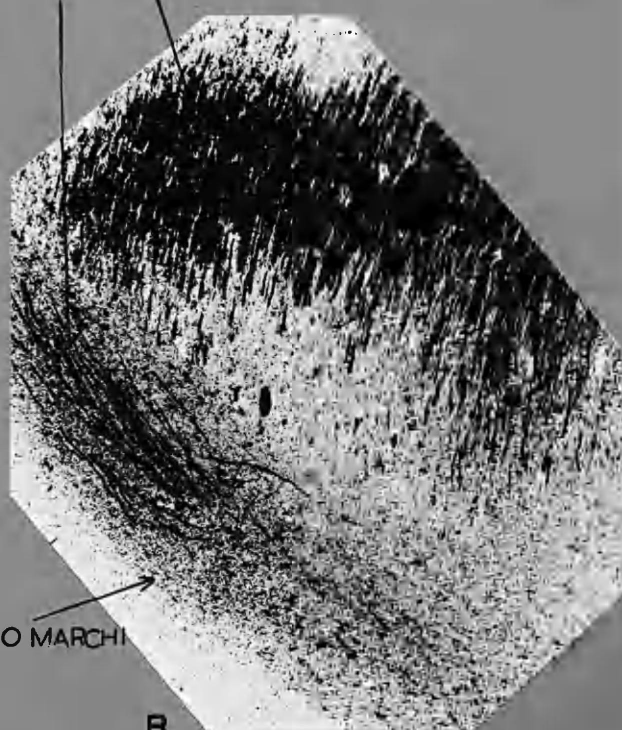
FIG 8



A

FIG 9

PSUEDO MARCHI STAINING OF NORMAL FIBRES



PSEUDO MARCHI DUST

B

reagents. These stained droplets have the same appearance as Marchi bodies; for they are in fact Marchi bodies. But they are not the Marchi bodies of true fibre degeneration. These droplets can usually be distinguished from true Marchi bodies on account of their distribution: they occur in the neighbourhood of fibres showing pseudo-Marchi degeneration; and they do not occur in particular association with the main mass of degenerating fibres which can be traced from section to section.

The appearance of pseudo-Marchi staining is shown in Figs.7.A and C, and Fig.12. Figs.7A and B and Fig.11 show the appearance of true degeneration at a period of survival of 81 days, and Fig.8.A and B. and Fig.10 at a period of survival of 23 days; these degenerating fibres can be contrasted with the fibres showing the pseudo-Marchi staining. All the fibres are seen in longitudinal section.

In Fig.7, this pseudo-Marchi staining is present in both fifth cranial nerves. In Fig.12, the constant diameter and the patchy staining of the normal fibres is particularly clear. In Figs.8 and 10, the appearance of true degenerating fibres at a stage when they are irregularly swollen, but not disrupted, is shown. In Figs.7.B and 11. the true

FIG. 10 DEGENERATING FIBRES (MARCHI BODIES) SURVIVAL 23 DAYS (FROM FIG 8)

FIG. 11 DEGENERATING FIBRES (MARCHI BODIES) SURVIVAL 81 DAYS (FROM FIG 7)

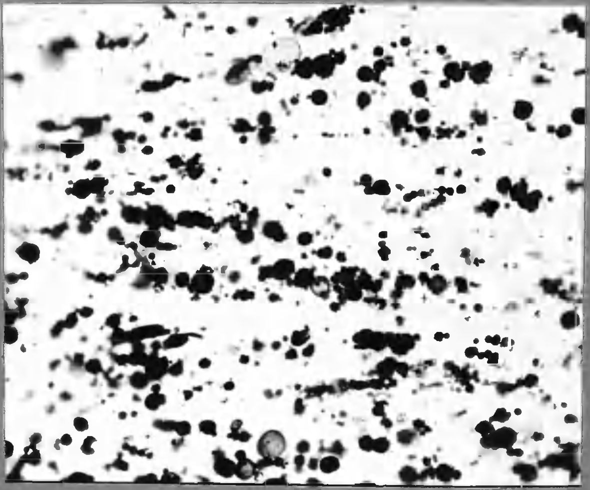
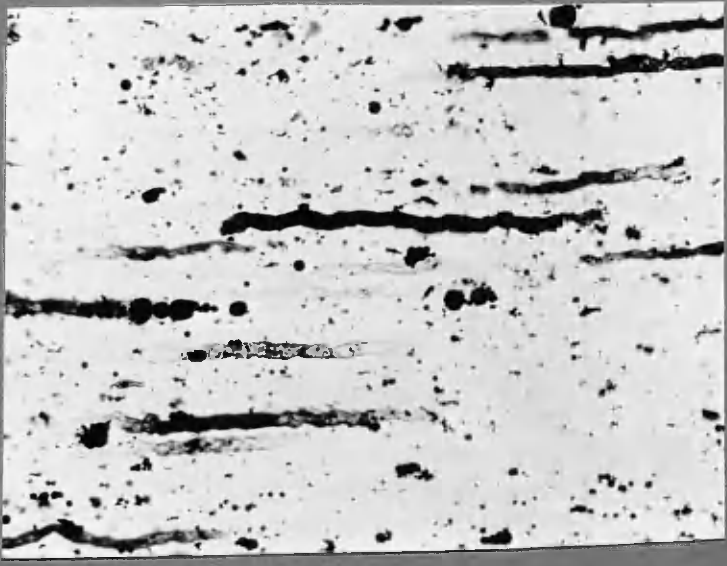


FIG 12 PSEUDO-MARCHI STAINING IN NORMAL FIBRES (FROM FIG 7)



degenerating fibres have broken up into rounded Marchi bodies of various sizes.

3. Massive pseudo-Marchi staining: Occasionally there occurs a very dense patch of black staining, with some characteristics like those described under (2). This massive black staining is particularly liable to occur deep in a large block, in an area of densely packed nerve fibres; it may enclose an unstained zone. It is characterised by the intensity of the coal black staining, confined to one area of the block. In sections through such an area, the whole region is usually found to be peppered with pseudo-Marchi dust. Every fibre within such an area is stained intensely black; such a mass of intense black staining does not occur with true degenerating fibres. When the fibres of such an area are examined at the edge of the area, the characteristics mentioned under(2) are seen - characteristics such as the constant diameter of the fibres and the patchy staining of the fibres; in this case the patchiness occurs as a demarcation at the edge of the black area; the fibres within the black area are deeply stained, and the same fibres continuing out of this area are left unstained.

This form of artefact differs from true degeneration in that the black staining does not spread along tracts or bands of nerve fibres, and it is not found in neighbouring sections, once the edge of the patch has been reached. The appearance of this form of artefact is shown in Fig.9.

One last feature of Marchi preparations which has not been mentioned is the occurrence of dark, cloudy areas. These are present in Fig.7. These are simply manifestations of irregular depth of staining. Under high power, such an area is seen to be more deeply stained than the rest of the section, the colour is brown, not black. The appearance in no way resembles degeneration of fibres.

d) <u>Length of period of survival during which the Marchi method is applicable, in human tissue.</u>

It is usually believed that degenerating myelin cannot be demonstrated when the patient survives more than six weeks. This belief may be based on the findings of those who work on laboratory animals. I have found that in man, clear Marchi staining can be obtained with periods of survival of 13 months. These results were published in 1951. Since that time I have found that material from patients surviving for periods of two and a half years can be stained by the Marchi method, and that such material can be used for tracing degenerating tracts for a considerable part of their course.

With regard to the shortest period of survival which is compatible with the use of the Marchi method, I have found that material from a patient dying twelve days after a cordotomy was useless; no Marchi bodies were seen. On the other hand, in one patient in whom the fifth cranial nerve was cut 10 days before death, Wallerian degeneration could be clearly shown by the Marchi method in the distal portion of the divided nerve. For the staining of tracts in the central nervous system, it seems that adequate preparations can be expected when the survival period exceeds 16 days; occasionally cases with a survival period of less than 16 days may be stained by the Marchi technique.

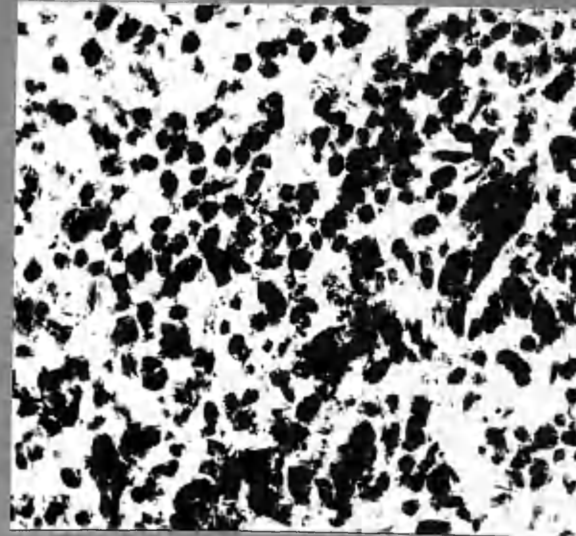
Some further points need emphasis. Clear evidence of degeneration in a tract may be obtained by the Marchi method at the site of a lesion and in its terminal parts earlier than in the main length of the tract. Marked staining may persist in the lesion and in the greater part of the tract for very much longer than in the terminal zone; but even in this zone clear degeneration has been seen in cases with survival periods of 5 months. Even when only a few fibres remain, the Marchi method still gives vivid evidence of degeneration, unequalled by any other method. From observations made on non-human material it appears to be likely that the process of degeneration varies from species to species, and from tract to tract. Hence no generalisation on the applicability of the Marchi method can be made.

e) Effect of prolonged storage in formol-saline.

It is universally believed that the prolonged action of formalin on a tissue renders it unsuitable for investigation by the Marchi method (Swank and Davenport, Mettler and Hanada and many others). It is always recommended that the tissue should not be kept in formalin for longer than 14-21 days. The following observations, however, show that in man the tissue can be kept in formol-saline for 9 years.

It has been found that material from patients with a survival period of less than 80 days cannot be

FIG.13. SURVIVAL 9 MONTHS
FIXATION 21 MONTHS



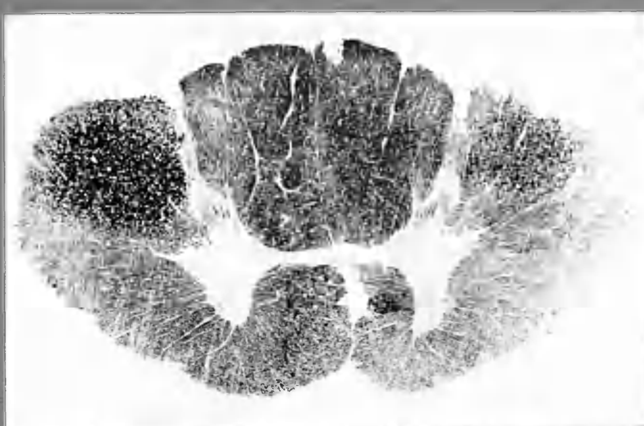


FIG 14 SURVIVAL 11 MONTHS
FIXATION 2 YEARS

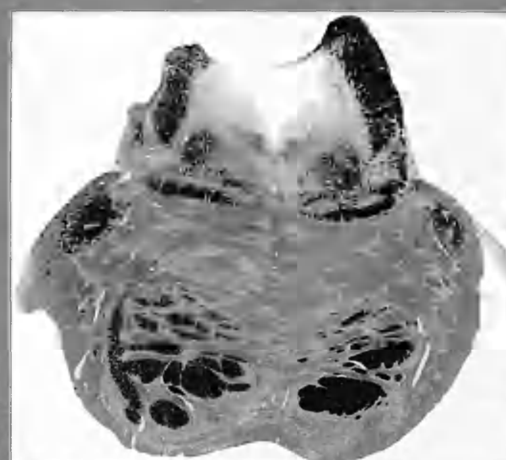


FIG 15 SURVIVAL 15 MONTHS
FIXATION 2½ YEARS

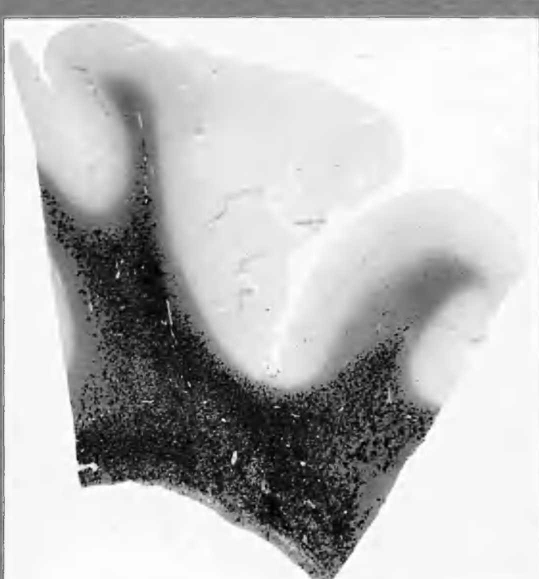


FIG.16 SURVIVAL 12 MONTHS
FIXATION 8+ YEARS

stained by the Marchi technique, if it has been kept in formol saline for more than about 18 months. But if the survival period exceeds 80 days, then definite Marchi staining can be obtained in all cases. The longest period of survival in this series was 2 years, and the longest period of storing the tissue in formol saline was a little less than nine years. Indeed, staining is particularly vivid in these cases. On plate 8 are photographs from patients who received serious head injuries at periods of 9, 11, 15 and 12 months respectively, before death. The length of time that the tissue was in formol saline was 21 months, 2 years, 2½ years and almost 9 years respectively. Clear Marchi staining is present in all the cases.

In over 20 cases the Marchi technique was used after 10-14 days in formol saline; and in these same cases, neighbouring blocks were stored for periods of 1-9 years in formol saline; these blocks were prepared by the Marchi technique. It was found that the distribution of the Marchi staining bodies was identical after the short and lengthy periods of fixation (in all the cases with periods of survival of over 80 days).

In the tissue which has been stored for years the appearance of the Marchi bodies differs from that seen in freshly fixed material. In the cases with longer survival periods increasing amounts of the Marchi material is contained in fat granule cells. It appears that it is this intracellular Marchi material which continues to stain despite the action of formalin. It is surprising that these cells do not move away, and are still to be found in the place where the original fibre degenerated.

This old stored material is particularly pleasant to study, for it does not contain pseudo-Marchi artefacts in frozen sections.

A further point of interest about this long-stored material is that the Marchi bodies tend to dissolve out into clearing reagents. A frozen section, mounted without clearing, in many cases contains far more Marchi bodies than the adjacent sections mounted after dehydration and clearing.

Thus it is definite that prolonged storage in formol saline does not prevent Marchi staining in the later stages of degeneration. This has probably never been appreciated by other workers as the applicability of the method in demonstrating degenerating myelin at survival periods longer than 6 weeks was not recognized. This observation is important, because it increases enormously the applicability of the Marchi method. It must be noted that all the remarks made in this context are applied to man only; they may be true for other species, but I have no evidence for this.

Papers dealing more fully with this aspect of the work are being prepared for publication, and further work on the nature of the alteration in degenerating myelin, and the action of formalin and osmic acid on the myelin is being continued.

f) Spontaneous myelin degeneration in "normal" tissue.

It is possible that there is some atrophy of cells and fibres occurring as a part of the gradual and normal process of ageing. If this is so, these degenerating fibres might give a positive Marchi staining reaction, and form a source of error in the kind of material investigated here. In order to investigate this question, control cases were examined by the Marchi technique. These controls consisted of cases of cancer, congestive heart failure, peritonitis and alcoholism, in the same age groups as the cases of cordotomy; the only difference between the material of the main study and the control group was that the former had the operation of cordotomy and the latter had no surgical operation on the nervous system. The features of the control cases and the results of Marchi staining of this material is shown in Table 2.

In all the cases except cases 35, 40 and 52, only a rare degenerating fibre was found, in the sites indicated in the table. In these three cases the fibres were slightly more numerous.

In the spinal cord degenerating fibres were seen in only 5 cases. In two of the cases the fibres were in the dorsal columns; it is likely that these fibres were degenerated because of carcinomatous involvement of the dorsal roots. In the other three cases, in which a very few degenerating fibres were in the central grey matter and ventral lumbar nerve roots, the central grey matter, and the direct pyramidal tract, respectively, no cause for the degeneration was found. In no case was there any degeneration in any of the secondary sensory fibres in the spinal cord. In

Case Number	Age	Complaint	DEGENERATING FIBRES IN THE SPINAL CORD	DEGENERATING FIBRES IN THE BRAIN
35	76	Carcinoma of upper jaw	None	In brachium of superior colliculus in retro-lenticular radiation
36	84	Carcinoma of stomach	None	None
37	73	Congestive heart failure	Not examined	None
38	53	Peritonitis from diverticulitis	In right pyramidal tract.	In right pyramidal tract
39	-	-	None	None
40	-	-	In dorsal columns	In both cuneate nuclei and in sensory decussation.
41	66	Carcinoma of stomach	None	None
42	51	Carcinoma of stomach	In left fasciculus gracilis. (Lumbar roots involved in tumour)	None
43	-	-	None	In fibrae perforantes pedunculi
44	67	Heart failure	None	None
45	65	Carcinoma of uterus	In central grey matter of cord	None
46	56	Carcinoma of salivary gland	None	None
47	51	Carcinoma of bronchus	In ventral roots of lumbar region and in central grey matter	None
48	76	Congestive heart failure	None	In fibrae perforantes pedunculi
49	75	Parkinsonism Heart failure	None	None
50	68	Carcinoma of bronchus	Not examined	None
51	55	Carcinoma of bronchus	Not examined	In fibrae perforantes pedunculi and in lamina of globus pallidus
52	56	Chronic alcoholism	None	On the right: in medial lemniscus and in latero-ventral nucleus of thalamus; in geniculo-calcarine radiation, in fibrae perforantes pedunculi. On the left: in limiting layer of thalamus, in retro-lenticular part of internal capsule and in fibrae perforantes pedunculi.

the sections of brain examined, degenerating fibres were seen more often in the perforantes pedunculi, and in the retro-lenticular part of the internal capsule, than in other sites, which varied from case to case. In cases 35 and 52, more numerous degenerating fibres were seen. No direct cause for the degeneration was found in any case.

It would appear from this study that although degenerating fibres may occur without evident cause in "normal" unoperated cases, they usually occur in very small numbers. In view of this they need not lead to any confusion with the fibres traced in contiginous sections from an operative lesion in the cord.

II. Weigert Pal Method.

The preparations stained by the Weigert Pal method were of definite value, only in showing the extent of the lesion in the cord. The method did not prove of value in tracing degeneration except in the cord, as a "negative" stain does not show up the loss of a small number of fibres, especially where there is an intermingling of several tracts.

The method was also used to determine that no degeneration antedating the operation was present.

III. Silver Impregnation Methods.

There were very few cases in which the survival period was short enough for the demonstration of axons in the process of degeneration. The silver impregnation methods were mainly used, like the Weigert Pal methods, to demonstrate by nonstaining the extent of the fibre loss.

I hope eventually to determine the details of the terminations of the spino-cerebellar tracts by using one of the silver impregnation methods (e.g. Glees and Clark (1941); Nauta and Gygax (1951)) on suitable material - cases with a survival of about 6-16 days.

Gros Bielschowsky preparations were made chiefly on celloidin sections. It was soon found, however, that when this method was used on spinal cord sections, there was a peripheral band where the axons were not impregnated. A similar artefact occurred also in sections from the brain stem and cerebellum; but in the spinal cord this defect was particularly unfortunate as the peripheral region is that in which the ascending degeneration under investigation occurs.

This defect was eventually overcome by observing the following precautions:-

(i) Blocks were stored a minimal time in alcohol and water before the sections were cut.

(ii) Sections were cut and put into distilled water instead of the routine alcohol and water.

(iii) Gros Bielschowsky preparations were made within 24 hours of cutting the sections before any other staining was done.

A further observation was made on the Gros Bielschowsky method when sections were counterstained with thionin. It was noted that thionin staining was exceptionally good, surpassing the ordinary thionin stained section, and with the advantage of a markedly reduced tendency to fade.

It is intended to investigate which step of the silver method enhances subsequent thionin staining.

Holmes method on paraffin sections was employed in a few cases. This method has the advantage of uniform staining without the "halo" artefact of the Gros Bielschowsky preparations, but it has the disadvantage of a far less vivid picture for photographic representation.

CHAPTER VI

ON INTERPRETATION OF THE SECTIONS IN DEGENERATION STUDIES.

The lesions in the ventral and lateral columns of the cord vary from entirely ventral to entirely dorsal, from small and superficial to so extensive as to leave intact little more than the dorsal columns and central grey matter.

The resultant degeneration of ascending fibres has been determined, and an attempt has been made to correlate the distribution of the fibres with the area of the cord involved. Similar studies have been made in relation to the retrograde cell changes.

I. Fibre degeneration.

The possible criticism that the appearances of the area destroyed may be very different according to the various lengths of time between the making of the lesion and the patient's death has been considered. The extent of the lesion in early and late cases has been confirmed by a number of stains. In early cases the lesion may be somewhat more extensive and less clearly delimited; there are a few degenerating fibres scattered near the region, which, as far as can be assessed, have not been actually severed by the knife. These fibres run among normal fibres; they are too few to have much functional significance. In these early cases in which survival was less than two months after the operation, the area of maximum, and presumably total destruction can be determined by excluding the scattered fibres around the periphery of the degenerating area. In the later cases, it was thought at first that owing to the disappearance of degenerated myelin the area of destruction might appear unduly small, and that the appearance in a Marchi preparation would minimise the actual area of destruction. But comparison of the outlines of the degenerated area shown in Marchi, Weigert Pal, and Gros' silver preparations, and sections stained by the other methods enumerated in Chapter IV showed such consistent limits in all cases that it was obvious that the Marchi method was reliable also in later cases.

A further criticism could be, that some of the tracts investigated might be composed entirely of small, thinly myelinated or unmyelinated fibres and that such fibres would not be shown up by myelin stains. But the total area of destruction demonstrated in myelin preparations has been shown to have the same extent as that shown in preparations stained to demonstrate axis cylinders. It may be concluded that such small fibres, if they are relevant to the tracts under consideration, are intimately mingled with larger myelinated fibres; and so the picture of myelin degeneration due to staining of the large degenerating fibres covers the area of degeneration whether all the fibres are large or small. Details of termination of finer fibres could not be made in this study.

The assessment of the size of myelinated fibres cannot be accurately gauged from Marchi preparations. For Marchi bodies are derived from disrupted myelin sheaths. It would be particularly fallacious to take the smaller bodies as representing only fine fibres, for they may represent degenerating myelin from thicker fibres which have broken up. Nevertheless, some deductions from the size of the larger Marchi bodies may be made. It has been observed that large Marchi bodies occur only in tracts known to contain thick fibres. In this work, no conclusions were made about the size of fibres from Marchi material unless they could be confirmed by silver preparations in normal material.

The absence of Marchi bodies was not accepted as significant unless it was a constant feature in many cases of varying post-operative survival intervals. Obviously the degeneration may have been present at an earlier stage, and subsequently have disappeared. Even a few degenerating fibres, on the other hand, may be highly significant, if they confirm the evidence from other cases that fibres of a certain system occupy a certain position.

II. Tracing of Fibres within Tracts.

The shifting position of tracts and fibres within tracts will be considered in some detail. The reason for this must be made clear. Tracts within the central nervous system are intermingled, and often it is very difficult to sub-divide a mass of degenerating fibres into its components. Only by a recognition of the individual course of certain groups of fibres can they be identified as separate tracts. Also, the possibility that fibres from different parts of the body are in a definite relationship to each other can only be investigated by following the detailed course of degenerating fibres.

III. Cell changes.

When the axon of a cell is injured, certain reactive changes appear in the cell body. The cell may become chromatolytic; it may then recover, and gradually return to its normal state. Or it may become chromatolytic; and then atrophy, becoming shrunken and pyknotic, or becoming a very pale "ghost" cell, without any nucleus or Nissl substance; it may even disappear completely. When this happens, there may be an increase in glial cells.

On the other hand, we have no grounds for assuming that all cells become chromatolysed when their axons are divided.

It is usually accepted that a more marked reaction may occur in a cell body if the proximal part of the axon is injured close to the cell body, than if it is injured in its distal part, remote from the cell body. This then shows that the cell shows various reactions. The presence of collaterals may also influence the reaction of the cell body. If the axon is poor in collaterals, it would seem likely that any damage to the axon would lead to the death of the cell; for one cannot understand what purpose it could serve if the cell body has lost it's means of transmission. But if the main axon is damaged, and there is a strong collateral system, then the cell may continue to function. In the latter instance, any axonal changes would be only temporary. This is one possibility. Other may very likely exist. The type of dendrites in a cell may also play a part in governing its reaction to injury. It may be that some cell bodies are more sensitive to damage of their axons than others. This has been noted by many other workers, e.g. Marinesco, (1898); van Gehuchten (1900); de Neef (1907); Bucy (1927, 1928); Geist (1933); Hare and Hinsey (1940); Romanes (1941, 1946).

In considering the subject of looking for the parent cells of divided axons, it is obvious that cells showing chromatolysis can usually be found easily, that very atrophic cells can be found often only with difficulty, and that cells which, having disappeared altogether, may never be found at all; for they may have left no trace. This latter occurrence constitutes a serious difficulty when search is being made for the cells of origin of axons divided long before death. When there is a disappearance of a large mass of cells or a large cluster of cells normally found in a nucleus, their absence may be easily observed. But when only some cells of a nucleus of sparse cell population and a diffuse character have disappeared, it may be impossible to be sure if cells have disappeared or not. Where cell loss, or alteration, is expected, the presence of many glial nuclei and fibres may be taken to represent reaction to the death of neurones. But a considerable range of differences in glia population was found in examining "normal" cords, and at different levels of the same cord. In this respect also, it was noted that some normal cords appear to contain fewer neurones in all cell groups than is usual.

When this general problem of cell changes following division of axons is particularized on to the present material, it was found that all forms of cell reactions were easily seen in Clarke's column, and that they were all harder to find elsewhere.

Chromatolysis was always found in Clarke's column when the period of survival was less than forty days, and very seldom found when the period was longer. After forty days, and even earlier, a disappearance of cells could easily be ascertained. Chromatolysis was found in the cells of the dorsal horn when the period of survival was as varied as 5 to 390 days, and was most marked when the period of survival was about 150 days. It is thus clear that the different groups of cells do not all have the same temporal pattern of reaction.

It has been found throughout this work on degeneration of the human nervous system that the period of survival after which marked axonal cell changes might be expected, varies with respect to different nuclei. This is important, for unless this "group" variability is appreciated, conclusions may be drawn with respect to findings which are negative solely because of the length of the period of survival.

In this material, the presence of gliosis did not help in deciding whether neurones had previously been present or not, if this was not already obvious. This is on account of the variation of the normal amount of glia, as has been mentioned, and also because the cells being sought do not occur in large clumps, but are likely to be scattered here and there among unaffected normal cells.

It is also possible, as has been mentioned, that many of these cells do not react to trauma by passing through the series of chromatolysis, death and gliosis.

The lack of changes in the cell groups, other than those of Clarke's column, caudal to a lesion, has often been noted before. Apart from the possible factors mentioned above, it might well be that the fibres of many of these cells form short chains; and so only a few of them would be damaged even when the cord is transected.

The position, it is true, is rather unsatisfactory. When many cells in a group show changes after a lesion we can safely deduce that many of their fibres were injured; when only a few cells of a group show changes, we can only deduce that a few fibres were injured, but we cannot decide whether the remaining fibres were injured or not.

CHAPTER VII

PREPARATION OF MAPS FOR AID IN LOCALISATION IN THE CEREBELLUM.

In examining the cerebella for degenerating fibres a difficulty was encountered in the absence of published drawings or diagrams of any comprehensive series of slices taken in different planes through the human cerebellum. In the majority of textbooks the only plane of section in which the folia are named is the sagittal, and here most workers have limited the labelling to the vermis itself.

The cerebella examined in the course of this topographical study have been cut in different planes in the various cases, in order to obtain a clearer three-dimensional image of the course of the spino-cerebellar fibres. Recognition of the folia was essential for this work; yet owing to the fact that the histological structure of the grey matter is the same throughout the cerebellar cortex, topographical localisation in the cerebellum is difficult. To meet this difficulty, maps of slices of the cerebellum, cut in different planes, were prepared, as follows.

The cerebellum and brain stem from each of twenty "normal" adult subjects were used. The meninges were stripped off, the divisions of the vermis were then determined, and their continuity laterally with the folia of the hemispheres was traced. The different divisions of the vermis were each painted in a different colour, the colour being continued laterally on to the adjacent folia. Thus the external surface of the cerebellum was coloured in such a way that a mere casual glance at any small piece of the structure immediately revealed to which division that piece belonged.

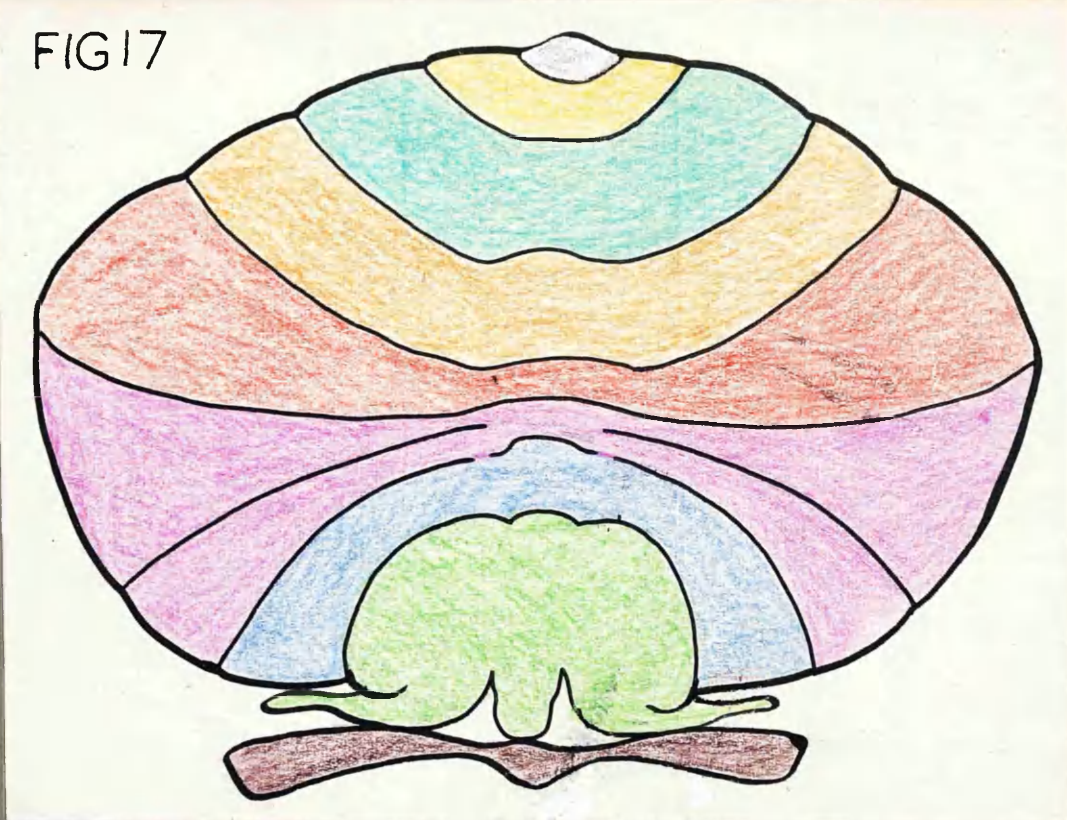
After I had tried various methods of colouring the cerebellum, I found that "Stabilo" water paint pencils were the most suitable. I also found that the colours could be made adequately fast, so that they could not easily be washed or rubbed away if the following technique was used. After the cerebellum was painted it was left for 24 hours exposed to the light, protected from over-drying by covering it with a bell-jar; some damp cotton-wool was also put under the jar, not touching the cerebellum, to keep the atmosphere slightly damp. After colouring the preparations photographs were taken of the uncut specimens. Kodak's ectachrome colour transparencies were used.

The preparations were then cut in slices. It was found that slices 4 mms. thick were most satisfactory for showing the topography of the cerebellum at different levels. The planes of section were a. Sagittal, b. Horizontal, c. Coronal, d. Oblique at right angles to the brachium pontis.

After slicing the cerebellum, the colour was then continued from the surface of the cerebellum onto the cut surface of the folia. In order to be certain about the correct colouring of the folia, as each specimen was coloured, a companion cerebellum was dissected at the same time, in the same plane. By dissecting the folia right down to their bases the distinction between each division of the cerebellum could be definitely ascertained. Colour photographs of these series of slices were also taken.

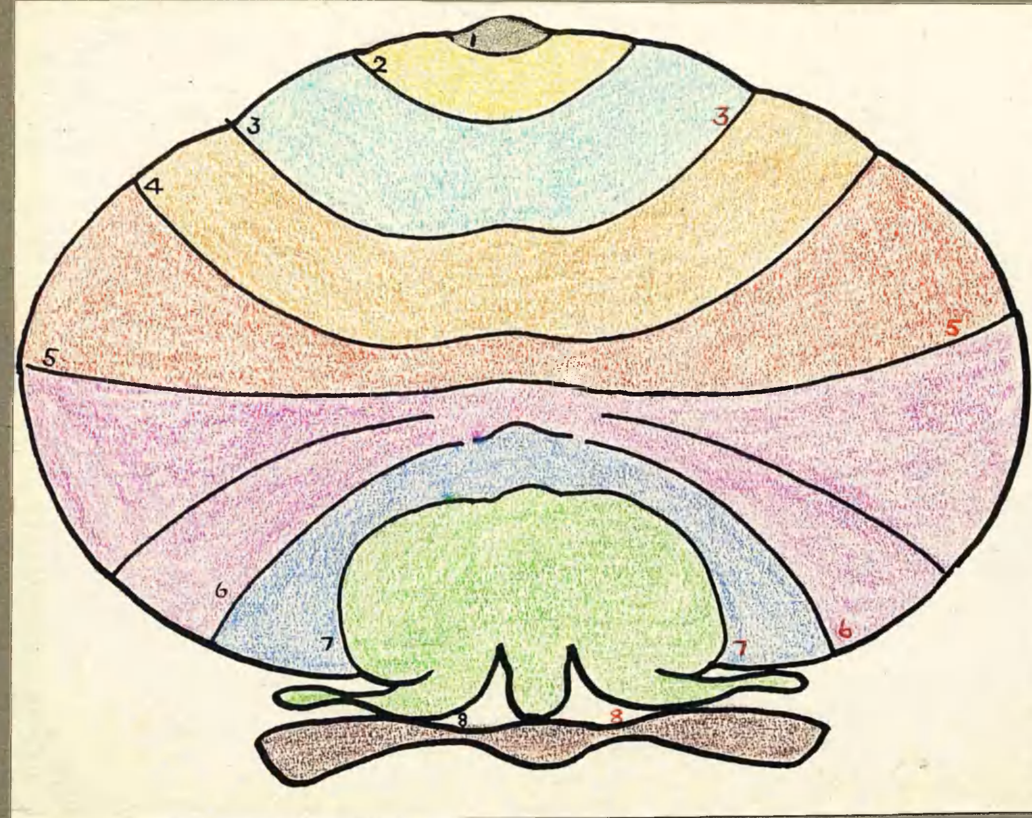
The colour transparencies are the negatives and not the positives or prints, and so it follows that each photograph produces only one transparency. Further, the material costs for each photograph was approximately 10/6, the whole set cost £13. 13. 0. It is then, unfortunate, but unavoidable, that only one set of these transparencies could be made: these

FIG 17



COLOUR	VERMIS		HEMISPHERES		LOBES
	LINGULA				
	CENTRAL LOBULE		CENTRAL LOBULE		ANTERIOR LOBE
	CULMEN	SUPERIOR VERMIS	ANTERIOR SEMILUNAR LOBULE		
	DECLIVE		POSTERIOR SEMILUNAR LOBULE	LOBULUS SIMPLEX	
	FOLIUM		SUPERIOR SEMILUNAR LOBULE	CRUS I } ANSIFORM LOBE	
	TUBER		INFERIOR SEMILUNAR LOBULE	CRUS II } ANSIFORM LOBE	
			GRACILE LOBULE	LOBULUS PARAMEDIANUS	POSTERIOR LOBE
	PYRAMIS	INFERIOR VERMIS	BIVENTRAL LOBULE	PARAFLOCCULUS DORSALIS	
	UVULA		TONSILLA	PARAFLOCCULUS VENTRALIS	
	NODULUS		FLOCCULUS		FLOCCULO-NODULAR LOBE

FIG 18



1 PRECENTRAL FISSURE
2 PRECULMINATE FISSURE
3 SUPERIOR ANTERIOR FISSURE — FISSURA PRIMA
4 SUPERIOR POSTERIOR FISSURE
5 HORIZONTAL FISSURE — SULCUS INTERCRURALIS
6 PREPYRAMIDAL FISSURE — FISSURA PRAEPYRAMIDALIS
7 POSTPYRAMIDAL FISSURE — FISSURA SECUNDA
8 UVULONODULAR FISSURE — POSTEROLATERAL FISSURE

FIG 19 ROSTRAL VIEW

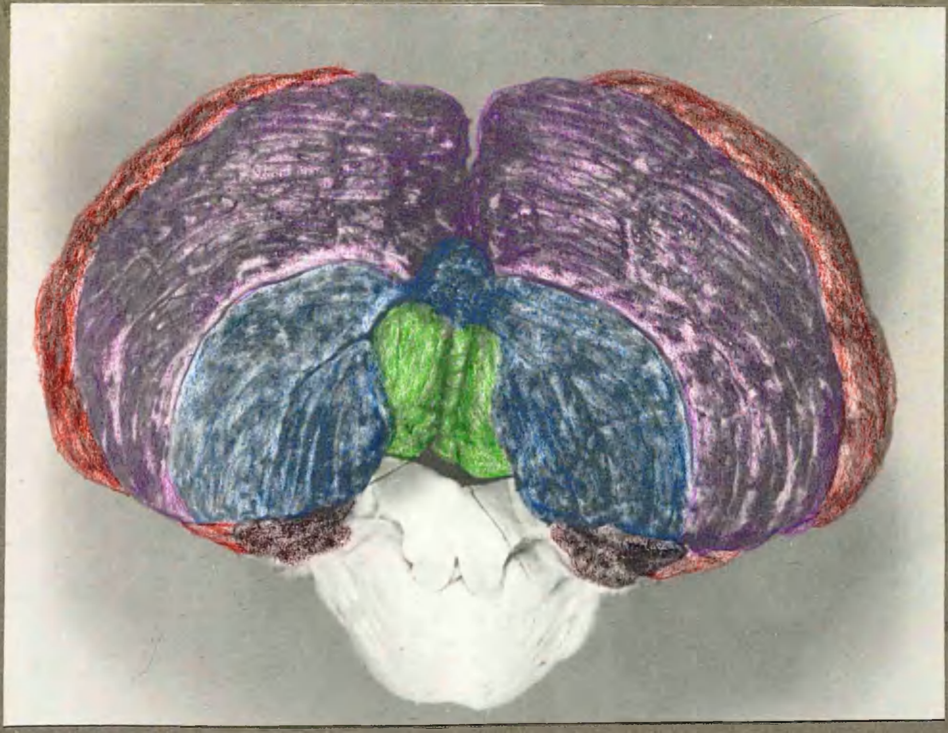


FIG 20 CAUDAL VIEW

FIG 21 POSTERIOR } VIEW
DORSAL

FIG 22 ANTERIOR } VIEW
VENTRAL

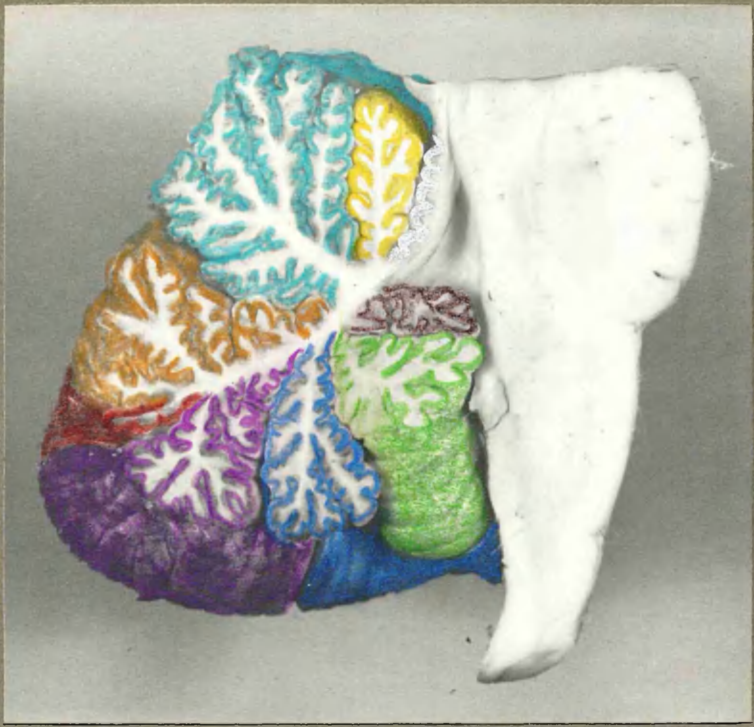


FIG 23A MID-SAGITTAL VIEW

FIG23BMID-SAGITTAL VIEW

FIG 24 HALF CEREBELLUM TO SHOW CUT PEDUNCLES

SAGITTAL SERIES

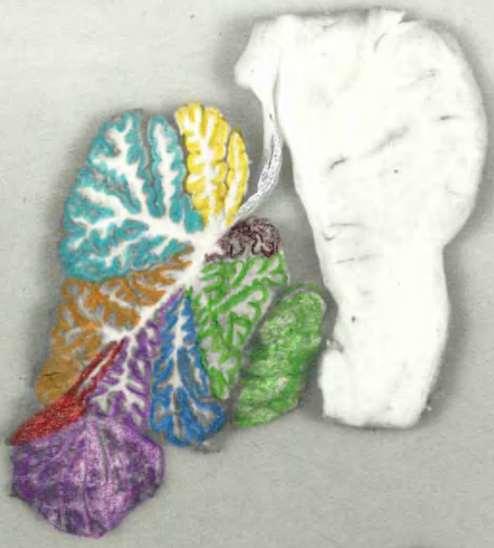


FIG 25

FIG 26

FIG 27

SAGITTAL SERIES

FIG 28

FIG 29

FIG 30

SAGITTAL
SERIES

FIG 31

FIG 32

FIG 33

FIG 34

HORIZONTAL SERIES

FIG 35

FIG 36

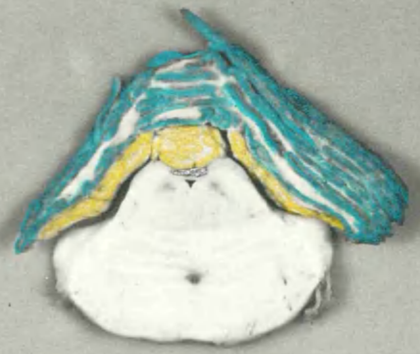


FIG 37

FIG 38

HORIZONTAL SERIES

FIG 39

FIG 40

HORIZONTAL SERIES

FIG 41

FIG 42

CORONAL SERIES

FIG 43

FIG 44

FIG 45

FIG 46

CORONAL
SERIES

FIG 47

FIG 48

FIG 49

CORONAL SERIES

FIG 50

FIG 51

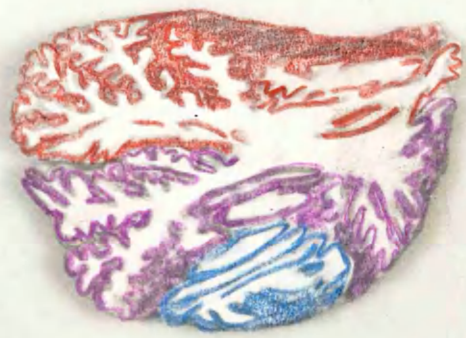
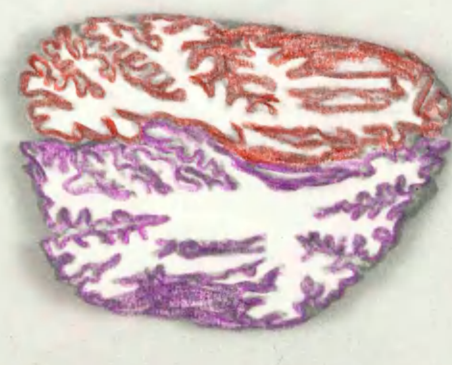


FIG 52



OBLIQUE SERIES

FIG 53

FIG 54

FIG 55

FIG 56

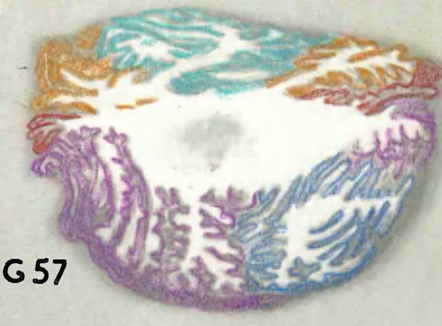


FIG 57

FIG 58

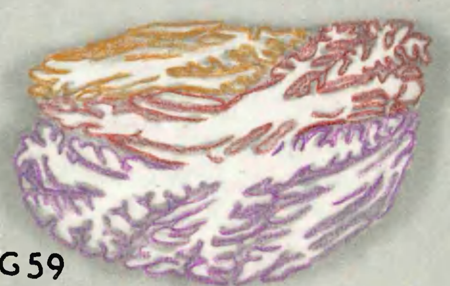


FIG 59

are now in the National Hospital, Queen Square. For the sake of this thesis, black and white photographs were also made of the external surface and the sections of the cerebella. These prints were tinted in the same colours as were used on the originals. They are presented in Plates 11-24. On Plates 9 and 10 diagrams are presented to show how the various divisions of the cerebellum have been coloured. These plates also show the commoner alternative nomenclatures used by various writers in studying their cerebellum.

Plates 11 and 12 show the external appearances of the cerebellum.

Plate 13 shows views of half cerebella, from the medial aspect. Attention is drawn to the variation which occurs in the structure of the lingula.

Plate 14 shows the appearance of half a cerebellum, removed from the brain stem by dividing the cerebellar peduncles, the middle cerebellar peduncle being cut at right angles to its long axis.

Plates 15-17 show the sagittal series of sections.

Plates 18-20 show the horizontal series of sections.

Plates 21-23 show the coronal series of sections.

Plate 24 shows the oblique series of sections.

CHAPTER VIII

THE ASCENDING DEGENERATION IN THE SPINAL CORD.

I. The Cordotomy Lesions. (Plates 25-35).

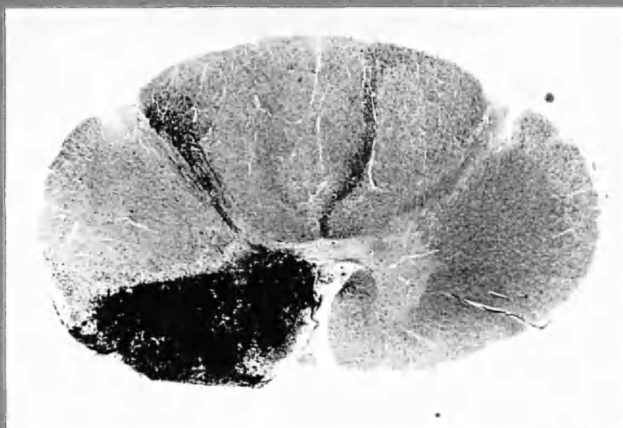
Photographs of transverse sections of the cords taken from that region cut through by the knife at operation, and thus showing the maximum area of destruction, are given on Plates 25-35. In all the cases the extent of the operation was verified by the use of a number of staining methods. The sections in Fig.92, case 4, were stained by haematoxylin and van Gieson's method, and in Fig.86, case 29; Fig.88, case 31; and Fig.89, case 32 by the Weigert Pal technique. In all the other cases Marchi preparations have been photographed, as they give a clear indication of the lesion at the low magnification used here, (x7), and the lesions in the different cases can be easily compared.

The level at which the operation was performed is shown in Table I and also on the photographs. In 7 cases the operation was in the cervical segments, in 26 cases in the thoracic, and in 1 case in the first lumbar segment. In 10 cases the

RIGHT

FIG 60

LEFT



(CASE 1) C1

FIG 61

(CASE 3) C3

RIGHT LEFT

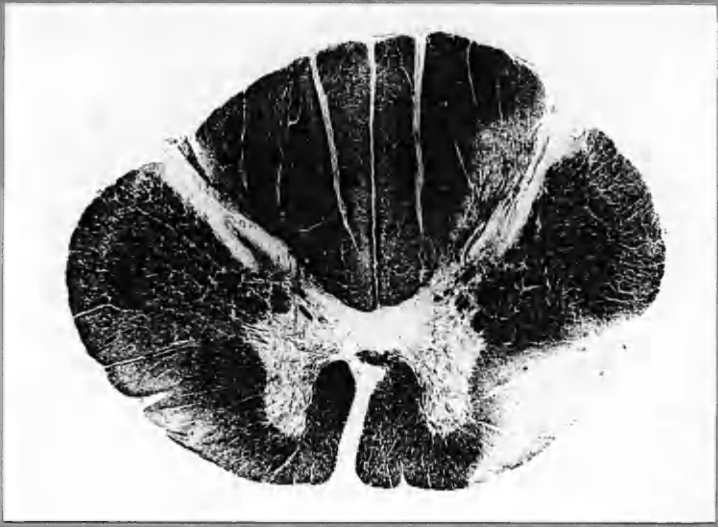


FIG 62 (CASE 2) C2

FIG 63 (CASE 5) C3

FIG 64 (CASE 6) C3

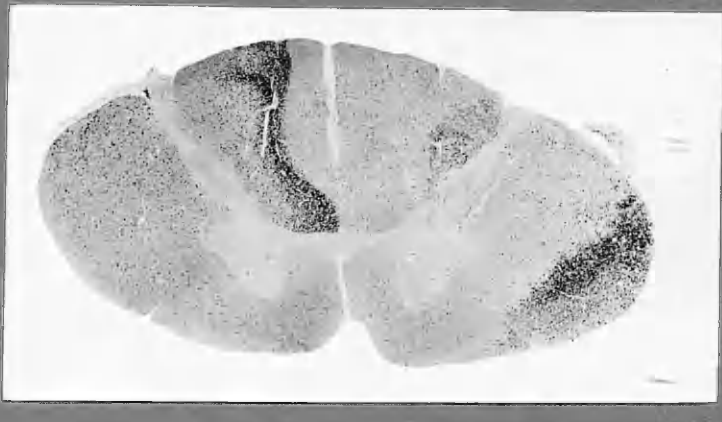


FIG 65 (CASE 7) C3

RIGHT LEFT

FIG 66
(CASE 8)

T3

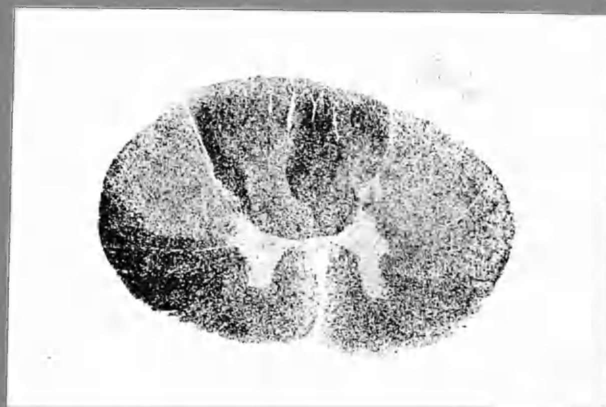


FIG 67
(CASE 9)

T5

FIG 68
(CASE 10)

T5

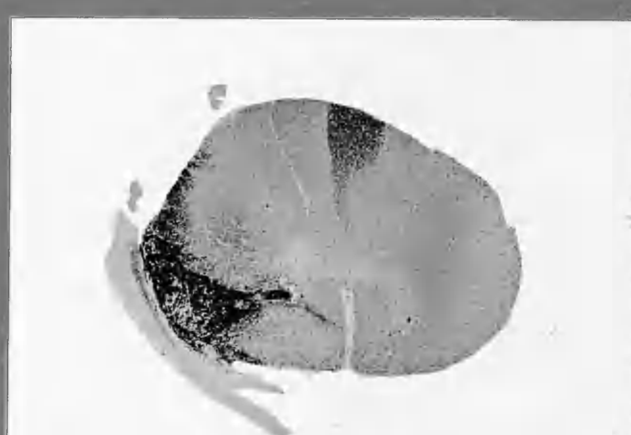
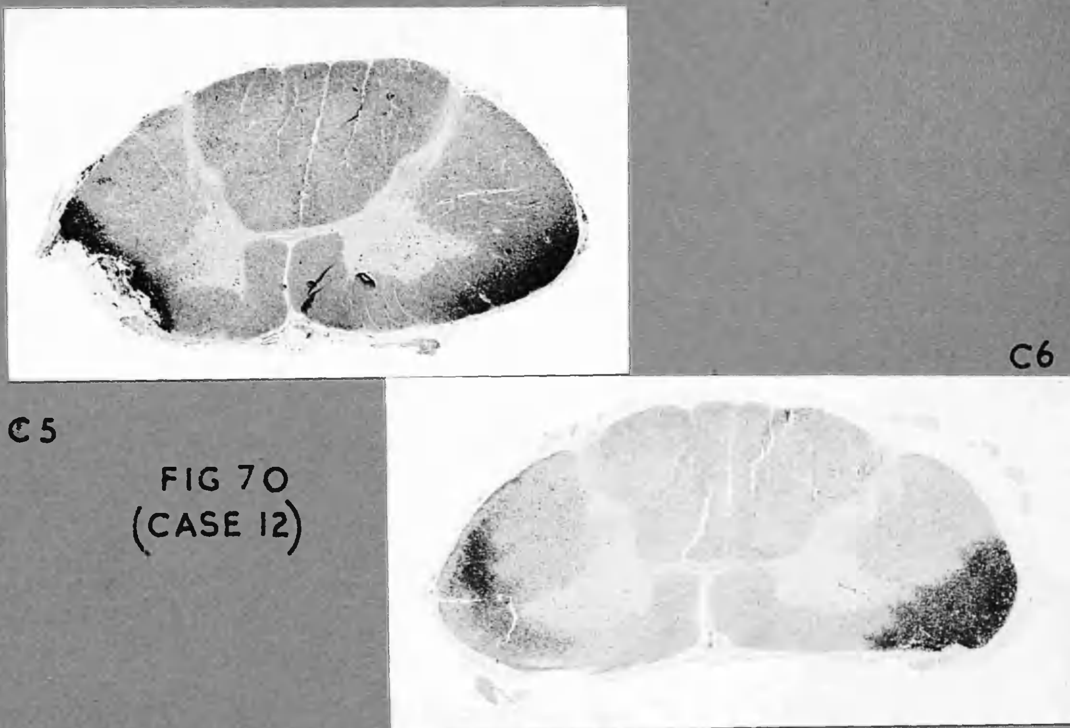


FIG 69
(CASE 11)

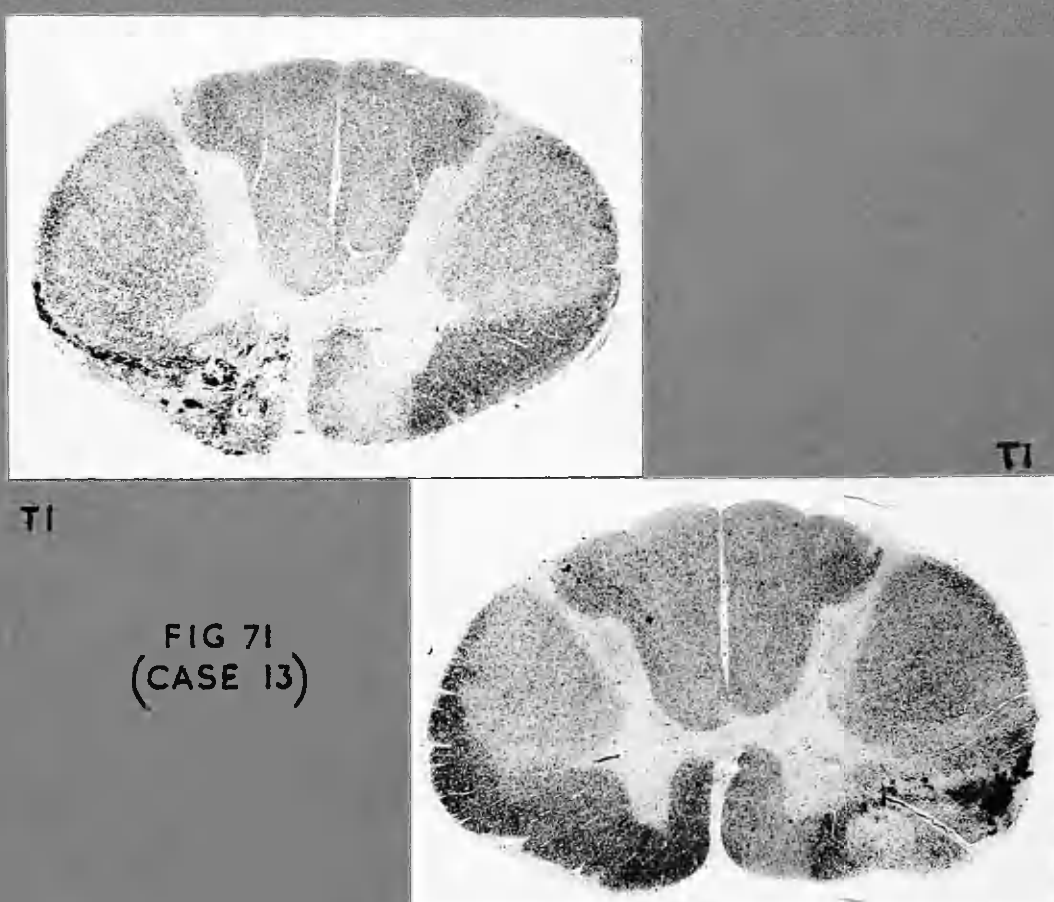
T8

RIGHT LEFT



C5 C6

FIG 70
(CASE 12)

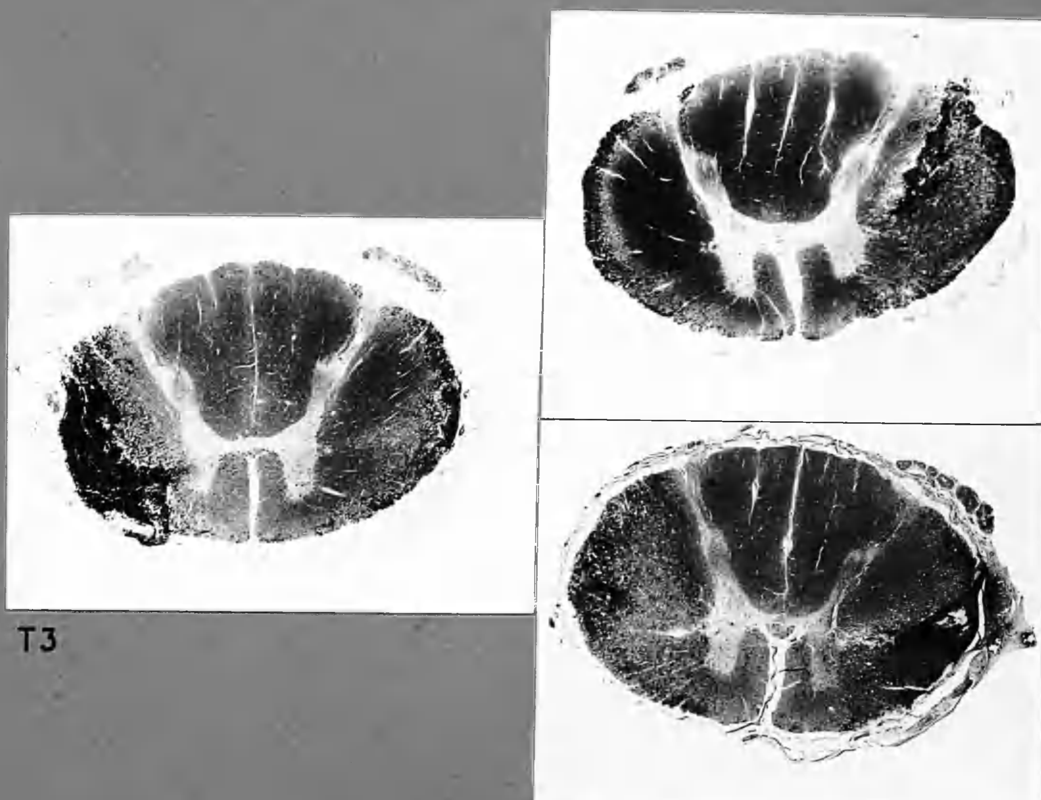


T1 T1

FIG 71
(CASE 13)

RIGHT LEFT

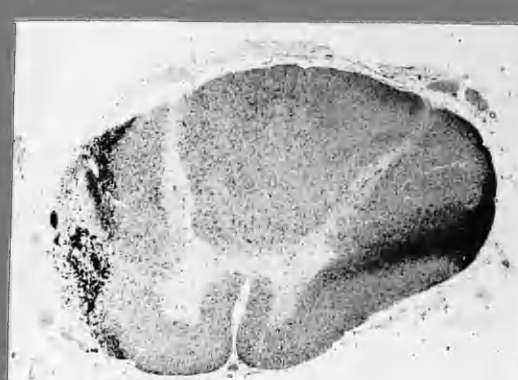
T7 FIG 72 (CASE 14) T2



T3

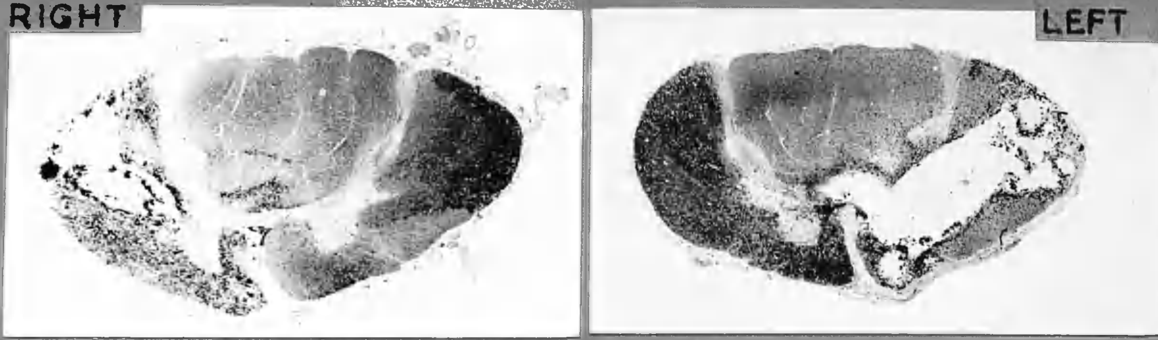
T3

FIG 73 (CASE 15)



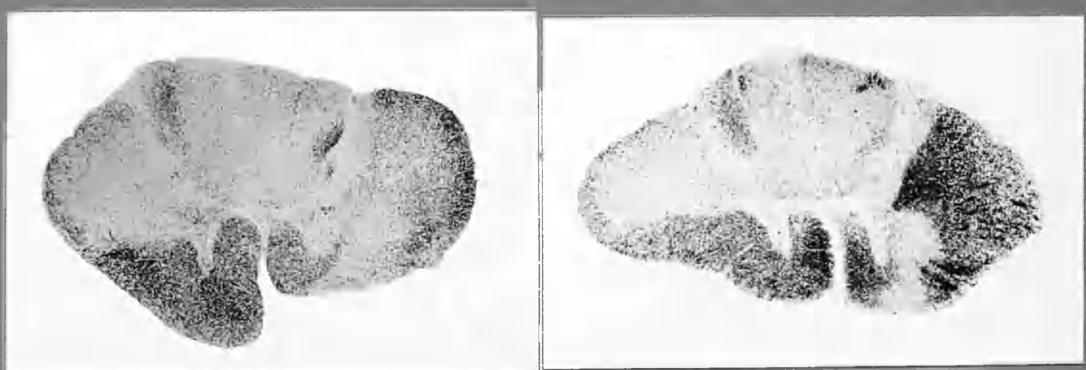
T3 (CASE 16) FIG 74

RIGHT LEFT



T3 FIG 75 (CASE 17) T4

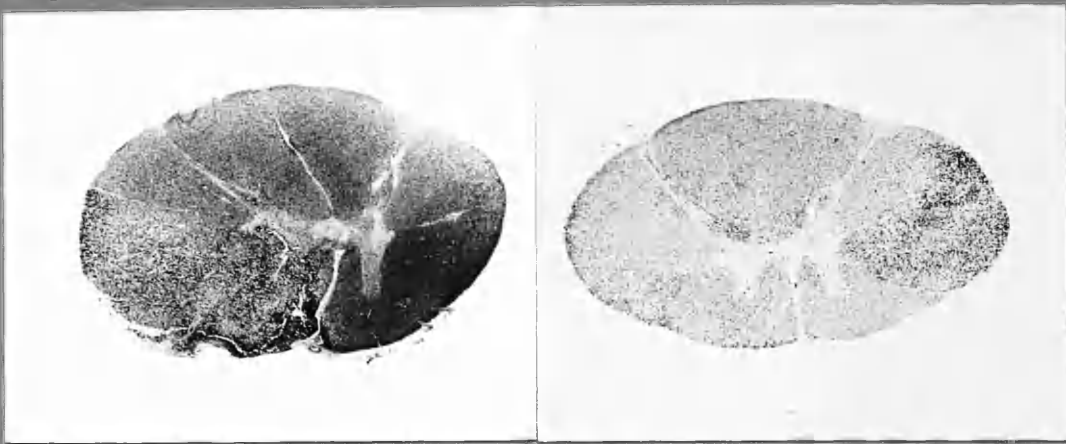
T4 FIG 76 (CASE 18)



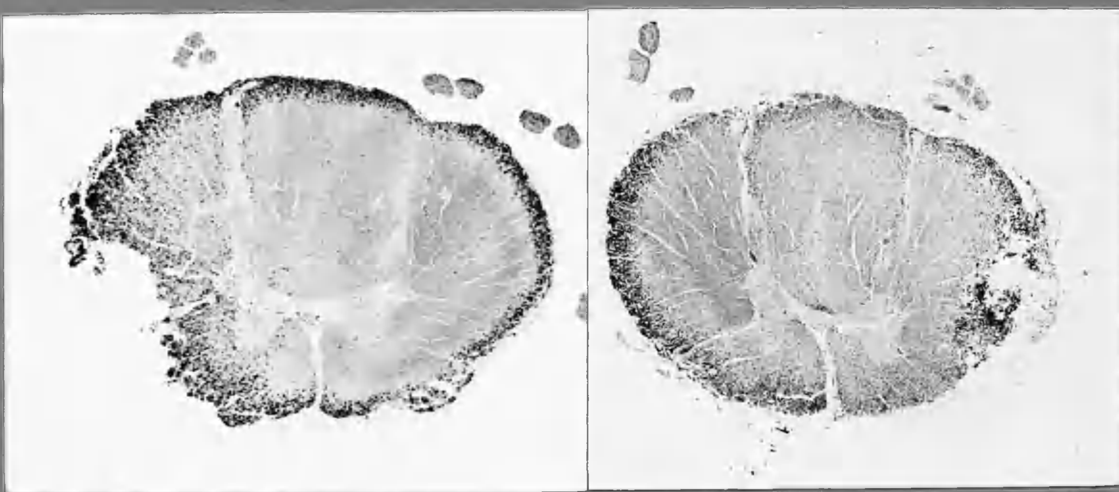
T4 FIG 77 (CASE 20) T5

T6 FIG 78 (CASE 21) T4

RIGHT LEFT



T5 FIG79 (CASE 22) T5

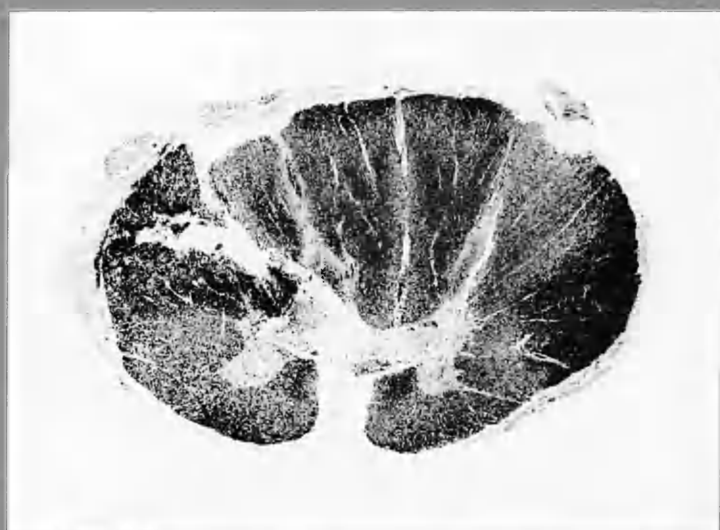


T5 FIG80 (CASE23) T5

T5 (CASE 24) FIG 81 (CASE25) FIG82 T5

RIGHT LEFT

T5 FIG 83 (CASE 26) T5



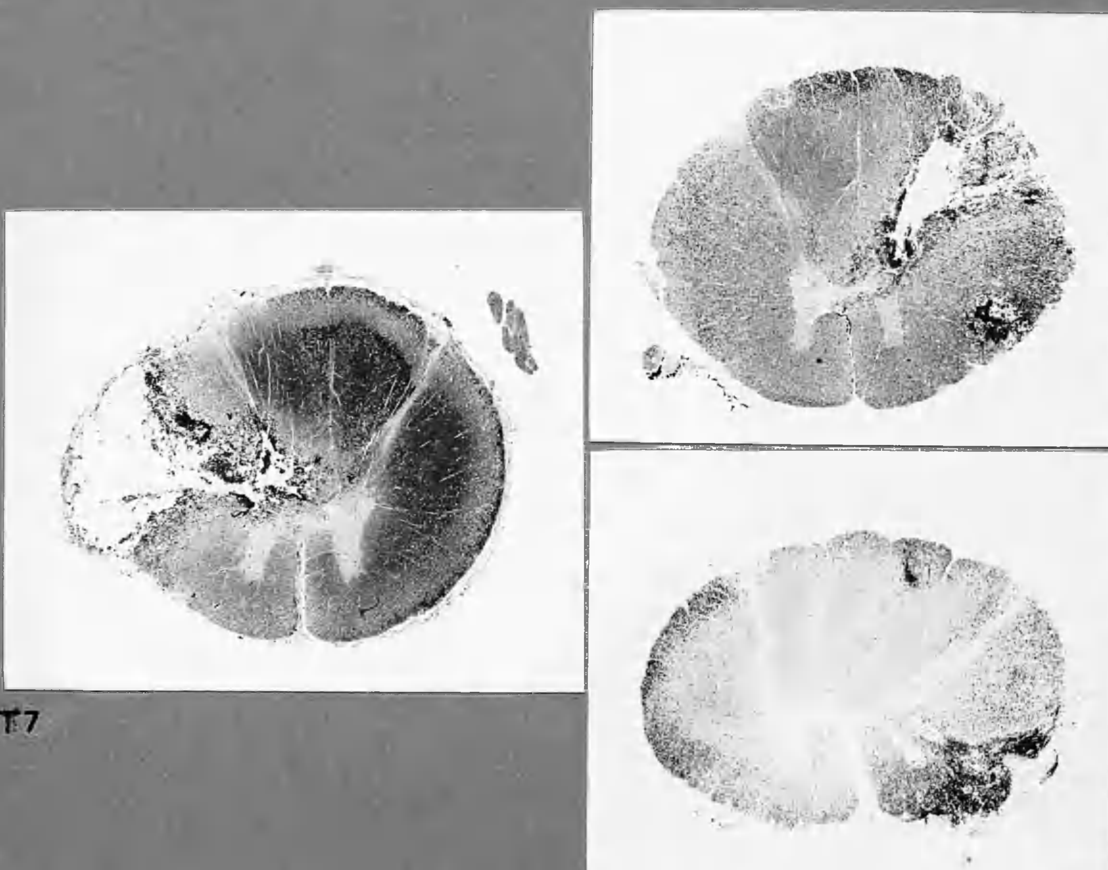
T5 FIG 84 (CASE 27)

T6 FIG 85 (CASE 28) T9

RIGHT LEFT

T6 T6

FIG 86 (CASE 29)



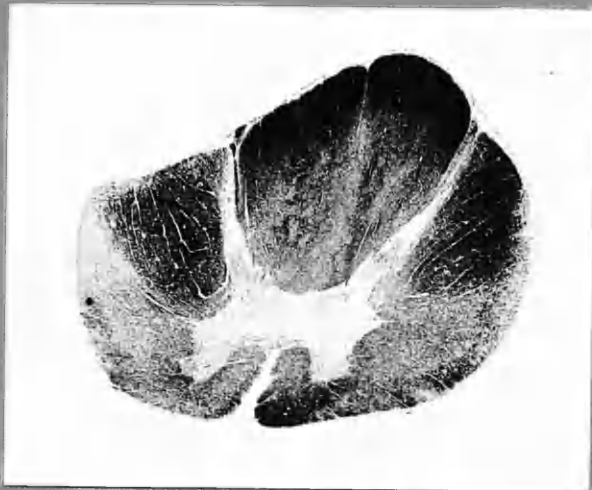
T7

T7

FIG 87 (CASE 30)

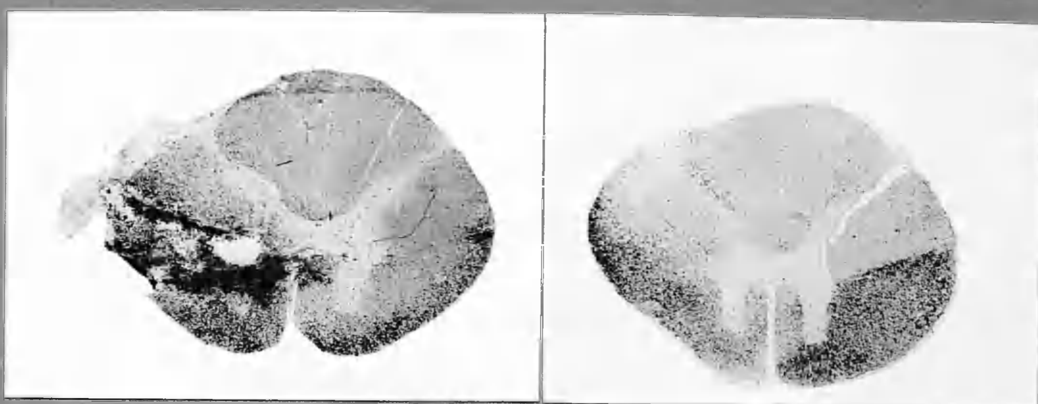
RIGHT

LEFT



T7 (CASE 31) FIG 88

(CASE 32) FIG 89 T8



T9 (CASE 33) FIG 90 T9

L1 (CASE 34) FIG 91

C3

FIG 92
(CASE 4)

C3

operation was unilateral, and in 24 cases it was bilateral. The periods of survival are shown in Table I.

It will be seen from the photographs that there is a very wide range of variations in the extent of the lesion, not only in different cases, but between the two sides of the same case in some instances.

In this work, the ventral and lateral funiculi of the cord will be considered as being arbitrarily divided into 3 columns, by two imaginary lines, one passing transversely across the cord through the central canal, and one along the line of the most medial of the ventral roots. The three columns are then dorso-lateral, ventro-lateral and ventral.

The operation may involve all three columns to some extent (e.g. Fig.75, case 17 (left), Fig.85, case 28 (right and left)); the dorso-lateral and ventro-lateral columns (e.g. Fig.87, case 30 (left), Fig.79, case 22 (left)); the ventro-lateral and ventral columns (e.g. Fig.82, case 25 (left), Fig.72, case 14 (left)); the dorso-lateral column only (e.g. Fig.83, case 26 (left)); the ventro-lateral column only (e.g. Fig.76, case 18 (right), Fig.64, case 6). In no case was the operation confined to the ventral column only; in Fig.60 case 1, and in Fig.91 case 34 (left) the main extent of the operation lay in the ventral column.

In all these cases the lesion extended medially through the greater part of the white matter up to, or close to, the grey matter. In a few cases the operation was much more superficial, involving only the more lateral part of the white matter (e.g. Fig.74, case 16 (right), Fig.80, case 23 (left)).

II. The Ascending Degeneration. (Plates 37-46).

The course of the ascending degenerating fibres in the lateral and ventral columns will be considered in this section. The general pattern of degeneration resulting from an extensive lesion of both the dorso-lateral and the ventro-lateral columns will first be shown. Then the general pattern of degeneration resulting from a lesion of the dorso-lateral column only will be compared with that resulting from a lesion of the ventro-lateral column only. The course of the fibres in the dorso-lateral column will then be considered in more detail, in those cases with varying lesions of this column. The course of the ventro-lateral fibres will be similarly considered.

It will be realised that partial lesions of a single tract are necessary in order to show the changing position of the fibres within this tract; complete lesions of the tract can show only the total position of this tract in relation to surrounding fibres. The greatest number of demonstrable degenerating fibres is found in the cases with a period of survival of under a hundred days. But cases with a longer survival are also useful. In such cases deductions concerning the significance of the absence of other fibres are made only when comparison between the two sides of the same case, or comparison with cases of similar periods of survival, is possible. Minor differences in the distribution of the degenerating fibres will not be interpreted as significant, unless they were consistently found in other cases.

a) Extensive lesion of both the dorso-lateral and the ventro-lateral columns.

A good example of the general pattern of the degenerating ascending fibres is case 20 (Plate 37, Fig.93). Here the surgical lesion was bilateral and was made in the mid-thoracic region (Fig.93A). On the left side the lesion involves nearly the whole of

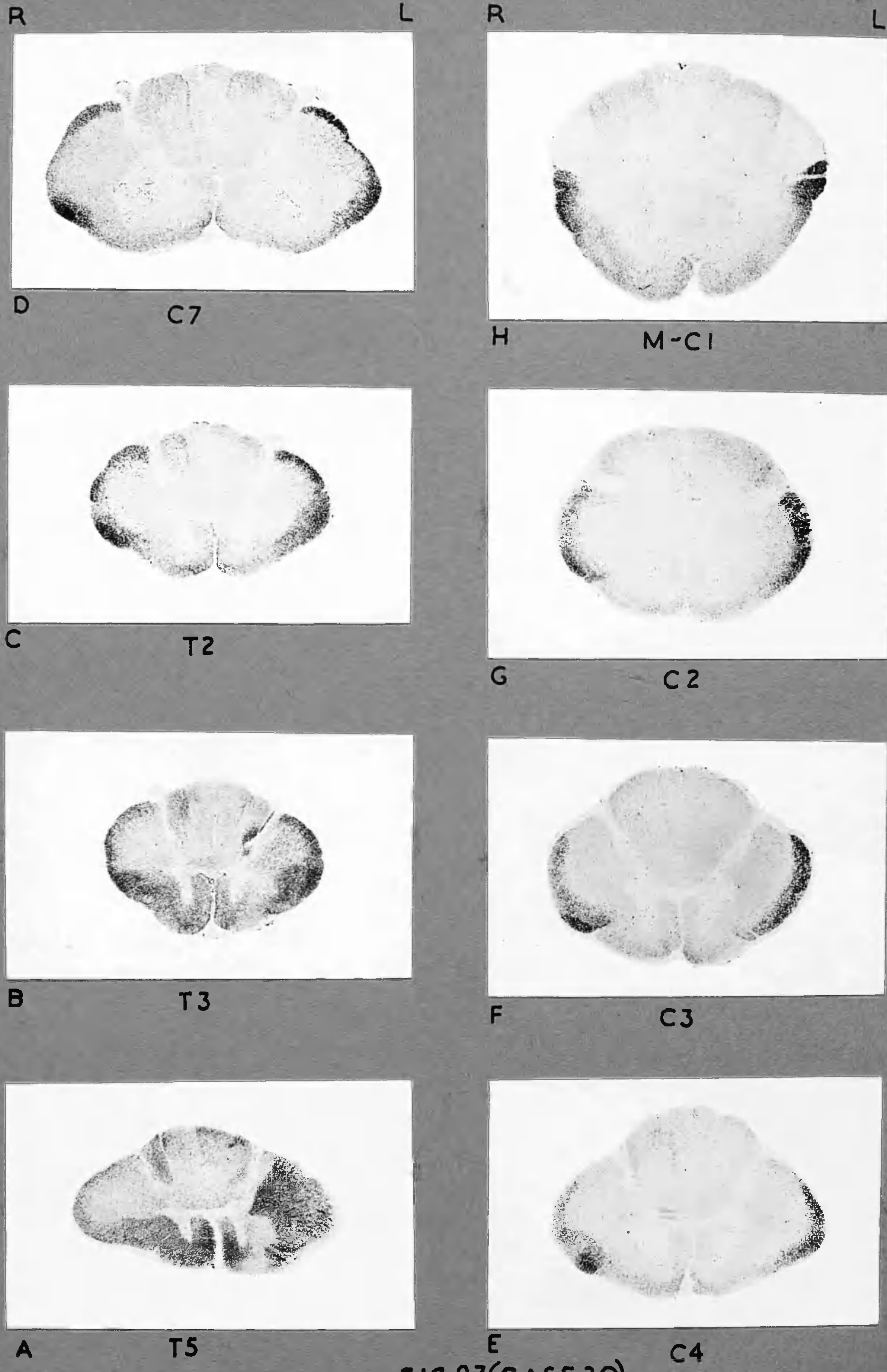


FIG 93(CASE 20)

the dorso-lateral column, the lateral part of the ventro-lateral column and the medial part of the ventral column. This side will be mainly used in showing the form of the ascending degeneration. The right side will be used as furnishing additional evidence on the degeneration after extensive lesions of the ventral quadrant; on this side the lesion involves the whole of the ventro-lateral and the ventral columns.

In the segments cranial to the lesion, up to the second thoracic segment (Figs.93B and C) there is a peripheral band of degeneration from the dorsal horn to about the level of the central canal, on the left side; there is some scattered degeneration medial to this concentrated mass of degenerating fibres, which gradually diminishes. This dorso-lateral degeneration is continuous with a much more diffuse ventro-lateral mass of degenerating fibres, which extends on the right side medially up to the grey matter and on the left, in the third thoracic segment (Fig.93B) as far medially as the extent of the operation lesion in the fifth thoracic segment (Fig.93A). The diffuse degeneration would appear to be due to two causes: first, the presence of numerous spino-spinal fibres in this part of the cord; secondly, the degeneration of fibres of the ascending systems, in that part of their course which lies between the grey matter and the periphery of the cord. The degeneration of the intrinsic fibres tends to obscure any immediate rearrangement of the long ascending fibres.

The degeneration in the ventro-lateral column gradually becomes concentrated on the periphery of the column, and except for a few scattered fibres is limited to the outer half of the white matter (Fig.93C T_2). In the seventh cervical segment (Fig.93D) degenerating fibres form a continuous band along the periphery of the cord, from the dorsal horn to about the level of the ventral limit of the ventral horn. In the dorso-lateral zone the degeneration is roughly divisible into two halves, by the sulcus ventrolateralis spinalis. In the dorsal half the degeneration forms a broader band than in the ventral half. The degeneration in the ventro-lateral column extends further medially than in the dorso-lateral column, with which it is continuous. Degeneration in the ventro-lateral column is more distinctly seen as a definite group of fibres on the right side. Here degenerating fibres in the ventro-lateral column are isolated to the lateral half of the white matter, from about the level of the dorso-lateral extremity, to the level of the ventro-lateral extremity of the ventral horn. The distribution of the degenerating fibres is the same in the sixth and fifth cervical segments as in the seventh cervical segment (and the eighth). In the fourth cervical segment (Fig.93E) there is a marked difference in the arrangement of the fibres. The periphery of the most dorsal part of the dorso-lateral column is at this level free from any degenerating fibres. There is a crescent-shaped band of degeneration extending from a point on the periphery, about mid-way between the dorsal horn and the level of the central canal, to about the level of the ventral extremity of the ventral horn. This band of degeneration is less spread out at the seventh cervical segment; it has a lesser dorso-ventral extent, and it is more extensive latero-medially. It therefore appears as if the degenerating fibres in the dorsal half of the dorso-lateral column in the seventh cervical segment had moved ventrally in the fourth cervical segment. The appearance in the third cervical segment (Fig.93F) is similar to that in the fourth; the dorsal zone being completely free from degeneration. In the second cervical segment (Fig.93G) the whole mass of fibres appears to move dorsally, so that the most dorsal fibres are contiguous with the dorsal horn. Between the fourth and the second cervical segment there is actually little change in the site of the band of degenerating fibres. The differences which are apparent on the Figs.93F and G are mainly due to the change in position and extent of the dorsal horn, and in particular of the root entry zone, for at the second cervical segment (Fig.93G) this becomes larger and wider in its dorso-ventral dimension, and it also shifts ventro-laterally. Within the band of degenerating fibres, fibres have shifted from the ventral part to the dorsal part, between the fourth and the second cervical segments. This makes the band of fibres broader and more concentrated in its dorsal half. In the first cervical segment (Fig.93H) there is a further migration and concentration of fibres dorsally and medially, so that the outline of the mass of degenerating fibres becomes roughly triangular rather than ribbon-shaped.

The general picture of the ascending fibres which we glean from this case is of two definite groups of fibres, running contiguously, and located between the dorsal horn and a point on the periphery at about the level of the tip of the ventral horn. The ventral group is somewhat broader than the dorsal group.

From our material some evidence can be obtained on the most caudal extent of these ascending fibres of the lateral column. In our series the most caudally placed lesion was at the first lumbar segment - case 34 (Plate 42, Fig.99). At this level these ascending fibres are already present in the lateral column; and some of these fibres end in the cerebellum. Thus already at the first lumbar segment, spino-cerebellar fibres are present in the lateral column of the cord.

With regard to the size of the fibres of the dorso-lateral, ventro-lateral and ventro-medial columns, it was found that there is a mixture of fibres, of small, medium and large calibre. There are more fibres of large calibre in the dorso-lateral column than in the ventro-lateral column. In the ventro-lateral column fibres of large calibre, equal

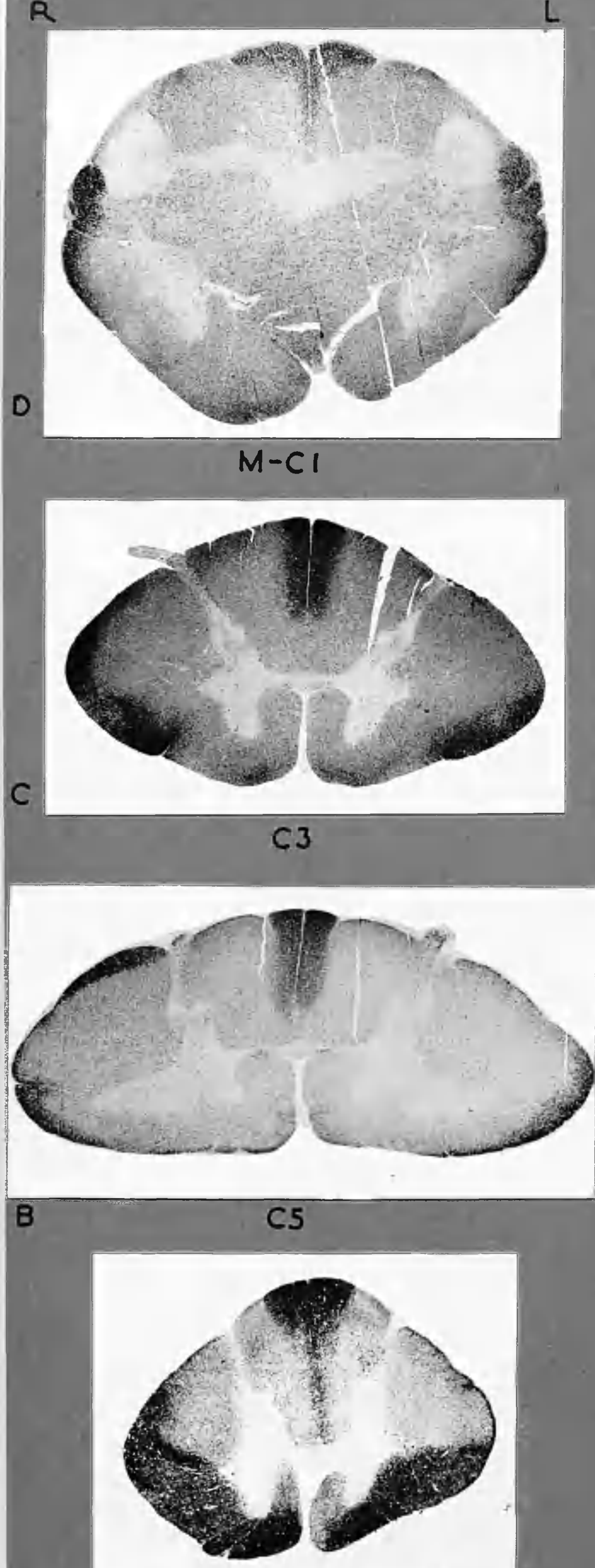


FIG 95 (CASE 25)

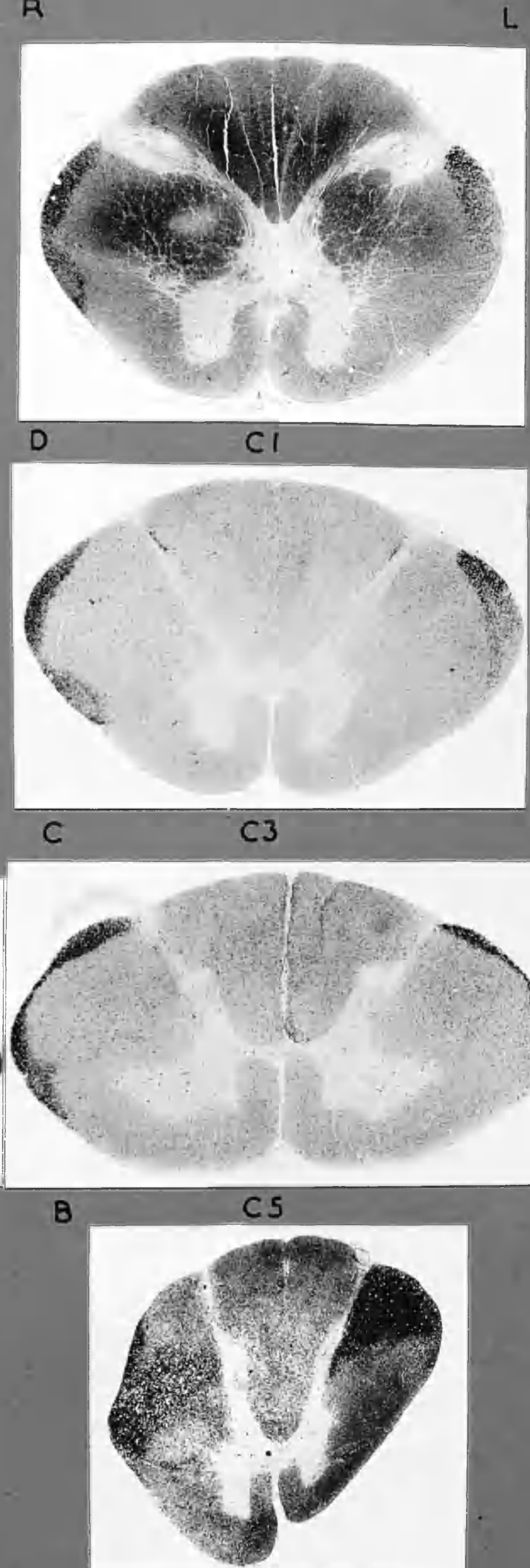


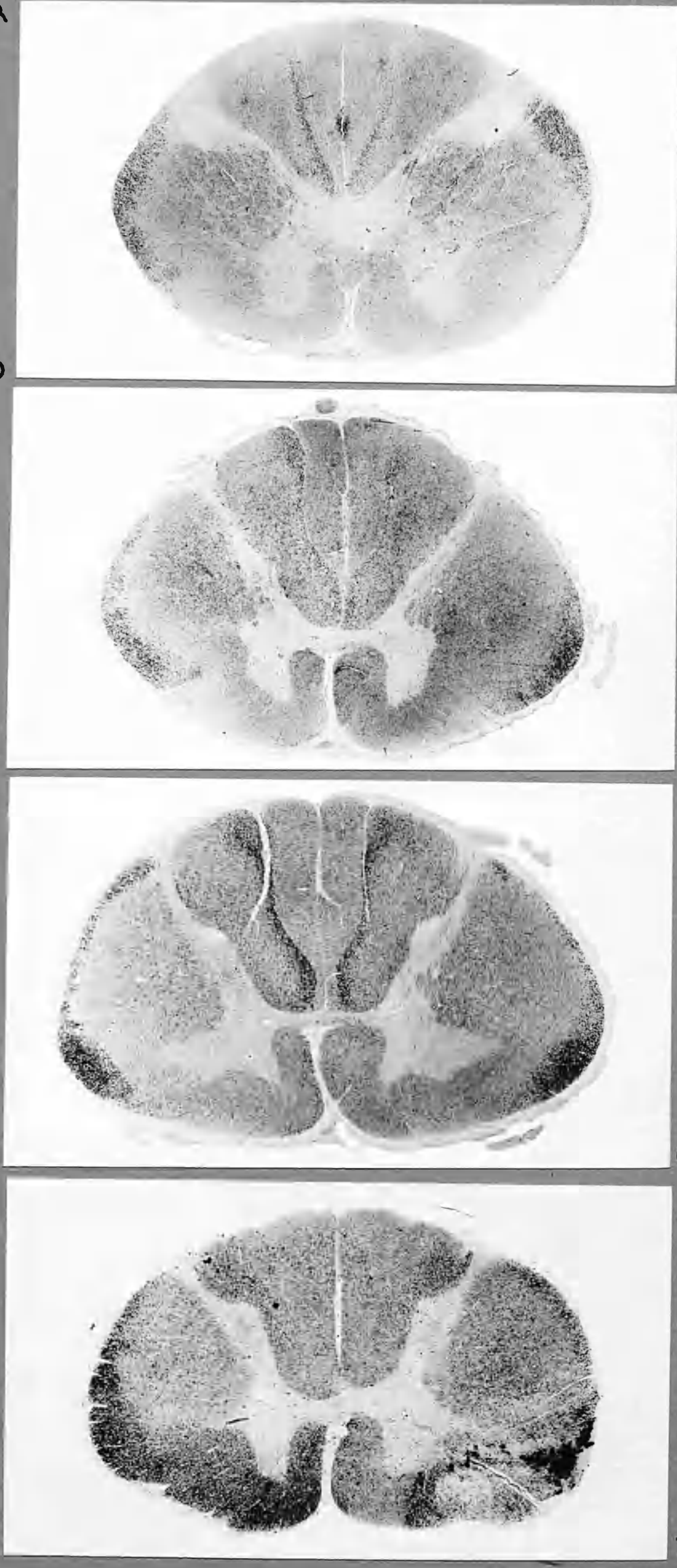
FIG 94 (CASE 26)

to those of the dorso-lateral column, are more numerous in the peripheral zone than more medially. Fibres of the ventro-medial group appear to be of finer calibre than in the other two groups.

b) Comparison of the pattern of degeneration between lesions affecting the dorso-lateral and lesions affecting the ventro-lateral columns.

In the two cases 25 and 26, on Plate 38, the cordotomies, which were bilateral, were carried out in the mid-thoracic region; the post-operative survival periods were 141 days and 154 days respectively; thus the two cases are comparable. If the left sides of these two cases are compared, it will be seen that the operation areas are totally different, and have no common zone (Figs.94A and 95A). At the fifth cervical segment, in case 26, the degenerating fibres are confined to the dorso-lateral column, and in case 25 they are confined to the ventro-lateral column, as were the respective lesions. These groups of fibres remain in their respective positions in the two cases (Figs.94C and 95C) until the first cervical segment (Figs.94D and 95D) is reached. At that level, the pattern of

FIG 96
(CASE 13)



degenerating fibres on the transverse section has become unexpectedly similar in the two cases. In both cases the area of degenerating fibres lies adjacent to the dorsal horn.

Thus we find that the fibres which lie in the ventro-lateral column between the fifth thoracic and the third cervical segments change their course over the upper two cervical segments, and come to occupy the area ventral to the dorsal horn in the first cervical segment - the same area which is occupied by ascending fibres of the dorso-lateral column.

This change in position of the ascending ventro-lateral fibres is a new fact that has been elucidated from this material containing lesions of different topography. This shift of the ventro-lateral fibres occurs in all cases, at whatever segment the lesion is made. The evidence for these statements will now be presented in a further four cases.

In case 13 (Plate 39), on the left side the operation, performed at the first thoracic segment, extends from the ventral surface, from slightly lateral to the medial border of the ventral horn to

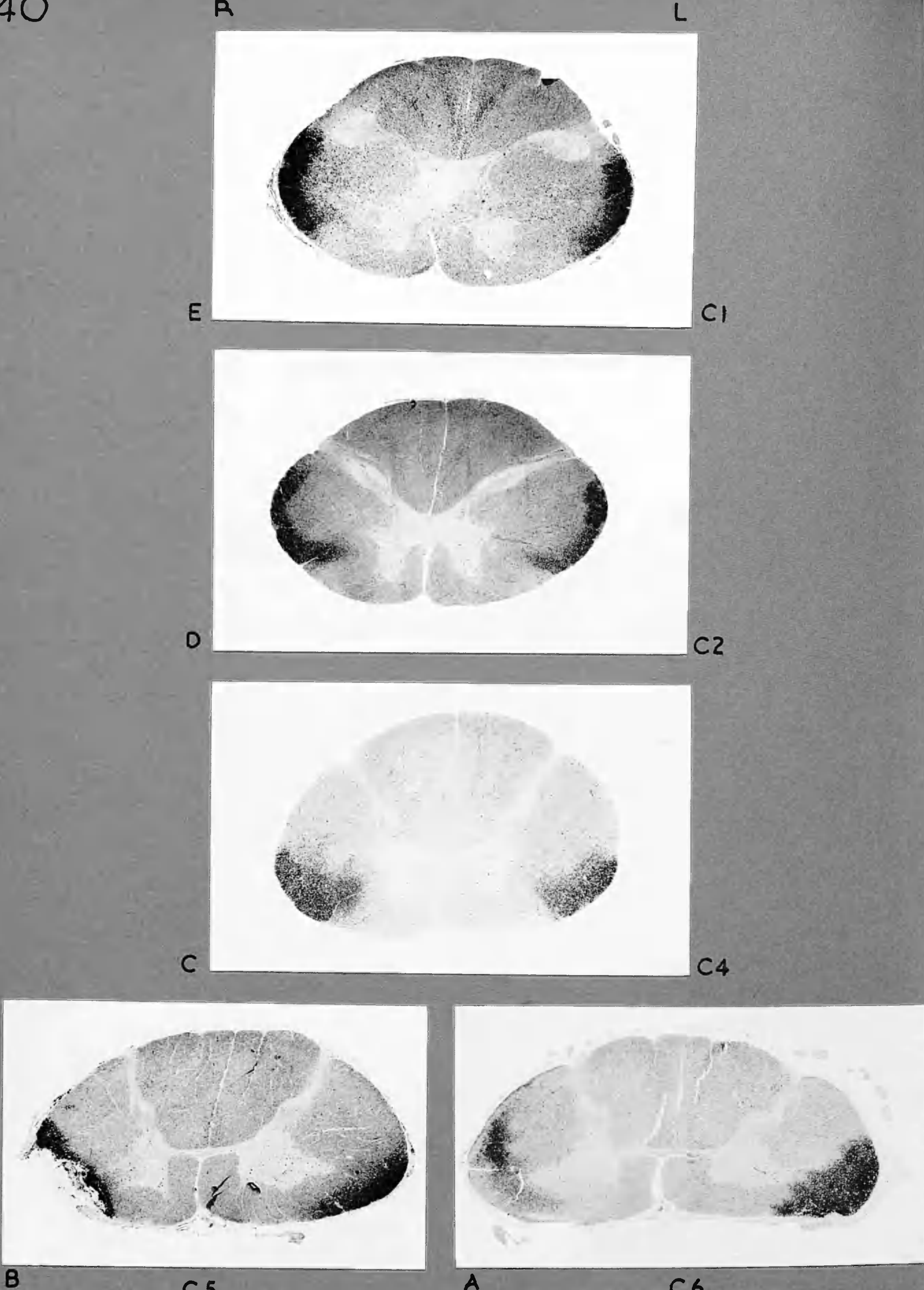
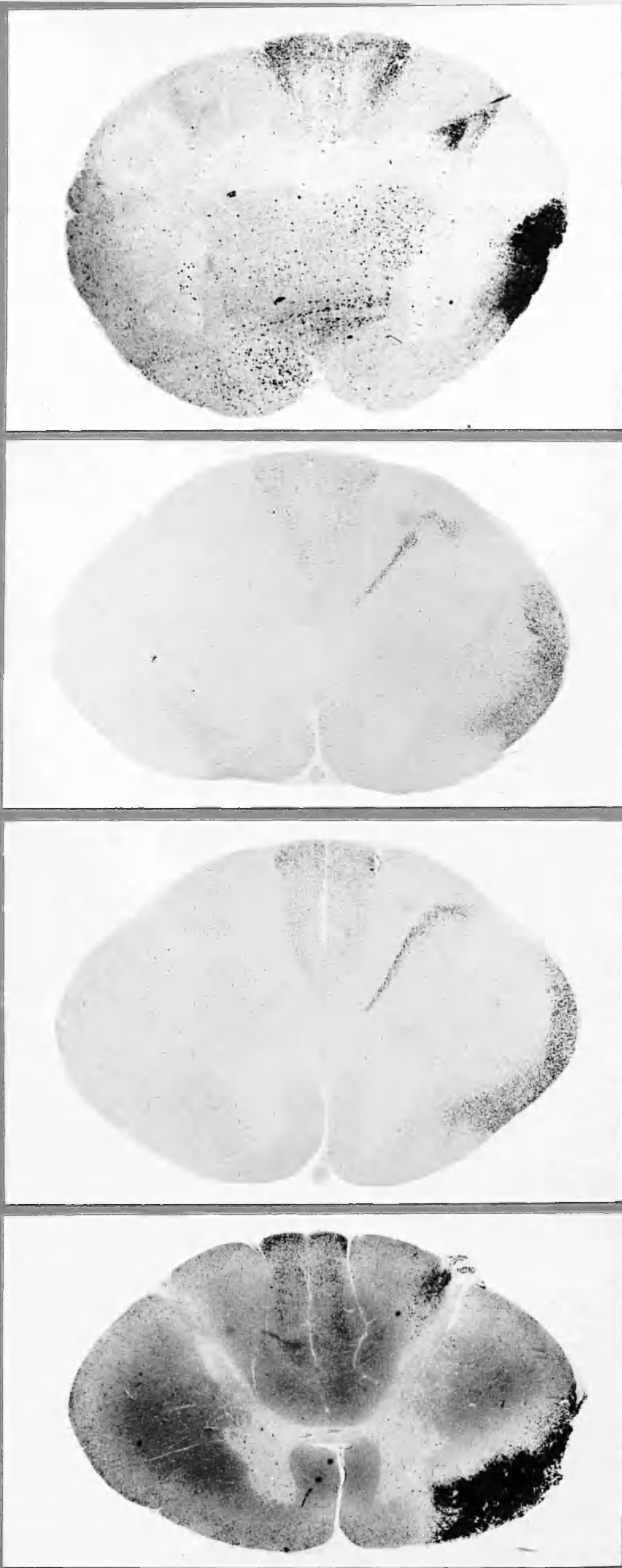


FIG 97 (CASE 12)

the level of the lateral horn; it leaves the entire dorso-lateral column free from degeneration (Fig.96A). The degenerating fibres at the fifth and the third cervical segments (Figs.96B and 96C) are almost completely confined to the ventro-lateral quadrant. At the first cervical segment however, the degenerating fibres have migrated dorsally into the dorso-lateral zone (Fig.96D). In case 12 (Plate 40), the operation was performed at the fifth and sixth cervical segments. On both sides the operation lesion involves the ventro-lateral part of the ventral quadrant, and extends only very slightly dorsal to the level of the central canal (Figs.97A and B). In the fourth cervical segment (Fig.97C) there is complete absence of any dorso-lateral degeneration. In the second cervical segment (Fig.97D), there is a very marked spreading out dorsally of some of the degenerating fibres so that many lie nearer the dorsal horn, and reach the dorso-lateral area in contact with by the first cervical segment (Fig.97E). At this level the degeneration is distributed throughout the whole dorso-lateral and the dorsal half of the ventro-lateral peripheral zone.

FIG 98
(CASE 6)



In case 6 (Plate 41) the operation was performed at the third cervical segment (Fig.98A) and involved the ventro-lateral column only. The dorsal shift of ventro-lateral fibres is particularly striking in this case (Figs.98B and 98C).

The next case, 34, (Plate 42) furnishes evidence that as low as the first lumbar segment of the cord there are fibres present in the ventro-lateral column which ascend in this column until the second cervical segment and then shift into the dorso-lateral column. In this case the operation, performed at the first lumbar segment, was limited on the left to the ventral quadrant of the cord, on the right the lesion involved the ventral part of the dorso-lateral column as well as all the ventro-lateral column. On both sides some fibres ascend in the ventro-lateral column until the third cervical segment, and then shift dorsally into the dorso-lateral column where some lie in juxtaposition with the dorsal horn (Figs.99C and D).

In all the cases described the pattern of degeneration in the upper three cervical segments is the same, regardless of the level of the lesion. The number of fibres varies but the distribution in

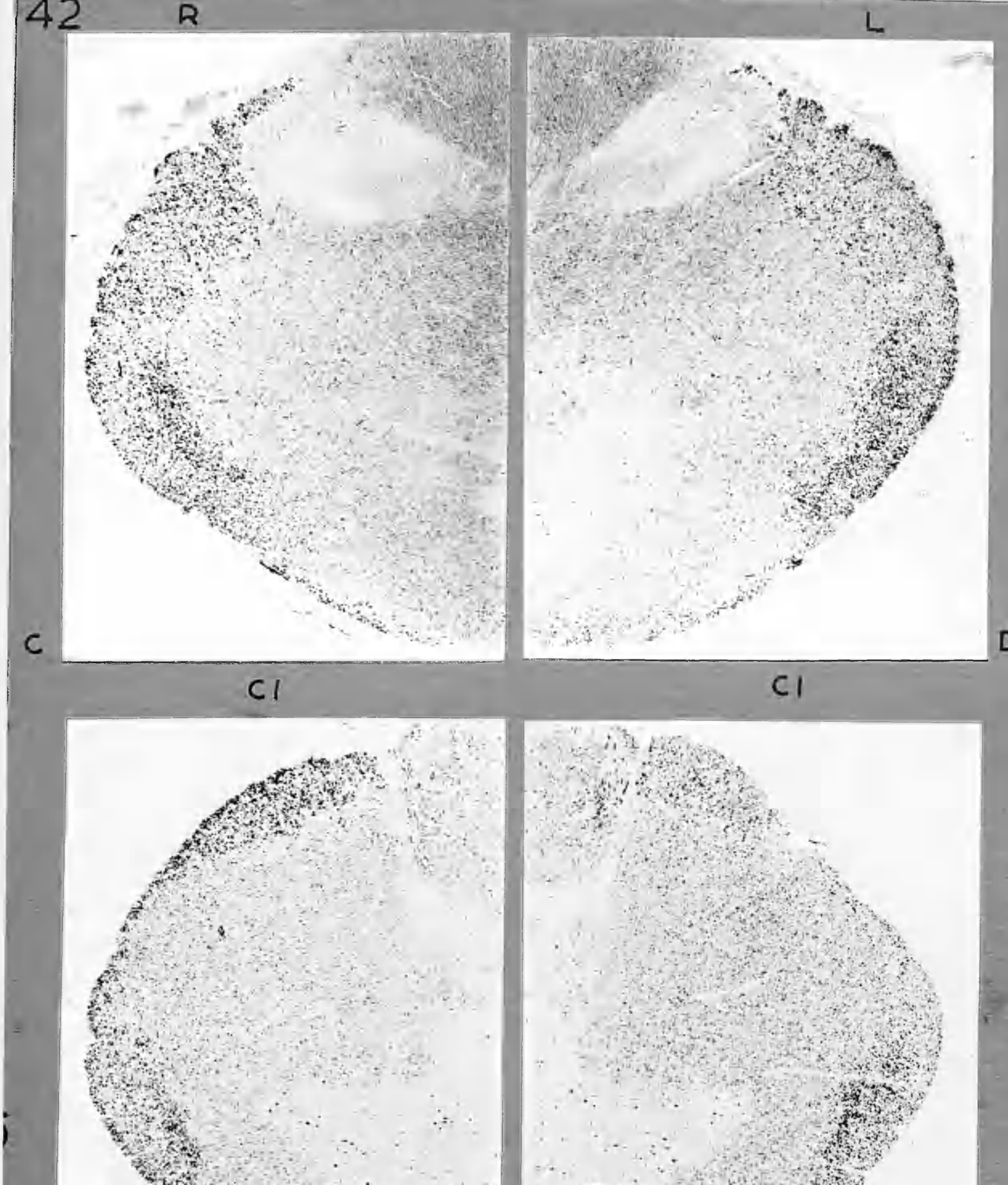


FIG 99
(CASE 34)

the first cervical segment is the same in all the cases.

The pattern of degeneration is quite different when a lesion is limited the ventro-lateral column, from when it is limited to the dorso-lateral column, caudal to the third cervical segment.

It has been shown that many fibres ascend in the ventro-lateral column of the cord, from at least as low as the first lumbar segment up to the third cervical segment, and that they then shift into the dorso-lateral column at the second and first cervical segments. Here they are intermingled with the fibres which lay in the dorso-lateral region throughout their ascent.

This dorsal shift cannot of course be made out when both the dorso-lateral and the ventro-lateral columns are cut, for in such a case the dorso-lateral column contains large numbers of degenerating fibres throughout the whole length of the cord, between the level of the incision and the upper part of the first cervical segment.

c. Arrangement of ascending fibres in the dorso-lateral column.

In all the cases in which the operation

involved the peripheral fibres in the ventral part of the dorso-lateral column, some fibres are seen to move gradually into the dorsal part of the column. This shift of fibres occurs in segments immediately cranial to the lesion; once the fibres reach the most dorsal zone they do not appear to alter their relationships until the fourth cervical segment. The dorsal shift of dorso-lateral fibres can be demonstrated clearly by comparing the two sides of the cord of case 26 (Plate 38, Fig.94). Both lesions were made at the fifth thoracic segment; that on the left involved the most dorsal part of the dorso-lateral column, whereas that on the right did not do so (Fig.94A). It will be seen that by the fifth cervical segment however (Fig.94B), the region immediately lateral to the dorsal horn contains degenerate fibres on both sides of the cord. But not all the fibres have moved dorsally, on the right side; for degenerating fibres are still seen at this level as far ventrally as they were immediately cranial to the operation lesion. Therefore, it will be understood that not all of the fibres of the lateral and ventro-lateral column move dorsally as they ascend the cord. This dorsal shift of fibres in the dorso-lateral column from the ventral to the dorsal half of the dorso-lateral tract can be seen in all the cases in which only the ventral part of the dorso-lateral column was involved in the lesion (see case 25, Plate 38, Fig. 95 right side; case 20, Plate 37, Fig. 93, right side). A comparison between cases 26 (Plate 38, Fig. 94B) in which the lesion was made at the fifth thoracic segment (both sides), and 34 (Plate 42, Fig. 99A) in which the lesion was made at the first lumbar segment, has shown that there is no lamination in the dorsal fibres.

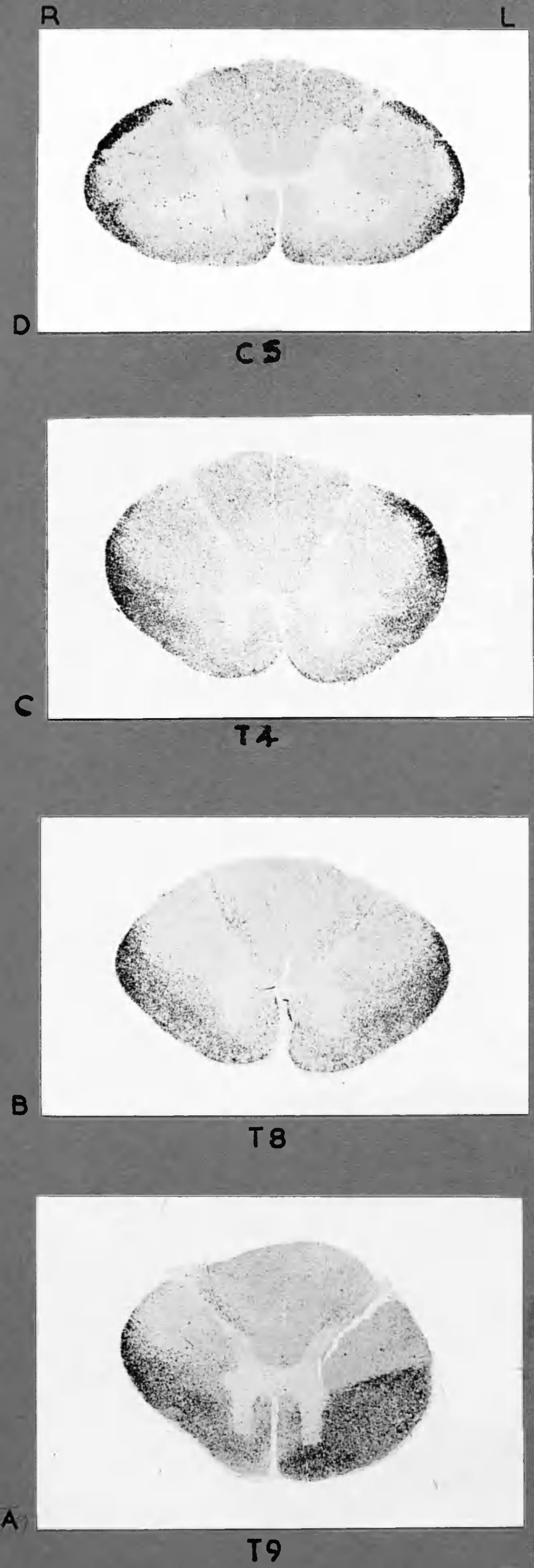
It is now necessary to determine as far as possible, how far ventral on the periphery of the cord these fibres lie, which in more cranial segments, will move dorsally. Their ventral extremity seems not to be identical at all levels. The evidence concerning this point of watershed will be considered now at the following three levels: mid-thoracic, upper thoracic, lower thoracic and upper lumbar. The bulk of evidence on this point comes from the mid-thoracic level.

Mid-thoracic: these fibres which move dorsally further cranially lie at this level dorsal to a line passing from side to side through the central canal. Case25, Fig.95 may be taken as an example. On the right side of the cord, the fibres move dorsally so that at the fifth cervical segment, they occupy the area adjacent to the dorsal horn. On the left side of the cord, they do not do this, but remain in the same ventro-lateral region, as they ascend. Thus the fibres dorsal to this line passing through the central canal move dorsally as they ascend, and those lying ventral to this line do not do so. The same can be seen from case 20 (Plate 37).

Upper thoracic: case 13 (Plate 39) may be taken to determine the watershed at the level of the first thoracic segment. On the left, the lesion lies ventral to the line passing through the central canal, and on the right, it includes some fibres lying dorsal to this line. It will be seen that at the fifth cervical segment (Fig.96B) there are no degenerated fibres lying contiguous to the dorsal horn on the left, whereas such fibres are present on the right.

Lower thoracic and upper lumbar: case 34 (Plate 42) may be taken to determine the watershed at the first lumbar segment. On the left, the

FIG 100
(CASE 33)



lesion involved only the ventral part of the ventro-lateral column; on the right, it involved many fibres lying dorsal to the line passing through the central canal. It will be seen that at the sixth cervical segment, (Fig.99A and B) in this case, there are some degenerate fibres from the left side lying contiguous to the dorsal horn at the fifth cervical segment; and there are also some on the right side, as would have been expected.

Case 33 (Plate 43) may be taken as an example when the lesion is at the ninth thoracic segment. In this case, both lesions extended dorsal to the line passing through the central canal; and on both sides at the fifth cervical segment degenerate fibres are lying contiguous to the dorsal horn. The important feature to note is the large number of fibres which have moved dorsally, considering the few fibres which were dorsal to the line at the level of the lesion. It would therefore appear that some of these fibres occupying the dorsal position at the fifth cervical segment must have been ventral to the line passing through the canal at the lower thoracic region. It is therefore suggested that at this level some fibres lying more ventrally than the level of the central canal also migrate dorsally.

It would then appear to be justified to conclude that in the middle and upper thoracic segments the majority, if not all, the fibres which shift dorsally in the dorso-lateral column never lie further ventrally than about the level of the central canal. It should be noted that the central canal is utilised in these descriptions because it is convenient to have such a landmark in describing sites in the cord. But it is intended to be used purely as an indication of approximate positions.

From the evidence available it appears probable that in the lower thoracic and first lumbar segments, some fibres actually shift from sites rather more ventral than the central canal line, into the dorso-lateral column. All descriptions of a dorsal shift of dorso-lateral fibres refer only to segments below the fifth cervical. For it has already been demonstrated that there is a considerable ventral shift of dorso-lateral fibres in the fourth and third cervical segments, so that the dorsal extremity of the mass is separated from the dorsal horn by non-degenerated

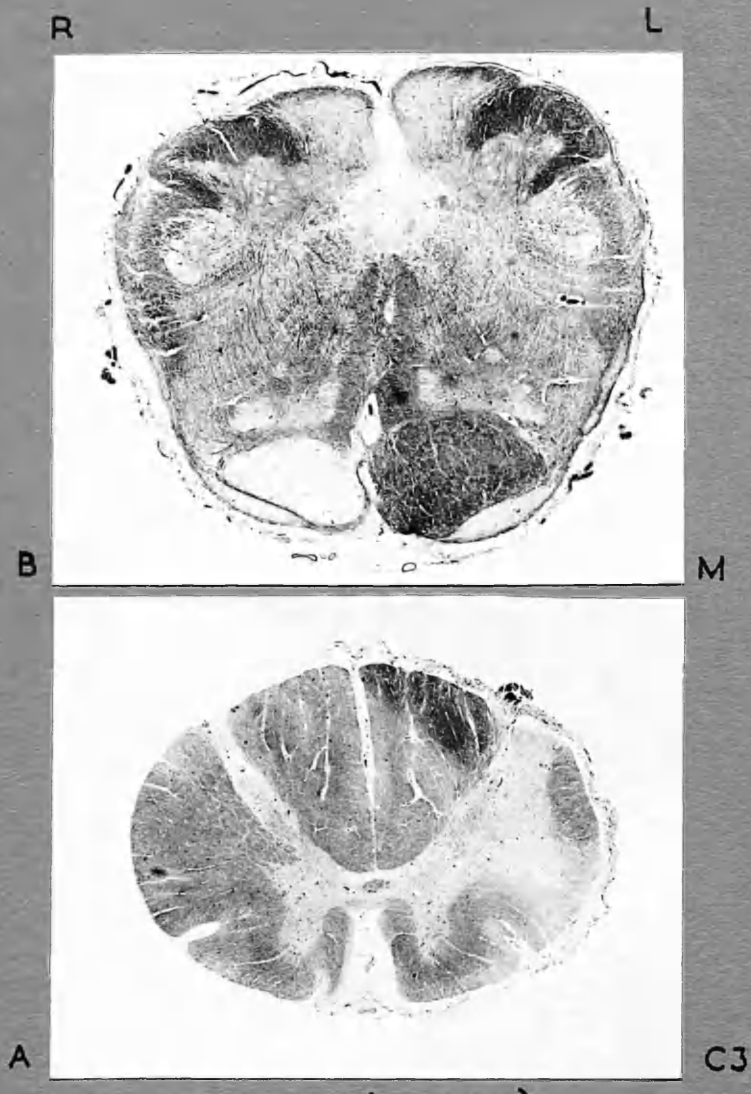


FIG 101 (CASE 53)

fibres. These non-degenerated fibres can be shown to be fibres of the crossed pyramidal tract. This point is most clearly established in cases in which the crossed pyramidal tract was degenerated, due to a lesion in the internal capsule. An example is case 53 (Plate 44). Fig 101B shows the degenerated right pyramid in the medulla; Fig.101A shows the degenerated left crossed, and right direct pyramidal tract at the third cervical segment. The crossed pyramidal tract extends laterally to occupy the most dorsal zone of the dorso-lateral column.

When, at the third and fourth cervical segments, the dorso-lateral fibres move ventrally, the shape of the whole mass of fibres is altered, as already described. It has not so far been possible to establish any consistent differences in the arrangement of the fibres, associated with the different lesions. In the upper two cervical segments, where the mass of fibres again comes to lie in contact with the dorsal horn, the dorso-lateral fibres are intimately mingled with the ventro-lateral fibres. No differences in the appearance of the degeneration at this level, such as were noted in the lower cervical segments, can be recognised.

d) <u>Arrangement of ascending fibres in the ventro-lateral and ventral columns.</u>

On pages 120-126 the general pattern of degeneration in the ventro-lateral column was described. Case 20 was shown as a typical example of the course of the ascending fibres, rendered degenerate by a lesion involving the entire ventral and lateral columns. It was learnt from this case that an extensive lesion of the ventral quadrant gives degeneration of ascending fibres in the ventral quadrant, and that these fibres as they ascend, become concentrated in the dorsal half of the ventral quadrant. This pattern of ascending fibres of the ventral quadrant will now be considered in more detail.

A case of particular importance is case 34 (Plate 42) even although the survival period was long, (91 days) and the ascending degeneration rather sparse. The importance of this case lies in the fact that the operation was performed at a caudal level - the first lumbar segment - and on the left side it involved only the ventral part of the ventral quadrant.

In segments immediately cranial to the lesion degenerating fibres are confined to the same part of the ventral quadrant involved in the operation, but in higher sections the degenerating fibres gradually move dorso-laterally and come to be in approximately the same location as the ventro-lateral group of fibres in case 20 (Plate 37). They occupy an area between the transverse line passing through the central canal and the ventral limit of the ventral horn. But the fibres are far fewer in number than in case 20.

There is, then a dorso-lateral shift of the fibres in the ventral quadrant, to the lateral part of the dorsal region of the ventro-lateral column. As the fibres are scattered over approximately the same extent of the column in the lower cervical region, after a lesion at the first lumbar segment (case 34, Plate 42, Fig.99A and B) as after a lesion at the fifth thoracic segment (case 20, Plate 37, Fig.93D) it is clear that there is considerable intermingling of fibres from different segmental cord levels.

In case 34 (Fig.99A and B) it will be seen that these ventro-lateral fibres tend to become concentrated into two areas; one group is along the periphery of the cord, the other group lies about midway between the periphery of the cord and the grey matter; but between these two main groups of fibres, the space still contains quite a lot of degenerate fibres.

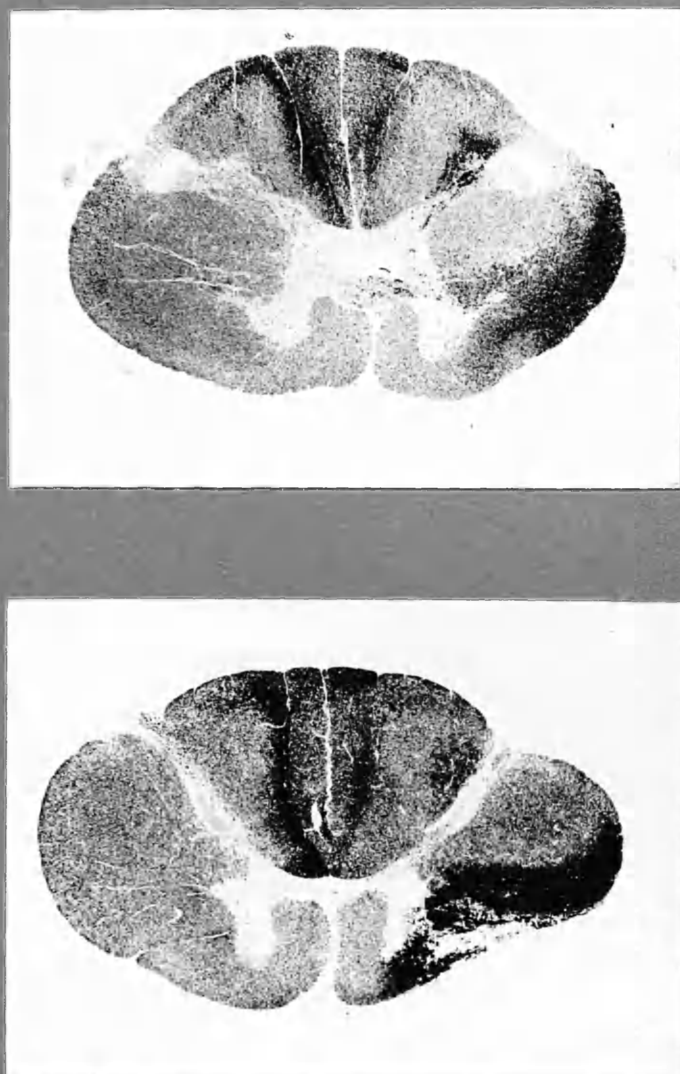
It is instructive to turn now to case 20 (Plate 37). In the sections of the second thoracic and the seventh cervical segments (Figs. 93C and D), particularly on the right side, the peripheral zone of dense degeneration and a medial zone of more diffusely scattered degenerated fibres can be distinguished.

When case 20 is compared with case 34, it will be seen that at the second thoracic and seventh cervical segments the area between the two zones is filled out with degenerating fibres; thus in case 20 the area between the two curved bands of degenerating fibres is not sparsely scattered with fibres, as it is in case 34. The reason for this difference is likely to be that in case 20 the lesion was at the fifth thoracic segment, and in case 34 it was at the first lumbar segment; the intermediate area is likely to be filled with the fibres from the segments cranial to the level of the lesion of case 34. If a case with a lesion at a level between these two cases, is examined, for instance at the ninth thoracic segment, as in case 33 (Plate 43) some indication is found of the space being moderately filled with fibres; there seem to be more fibres in this space than in case 34 (Plate 42) and less than in case 20 (Plate 37). When the lesion is made further cranial than the ninth thoracic segment, these two separate groups of ascending fibres in the ventro-lateral column become harder to distinguish ; they can still be made out in case 20 (Plate 37), when the lesion was made at the fifth thoracic segment; but in cases where the lesion was made further cranially the space between the two curved bands is no longer clearly seen (e.g. case 12, Plate 40).

It can also be seen that the more cranial the lesion, the more fibres are present in the medial of the two curved bands; this band comes to extend further ventro-medially.

A further point is that the size of the Marchi bodies tends to differ in the two groups:

R L



B C1

A C3

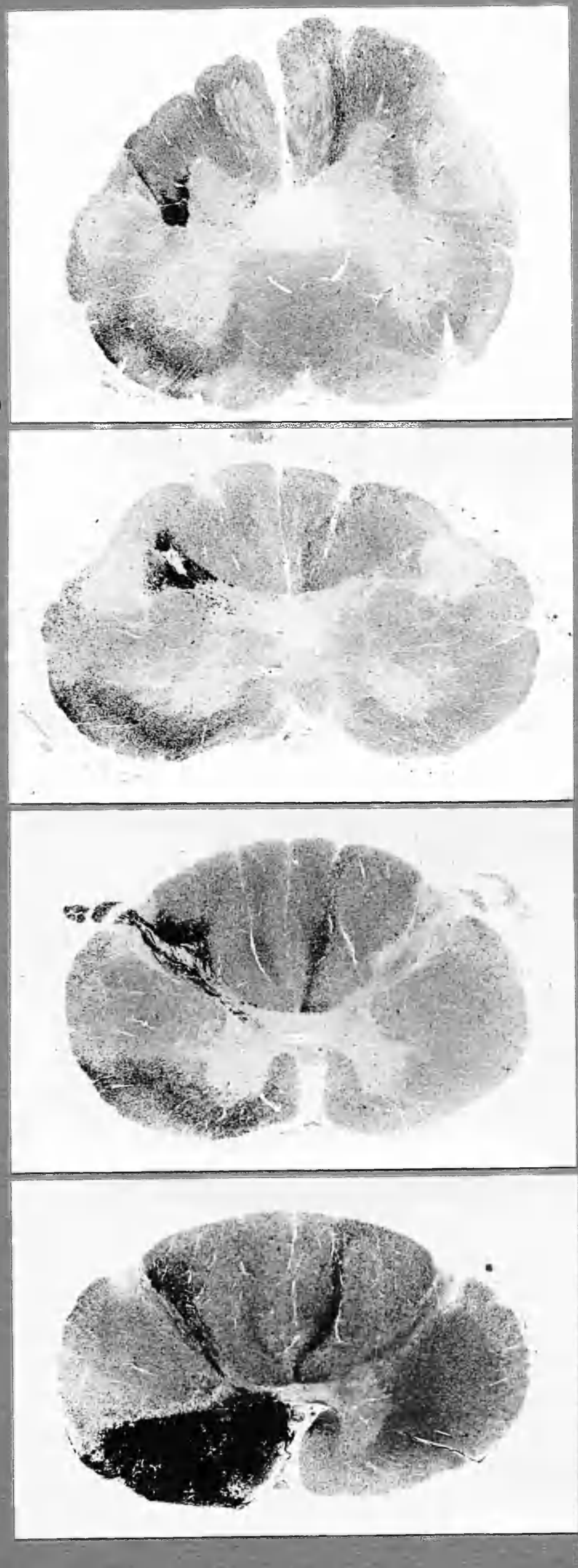
FIG 102
(CASE 3)

the peripheral band contains more numerous large Marchi bodies than the most medial band.

Case 12 (Plate 40) forms an example of the pattern of ascending degeneration when the lesion is made at the fifth and sixth cervical segments. The two separated bands can no longer be found, but some distinction can be seen between the lateral half of the degenerating area of fibres and the medial half. In the lateral half, the Marchi bodies are larger, and in the medial half they are finer. The more medial group of finer Marchi bodies extends further medially and ventrally than the medial group in case 20. Also, the total mass of degenerating fibres is greater than that in case 20, where the lesion was at a more caudal level.

It will be seen from case 20 (Plate 37) and case 12 (Plate 40) that the more medial group of degenerating fibres extends more ventrally and medially than the lateral group of fibres. This is also shown in the cases in which the operation lesions were made further cranially. An example of this is case 3 (Plate 45) where the operation was performed at the third cervical segment. It is

FIG 103
(CASE I)



also clearly shown in case 1 (Plate 46) where the operation was performed at the first cervical segment.

Now if the sections of the first cervical segment of case 1 (Plate 46, Fig.103B) are compared with the sections of the first cervical segment of case 34 (Plate 42, Figs. 99 C and D), the following feature will be observed: the most dorsal part of the medial band of degenerating fibres in case 1 lies in approximately the same position as the most ventral part of the medial band of degenerating fibres in case 34, or slightly more medially. Thus these ventro-medial fibres occupy essentially the same position at the first cervical segment in the two cases. It therefore seems likely that the fibres in this position belong to the same system.

It is hoped that further cases will eventually fill in the main outlines shown by these cases.

To sum up, it has been shown that there are at least two sets of long ascending fibres in the ventro-lateral column, and that the lateral set is more compact than the medial, and does not extend so far ventrally. In their ascent in the cord all the fibres move dorso-laterally. No lamination was found in the lateral ascending groups. It seems that there may be some dorso-lateral ventro-medial lamination in the more medial group fibres entering this band from more cranial segments taking up the more ventro-medial position. It is more difficult to work out the topography of the more medially lying fibres than the lateral fibres, owing to their small calibre.

The course of this whole ventral group of fibres in the upper cervical segments has already been described on pages 120-126, and 126-130.

CHAPTER IX

THE ASCENDING DEGENERATION IN THE MEDULLA AND PONS.

A brief account of the pattern of degeneration in the brain stem in a case with an extensive lesion of both the dorsolateral and the ventrolateral columns at the third cervical segment will be demonstrated from a series of transverse sections. Then the degeneration following lesions at different cord levels, and of varying topography will be compared. Certain other features will also be described. Finally a case with a lesion confined to the ventral quadrant at the first cervical segment will be described, and the ascending degeneration demonstrated in sagittal sections.

I. General Pattern of Degeneration.

(case 5, Plates 47-49).

In case 5 there is an extensive operation lesion in the third cervical segment (Fig.104A) which includes the greater part of the peripheral zone in the dorso-lateral and the ventro-lateral columns. This case is particularly useful because

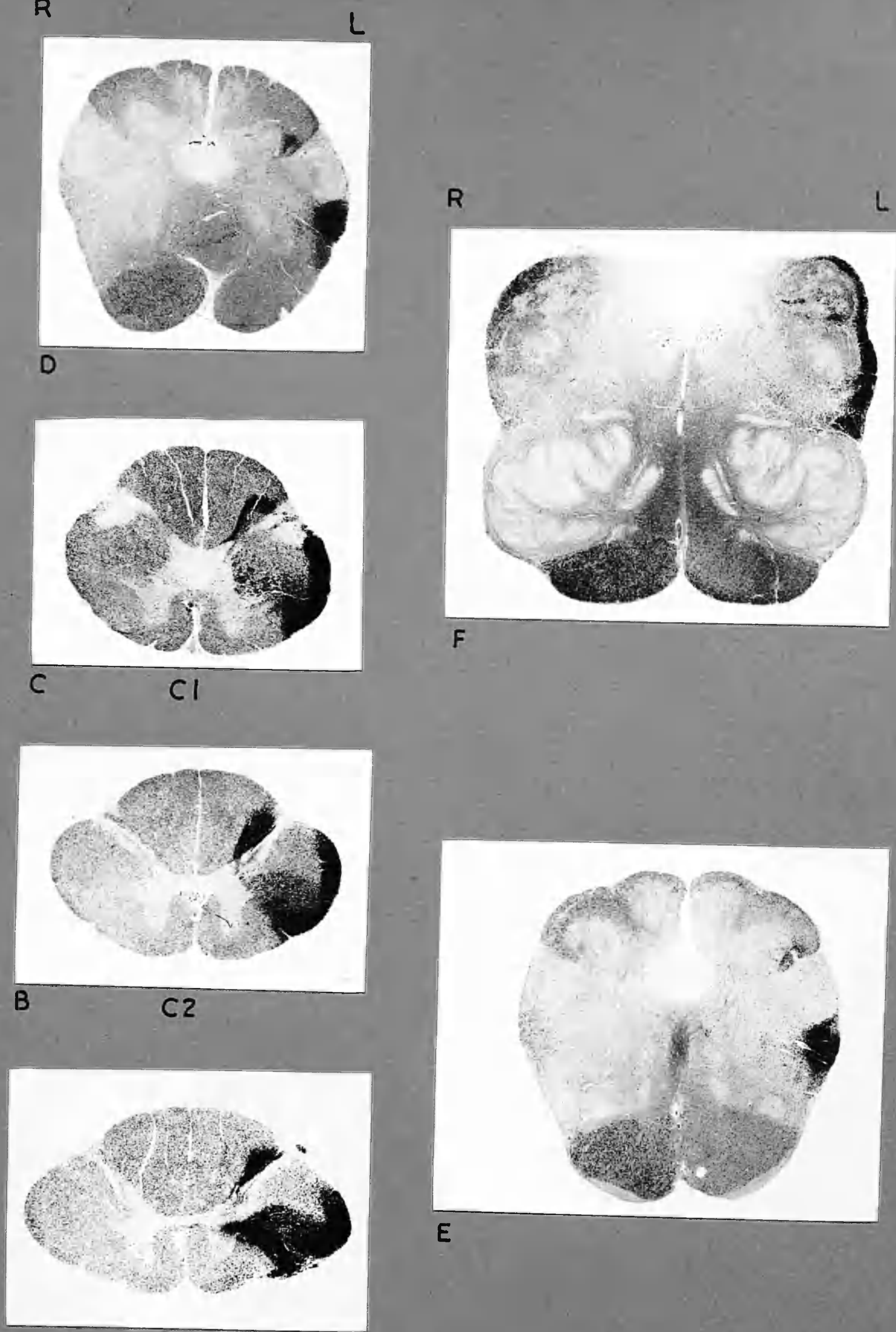


FIG 104 (CASE 5)

the lesion, made at the third cervical segment, must involve most, if not all, of the ascending fibres of the lateral column. It is only in the third and fourth cervical segments that these fibres occupy an extreme lateral position; for there the cortico-spinal tract comes to the periphery of the cord, and displaces the dorso-lateral fibres laterally. Also, by this level, all the long ascending fibres of the dorso-lateral and ventro-lateral groups, are gathered together in this lateral column. Thus the lesion in case 5 involves all ascending fibres of the dorso-lateral and ventro-lateral systems. In this case, it will be seen that at the segment above that of the operation - at the second cervical segment (Fig.104B) - the degenerated region is in the ventro-lateral and dorso-lateral columns. (There is an unusual feature here: there is a large mass of degenerating fibres, between the peripheral band and the central grey matter. These have been investigated in this and other cases, and a paper on them entitled "Spino-cortical fibres in man" has been accepted for publication in the Journal of Neurology, Psychiatry and Neurosurgery).

In the next cranial section the peripheral band of degenerating fibres is seen to lie in juxtaposition with the dorsal horn (Fig.104C).

In Fig.104D, at the level of the upper part of the pyramidal decussation, the degenerating fibres are closely packed in the region immediately ventral to the descending nucleus of the fifth cranial nerve. The mass of fibres presents a roughly triangular appearance in transverse section. The hypotoneuse of this triangle extends along the periphery of the medulla from the fifth nerve nucleus almost to the pyramid. The shortest side of the triangle lies along the ventral aspect of the fifth nerve nucleus, and extends into the reticular formation. The mass of degenerating fibres is stained more intensely in its dorsal two thirds than in the ventral third. This suggests a concentration of degeneration fibres in the dorsal part.

In Fig.104E, at the level of the lower part of the sensory decussation, the degenerating fibres are still massed in a triangular area, ventral to the spinal nucleus, lying in the dorsal two-thirds of the distance between this nucleus and the pyramid.

FIG 104 (CASE 5)

R L

H

R L

G

There is scattered degeneration in the reticular substance, medial to the main mass of degeneration.

In Fig.104F, at the caudal limit of the fourth ventricle, the degenerating fibres now form a peripheral band extending dorsally from the post olivary sulcus to the level of the dorsal border of the cuneate nucleus; the degenerating fibres lie lateral to the descending nucleus of the fifth cranial nerve and the cuneate nucleus. Except for the most ventral fibres, the fibres have run dorsally and are cut in longitudinal or oblique section. Degenerating fibres also in this section lie in the formatio reticularis.

In Fig.104G, at the upper medulla, the majority of the fibres have collected dorsally in the lateral part of the restiform body, where they are cut in transverse section. A smaller mass of fibres lies on the periphery of the medulla in the depression between the olive and the restiform body. A few fibres are scattered along the periphery of the medulla, between the two masses of fibres, lateral to the descending nucleus of the fifth cranial nerve.

In Fig.104H., through the lower pons,

R L

I

FIG 104 (CASE 5)

the dorsal mass of fibres is still in the restiform body; the smaller ventral mass now lies further dorsally than in the medulla, deep in the pons. The ventral fibres are scattered in the lateral lemniscus, which lies dorsal and medial to the fibres of the brachium pontis, ventral to the fifth nucleus and lateral to the medial lemniscus.

In Fig.104I, at the level of the brachium conjunctivum, a few fibres are scattered diffusely through the lateral lemniscus, mainly in the lateral part, and in the stragulum on the periphery of the pons. A thin band of fibres also extend from the base of the brachium over its dorsal surface, and into the superior medullary velum.

Certain parts of the course will now be considered in more detail.

II. Cases Showing Particular Features.

A. Sections of the medulla will be shown to demonstrate:-

a) The location of the degeneration fibres, after a lesion of both the dorso-lateral and ventro-lateral columns made at:

(i) the upper cervical level

(ii) The mid-thoracic level

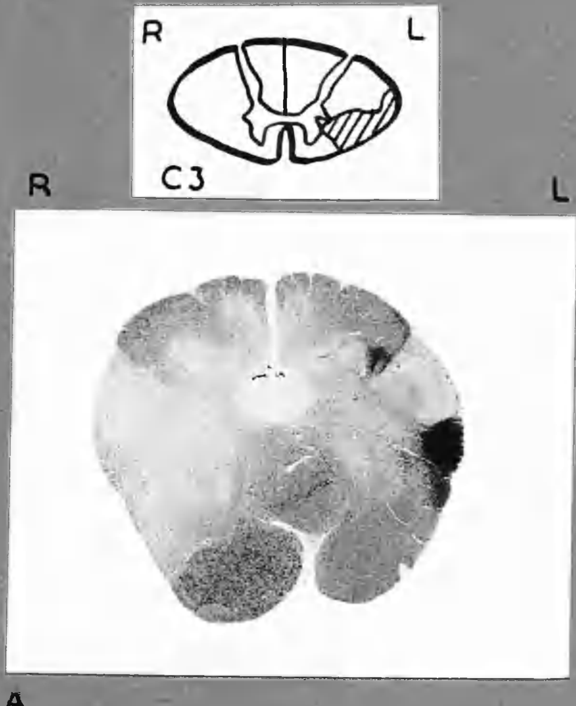


FIG 105 (CASE 5)

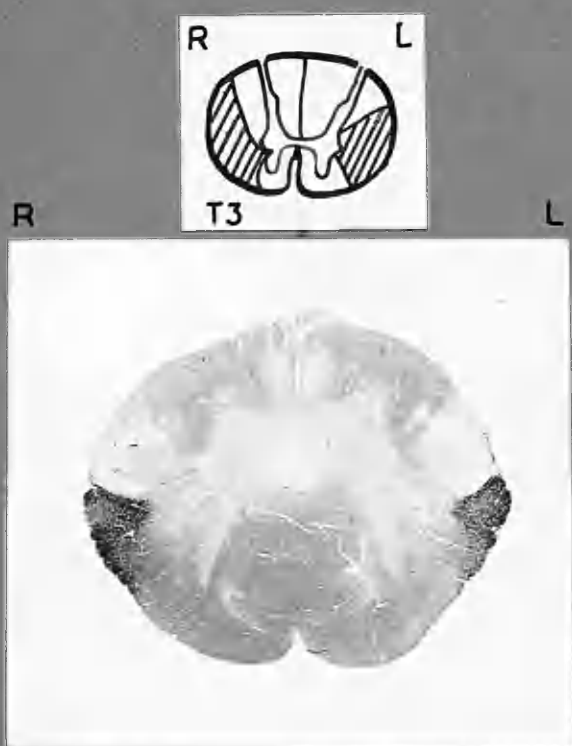


FIG 106 (CASE 15)

b) The location of the degeneration after a lesion of:

(i) the dorso-lateral tract only

(ii) the ventro-lateral tract only.

Sections will also be shown to demonstrate:-

c) The connection of the fibres with the restiform body.

d) Degenerating fibres in the formatio reticularis.

a) <u>Location of the degenerating fibres after a lesion of both the dorso-lateral and ventro-lateral column</u>. (Plate 50).

(i) Lesion made at the upper cervical level (case 5, Fig.105).

Case 5 was utilised as an example of the general pattern of degeneration in the brain stem, (pages 144-148). Fig.105B is an enlarged view of Fig.104D, and shows more clearly the distribution of the degenerating fibres in the medulla, after a lesion of both the dorso-lateral and the ventro-lateral columns at the third cervical segment.

(ii) Lesion made at the mid-thoracic level (case 15, Fig.106).

In case 15 the lesion, which was comparable in extent to that in case 5, was made at the fifth thoracic segment.

It will be seen from Fig.105 that the area throughout which degenerating fibres are present in the case of a mid-thoracic lesion is very similar to that in the case of a high cervical lesion.

In case 15, the degeneration extends a little further medially than in case 5, and the dorso-lateral part of the degeneration is less intensely stained than in case 5. The presence of degenerating fibres throughout the triangular area, ventral to the descending nucleus of the fifth nerve is a consistent finding in all cases with an extensive lesion of both dorso-lateral and ventro-lateral columns, no matter at what cord level the lesion was made.

Although it will be seen that in case 5 there are more fibres degenerated in the dorsal part of this triangle than there are in case 15, this difference in distribution is not found in other cases; and no significance is attached to it.

b) <u>Location of the degenerating fibres after a limited lesion of the lateral column.</u> (Plates 51-52).

(i) Lesion of the dorso-lateral column only (case 26, Fig.107).

In case 26 the period of survival was rather

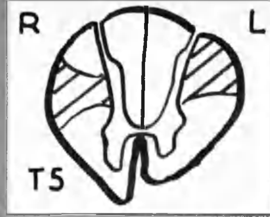


FIG 107 (CASE 26)

R L

L

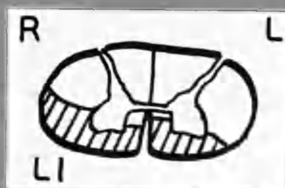


FIG 108 (CASE 34)

R

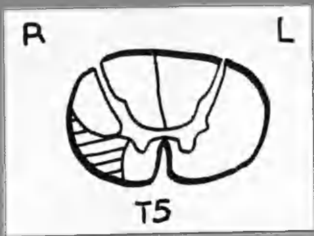
L

long (150 days), so that only the positive findings can be accepted as evidence: i.e. no deductions can be drawn respecting the absence of Marchi material in any area.

The extent of the degeneration in the medulla is approximately the same as in the dorsal two thirds of the degeneration mass in case 5. There are, however, far fewer fibres.

(ii) Lesion of the ventro-lateral column only, (case 34, Fig.108, case 9, Fig. 109, case 18, Fig.110).

In case 34 (Fig.108) the bilateral operation was at the first lumbar segment. On the left side, the lesion was confined to the ventral quadrant; on the right side the ventral quadrant was mainly involved. The degeneration in the medulla is sparse, but in distribution closely resembles that of case 26, (Fig.107), in which the lesion was wholly dorsal. In case 9 (Fig.109) and in case 18 (Fig.110) the lesion, made at the mid-thoracic level, was mainly ventro-lateral. In both these cases the distribution of the degeneration in the medulla is very similar to that in case 5 (Fig.105), and in the dorsal two thirds, therefore, similar to that in case 26. (Fig.107).



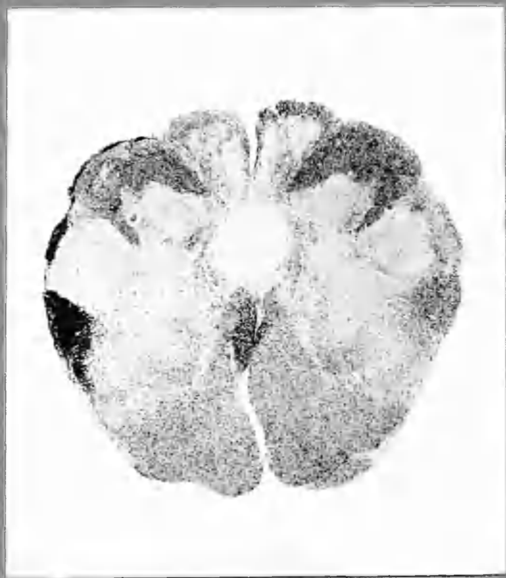


FIG 109 (CASE 9)

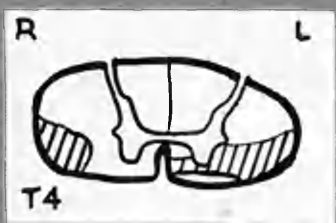


FIG 110 (CASE 18)

These cases show that the ascending fibres of the lateral column of the cord lie, in the medulla, in the dorsal half of the peripheral zone between the spinal nucleus of the fifth nerve and the pyramid. In the dorsal two thirds of this triangular area are fibres from both the dorso-lateral and the ventro-lateral columns of the cord. These fibres are so intermingled and scattered throughout this region that the distribution of the degeneration is the same whether the lesion was confined to the ventral or the dorsal part of the lateral column. In the ventral third of the triangular area there are more diffusely scattered fibres which come from the ventral part of the cord only.

Thus one is in a position to conclude that when degenerating fibres in the ventral part of this triangle are found, there must be a lesion of the ventral quadrant of the spinal cord; and when degenerating fibres are found in the dorsal part, the lesion must be in some part of the lateral columns. When one considers the rostro-caudal level of the spinal lesion, one finds that in the dorsal part of this triangular area there tends to be more fibres after a lesion in the rostral part of the cord, than

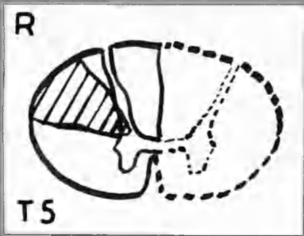


FIG 111 (CASE 27)

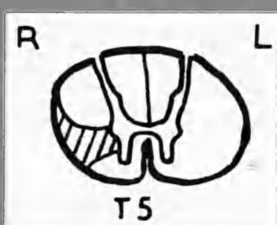
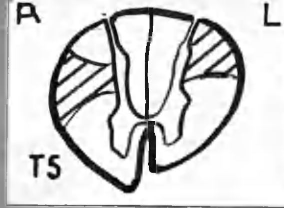


FIG 112 (CASE 9)

FIG 113
(CASE 26)



R L

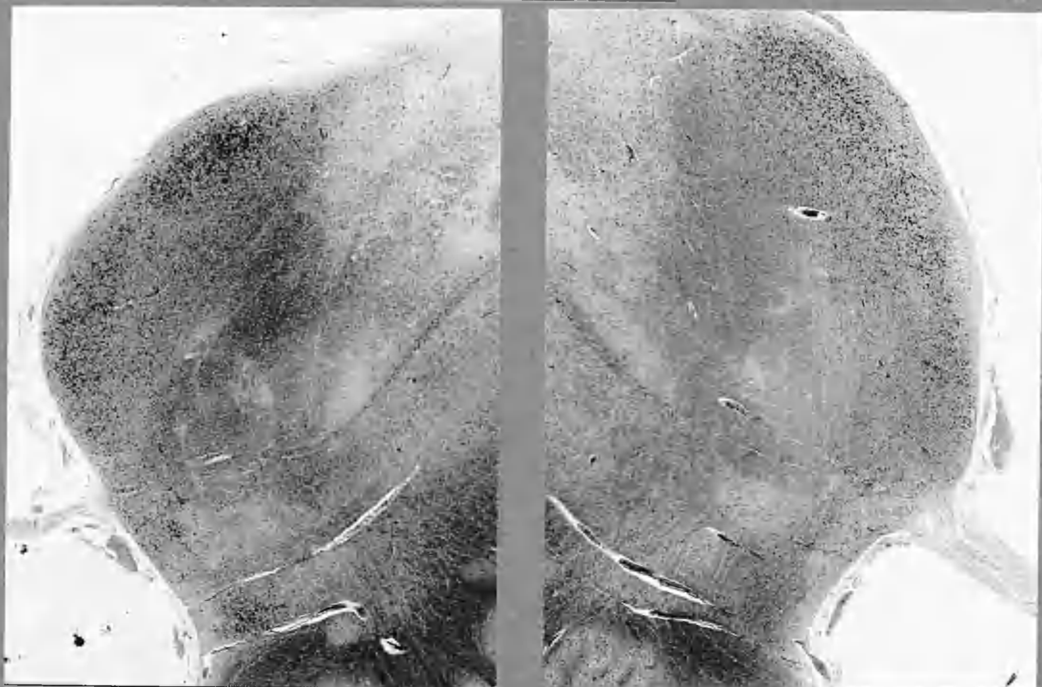
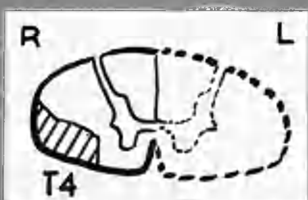
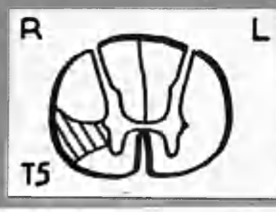


FIG 114
(CASE 18)



R

FIG 115
(CASE 9)



R

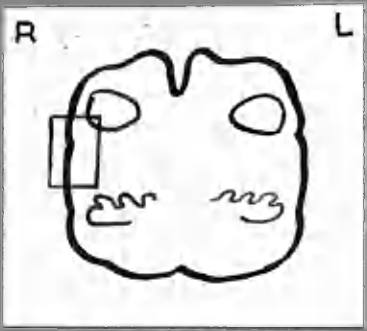
after a lesion in the caudal part.

c) The connection of the fibres with the restiform body. (Plates 53-56).

At the level of the mid-medulla, the majority of the degenerating fibres may be seen to pass dorsally, to enter into the formation of the restiform body.

On plates 53-56 are photographs to show the pattern of degeneration at this level in a case with a lesion of the dorso-lateral column of the cord (case 27, Fig.111), and in a case with a lesion of the ventro-lateral column (case 9, Fig.112). The evidence is insufficient to permit a definite conclusion about the ventral part of this triangle; but it does look as though the rostro-caudal disposition of the lesion does alter the content of fibres in the ventral part. A further observation on the fibres in the medulla is that those in the dorsal group are predominantly of larger calibre than those in the ventral group.

As might be expected from the fibre pattern in the lower medulla, the distribution of the degenerating fibres dorsal to the olive and along the periphery of the dorsal part of the medulla is very



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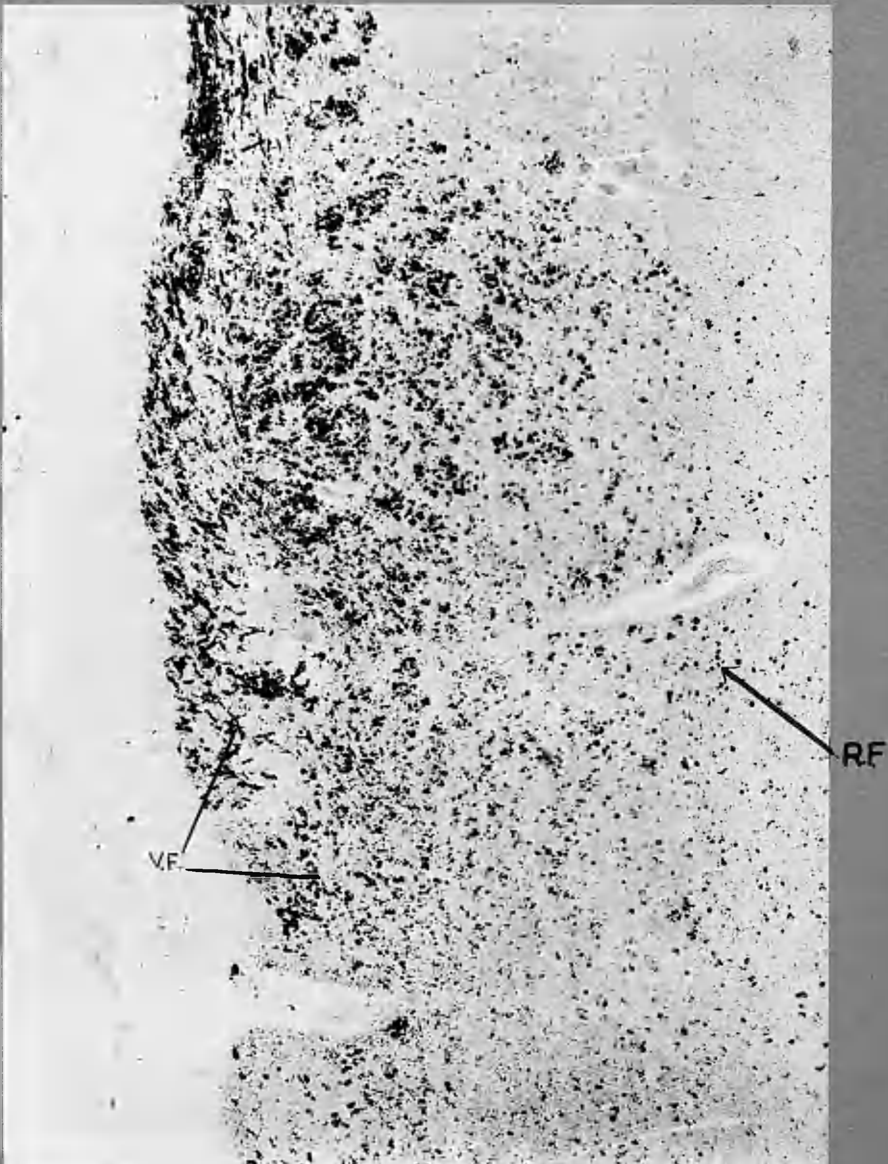


FIG 116 (CASE 23)

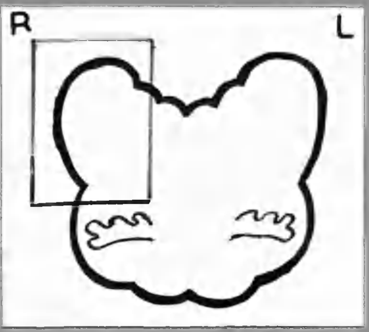


FIG 117 (CASE 23)

similar in the two cases. It is obvious from these photographs, and from those on plate 54, from a slightly higher level, that all the dorsal group of fibres pass dorsally into the restiform body. The next photograph (case 23, Fig.116) shows that some of the fibres in the ventral part of the degenerated area also pass dorsally towards the restiform body (V.F.). This passage of fibres from the ventral tract dorsally can be seen also in Fig.109 (case 9). In Fig.117, (case 23), at a slightly higher level than Fig.116, it may be seen that few fibres lie here in the most lateral zone of the ventral group of fibres. It appears that many of them have passed dorsally. The majority of the fibres pass in the most lateral part of the medulla to reach the restiform body. In a few cases, however, some fibres have been seen to take a slightly more medial course, and reach the restiform body, after traversing the descending nuclei of the fifth nerve. An example of this course can be seen in Fig.117 (case 23).

d) <u>Degenerating fibres in the formatio reticularis.</u>

Numerous fibres appear to leave the main degenerating mass and end in the formatio reticularis.

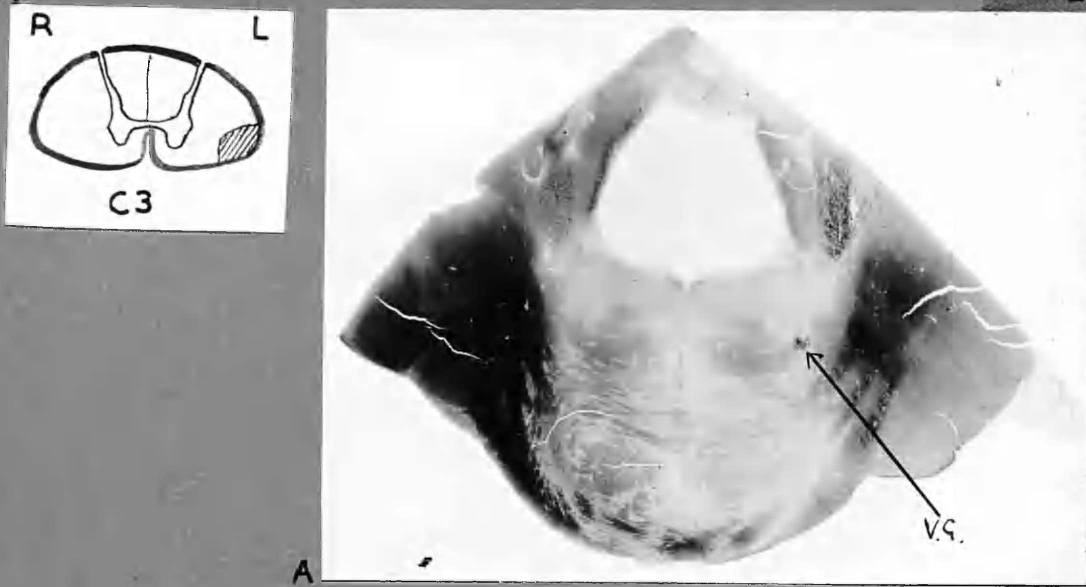


FIG 118 (CASE 7)

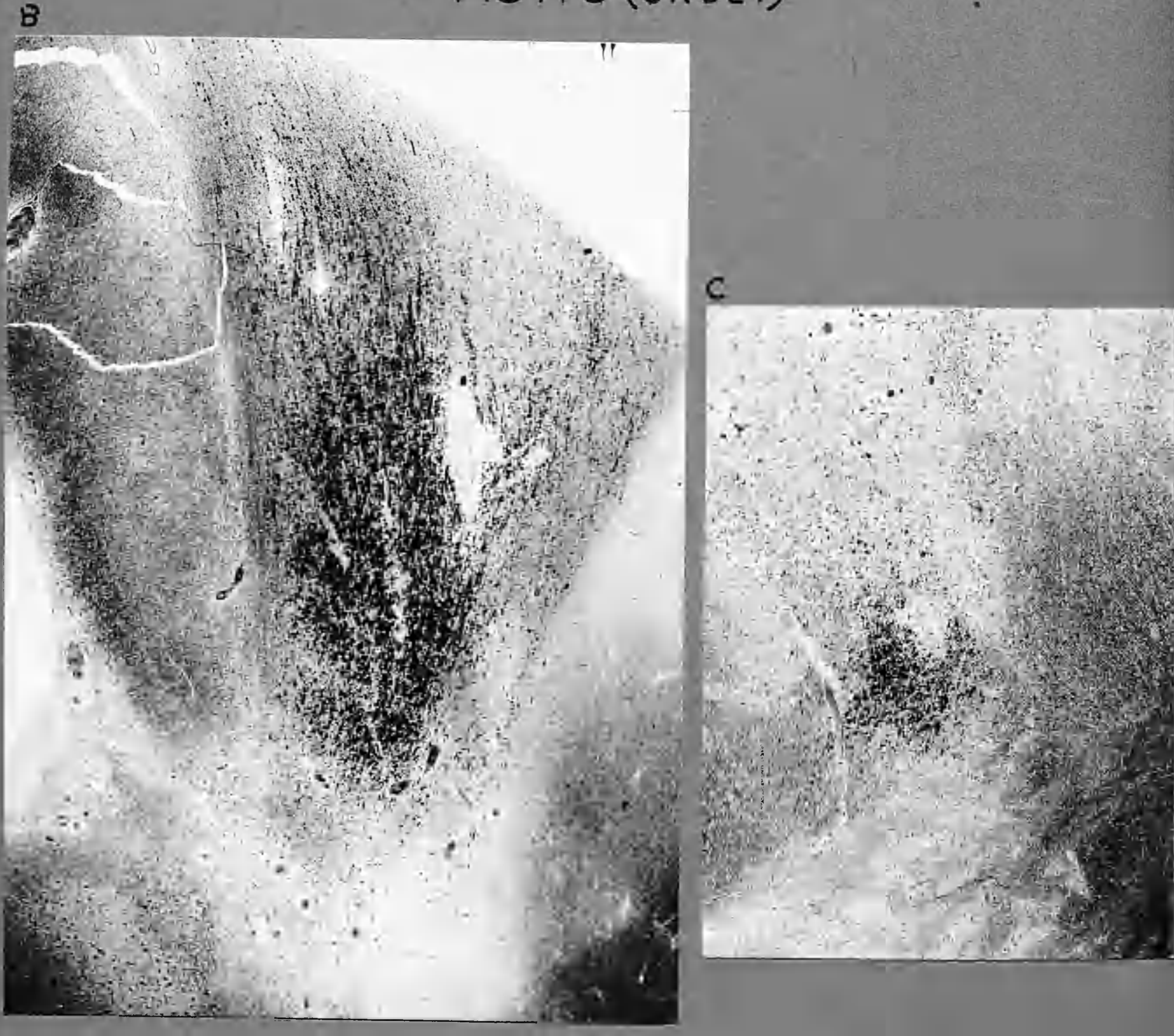


FIG 119
(CASE 15)

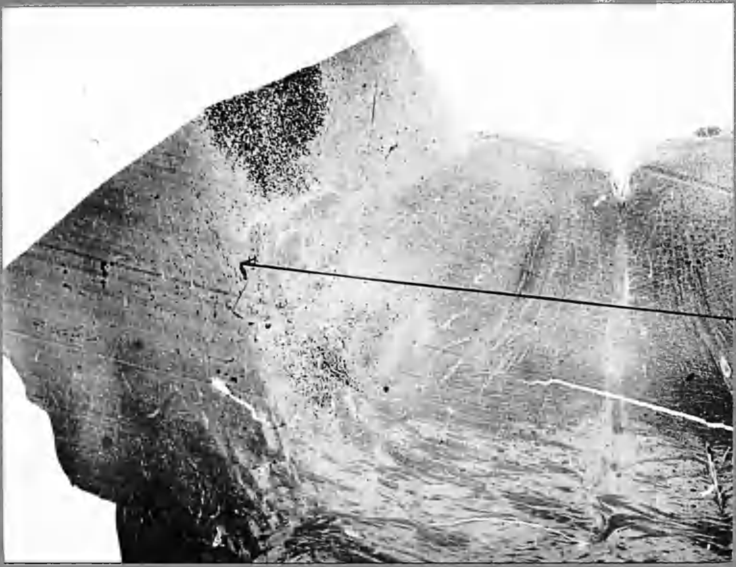


FIG 120
(CASE 28)

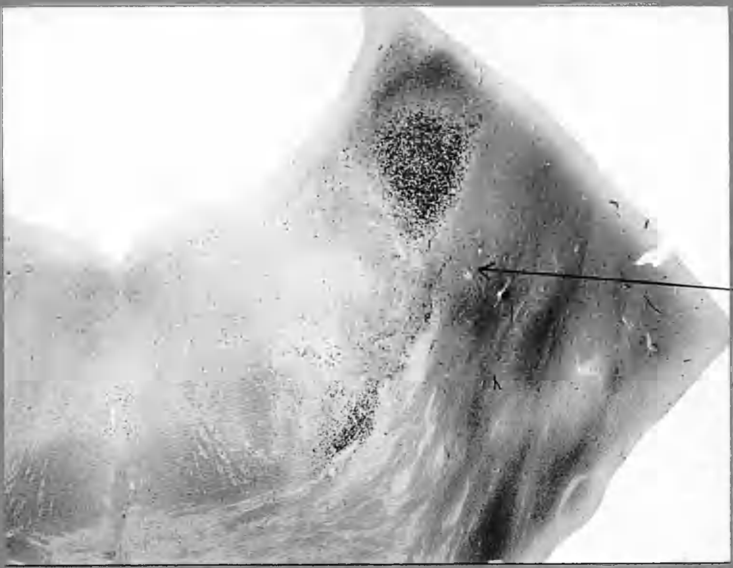


FIG 121
(CASE 7)

Some of these are shown in Fig.116 (case 23, R.F.). These fibres, and others leaving the main bundle of ascending fibres at higher levels, are being analysed in a separate piece of work, and will not be considered further here.

B. With regard to the pons, three points need to be stressed. (Plates 57-59).

a) Of the ascending fibres, the great majority have now passed into the restiform body. This can be seen in Fig.118, (case 7). Only a small percentage of the total fibres now remain in the ventral group. (V.G.). In comparing the number of fibres in these two groups it must be remembered that the ventral group is cut in transverse section, and therefore all the fibres are seen in one section, whereas those in the dorsal group are cut in longitudinal section, and therefore only some are seen in one section.

b) The fibres that remain in the ventral group are scattered in the lateral lemniscus. This is shown best in Figs.119 and 120 (cases 15 and 28).

c) A few of the ascending fibres consistently enter the cerebellum via the brachium pontis. These can be seen (F.B.P.) in Figs.119, 120, 121, (cases 15, 28 and 7).

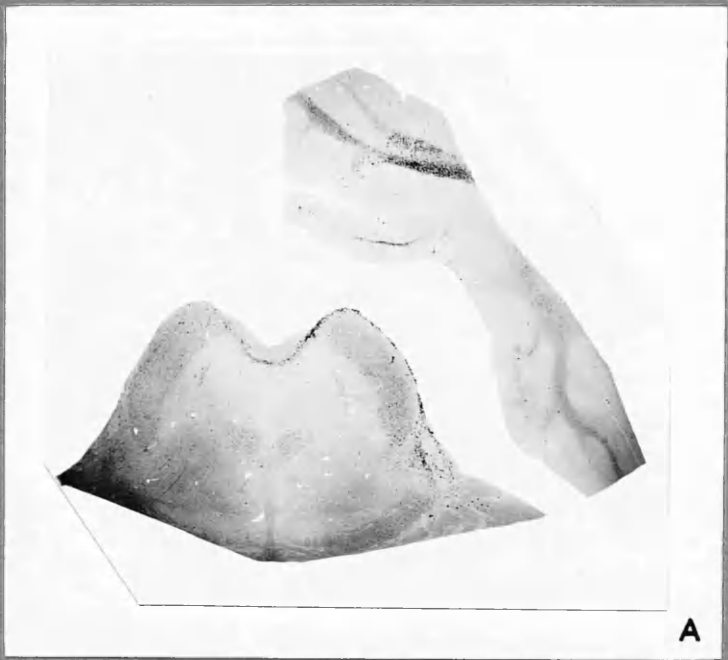
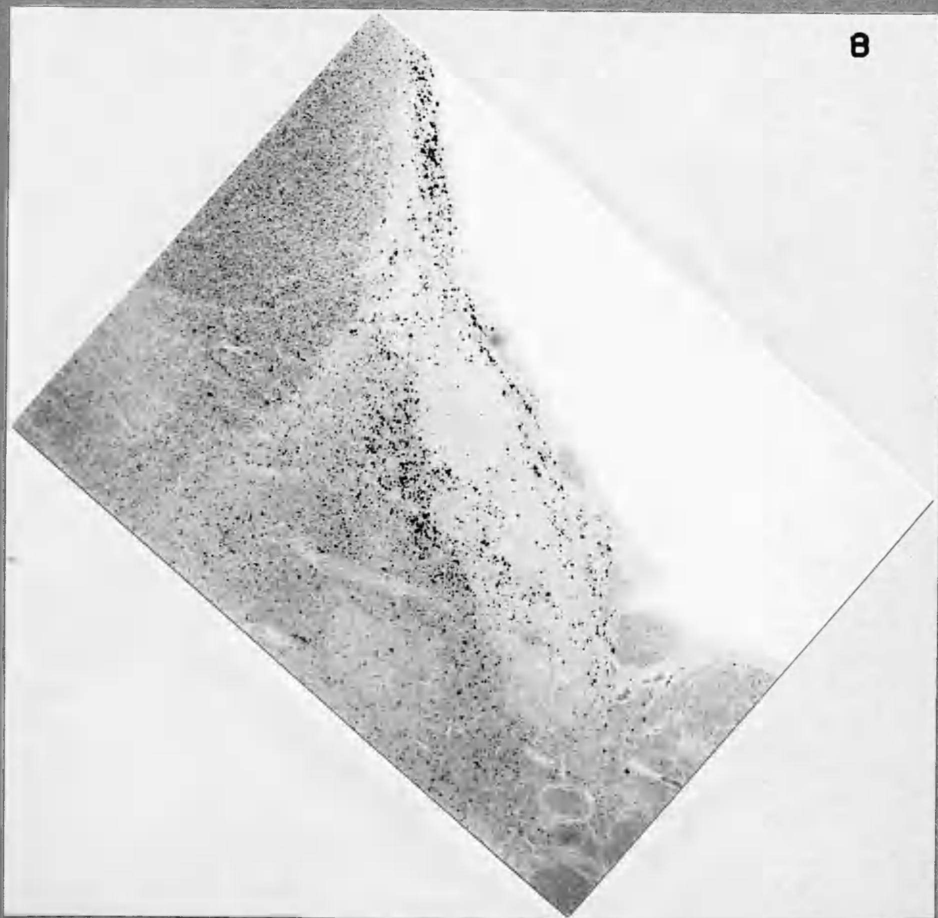


FIG 122 (CASE 5)



It has so far been shown that after lesions of either the ventro-lateral or of the dorso-lateral columns of the cord, the great majority of the degenerating fibres pass into the restiform body. The remainder of the fibres have been traced to the base of the brachium conjunctivum, where a few fibres move dorsally over the periphery of the brachium, Fig.122, case 5.

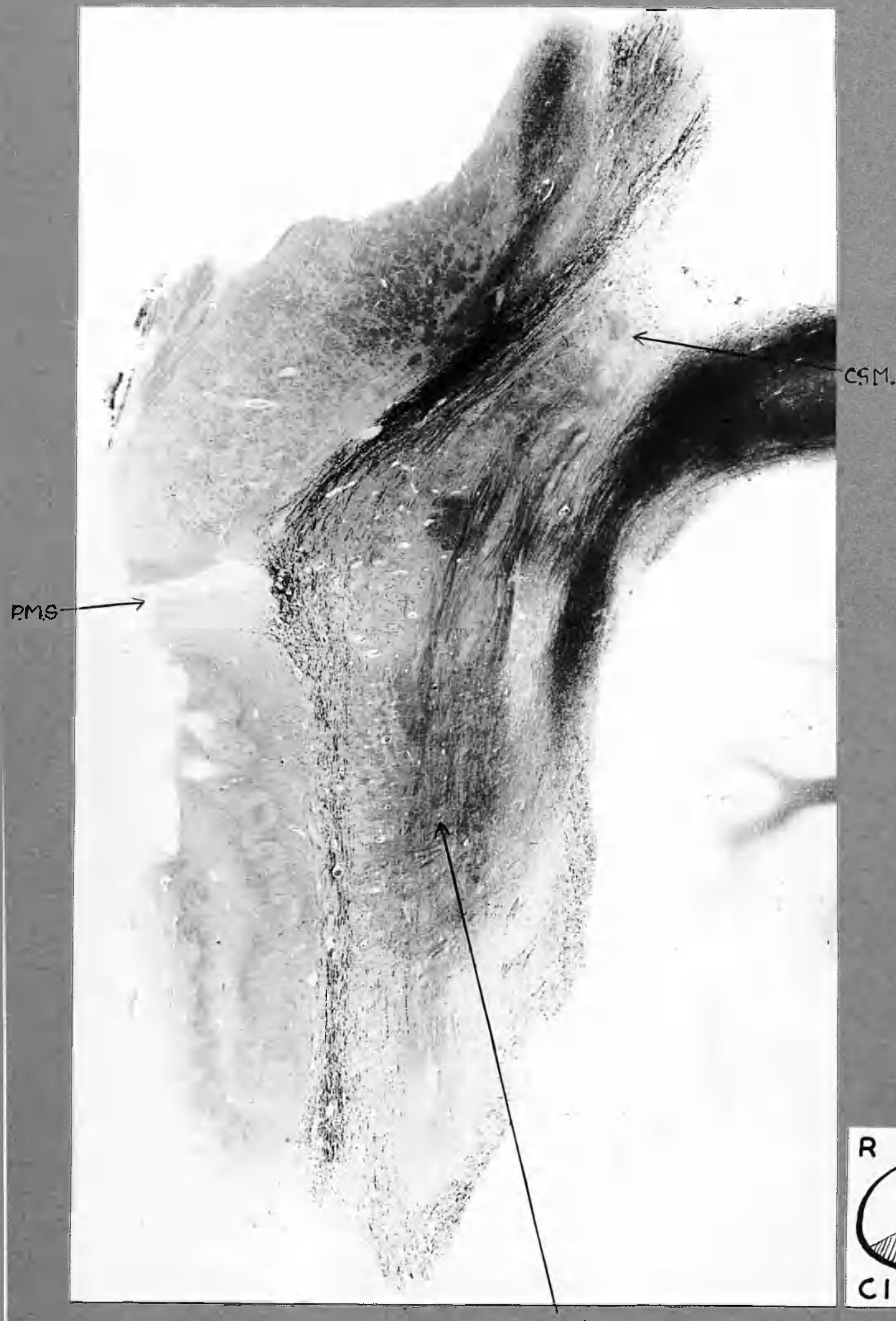
These observations are derived from all the cases in this series in which the lesions were made between the second cervical and the first lumbar segments.

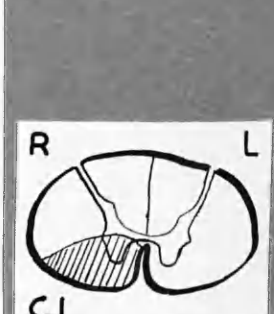
III. <u>Pattern of Degeneration after Lesion confined to the Ventral Quadrant</u>. (Plates 60-62A)

The next case, case 1, is of particular importance, as has been mentioned on page 144. For, in this case, the lesion was made in the first cervical segment. Thus the lesion is cranial to the dorsal shift of most lateral column fibres, described in the previous chapter (pages 117-143). The lesion involved only the left ventral quadrant of the cord.

The degenerating fibres seen in transverse section of the upper part of the first cervical segment and of the lower medulla have already been

FIG 123 (CASE I)





described (page 142, and Plate 46).

Attention is drawn again to the small group of degenerating fibres on the periphery of the lateral column. These fibres must correspond to the most ventrally placed fibres in the peripheral band of degenerating fibres present in the first cervical segment in all other cases (C/F. case 5). The mid and upper medulla, pons and lower mid-brain were cut in sagittal sections.

In the sagittal section, Fig.123, taken through the most lateral part of the olive, the course of the ventral group of fibres from the medulla into the lower brain stem is seen.

As was clear from the transverse sections of the medulla in the other cases (Plates 47-59) the ventral fibres in the medulla ascend in the area immediately dorsal to the olive. They then lie in the periphery of the ventral surface of the brain stem at the base of the ponto-medullary sulcus (P.M.S.). In the pons their course is directed obliquely rostrally and dorsally so that they pass from the ventral surface to the dorsal surface of the pons. In the first part of their pontine course they lie in the lateral lemniscus, dorsal to the bulb of the

FIG124
(CASE 1)

pons, and ventral to the nucleus of the fifth nerve (N.V.N.). As they approach the dorsal surface, the fibres lie at first ventral and then rostral to the circumferential grey mass at the base of the brachium conjunctivum (C.G.M.). Many of the fibres continue to ascend cranially. These do not concern us in the present study.

In a series of sections taken medially from that on Plate 60, fibres may be seen to separate from the large mass of fibres at the base of the brachium conjunctivum, and to run obliquely in a dorso-caudo-medial direction in the peripheral layer of the brachium conjunctivum, to enter the cerebellum. Fig.124 on Plate 61 is from a section medial to Fig.123. In it the numerous degenerating fibres on the dorsal part of the brachium can be seen. In view of the direction taken by the fibres going to the cerebellum, their separation away from the whole complex of ascending fibres, and their course along the brachium cannot be shown in the same sagittal section.

It cannot be decided which of these fibres at this level near the base of the brachium conjunctivum are destined for the cerebellum. There

FIG 125
(CASE 1)

may already be a segregation of the spino-cerebellar fibres, but it seemed as if the fibres entering the brachium conjunctivum came from the whole mass of degenerating fibres.

It should be remarked here that the number of fibres entering the cerebellum by way of the brachium conjunctivum is, in this case, far higher than in any of the other cases examined.

In the cases already described, and illustrated by transverse sections, a notable feature of the course of the ascending fibres in the medulla was that the great majority of all the degenerating fibres entered the restiform body.

It was emphasised earlier that this case is unique, because the operation lesion involved only ventral quadrant fibres, in the first cervical segment. It is striking that in this case 1, also, some fibres may be seen to move dorsally in the medulla to enter the restiform body. Fig.125, an enlarged view of the caudal part of Fig.123. Degenerating fibres (indicated by D.F.), run obliquely dorsally into the restiform body, where they are shown in Fig.126. These fibres appear to arise from the most peripheral degenerating fibres

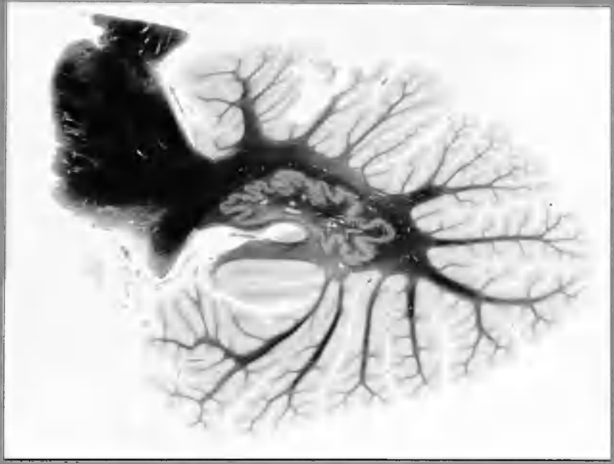


FIG 126
(CASE 1)

seen in the transverse sections of the lower medulla, for they are most numerous in the first section of the sagittal series which pass through the medulla.

From the evidence of this chapter and the previous chapter, it can be understood that almost all (or perhaps all) of the fibres of the peripheral band of the dorso-lateral and ventro-lateral columns of the cord which enter the cerebellum, do so via the restiform body. Fibres from the ventro-medial part of the cord, enter the cerebellum by way of the brachium conjunctivum. It is possible that a few fibres from the ventro-lateral region of the cord also reach the cerebellum by this route, but if so they must be extremely few.

KEY TO ABBREVIATIONS ON PLATES 63-76.

L.	Lingula
C.L.	Central Lobule
C.	Culmen
D.	Declive
F.	Folium
T.	Tuber
P.	Pyramis
U.	Uvula
N.	Nodulus
A. S.L.	Anterior Semi-Lunar Lobule.
P.S.L.	Posterior " " "
S.S.L.	Superior " " "
I.S.L.	Inferior " " "
B.L.	Biventral Lobule
To.	Tonsil
B.C.	Brachium Conjunctivum
R.B.	Restiform Body
P.M.	Pseudo-Marchi Staining.

CHAPTER X

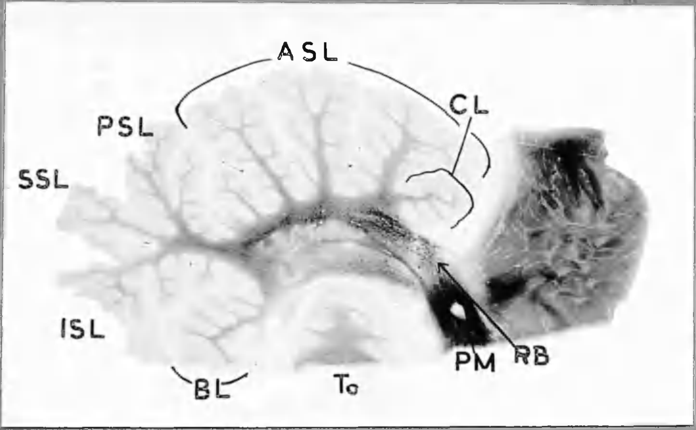
DISTRIBUTION OF DEGENERATING FIBRES IN THE CEREBELLUM.

I. General Pattern of Distribution of Fibres. (Plates 63-71).

Case 9 will be described in detail, and then other cases will be used for confirmation and additional information.

The lesion in case 9, a unilateral cordotomy, was performed on the right side of the cord, at the level of the fourth thoracic segment.

Numerous degenerating ascending fibres enter the cerebellum by the restiform body, and a few by the brachium conjunctivum. The degenerating fibres in the cerebellum will be described in sagittal sections, in a series passing from the right to the left side. The first section passes through the lateral part of the right restiform body. In the section of the right half of the cerebellum the ventral aspect of the cerebellum is on the right of the page; in the sections of the midline and left side the ventral aspect is on the left side of the page.

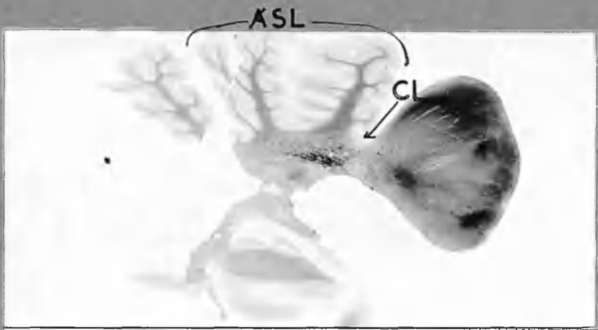


A

RIGHT

B

FIG 128 (CASE 9)



A

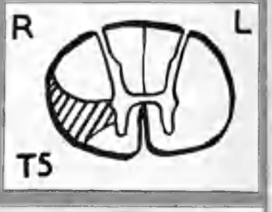
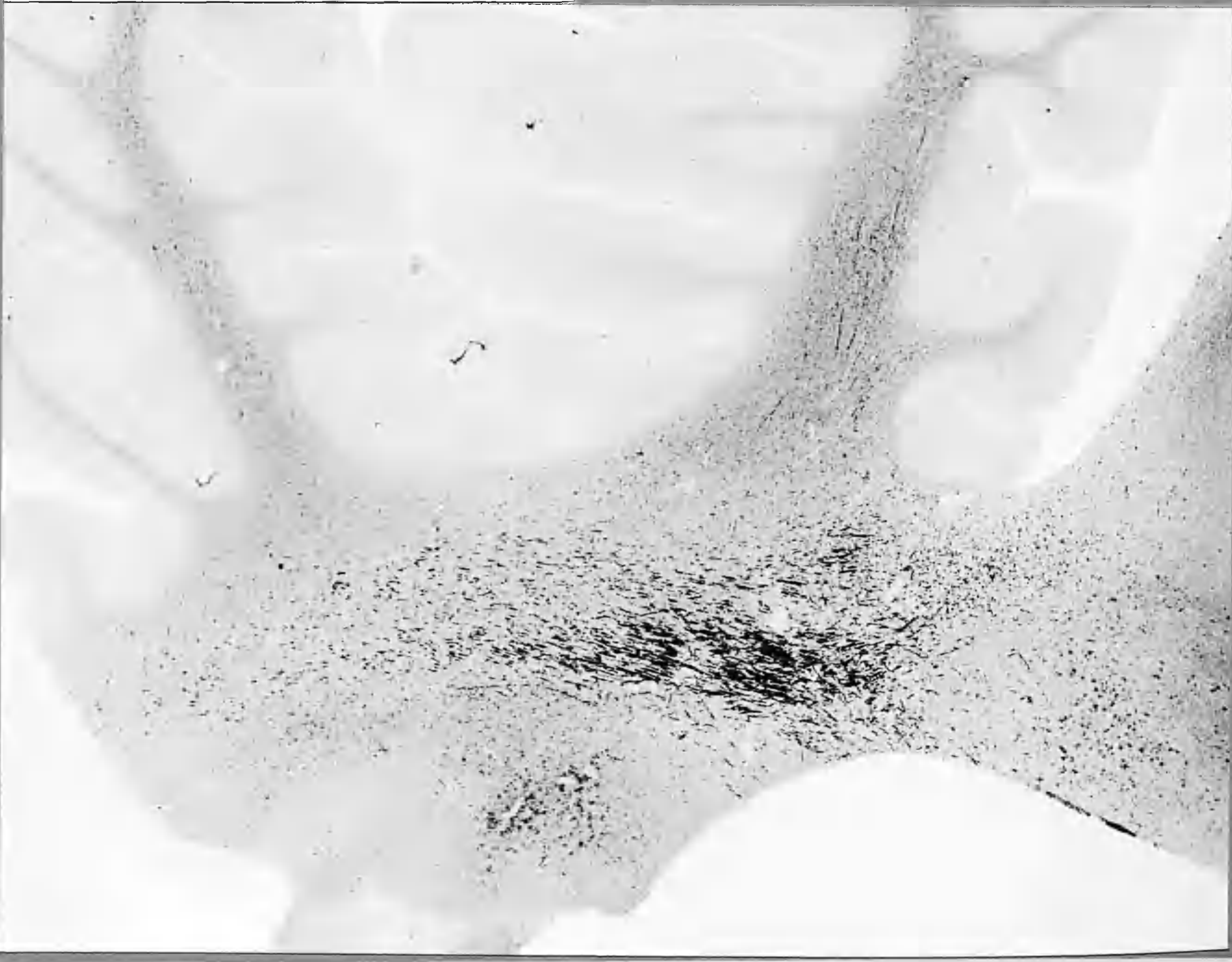


FIG 127 (CASE 9)

B



As the fibres which enter the restiform body form a dorsal group in the medulla, and those which enter the brachium conjunctivum form a ventral group, they will be referred to as "dorsal" and "ventral" fibres in the cerebellum, for convenience of description. No inference regarding their distribution in the cerebellum is intended by this term.

Figures 127 and 128 may be considered together. In Fig. 128 the section passes through the restiform body (R.B.), as it enters the cerebellum. There is a dark patch of pseudo-Marchi staining in the most caudal part of the restiform body (P.M.). Degenerating fibres, cut in longitudinal section, extend rostrally and dorsally from this pseudo-Marchi area, into the cerebellum. Here they lie in the caudal part of the central white matter, extending almost to the second large branch on the dorsal aspect, i.e. to the second lobule of the anterior semilunar nodule. The dentate nucleus lies dorso-caudally to these fibres. In Figure 127, which passes through the most lateral part of the restiform body, there are fewer fibres, in the same region.

A

RIGHT

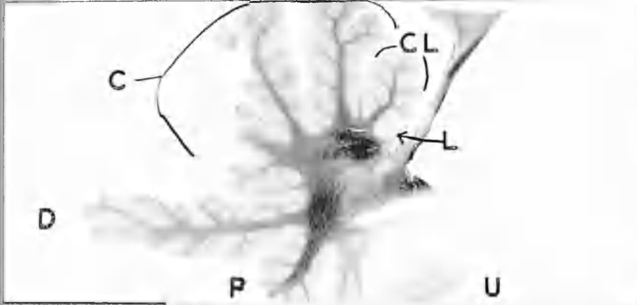
FIG 129 (CASE 9)

B

A very few degenerating fibres are present in the central white matter of the anterior semilunar lobule (Fig. 127) and of the biventral lobule (Fig. 128). No degenerating fibres were seen entering the dentate nucleus in any section.

In Figure 129, medial to the entrance of the restiform body, the dorsal fibres form a large mass in the ventro-rostral part of the central white matter of the cerebellum, immediately ventral to the main branch of the central lobule and of the most ventral lobule of the anterior semilunar lobule. The fibres are cut in transverse section, so it is clear that they are running in a latero-medial direction at this level. There are only few fibres in the white matter of the anterior lobe, and of the biventral lobule, mainly in the peripheral folia.

Figure 130 passes through the lateral part of the brachium conjunctivum, and the transitional zone between the vermis and the hemispheres of the cerebellum. The dorsal mass of fibres maintain the same relation, ventral to the ventral branches of the anterior lobe, as in the previous section.



A

RIGHT

FIG 130 (CASE 9)

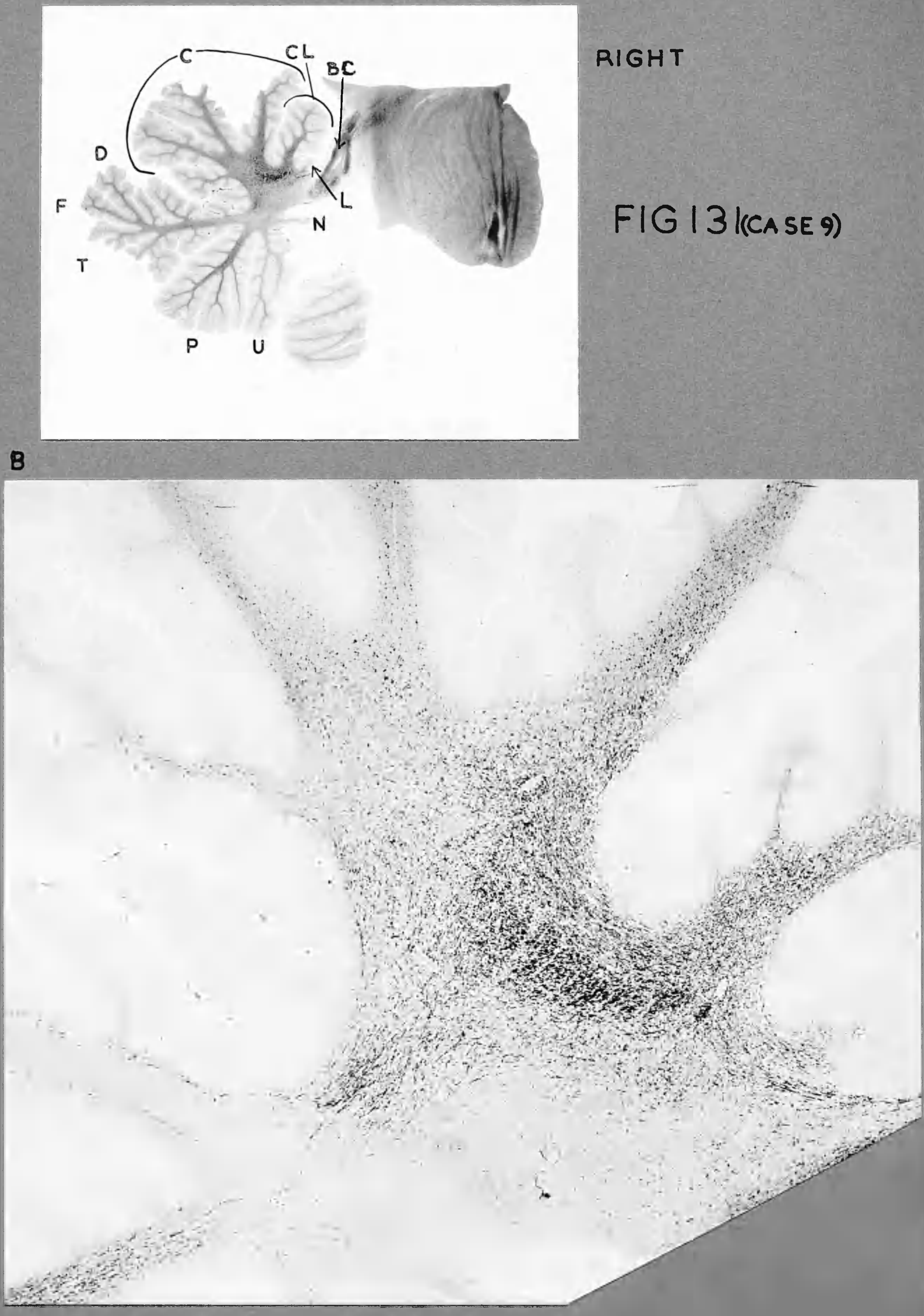
B

number of the fibres in the mass are now cut in oblique or longitudinal section, but the majority are still cut in transverse sections. A large number of fibres run in a caudal and slightly dorsal direction into the pyramis. These fibres pass the root nuclei on their dorsal aspect. In a series of sections through this region the continuity between the main mass of dorsal fibres and the fibres in the pyramis can be more clearly established.

A few black bodies are scattered in the branches of the anterior lobe and in the declive; some of these few granules may be genuine degenerating fibres cut in transverse section. No degenerating fibres were seen in the uvula nodulus or in the roof nuclei.

As the vermis is approached, the plane of section passes through a more foliated part of the cerebellum. The white matter is seen to be more divided into branches; in the more lateral planes of section, it forms a large central mass. Thus in sections 131-134 the white core of the culmen consists of a central stem, which gives origin to two main

A



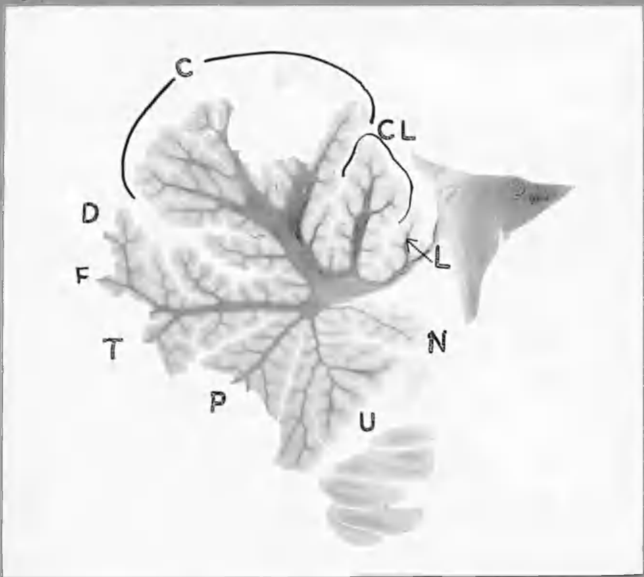
RIGHT

FIG 131 (CASE 9)

branches (Fig.132). In sections 128, 129 and 130, the white central core of the most ventral lobule of the anterior semilunar lobule meets the central core of the central lobule at an acute angle, so that the two branches of white matter form a V. In sections 131-134 these two central brnaches of white matter form a U; and as the sections come nearer the midline, the horizontal limb of the U becomes longer. With this spreading out of the white matter, the dorsal mass of degenerating fibres spread out along a wider zone than in previous sections.

In Figure 131 there are numerous degenerating fibres in the central lobule and in the ventral lobule of the culmen. In the zone between these two lobules there are many degenerating fibres cut longitudinally. Immediately caudal to this zone there is still a mass of fibres cut in transverse section. A few degenerating fibres also lie in the other lobules of the culmen. At the base of the brachium there is a small group of "ventral" degenerating fibres cut in longitudinal section. It is not possible in any section to distinguish unerringly between the fibres from this small ventral

A



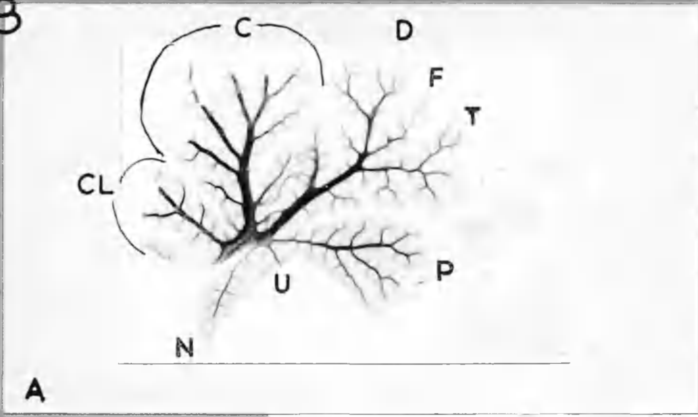
RIGHT

FIG 132 (CASE 9)

B

group, and those of the main "dorsal" group. Deductions as to the final destination of this small group from the brachium conjunctivum cannot therefore be made. A moderate number of fibres run in a dorso-caudal direction into the pyramis. A few fibres lie in the declive and a very few fibres in the folium and tuber; no degenerating fibres are present in the roof nuclei, nor in the uvula or nodulus.

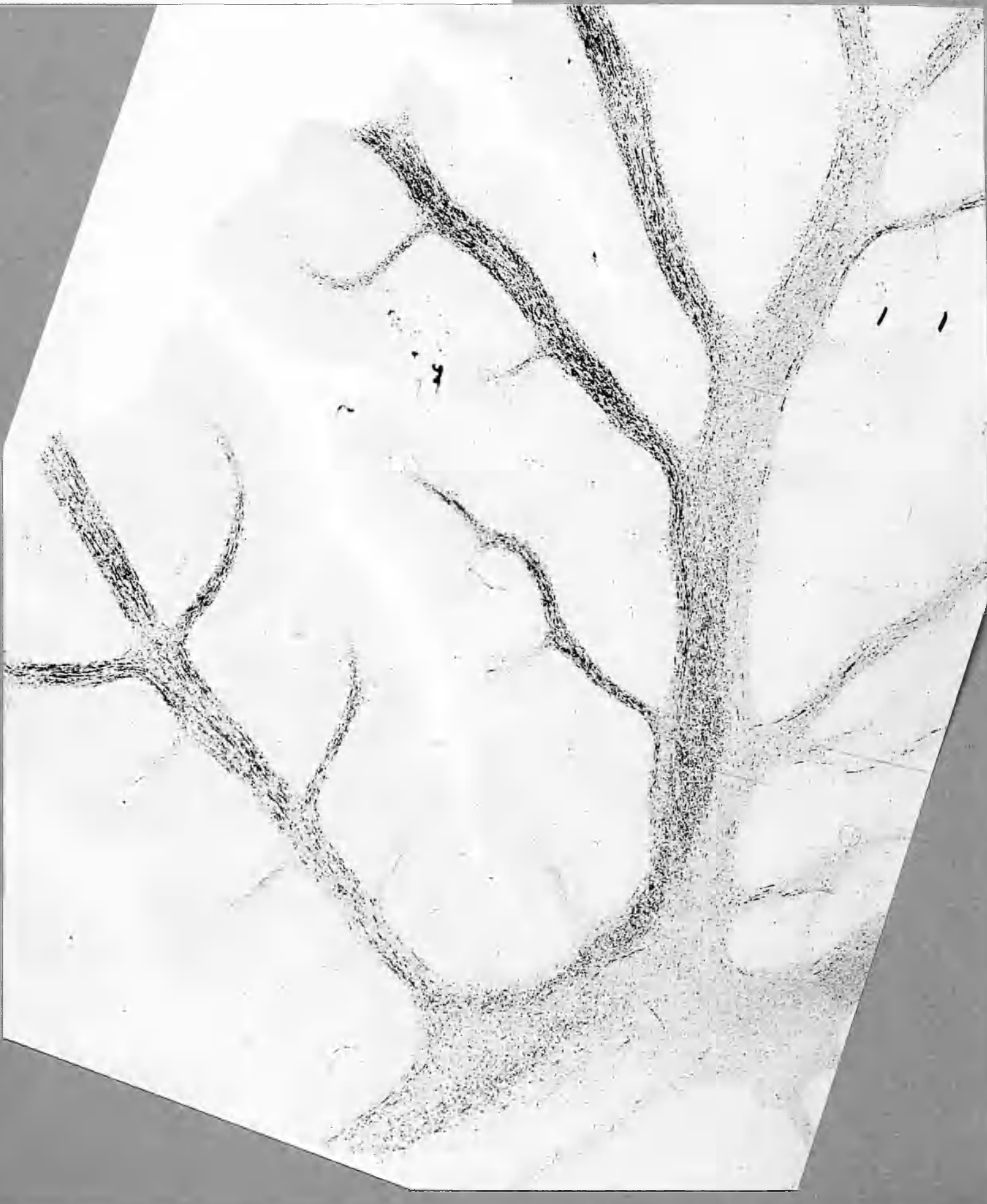
In Figure 132 the section approaches the midline of the vermis. In this section the ventral group of fibres are present in the brachium conjunctivum. They form a small definite group of fibres which divides into two - a rostral and a caudal part. The more rostral part can be traced to the region between the lingula and the central lobule, where they cannot be distinguished among the rest of the degenerating fibres. The more caudal part runs into the substance of the fastigial nucleus, and a few fibres can also be seen in more lateral sections, in the emboliform nucleus. Whether these fibres actually end in these nuclei, or merely pass through them on their way to the pyramis could not definitely be decided.



MIDLINE

FIG 133(CASE 9)

B



In this section, the degenerating fibres are almost completely confined to the anterior lobe. They are very numerous in the lingula, the central lobule and the culmen. In Figure 132 the culmen is seen to be in the form of a Y. The degenerating fibres are much more numerous in the ventral half of the common stem of the Y and of the ventral branch. In this region the more dorsal and caudal fibres are cut in transverse section, the rest are cut in longitudinal, oblique and in transverse section - all intermingled.

Some degenerating fibres are also present in the other branches of the culmen; a very few fibres are in the declive; no degenerating fibres are in the uvula or the nodulus. A few degenerating fibres are present in the more ventral part of the fastigial nucleus.

Figure 133 is from a section through the midline of the vermis. The distribution of the degenerating fibres in this section is very similar to that in the previous section, the fibres being rather less numerous at this level.

Figure 134 is a section slightly to the left of the midline. There are slightly fewer

69

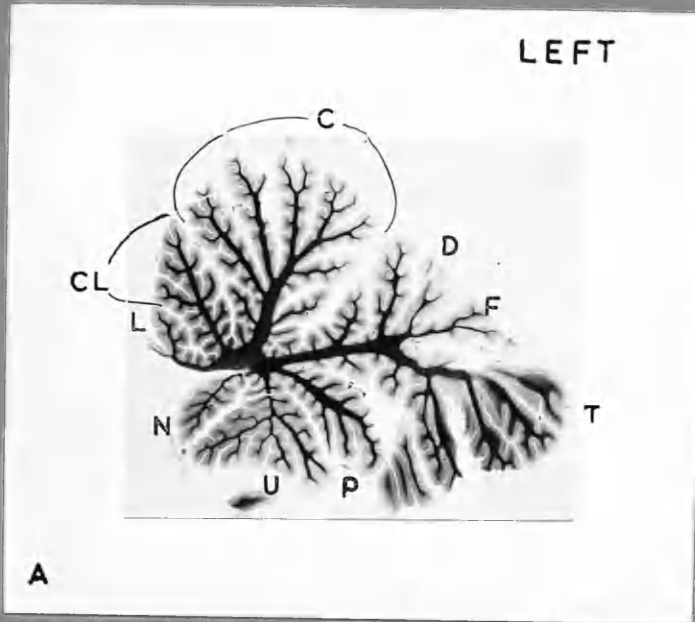
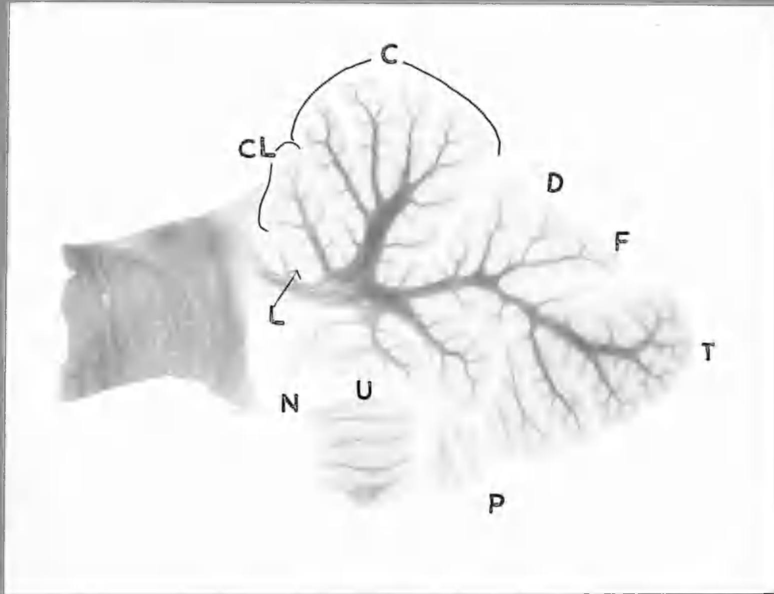


FIG 134 (CASE 9)

B



LEFT

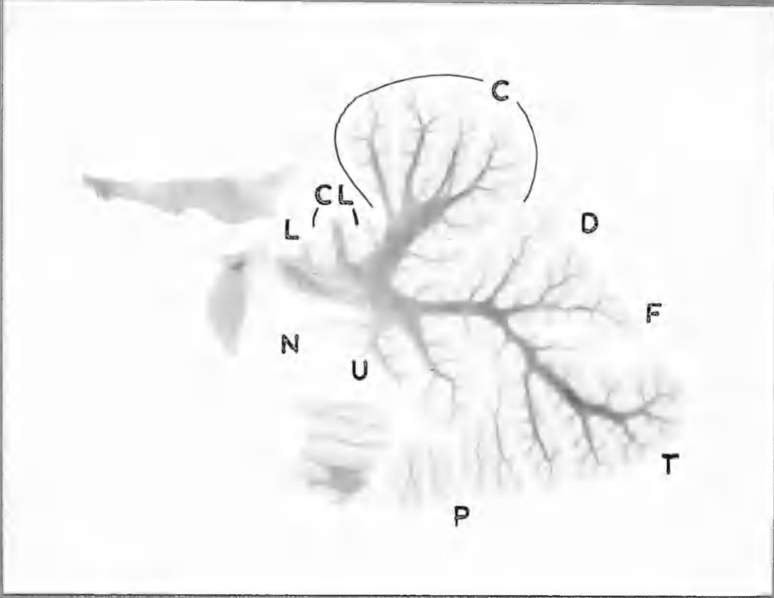
FIG 135 (CASE 9)

B

fibres than in the midline section, and they are in a comparable distribution to those in Fig.132. It is to be noted that some clear degeneration is present in the superior medullary velum, and in the lingula, as well as in the central lobule and the culmen, mainly in its ventral part. In Figures 132, 133 and in 134, most of the degenerating fibres in the branches of the culmen run longitudinally; dorsal and caudal to these fibres there is a long narrow branch of fibres mainly cut in transverse section; this branch continues along the base of the central lobule.

In Figures 135, 136 and 137 which pass through the root nuclei, there is rather more pseudo-Marchi and also dark staining of the normal fibres than in the previous sections; it is particularly marked in the fibres of the brachium conjunctivum. Caution is therefore required in interpretation of degeneration in these sections.

In Figures 135 and 136 there is a moderate number of degenerating fibres in the lingula, the central lobule and the culmen. In the culmen the fibres are more diffusely dispersed in the central white matter than in the previous section, although



LEFT

FIG 136 (CASE 9)

they are still more numerous in the branches of the ventral folia. Most of the fibres run longitudinally, and few are cut in transverse section. A moderate number of fibres forming a scattered grouppasses dorso-caudally from the base of the anterior lobe, dorsal to the roof nuclei, into the pyramis. These fibres can be seen to come from the region of the culmen, and also of the central lobule. There are one or two degenerating fibres in the declive; there are none in the nodulus or the uvula. A few fibres are present in the ventral part of the fastigial nucleus and in the emboliform nucleus, in the same distribution as on the right side. In the medial part of the central white matter, extending into the roof is a patch of pseudo-Marchi artefact (P.M.). It could not be decided whether any of these black staining bodies definitely represented degenerating fibres, most at least are artefact. Degenerating fibres are found in sections slightly more lateral to this section, in steadily decreasing numbers. None were found more laterally than the level of the medial aspect of the dentate nucleus. The number of fibres decussating, compared to those which terminate on the same side may be estimated as about 1 in 5.

From this case the following conclusions can be drawn. The majority of the spino-cerebellar fibres enter the cerebellum in the restiform body. They run in an oblique direction dorsally and rostrally to lie in the dorsal part of the white matter, immediately caudal to the ventral lobules of the anterior lobe, and rostral to the ventral part of the dentate nucleus. They then turn abruptly medially, remaining in a definite bundle of fibres, oval in transverse section; here they have the same relationship to the anterior lobe, being caudal to its anterior part. A very few fibres leave the main dorsal bundle of fibres at this level to enter the white matter of the anterior lobe, and of the biventral lobule. But until the lateral border of the emboliform nucleus, the number of fibres which leave the main bundle is very small. At this level a large number of fibres leave the main bundle and pass in a dorso-caudal direction into the most lateral part of the pyramis, which is the vermal "continuation" of the biventral lobule. The main dorsal bundle continues in a medial direction towards the midline.

From it fibres continually pass rostrally into the white matter of the anterior lobe. These fibres are distributed to the whole of the lingula, to the central lobule and the culmen; in the culmen they are distributed mainly to the ventral part. In the more lateral part of the anterior lobe these fibres in the folia run in all directions rostrally, medially, laterally and ventrally; in the more medial part, the majority of the fibres are directed rostrally, along the length of the lobula.

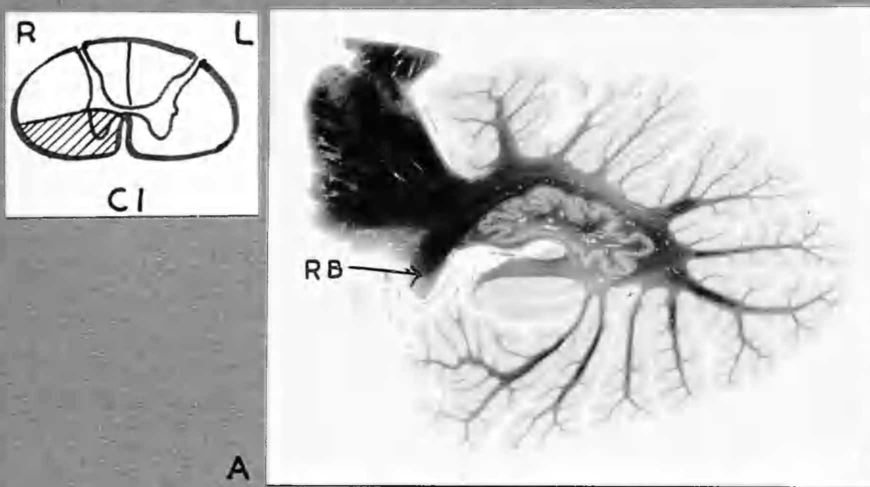
A small group of ventral fibres enters the cerebellum by way of the brachium conjunctivum. Most of the spino-cerebellar fibres coming in from this source immediately mingle with those from the restiform body, when fibres from the two peduncles meet. A few fibres pass into the substance of the fastigial nucleus, but whether they terminate there or continue to the pyramis has not been determined. Throughout, a very few fibres pass into the declive. Near the midline, very few fibres enter the pyramis. There are no spino-cerebellar fibres going to the uvula or the nodulus.

After the rostral fibres have run off into the anterior lobe, the band of fibres crosses the midline;

as it has lost so many fibres to the ipsilateral anterior lobe, it has become attenuated, and so it is rather a thin band when it reaches the contralateral lobe of the cerebellum. In the contralateral lobe, the distribution of the fibres is similar to that in the ipsilateral lobe going to the same parts of the anterior lobe and to the most lateral part of the pyramis. In addition to this main band of crossing fibres, a few fibres appear to cross in the superior medullary velum. They mingle with the main band of crossing fibres in the contralateral lobe. In this case, only a small contingent of degenerated fibres reached the cerebellum via the brachium conjunctivum; nearly all came in from the restiform body. It is therefore highly probably that every lobule of the anterior lobe and the pyramis and biventral lobule which contain degenerating fibres, has received a high proportion of them from the restiform body.

The question of the topographical distribution of the fibres arriving from these two sources - brachium conjunctivum and restiform body - will receive particular attention now, when subsidiary cases are examined.

RIGHT



A

FIG 137
(CASE 1)

B

A

RIGHT

FIG 138
(CASE I)

B

II. Cases Showing Particular Features.

(Plates 72-82).

In case 1, the unilateral operation, which was at the first cervical segment, was confined to the ventral quadrant of the cord.

The majority of the degenerating fibres entered the cerebellum via the brachium conjunctivum; only a minority entered via the restiform body. Thus the disposition of the fibres entering the cerebellum is exactly the opposite to that observed in the main case, case 9.

The most striking feature immediately apparent is the very much smaller number of degenerating fibres in the cerebellum in this case, than in case 9. In Figure 137, which passes through the restiform body where this body enters the cerebellum, a few degenerating fibres are seen in the restiform body. In Figure 138 degenerating fibres are scattered through the lateral part of the central white matter, and in the central lobule, the culmen,declive and pyramis; they are most numerous in the pyramis.

In Figure 139, the degenerating fibres entering the cerebellum along the dorsal aspect of the brachium conjunctivum are seen. In this section the fibres

RIGHT

A

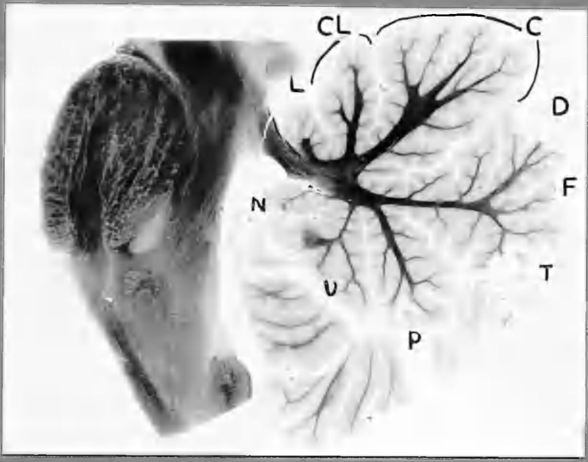


FIG 139
(CASE I)

B

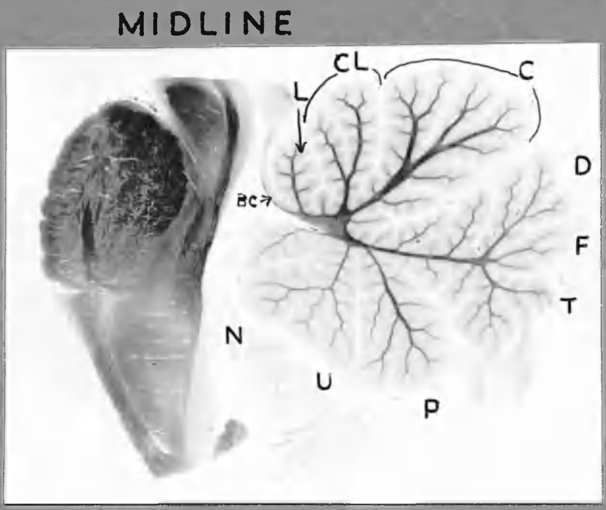
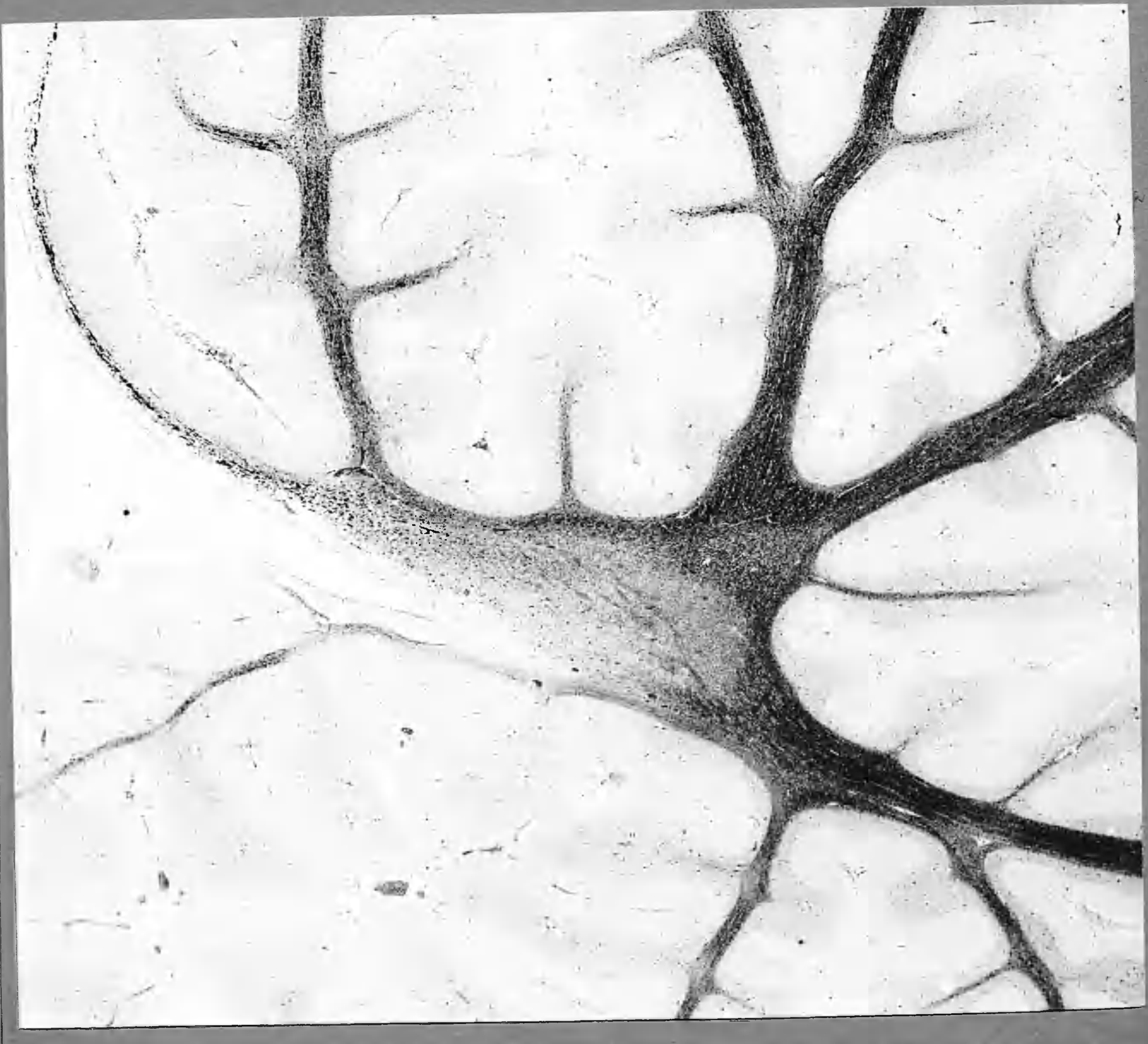


FIG 140
(CASE I)



A

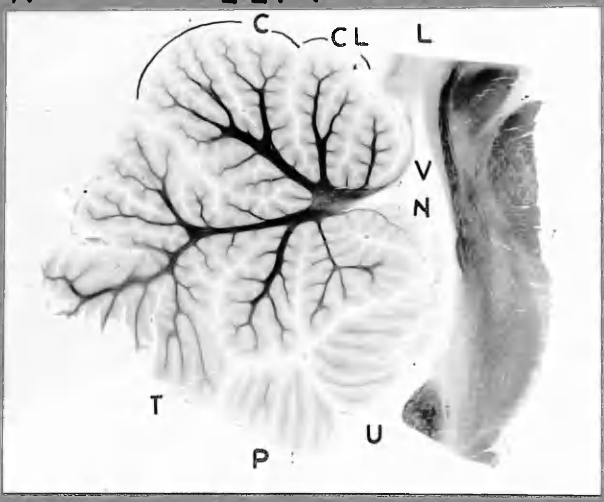


FIG 141
(CASE I)

B

are most numerous in the lingula, and in the distal part of the central lobule. A very few are present in the culmen, declive and pyramis. A few fibres pass from the group in the brachium conjunctivum into the substance of the fastigial nucleus, but whether they end there or continue to the pyramis could not be decided.

In Figure 140, which is very close to the midline, there are some degenerating fibres in the velum interpositum, and in the lingula, and a few fibres in the central lobule and the culmen. In the culmen the fibres are scattered equally throughout. In Figure 141, the section passes through the left side of the vermis. Some fibres are present in the velum interpositum and in the lingula; a few fibres are scattered throughout the ventral lobule and the culmen. In sections slightly more further to the left of the midline, a very few fibres are present in the declive and in the pyramis and in the fastigial nucleus. No degenerating fibres are found on the left side at levels corresponding to figures 137-139. No degenerating fibres are seen, in any section, in the dentate nucleus, nor in the uvula nor the nodulus. As a rough estimate the number of fibres in the contralateral side of the cerebellum in this case may amount to 1 in 10 of those distributed to the ipsilateral side.

From this case the following conclusion can be drawn. Fibres of the ventral group entering the cerebellum by the brachium conjunctivum are largely distributed to the anterior lobe. They terminate mainly on the side of entrance, about 1 in 10 fibres cross in the superior medullary velum to the opposite side. The fibres are most numerous in the lingula, and are sparser in the central lobule and in the culmen; they are scattered throughout the medial part of the culmen, and are not concentrated in any particular area. There are fewer fibres distributed in the central zone of the vermis than in planes slightly lateral to this. The fibres which cross to the contra-lateral side of the cerebellum are distributed in the vermis near the midline only. From this case it is also tentatively concluded that some fibres of the ventral group may terminate in the lateral part of the pyramis, almost entirely ipsilaterally. A few scattered fibres are also distributed to the posterior semilunar lobule, mainly ipsilaterally. A few fibres also pass into the substance of the ipsilateral fastigial nucleus; but it could not be

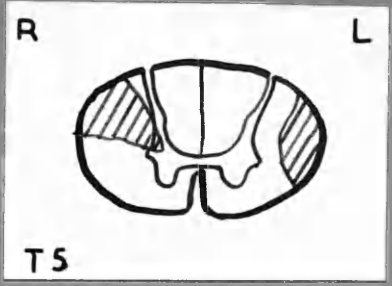


FIG 142 (CASE 27)

FIG 143 (CASE 28)

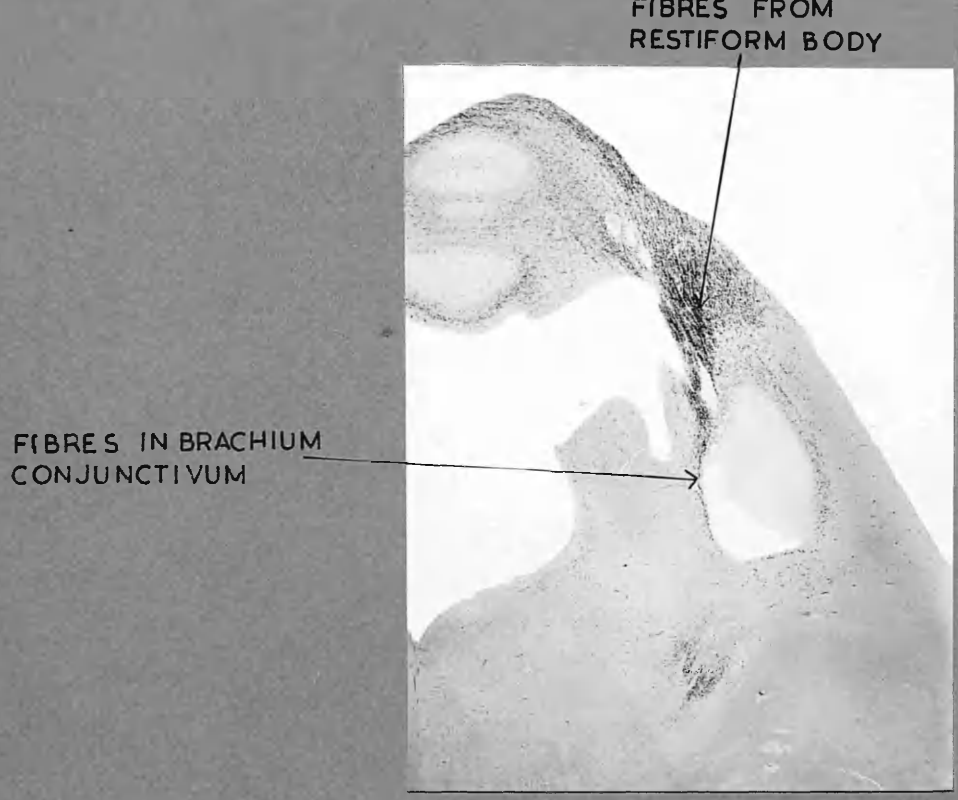


FIG 144 (CASE 28)

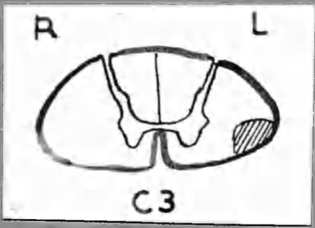
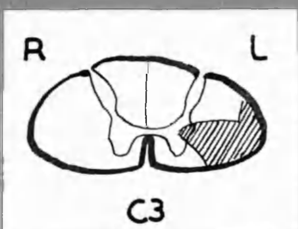


FIG 145 (CASE 7)

FIG 146 (CASE 7)

FIG 147
(CASE 5)



A

B

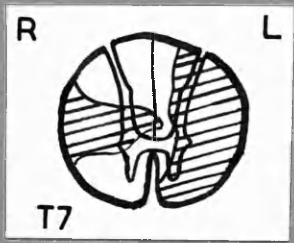
ascertained whether these fibres terminate in the nucleus or not.

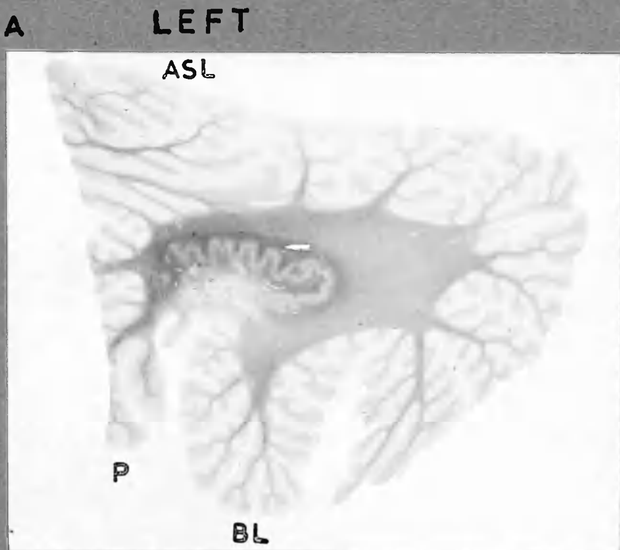
As case 1 is the only case in the series with more degeneration in the ventral fibres than in the dorsal fibres, deductions regarding the distribution of these ventral fibres must await confirmation in similar cases. Optimally, the evidence should be obtained from a case in which the lesion is confined to the ventral group of fibres only. In view of the very extensive distribution of dorsal spino-cerebellar fibres in the cord, such a case has not yet been obtained.

A few sections from other cases are now shown to illustrate certain features.

Figure 142 (case 27) and figures 143 and 144 (case 28) show the difficulty of distinguishing, in horizontal sections, between the fibres of the dorsal and the fibres of the ventral groups after they have entered the white matter of the cerebellum.

Figure 145 and 146 (case 7) and Figure 147 (case 5) show the preponderance of fibres in the ipsilateral side of the anterior lobe in a case with a unilateral lesion. The majority of the fibres lie slightly lateral to the midline.





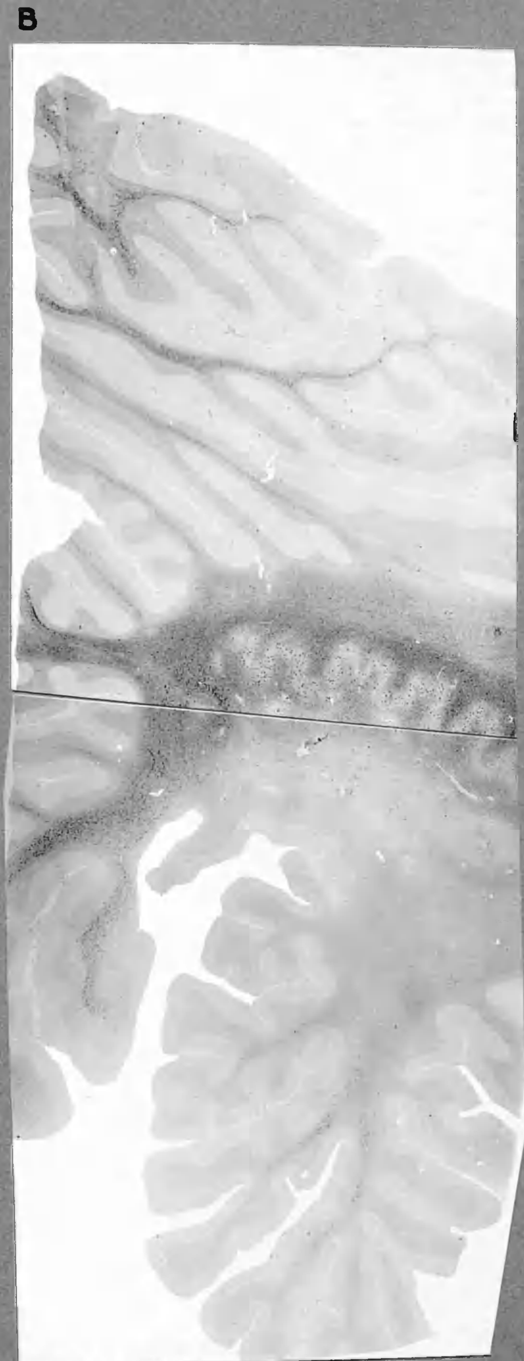


FIG 148(CASE 30)

Figure 148 (case 30) shows the presence of degenerating fibres in the folia of the anterior lobe, the pyramis and the biventral lobule, in sections from oblique series. Degenerating fibres may be found in the peripheral folia, even when no degenerating fibres are found in the main stem. Thus it is seen that a few fibres extend laterally into the peripheral folia of the hemispheres.

The next point to be considered is whether there is any difference in the distribution of the degenerating fibres with regard to the situation of the lesion, in particular, when in relation to its rostro-caudal, and its dorso-ventral position. For this purpose cases with a variety of lesions have been selected. The main distribution of the degenerating fibres is shown on diagrams Figure 149. In some of these cases, certain parts of the vermis were not examined by the Marchi method. Hence, conclusions concerning degenerating fibres in these blocks could not be drawn.

It will be seen that degenerating fibres are present in the same lobules of the cerebellum in every case. This is so whether the lesion was made in the first lumbar segment (case 34), in a thoracic segment

FIG 149

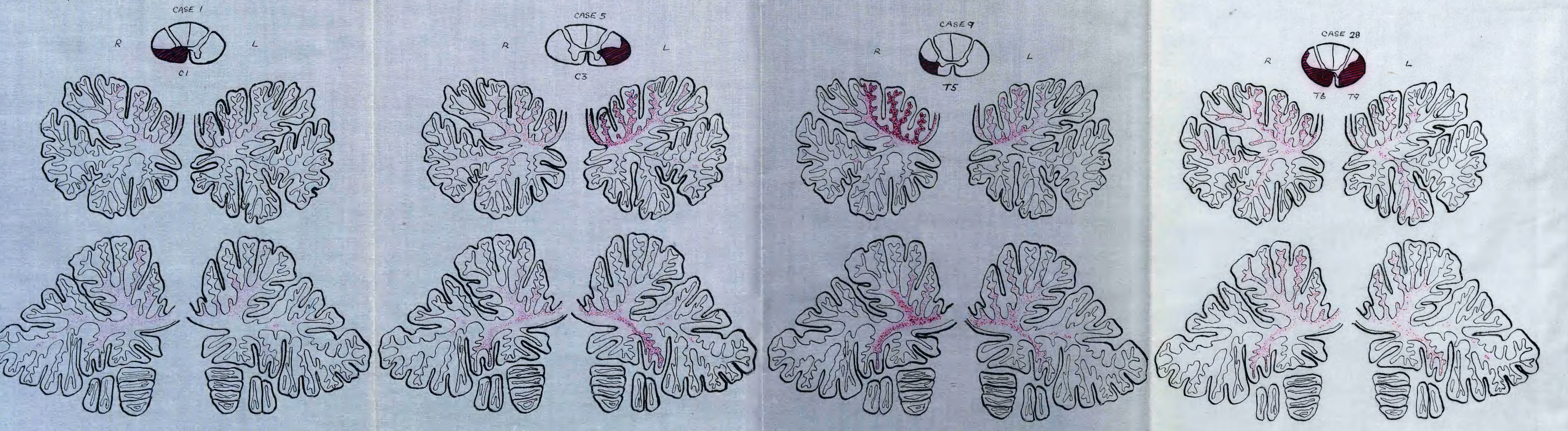
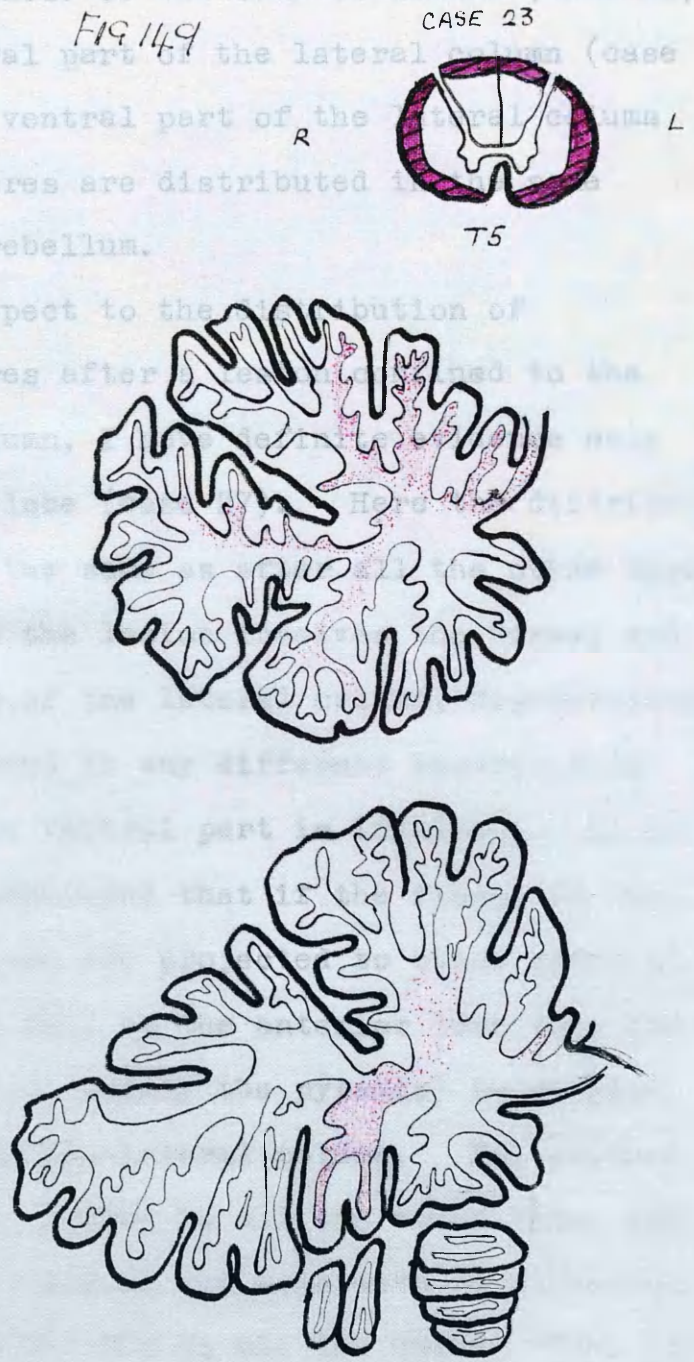
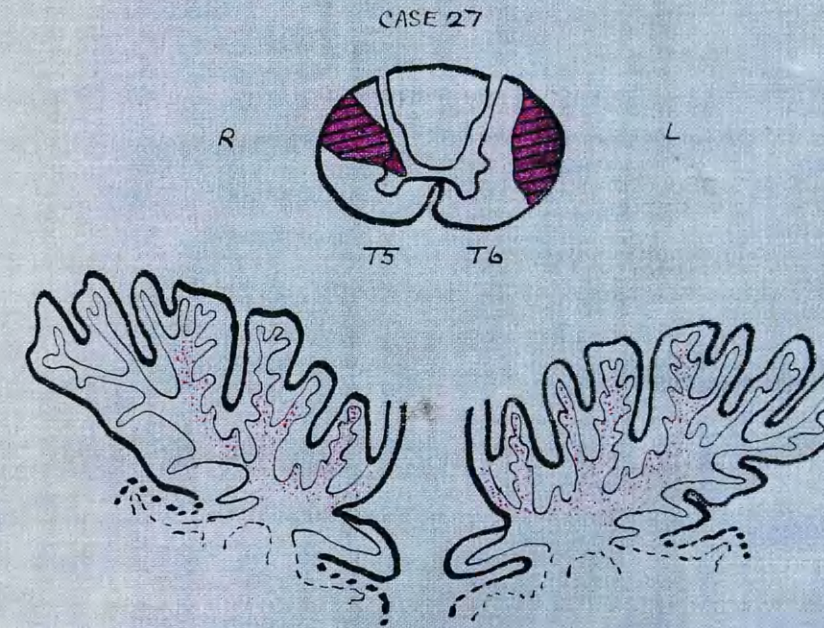
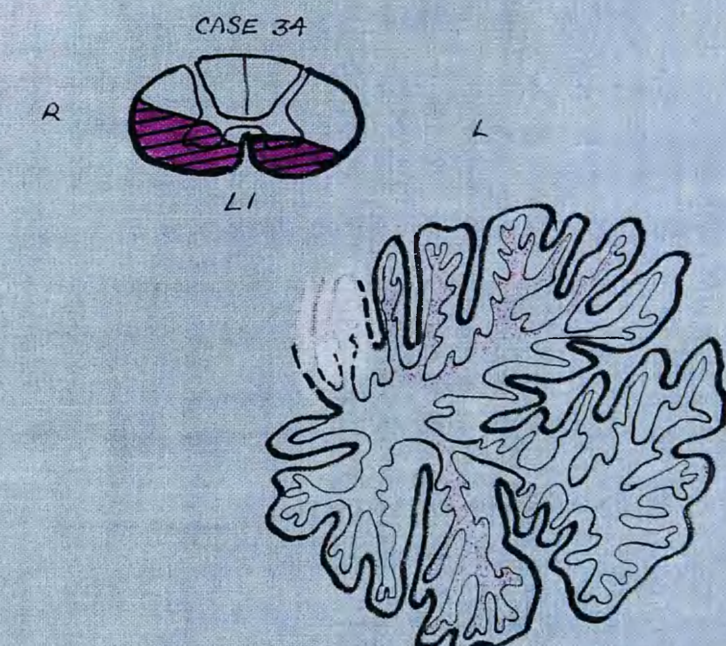


FIG 149







(case 9), or in an upper cervical segment (cases 1 and 5). Similarly, whether the lesion affected practically the whole of the lateral column (case 28), only the peripheral part of the lateral column (case 23), or only the ventral part of the lateral column (case 9), the fibres are distributed in the same region of the cerebellum.

With respect to the distribution of degenerating fibres after a lesion confined to the dorso-lateral column, I have definite evidence only for the anterior lobe (case 27). Here the distribution of the fibres is the same as after all the other types of lesion. When the lesion involves the dorsal and the ventral parts of the lateral column, degenerating fibres are not found in any different distribution than when only the ventral part is involved. So at least it can be concluded that if the fibres in the dorso-lateral column are projected to other parts of the cerebellum as well as the anterior lobe they are the same parts (i.e. mainly the pyramis) as receive fibres from the ventro-lateral column. Not evident in these diagrams, common to all the cases are: one, that the lateral limit of the main mass of degeneration is approximately the same in all the cases; two, there are some degenerating fibres in the biventral lobule, and a few degenerating fibres in the declive, folium and tuber, and lateral hemispheres.

Certain precautions in interpreting the results are necessary, on account of the periods of survival varying in the different cases; hence the picture of degeneration might be different in some of the cases had the patients not survived so long. Were all the cases identical in post-operative survival periods then they could, of course, be strictly comparable. Nevertheless, certain conclusions are permissible.

To sum up, the great majority of the long spino-cerebellar fibres enter the cerebellum by the restiform body, and a minority by the brachium conjunctivum. Fibres which lay in the ventral, the peripheral or the dorsal part of the cord are all distributed within the same parts of the cerebellum. The majority terminate in the anterior lobe, mostly in the medial part, and in the lateral part of the pyramis and the most medial part of the biventral lobule; a small minority terminate in the declive, folium tuber and in the middle lobe of the cerebellum. The majority of the fibres are ipsilateral in distribution, about 1 in 5 - 10 are distributed contralaterally.

No difference was found from case to case in the proportion of fibres distributed to the vermis lobules, when the great majority of the fibres entered the cerebellum via the restiform body. Only one case was collected where the majority of the fibres entered the cerebellum via the brachium conjunctivum. In this case there were more degenerating fibres in the lingula than in the other lobules, and in all the lobules containing degenerating fibres these did not extend so far laterally as when there are many degenerating fibres entering the cerebellum by the restiform body. It is clear that further evidence on the actual progress and distribution of the fibres can only be obtained from cases having strictly comparable survival periods. The evidence however, of these 7 cases and of the 13 other cases examined (not presented in detail here), indicates that the spino-cerebellar fibres , whatever position they occupy in the spinal cord, entering the cerebellum via the restiform body, are distributed throughout the lobules enumerated above.

CHAPTER XI

CELL GROUPS SHOWING RETROGRADE CHANGES

The purpose of this part of the work is to determine which cells in the spinal cord show changes attributable to transection of their axons. It is hoped that by correlating a sufficiently large number of varying lesions, made at various periods before the patients' deaths, the origin of the different groups of ascending fibres will eventually be made clear.

The cells have been considered in seven groups: cells of Clarke's column (nucleus dorsalis); apical cells of the dorsal horn (cellulae posteromarginales); cells of the substantia gelatinosa; cells of the nucleus proprius; cells at base of dorsal horn and in intermediate grey matter; cells of the ventral horn; cells of the lateral horn. The findings in these cell groups are presented at the end of this section in condensed form in Table 3. A selection of the material will be presented with photographs.

In illustrating these retrograde changes in cells, the point has been to show any changes in

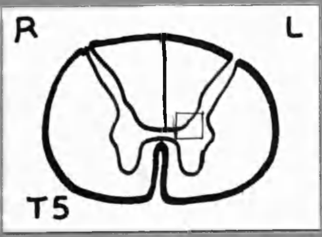
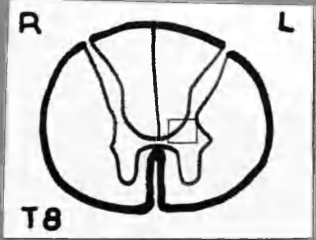


FIG 150



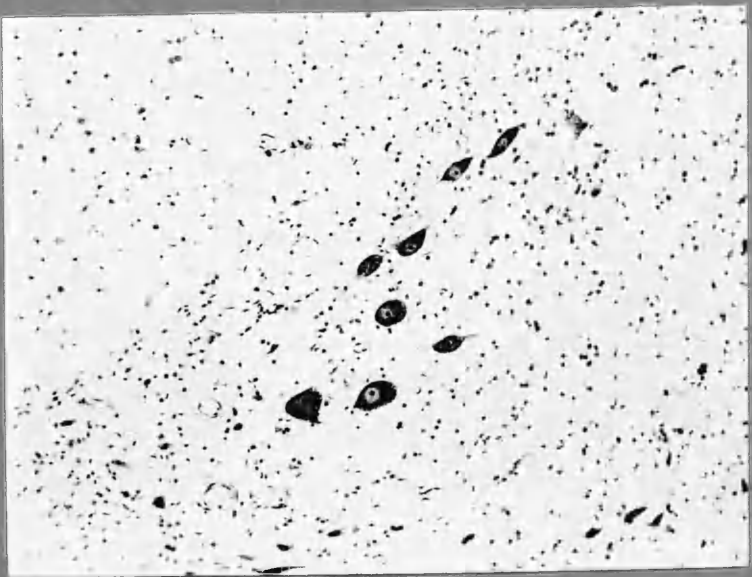


FIG 151

groups of cells. Low power photographs only are given. The fine details of cytology are not mentioned. For, from the point of view of determination of the cells of origin of degenerating fibres - which is the only point of view which interests us here - the question is the simple one: are these cells affected by the lesion or not.

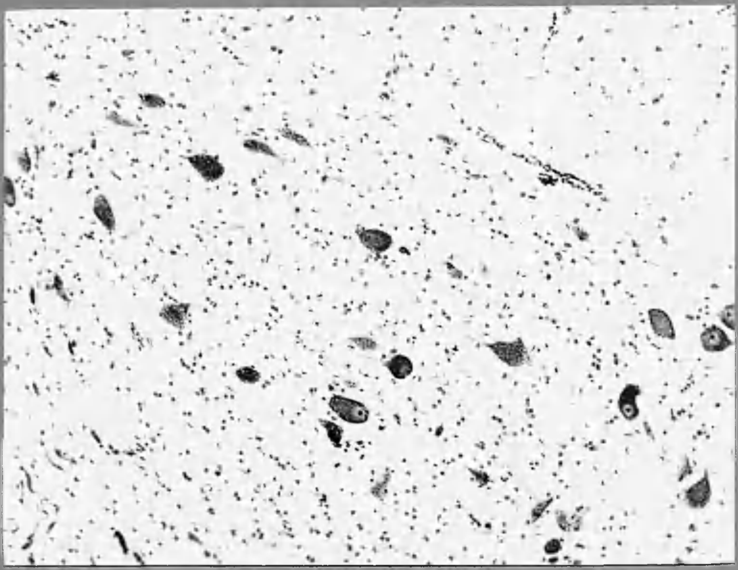
The cord level and the extent of the lesion are shown in small diagrams for each case. In all groups except Clarke's column the area in the cord shown in the photograph is also indicated in a diagram. This has not been done in the case of Clarke's column as the site of this nucleus is constant.

In the discussion of each of these cases the period of survival, measured in days, is given after the figure number.

I. Cells of Clarke's Column. (Plates 83-96).

a) Normal cells. (Figs.150, 151 and 152).

As there is some discrepancy in different textbooks as to the distribution of the cells of Clarke's column, personal observations on this point are given here. The upper limit of the column is usually at the first thoracic segment, but it is



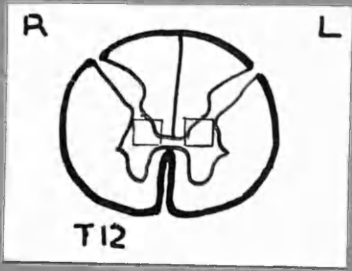


FIG 152

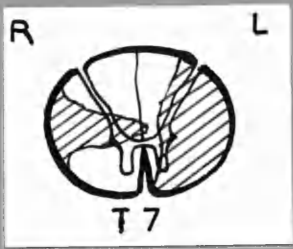
occasionally at the eighth cervical segment; the lower limit is at the first or second lumbar segments, or occasionally at the third lumbar. A few cells, similar to those of Clarke's column in appearance and site, are occasionally seen in the cervical and lumbo-sacral segments. The cells of Clarke's column are sparse in distribution from the first to the sixth thoracic segments; in normal cords the numbers may vary, in a transverse section, from 0-8 in each Clarke's column. From the seventh to the ninth thoracic segments there are usually more numerous cells in both Clarke's column in each section, most frequently 4-10, but sometimes no Clarke's column cell is present. From the tenth thoracic to the first lumbar segment Clarke's column is larger, containing 10 to 20 cells. In some cords no Clarke's column cells are seen below the first lumbar segment, in others numerous cells are present in the second lumbar segment, and there may be even a few in the third lumbar segment. The cells of Clarke's column are much larger in the lower thoracic and lumbar segments than in the middle and upper thoracic segments. In the normal cord the cells have, as is well known, an appearance which might in motor cells suggest chromatolysis. The cell is of vesicular appearance, the nucleus is frequently placed excentrically in the cell, the nucleus is excentric, and the Nissl granules tend to be confined to the periphery.

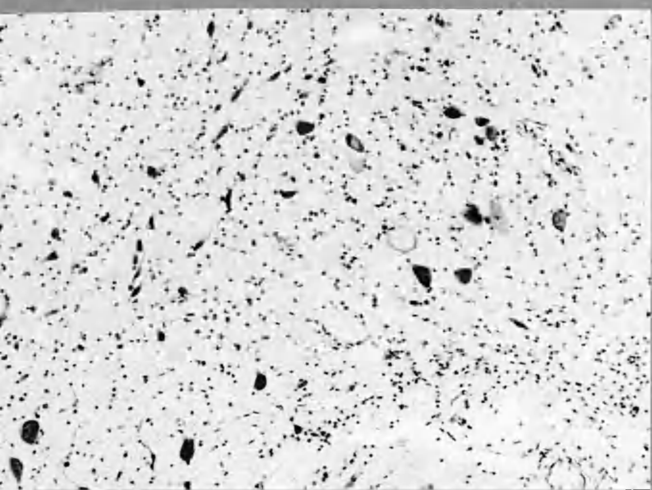
b) <u>Axonal reactions in cells</u>.

Chromatolysis of the cells of Clarke's column is characterised by ballooning of the cell, marked pallor and the disappearance of the Nissl substance. These changes make it clearly distinguishable from the normal cells.

Clarke's column cells appear to be particularly sensitive to damage of their axons; five days, or possibly sooner, after a lesion of their axons, marked chromatolysis of many of these cells may occur.

"Dropping-out" of Clarke's column cells, as shown in Table 3, may be well established by 39 days after a lesion. Thus in regions where there are normally very few of these cells it may be difficult to establish the loss of cells, unless examination of many sections from each segment is undertaken. Comparison of the two sides may likewise lead to error unless a smaller number of cells on one





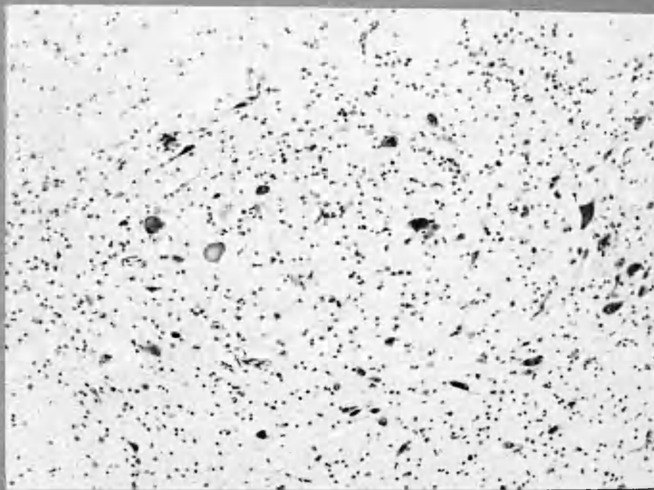
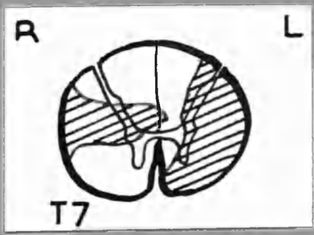


FIG 153 (CASE 30)



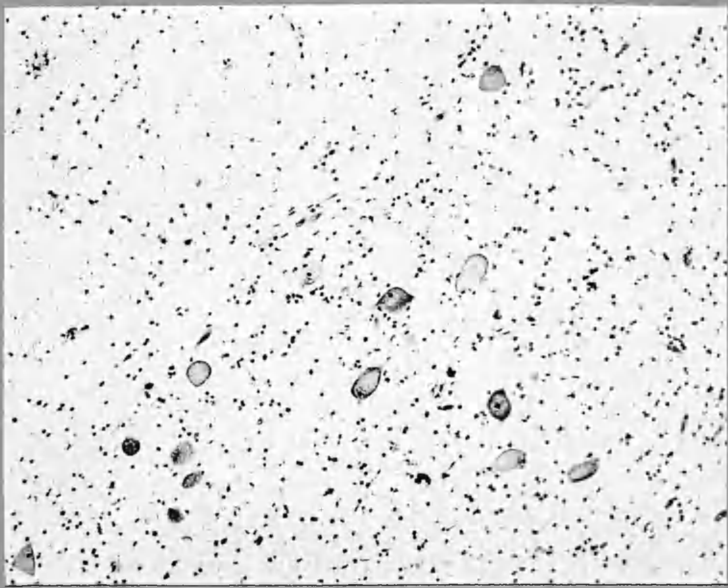
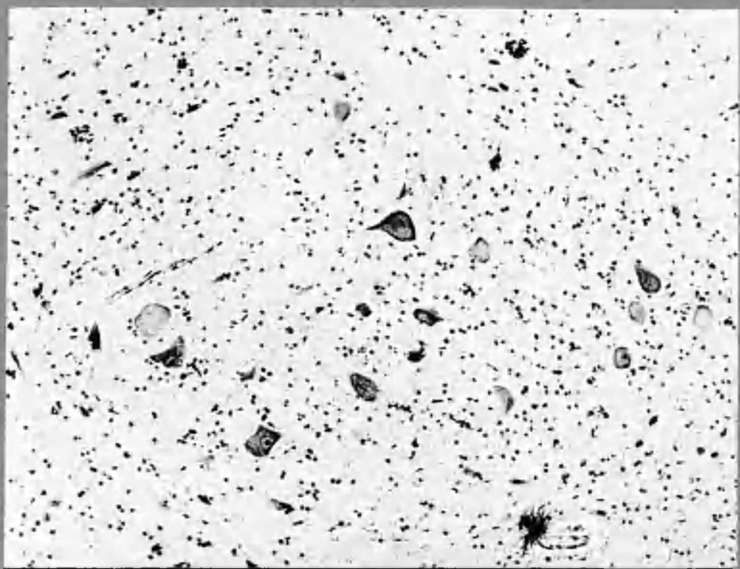


FIG 154 (CASE 30)



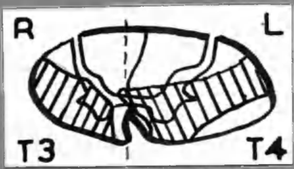


FIG 155 (CASE 17)

side is a consistent finding throughout a large number of sections.

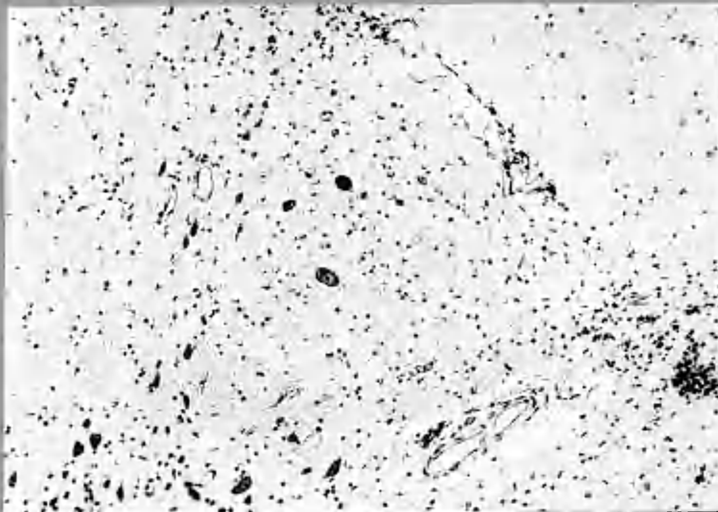
After a lesion of their axons some of the Clarke's column cells appear to persist indefinitely in a pale-staining ghost form, without nuclei. Other cells persist in a shrunken dark-staining pyknotic state.

Extensive bilateral lesions of the dorso-lateral and ventro-lateral columns.

Case 30: Figs.153 and 154 (23 days). In this case there are changes in Clarke's column cells at all levels caudal to the lesion. Many cells are chromatolytic, others are pyknotic; rosettes of glia are also present.

Case 17: Fig.155 (390 days). In this case there is a great loss of cells in Clarke's column of both sides, most marked on the right. Some cells persist, mostly in a rather shrunken state.

These two cases serve to illustrate the general finding that when there is an extensive bilateral lesion of the dorso-lateral and the ventro-lateral columns, many Clarke's column cells caudal to the lesion at first show chromatolytic changes, and at later stages many disappear.



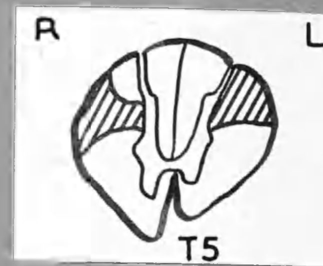
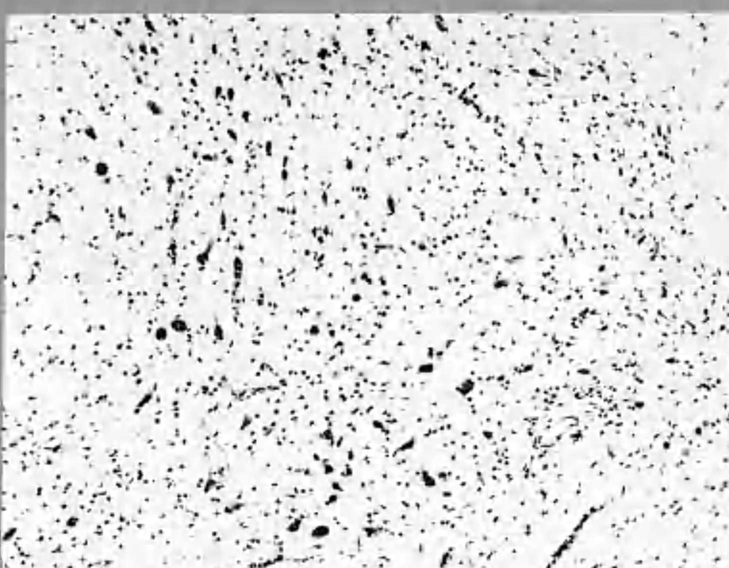
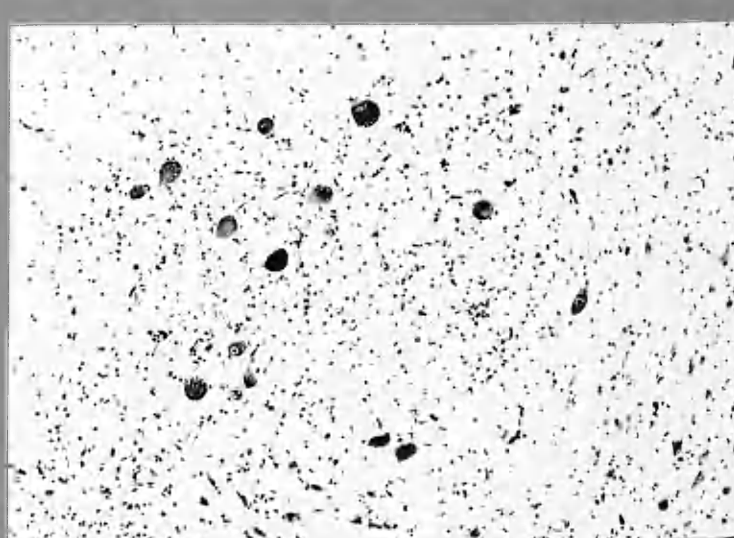
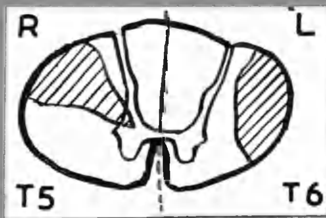


FIG 156 (CASE 26)







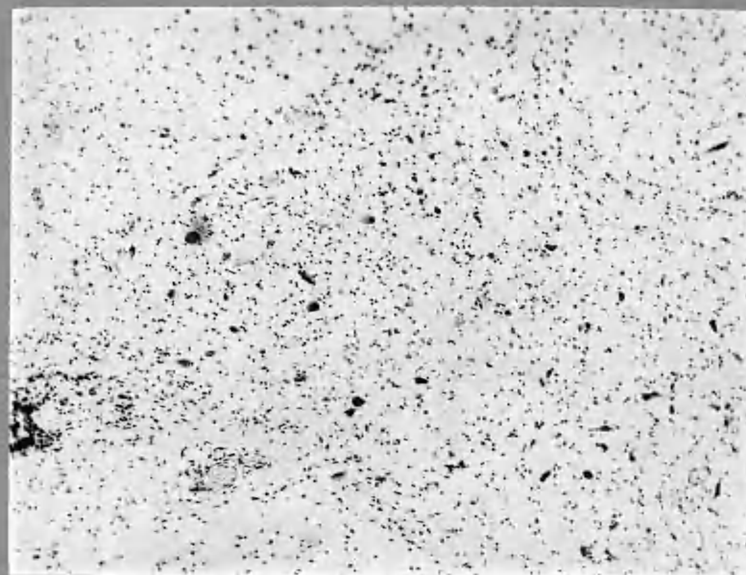
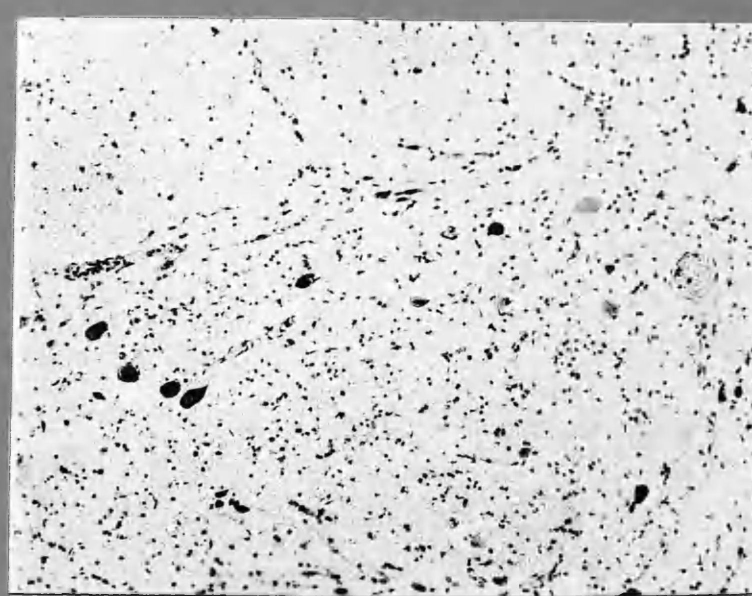
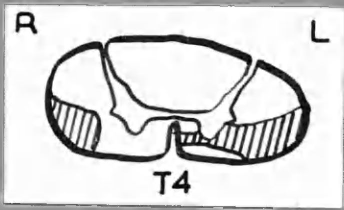


FIG 157 (CASE 27)





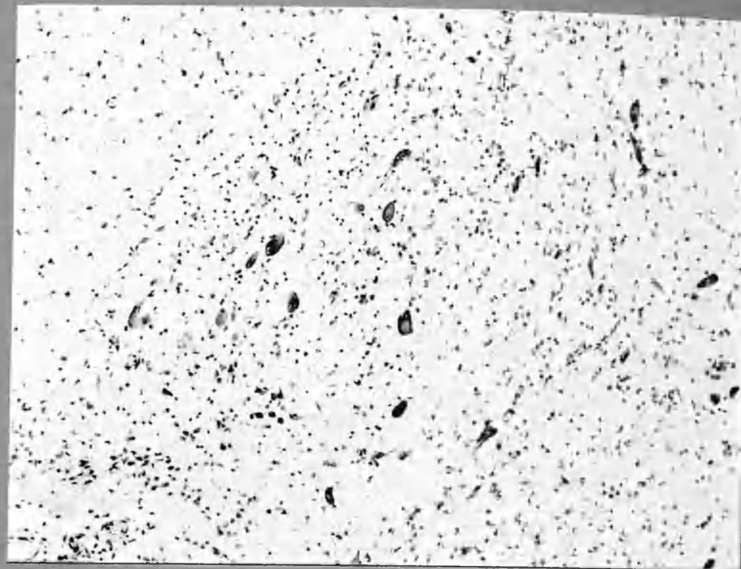
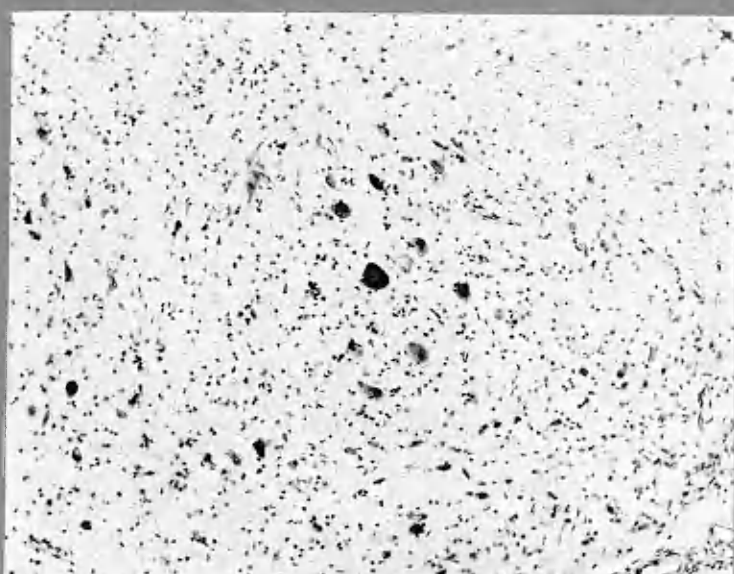
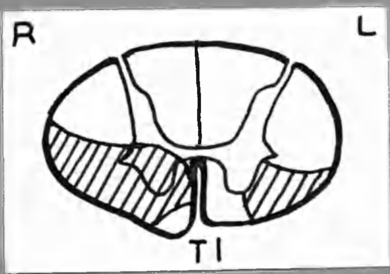


FIG 158 (CASE 18)





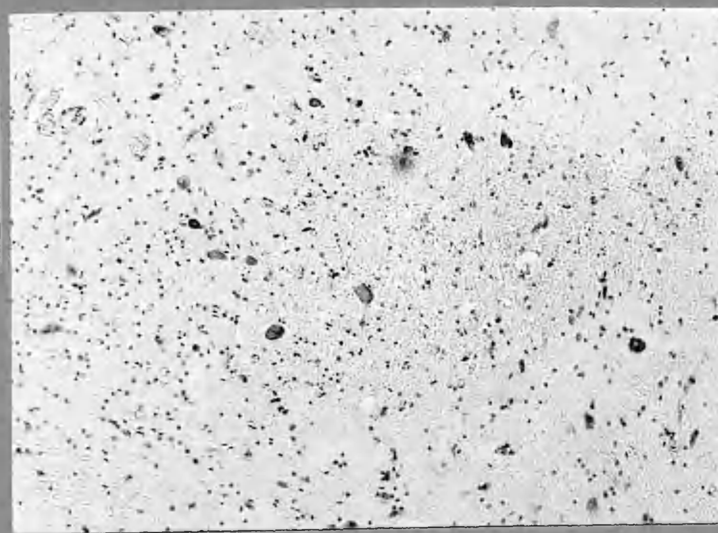
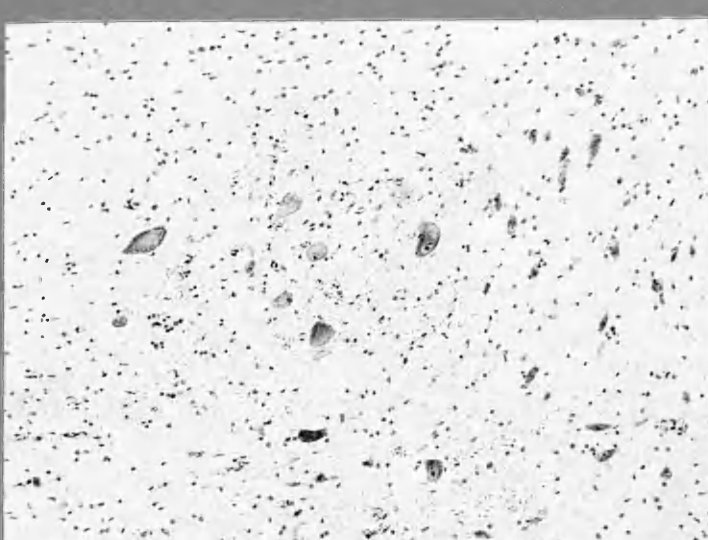


FIG 159 (CASE 13)



<u>Bilateral lesions of the dorso-lateral columns.</u>

Case 26: Fig.156 (154 days). In this case there is a loss of cells in Clarke's column from immediately caudal to the lesion to its lowest level. This is most marked on the right side.

Case 27: Fig.157 (42 days). In this case there is marked bilateral cell loss and gliosis in Clarke's column at all levels caudal to the lesion.

These two cases serve to illustrate the general finding that if there is a bilateral lesion of the dorsolateral columns many Clarke's column cells in the segment containing the lesion and at all levels caudal to the lesion show reactive changes.

<u>Bilateral lesions of the ventro-lateral columns.</u>

Case 18: Fig.158 (66 days). In this case there is bilateral loss of Clarke's column cells, some shrunken pyknotic cells, and an increase of glial cells at all levels caudal to the lesion.

Case 13: Fig.159 (159 days). In this case there is a marked bilateral loss of Clarke's column cells at all levels caudal to the lesion.

Case 22: Fig.160 (24 days). In this case the lesion on the left side mainly involved the ventro-lateral column; on the right the lesion

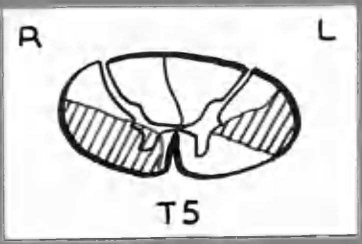
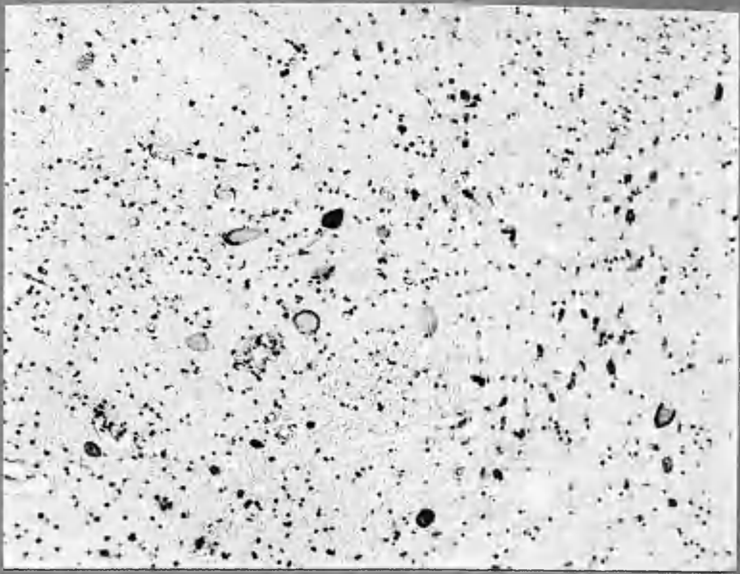
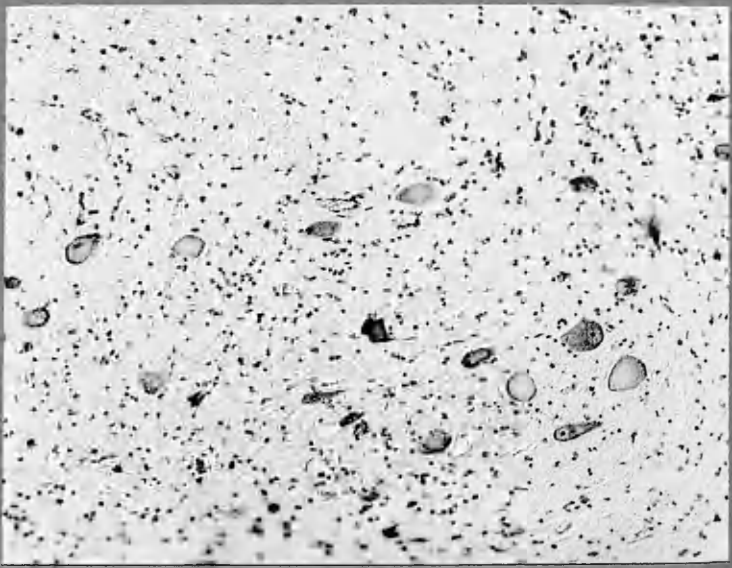
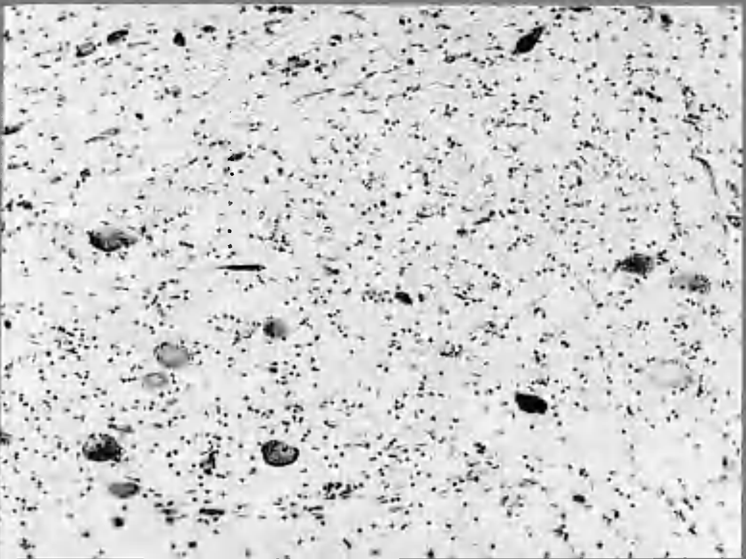
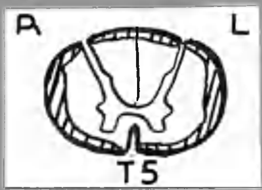


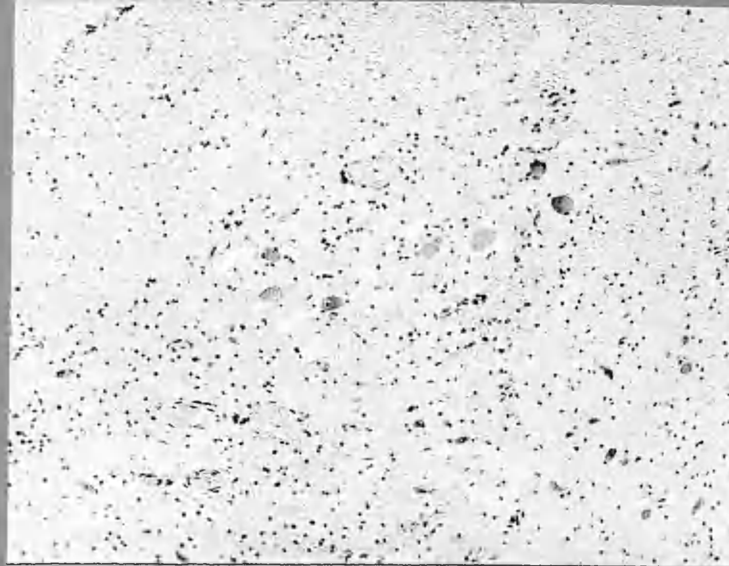
FIG 160(CASE 22)











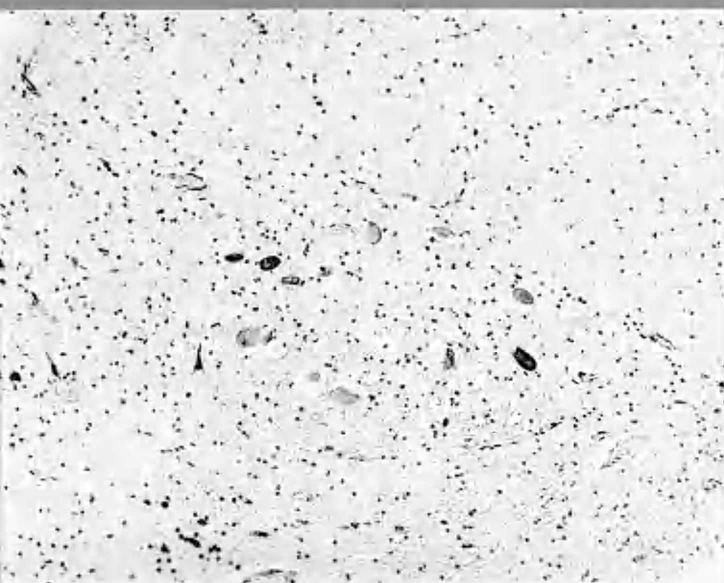
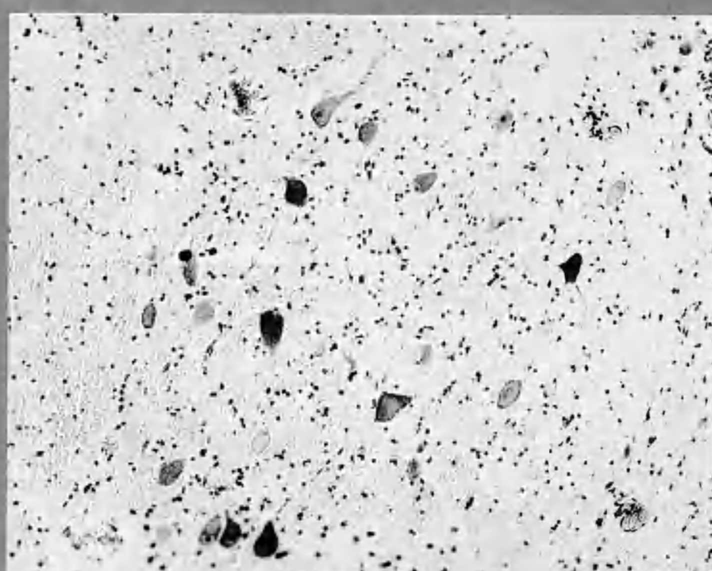


FIG 161 (CASE 23)



involved the ventro-lateral column and a considerable part of the dorso-lateral column as well. At all levels caudal to the lesion many Clarke's column cells on both sides are chromatolytic, and there is an increase of glia in the column; it is possible that there is also a reduction in the total number of cells.

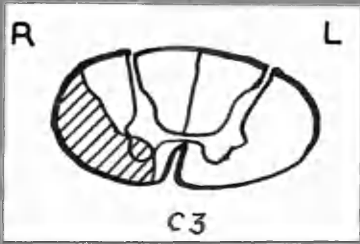
These three cases serve to illustrate the general finding that if there is a lesion of the ventro-lateral column, many cells of Clarke's column caudal to the lesion exhibit reactive changes.

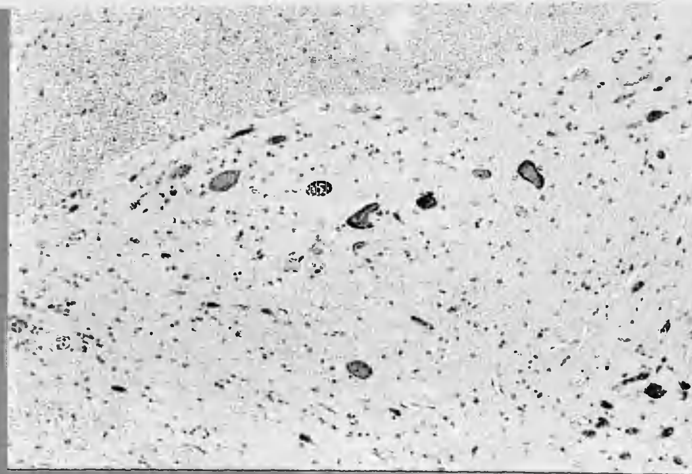
Whether the lesions involved the dorso-lateral column or the ventro-lateral column, no difference could be seen in the distribution of the altered cells or of the areas of cell loss.

Superficial bilateral lesions of the ventro-lateral and the dorso-lateral columns.

Case 23: Fig.161 (39 days). In this case the lesion was extensive bilaterally, but was confined to the periphery of the cord. Many of the cells in Clarke's column caudal to the lesion have degenerated to "ghost" forms, and a few cells are chromatolytic.

This case serves to illustrate that if there





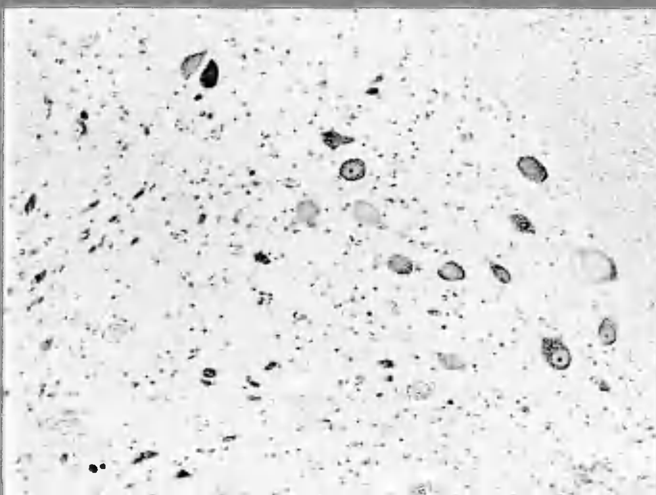
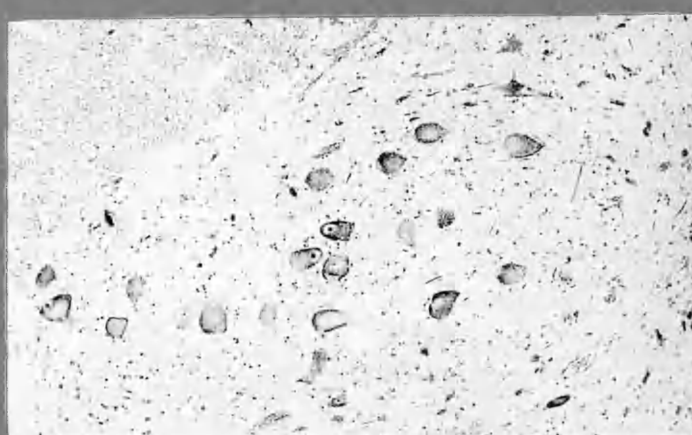
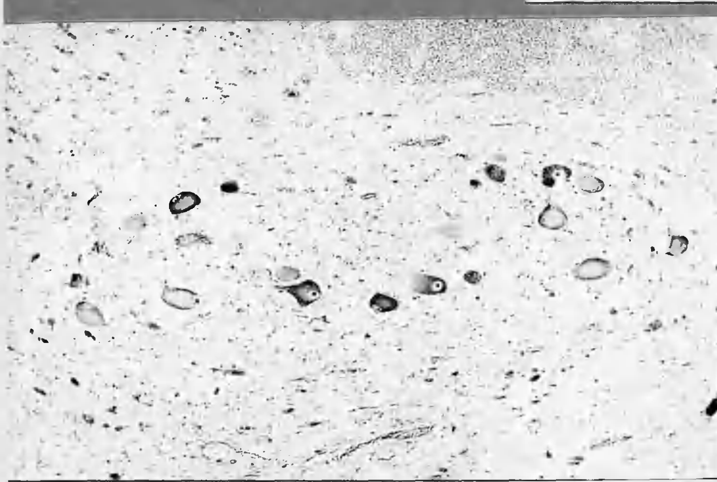


FIG 162 (CASE 4)





is a lesion of the periphery of the dorso-lateral and ventro-lateral columns, many cells of Clarke's column caudal to the lesion show reactive changes.

All the cases considered so far had bilateral lesions, and so no evidence is forthcoming from these cases whether the cells of one side are showing changes because of injury to the ipsilateral or to the contralateral tracts.

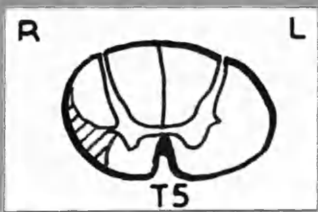
In the following three cases the cordotomy was unilateral.

Unilateral lesion of both the dorso-lateral and the ventro-lateral column.

Case 4: Fig.162 (5 days). In this case the lesion was made at the third cervical segment, only five days before death. Chromatolysis is present in the cells in the caudal half of Clarke's column. It will be seen that most of the affected cells were ipsilateral to the lesion (on the left side). There were also some degenerating cells on the contralateral (right) side in the more caudal segments.

Unilateral lesions of the ventro-lateral column.

Case 9: Fig.163 (23 days). In this case the lesion mainly involved the ventro-lateral column; There was slight involvement of the dorso-lateral



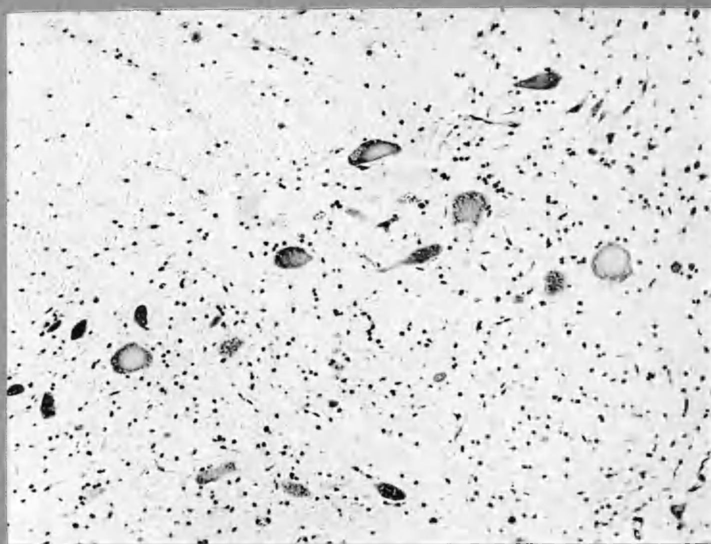


FIG 163 (CASE 9)

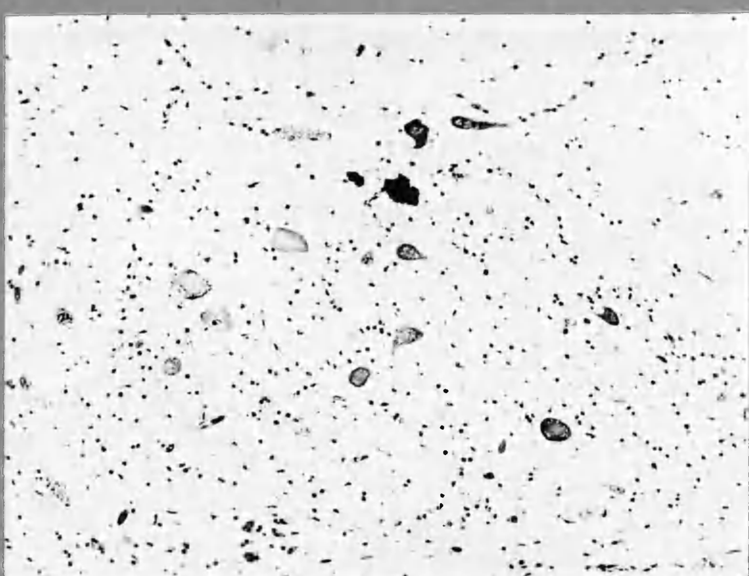
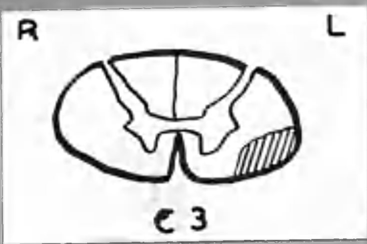
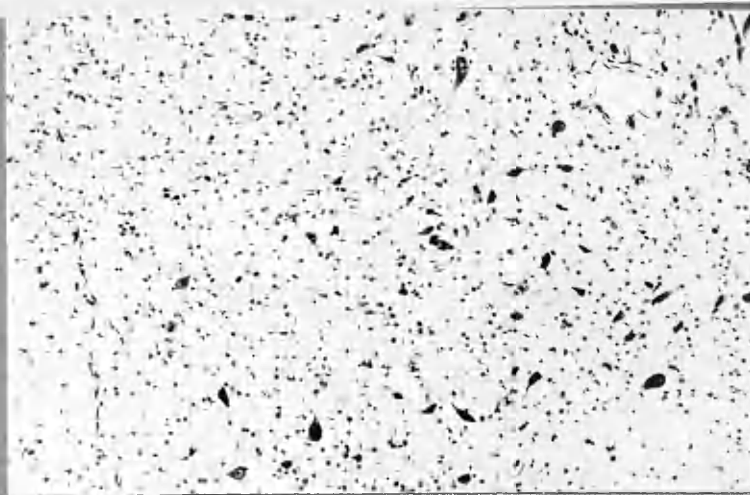
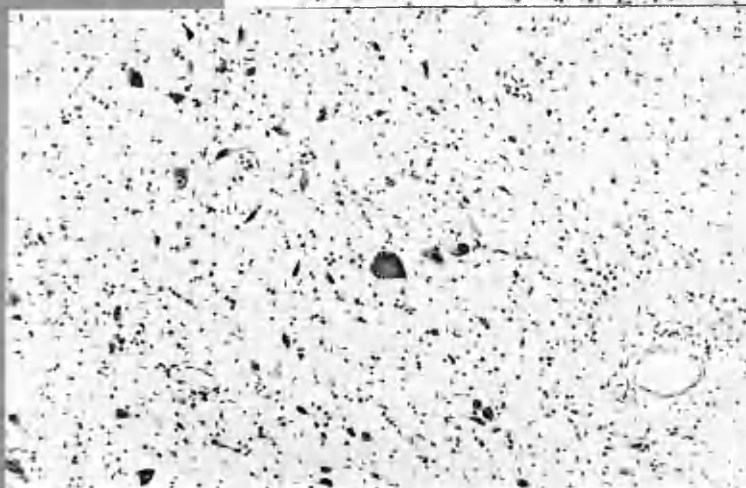
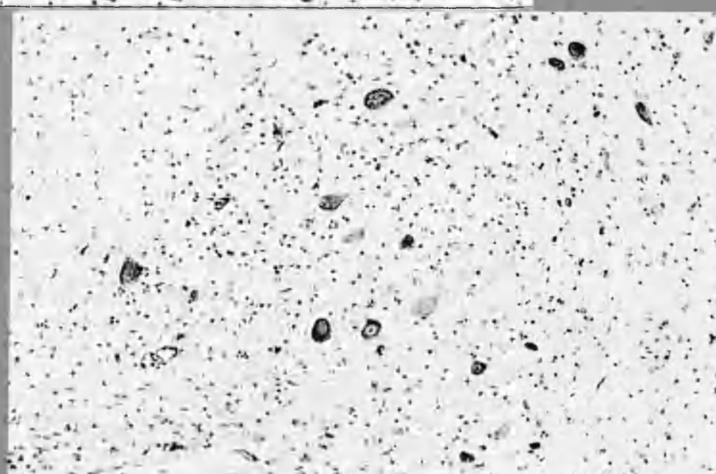


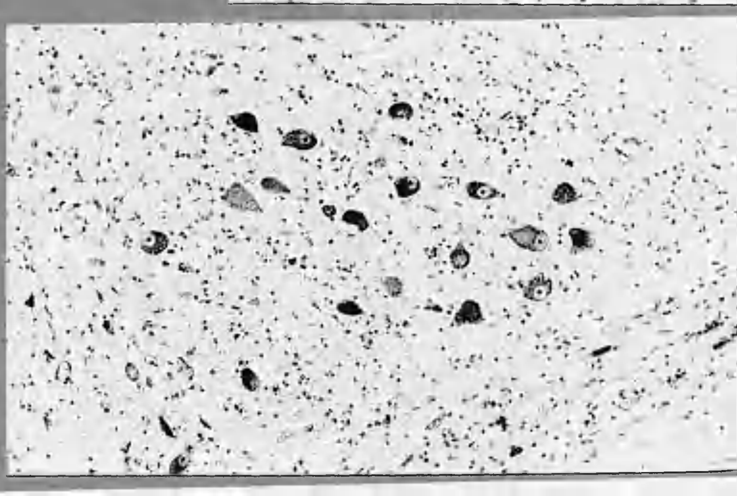
FIG 164
(CASE 7)











column. The Clarke's column cells of the left, (ipsilateral) column show very considerable changes; there are some chromatolytic cells and there is also some cell loss. In the right contra-lateral column there are a few cells which might be chromatolytic, but this is not so definite as in the previous case.

Case 7: Fig.164 (112 days). In this case the lesion mainly affected the ventro-lateral column. There is very definite cell loss on the left, (ipsilateral) Clarke's column, but it is not possible to say whether a few cells have fallen out from the right (contralateral) Clarke's column or not. This case is included to show the difficulty of recognising the loss of a few cells in Clarke's column nucleus, if no other cell changes occur concurrently.

The first of these 3 unilateral cases serves to show that a lesion of the ventro-lateral and the ventral part of the dorso-lateral columns in the upper cervical cord causes reactive changes in many cells of Clarke's column on the same side, and in a few cells of Clarke's column on the opposite side. The second case gives some evidence that when the lesion is confined to the ventro-lateral column in the mid-thoracic level, reactive changes are seen in

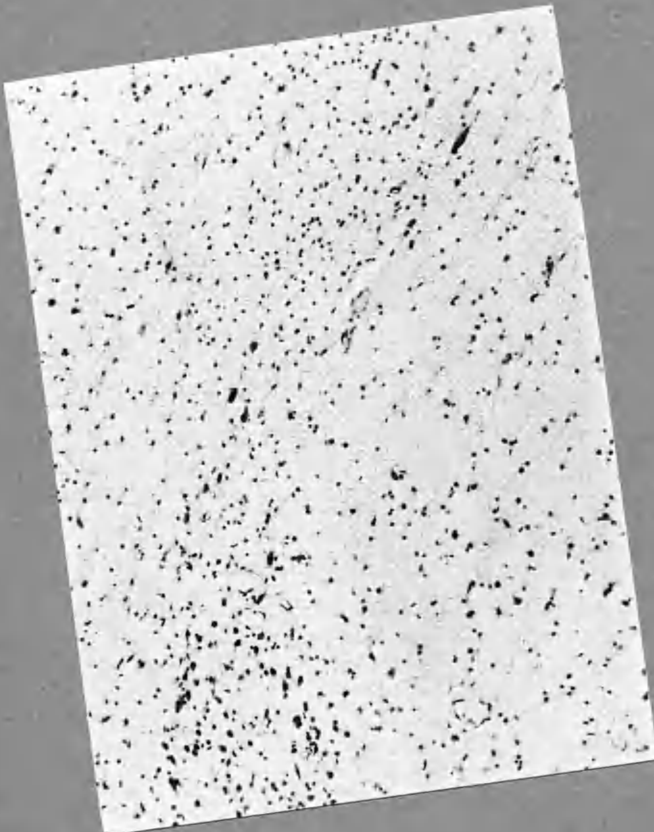
Clarke's column cells of the same side, and possibly in a few cells of the opposite side. The last observation is not definitely proved.

The third case might be expected to show as widespread an involvement of Clarke's column as the first case did, but at a later stage of degeneration. On the same side as the operation the column does show severe loss of nerve cells, but loss of cells on the opposite side cannot be definitely established.

<u>Reaction of ascending lateral column fibres to Clarke's column cells</u>.

From all the cases shown so far, certain conclusions can be drawn. Cells of Clarke's column give rise to fibres which ascend the cord both in the dorso-lateral and in the ventro-lateral column. Some, at least, of these fibres, lie on the periphery of the cord. Some, at least, of these fibres reach the periphery of the cord in the same segment as their cells of origin.

The course of most of the fibres in the cord is ipsilateral to their cells of origin; a few have a contralateral course. There is no final evidence whether the contralateral fibres run in the



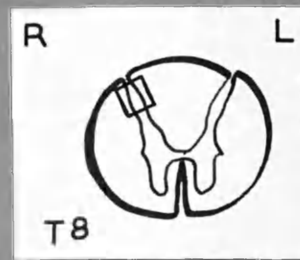
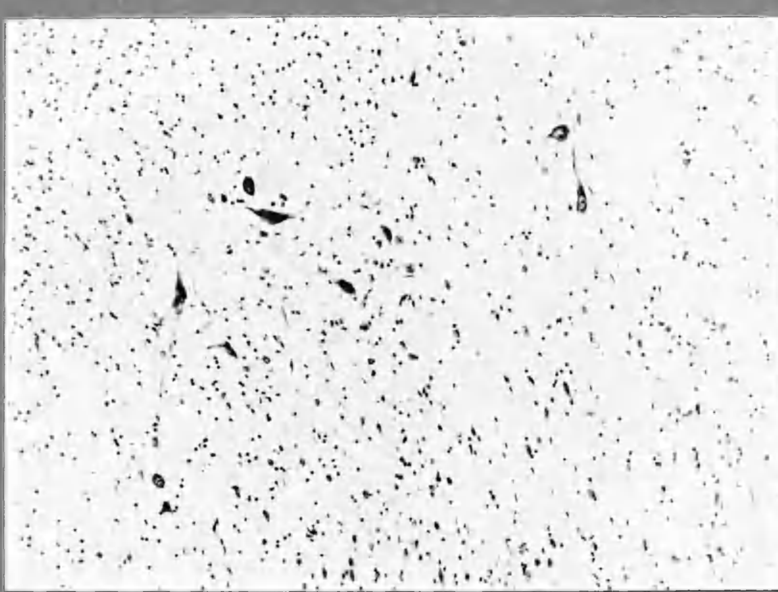


FIG 165



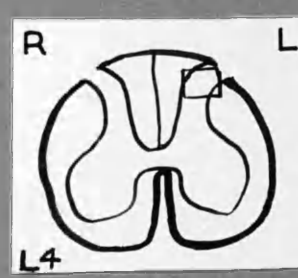


FIG 166

ventro-lateral or in the dorso-lateral column, but some evidence that at least some of the crossed fibres run in the ventro-lateral column.

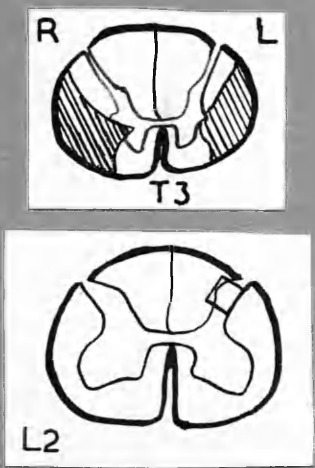
No correlation was found between the site occupied by the ascending fibres, and the distribution of the cells of Clarke's column, in either a rostro-caudal, or in a dorso-ventral direction.

II. Apical Cells of the Dorsal Horn. (cellulae posteromarginales). (Plates 97-102).

a) Normal cells: (Figs.165 and 166).

The number of small and medium sized apical cells seen in a transverse section vary from none at all to about eight. In the cervical cord there are most commonly 0-4 cells; in the thoracic cord there are frequently no large or medium sized cells in a section, or there may be one or two cells. In the lumbo-sacral cord there is a wide variation in the number in different segments, and in different sections; in the lumbar segments there are most commonly 3-8 cells, in the sacral segments 5-20 cells. As seen in transverse section the cells are narrow, pointed and dark staining.

b) Axonal reactions to cells: As can be seen in Table 3, chromatolysis tends to occur rather later in these



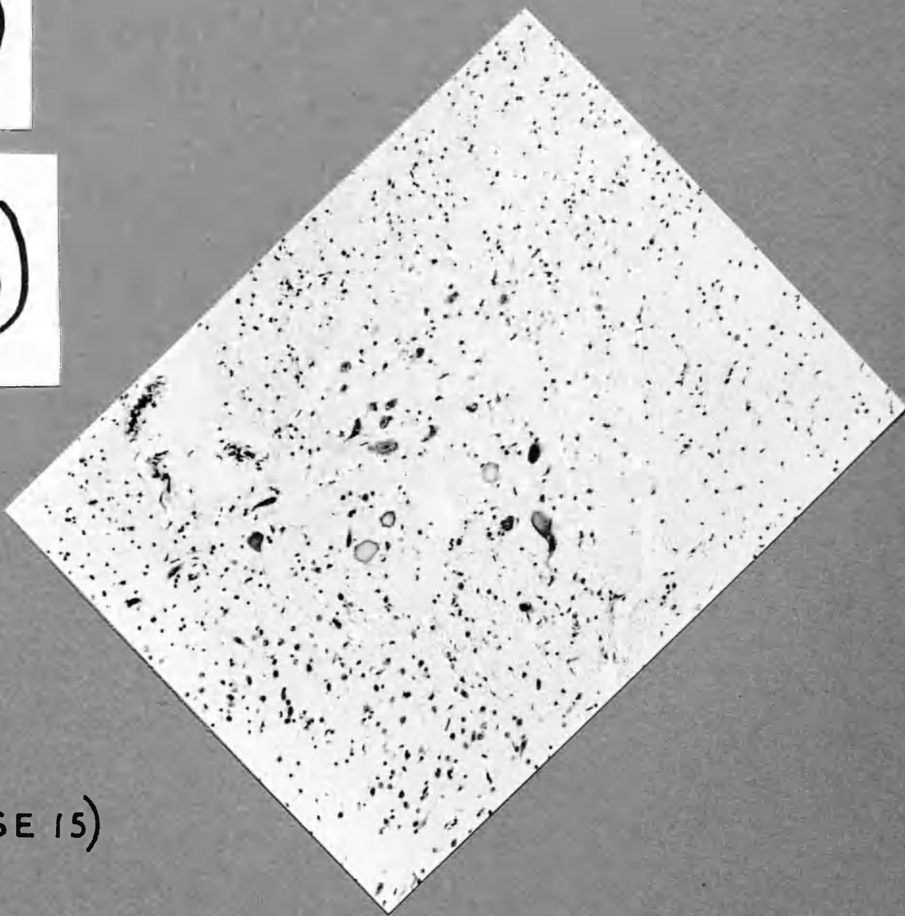


FIG 167 (CASE 15)

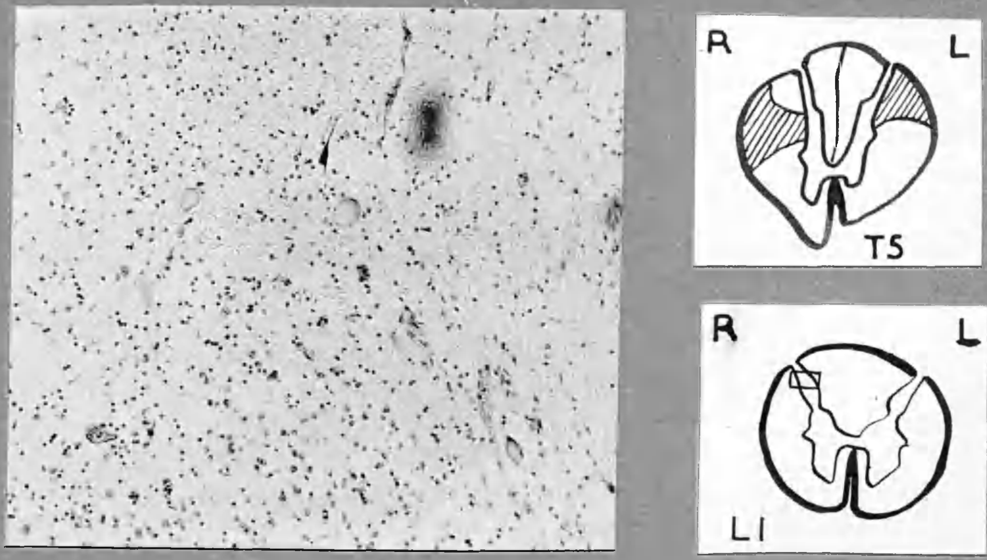


FIG 168 (CASE 26)

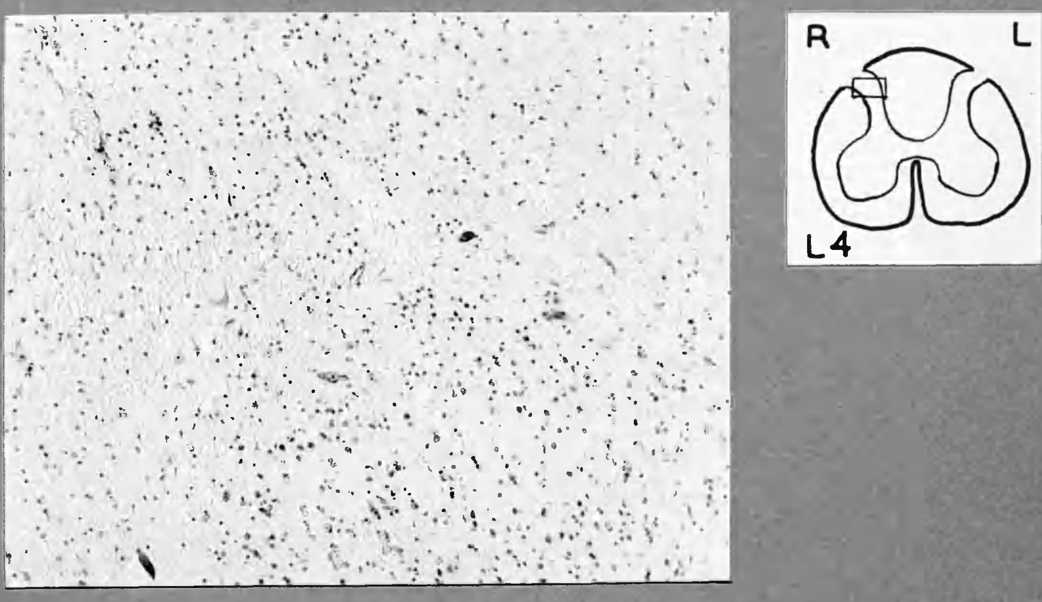
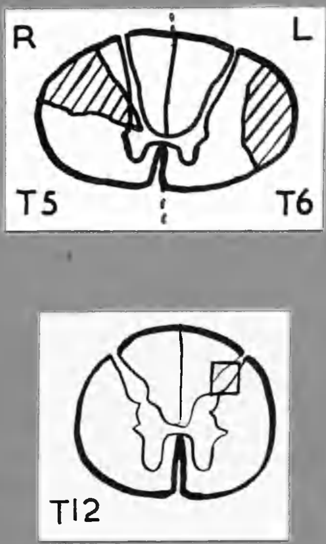


FIG 169 (CASE 26)



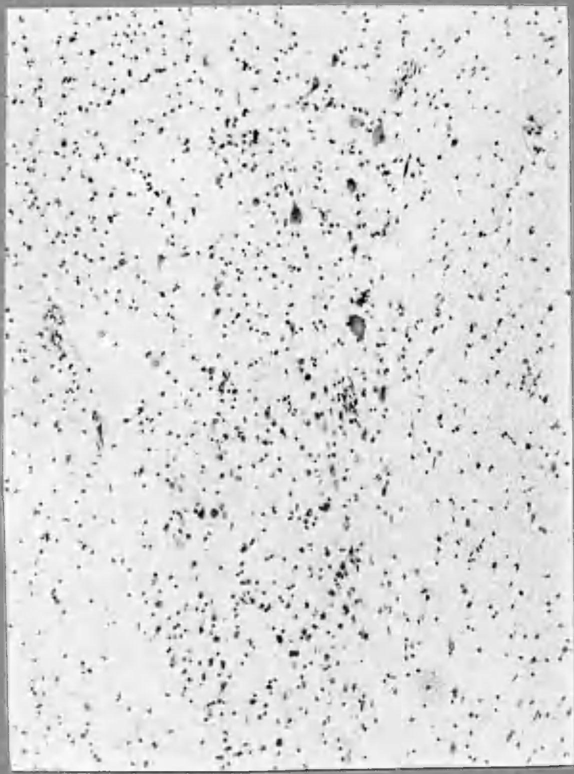
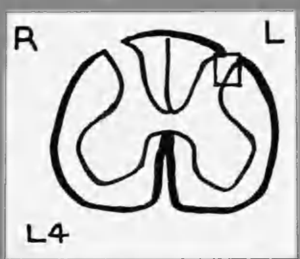


FIG 170 (CASE 27)



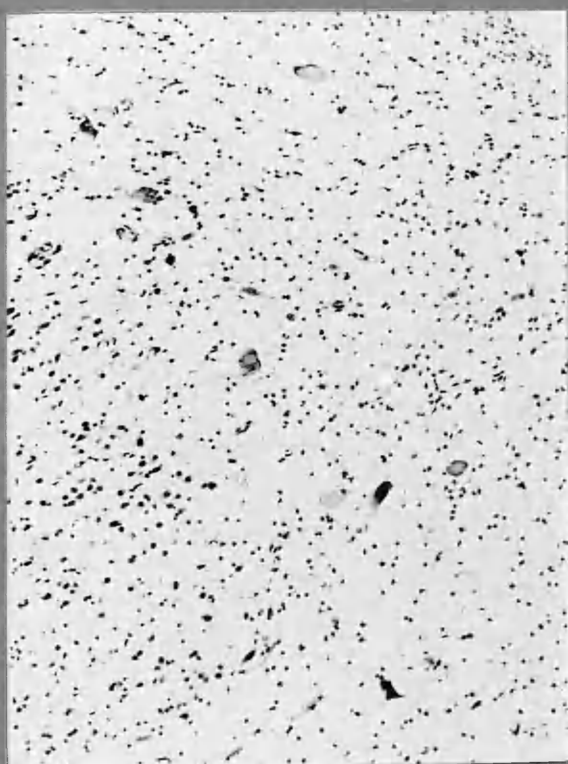


FIG 170A (CASE 27)

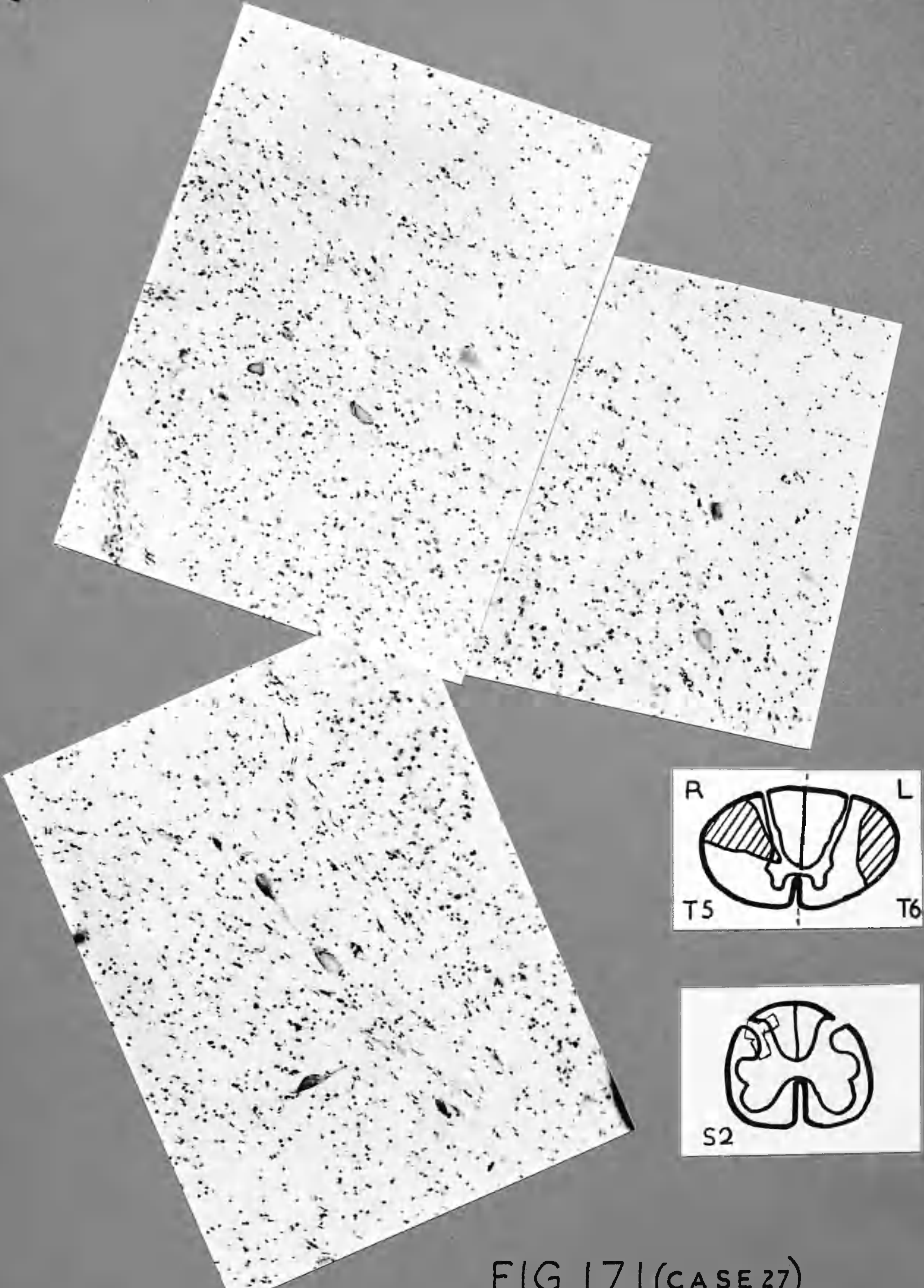


FIG 171 (CASE 27)

cells than in the cells of Clarke's column. Owing to the greater number, and larger size, of these cells in lower segments it is easier to recognise the occurrence of retrograde changes at these levels than in the upper segments. An important feature is that no matter how extensive the lesion is, changes are present in only some of the cells. Owing to this, the actual loss of cells is difficult to detect, and similarly there may be no evidence of any increase of glial nuclei.

Extensive bilateral lesions of dorso-lateral and ventro-lateral columns.

Case 15: Fig.167 (53 days). No chromatolytic cells have been seen in any sections of the thoracic segments. In the lumbo-sacral segments there are fairly numerous cells showing chromatolysis, as shown in Fig.167.

Bilateral lesions of the dorso-lateral columns.

Case 26: Figs.168 and 169 (154 days). In this case a few chromatolytic cells are present in the lumbo-sacral segments.

Case 27: Figs.170 and 171 (42 days). In this case also some chromatolytic cells are present in the lumbo-sacral segments.

FIG 173 (CASE 18)

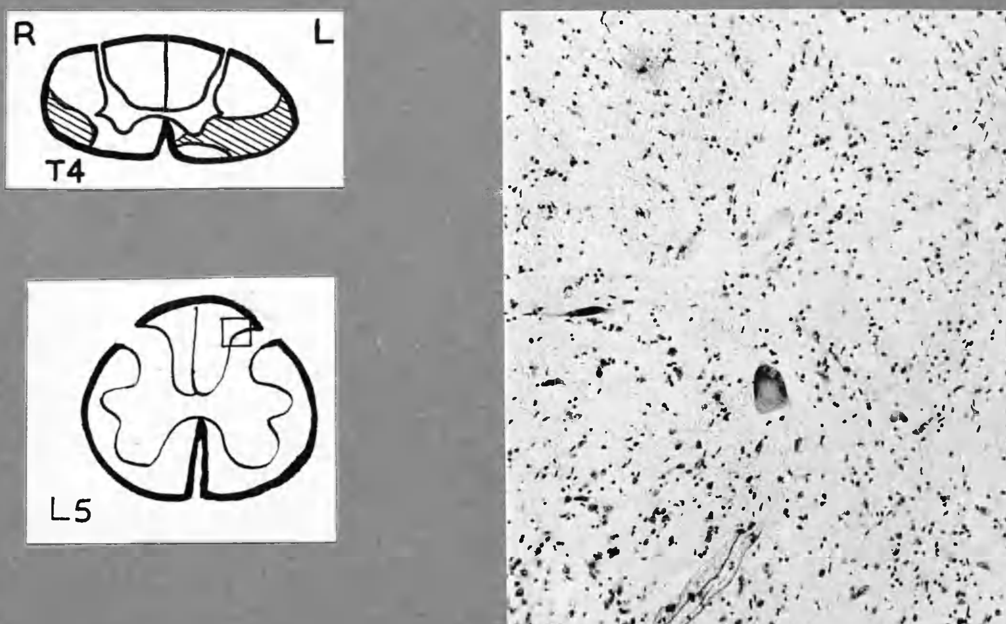
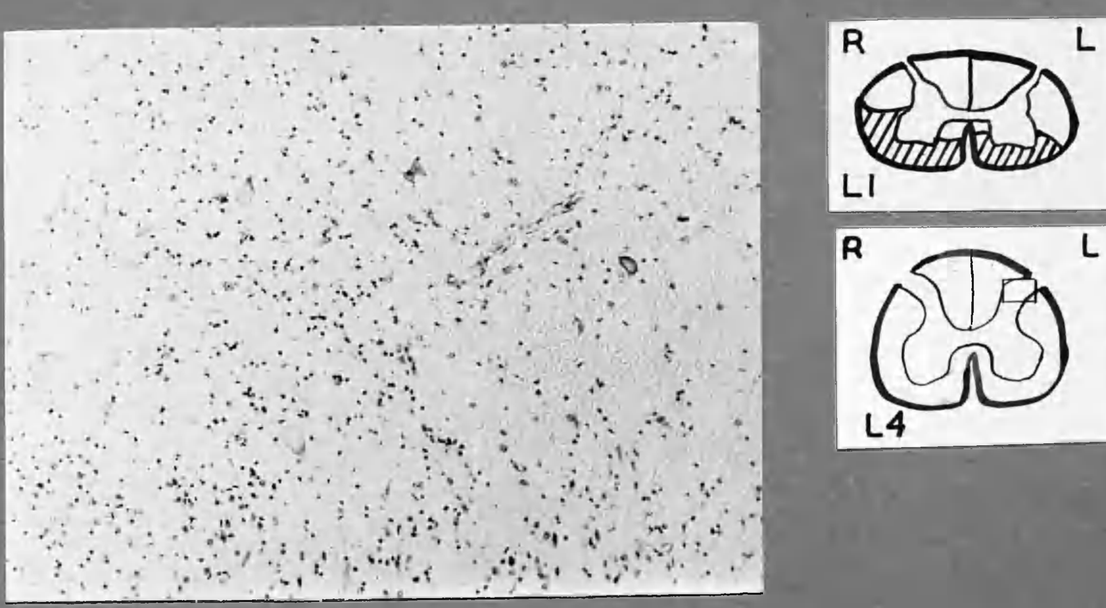


FIG 172 (CASE 34)



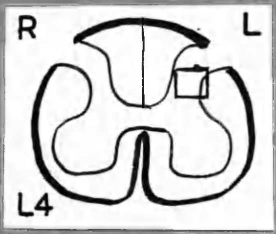
Bilateral lesions of the ventro-lateral columns.

Case 34: Fig.172 (91 days). In this case there are few chromatolytic apical cells present in all segments caudal to the lesions; they were particularly numerous in the fourth lumbar segment.

Case 18: Fig.173 (66 days). In this case a few chromatolytic cells are present in all segments caudal to the twelfth thoracic segment on the right, and the second lumbar segment on the left.

In all these cases showing chromatolysis in the apical cells, the lesions are bilateral. It will be seen from Table 3 that in those unilateral cases in which retrograde changes in this group of cells occur, the retrograde changes are usually contralateral to the lesion, although some are ipsilateral. In only one of the cases in which the lesion was at the upper cervical level have any changes been seen in the cervical segments. In this case a very few chromatolytic cells were present contralateral to the lesion.

Relation of ascending lateral column fibres to apical cells of dorsal horn: Retrograde changes are not pronounced among the apical cells, and in some cases no changes have been found. From this material



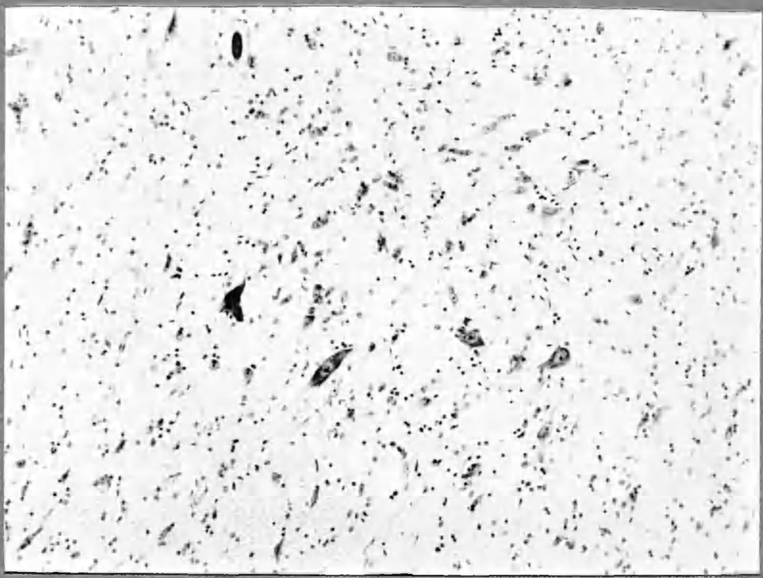


FIG 17.4

it may be concluded that at least some of the fibres which arise in the apical cells run in the dorso-lateral and the ventro-lateral columns.

The course of most of these fibres in the cord is contralateral to their cells of origin, some of the fibres have an ipsilateral course; some of the fibres reach the lateral column within the same segment as that containing the apical cells of origin.

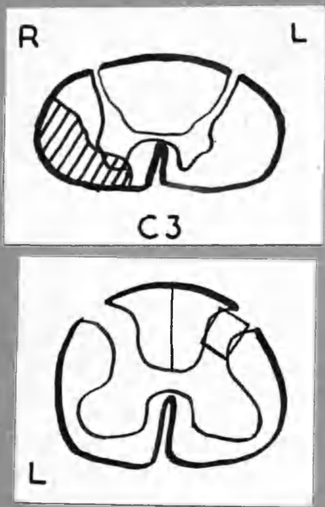
III. Cells of the Substantia Gelatinosa.

As is well known, the cells of the substantia gelatinosa are small, and changes in such small neurones are very difficult to determine. In this work, convincing evidence of marked changes in the substantia gelatinosa have not been seen. In a few cases, it appears that there might be some loss of neurones, and an increase of glial cells on both sides of the cord. But no definite conclusions have been drawn in relation to a connection between these cells and fibres of the lateral column.

IV. Cells of the Nucleus Proprius of Dorsal Horn.
(Plates 103-106).

a) Normal cells. (Fig.174).

The number of cells seen in a transverse section of this group varies from 0 to about 25.



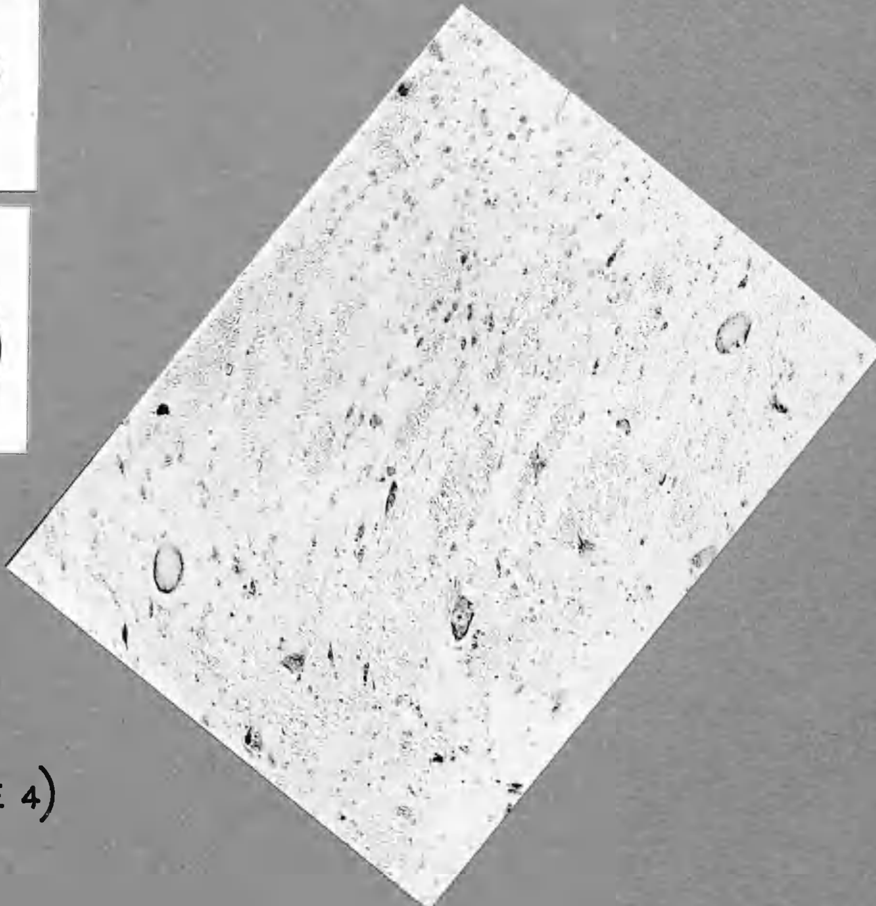
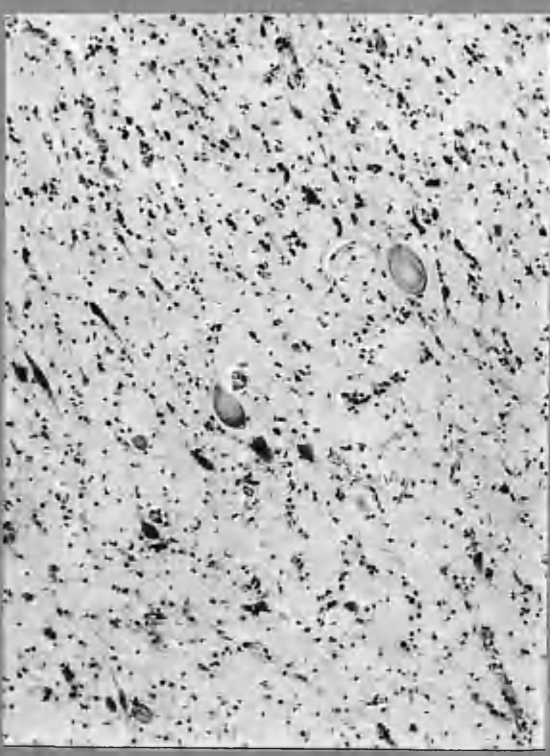


FIG 175 (CASE 4)



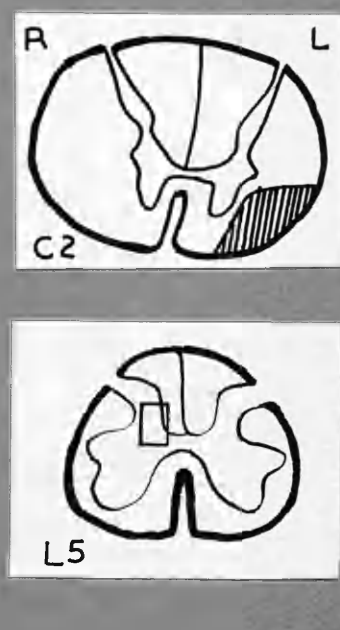


FIG 176 (CASE 2)

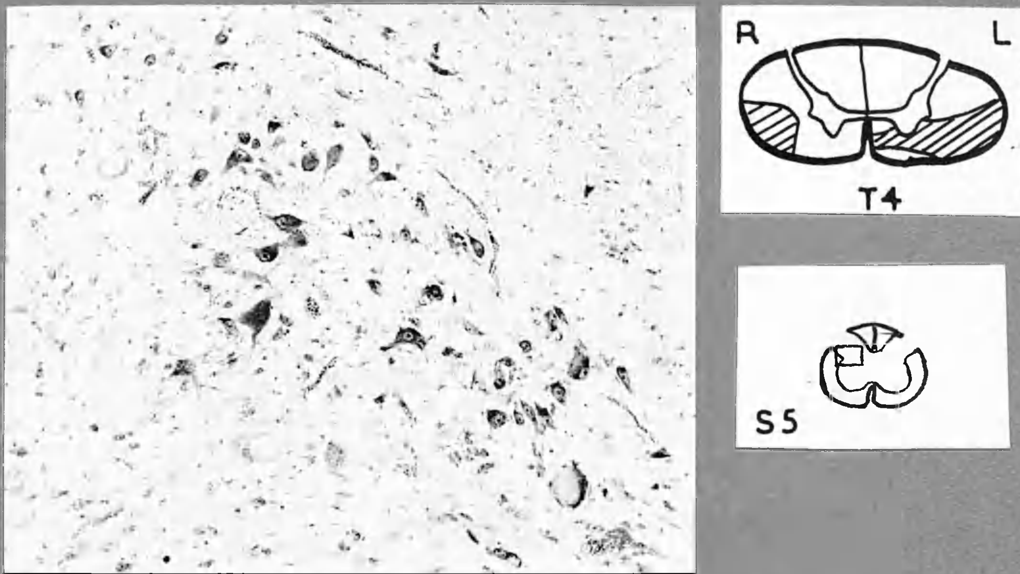
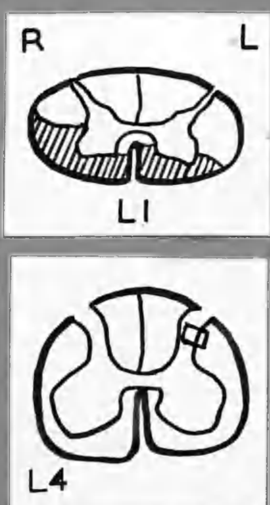


FIG 177 (CASE 18)



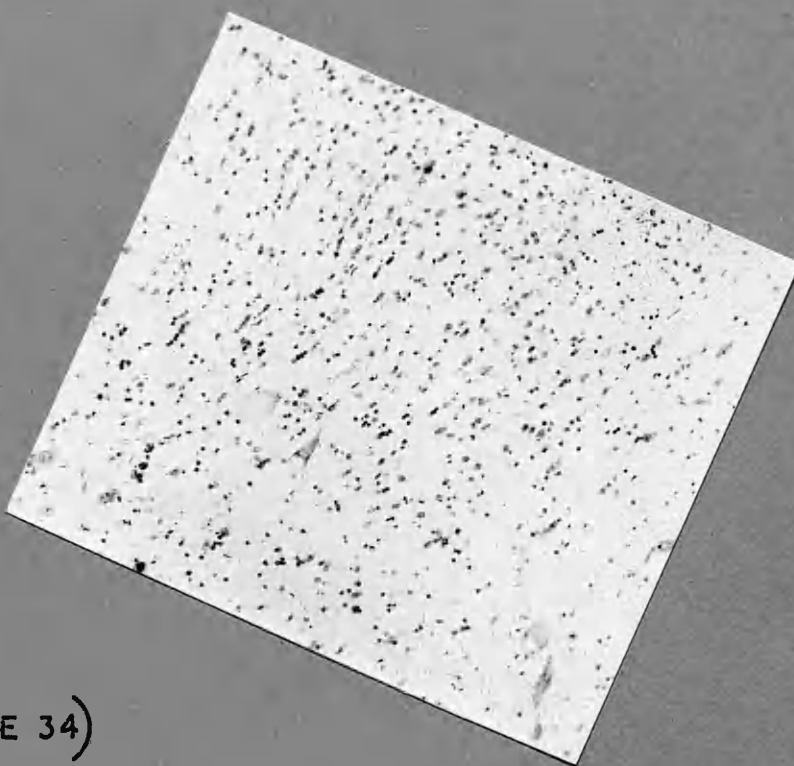
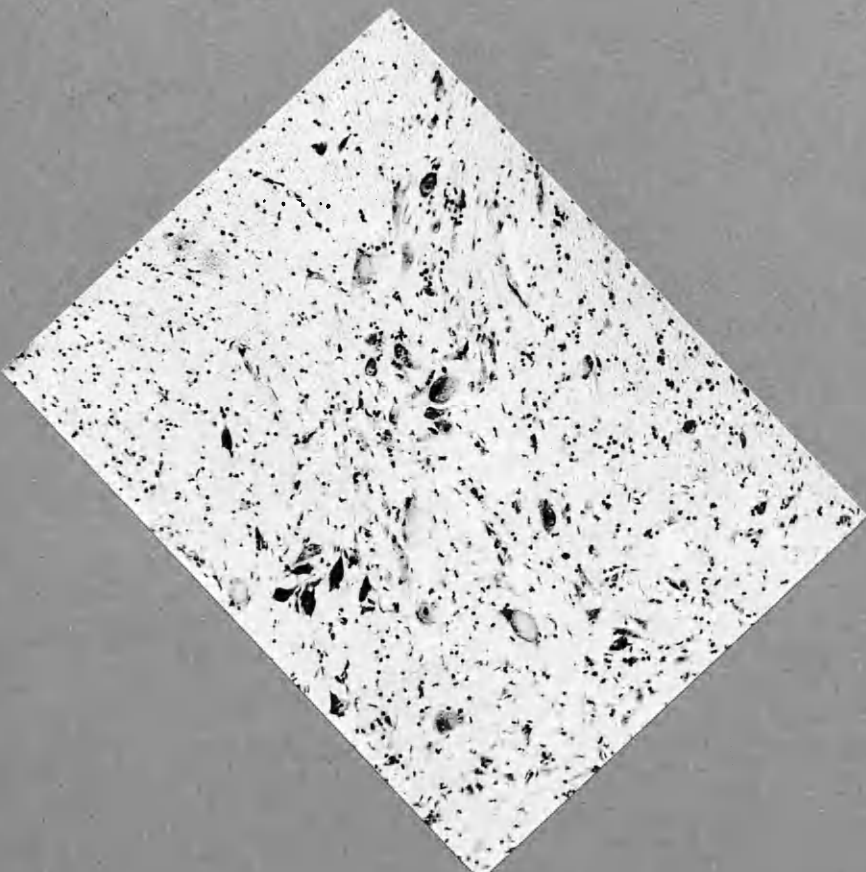
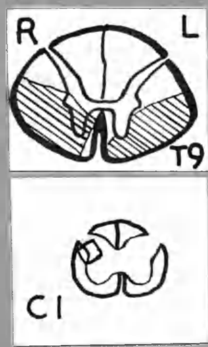


FIG 178 (CASE 34)

FIG 179 (CASE 33)





In the cervical cord there are most commonly 2-6 cells; in the thoracic cord 0-4; in the lumbo-sacral cord 3-20, the larger number being found in the sacral cord.

The cells are mostly of medium size in the cervical cord, smaller in the thoracic cord, and medium or large in the lumbo-sacral cord. The cells have a clearly defined nucleus and definite Nissl substance.

b) Axonal reactions in cells.

Chromatolysis can be easily recognised in the cells of this group. As with the previous group, a few chromatolytic cells were found in cases with widely different periods of survival. Examples of these chromatolytic cells are shown on plates 103-106.

Case 4: Fig.175 (5 days)
Case 2: Fig.176 (313 days)
Case 18: Fig.177 (66 days)
Case 34: Fig.178 (91 days)
Case 33: Fig.179 (109 days)

The few scattered chromatolytic cells seen in segments caudal to the lesion occurred in cases with only dorso-lateral lesions and cases with only ventro-lateral lesions; they were found bilaterally

FIG 180

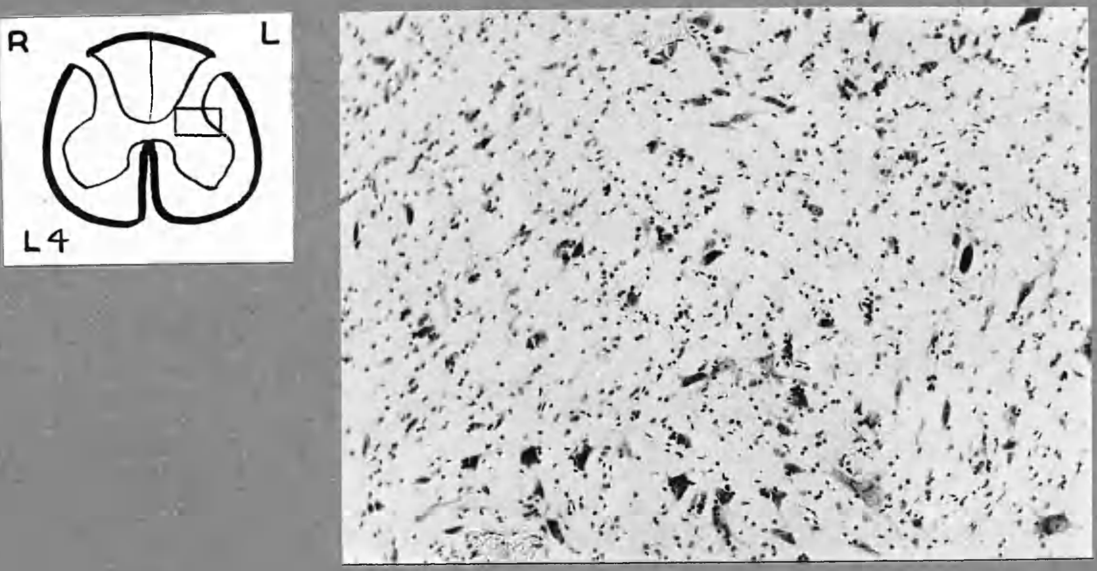
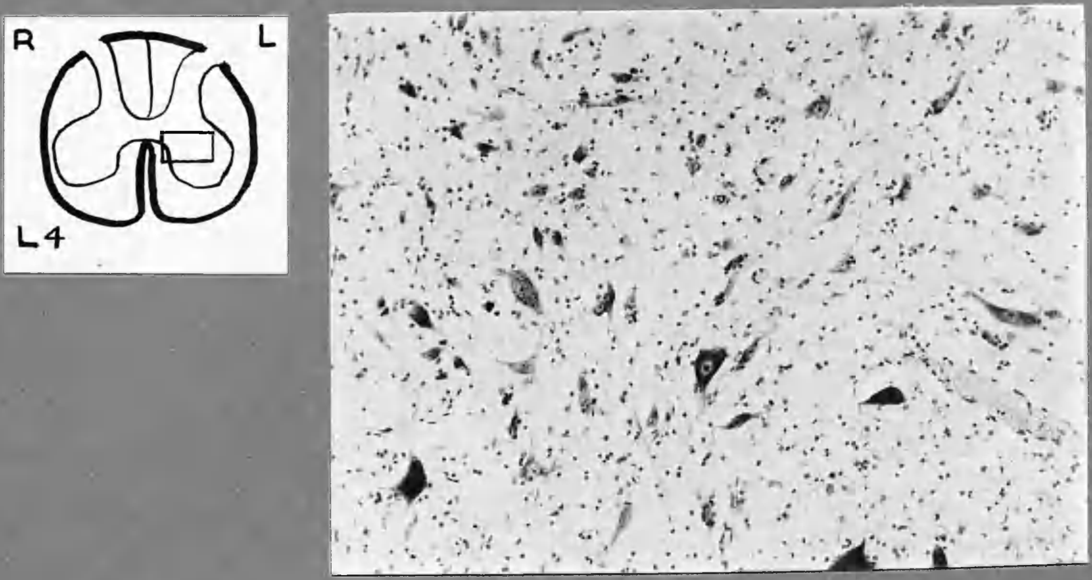


FIG 181



in unilateral cases. In the cervical segments chromatolytic cells were a very rare finding. In a few cases there is some gliosis in this scattered distribution. It was too scarce and inconstant to permit conclusions to be drawn about the number of fibres originating in this area. In no case have many chromatolytic cells been seen; and in some cases there were no changes to be seen in this group of cells. This absence of axonal reaction among these cells is quite definite; for they were looked for in serial sections throughout many segments in all cases. Also, there was no loss of cells (compared with the normal) in this group.

Relation of ascending lateral column fibres to cells of nucleus proprius.

It is concluded that some fibres ascending in the dorso-lateral and ventro-lateral columns take origin from the proprius cells. These fibres are both ipsilateral and contralateral.

V. Cells at the Base of the Dorsal Horn and in Intermediate Grey Matter. (Plates 107-110).

a) Normal cells. (Figs.180 and 181).

There are numerous cell groups in this region. Many of these groups consist of small cells, in which retrograde changes cannot be recognised.

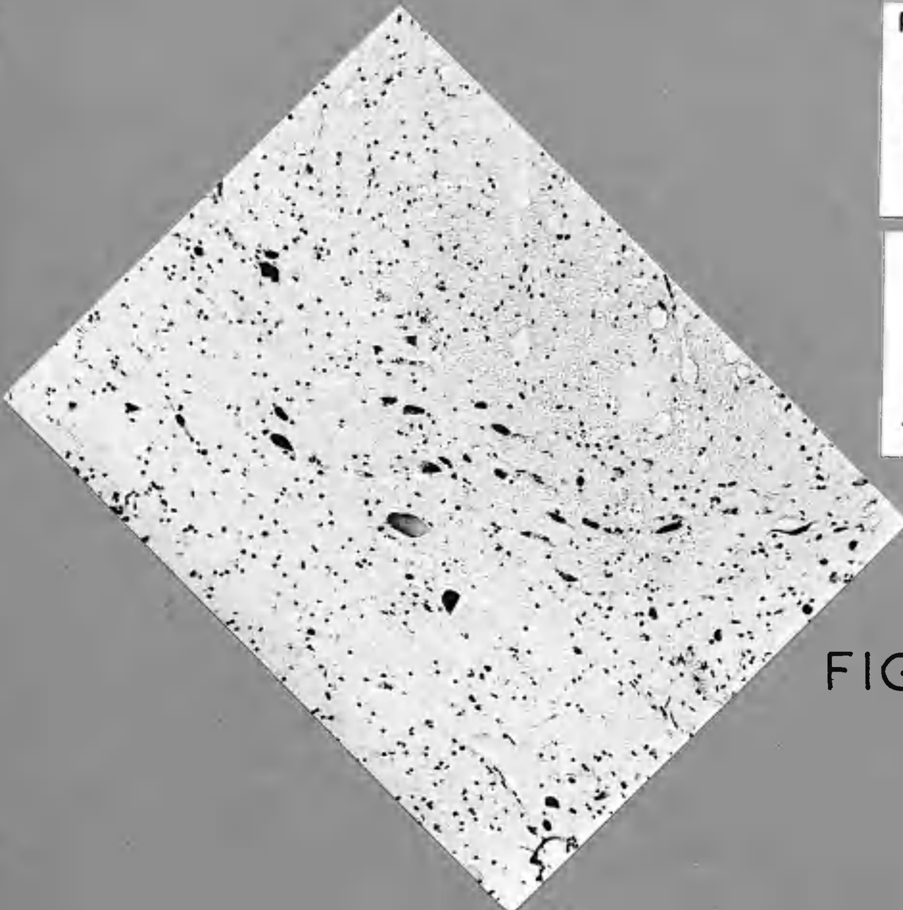
There are also some medium sized and larger cells scattered about in this region, being more numerous in the cervical and lumbo-sacral region. Average numbers per section in the normal have not been calculated for these cells. The cells have definite nuclei, and Nissl substance.

b) Axonal reactions in cells.

Chromatolysis is easily recognised in the cells of this region; loss of cells could not be seen; occasionally gliosis was noted, but it was always a rare localised finding, too inconstant for a definite interpretation of its significance.

Definitely chromatolytic cells were seen in only 8 out of the 23 cases. These cases had periods of survival varying from 23 to 170 days. The chromatolytic cells occur in only a few sections, and were not in sufficient numbers in any segment for their significance to be determined.

Chromatolytic cells were seen in cases with extensive lesions of the dorso-lateral and ventro-lateral columns, and also in cases with lesions of the ventro-lateral column only. In neither of the cases (cases 26 and 27) with lesions confined to the dorso-lateral column were cell changes seen in this



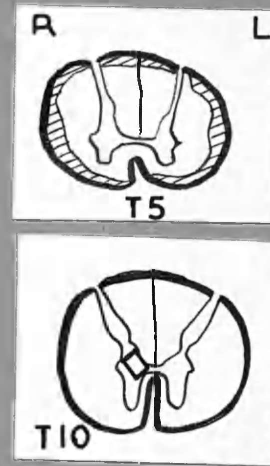


FIG 182 (CASE 23)

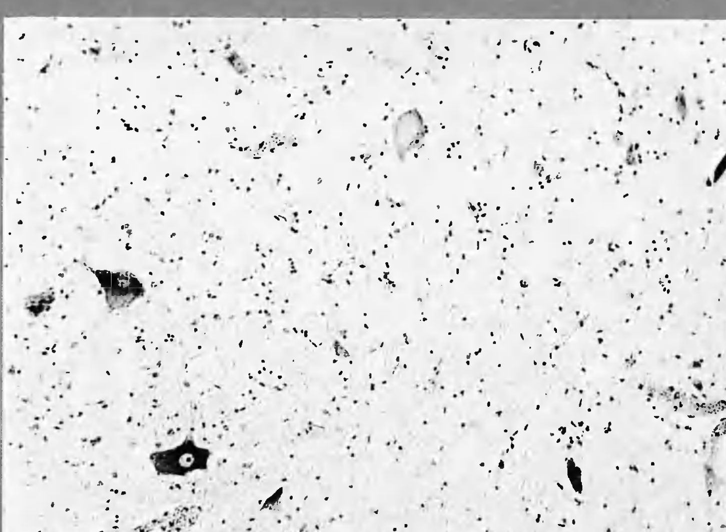
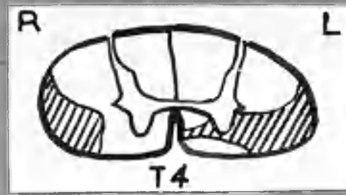
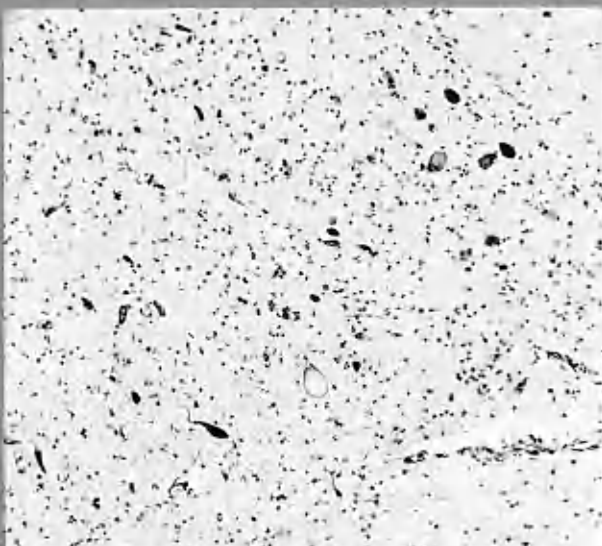


FIG 183 (CASE 23)



(CASE 18)



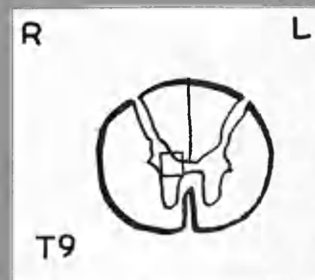
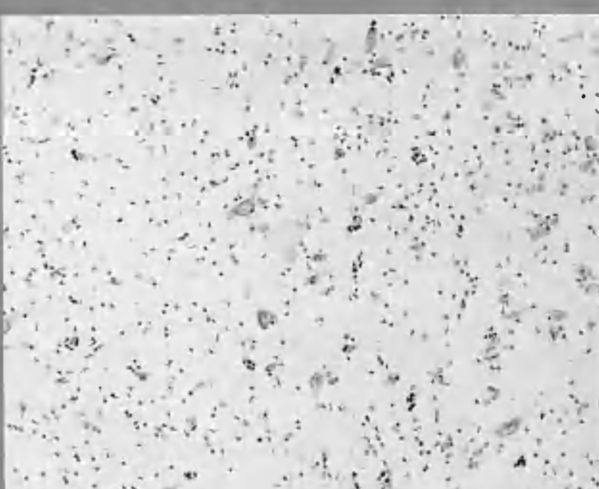


FIG 184



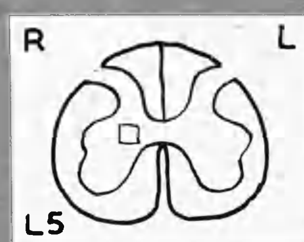
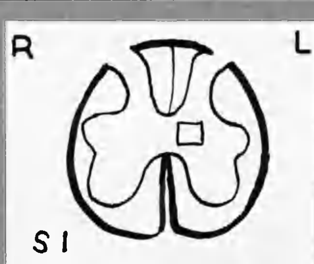


FIG 185



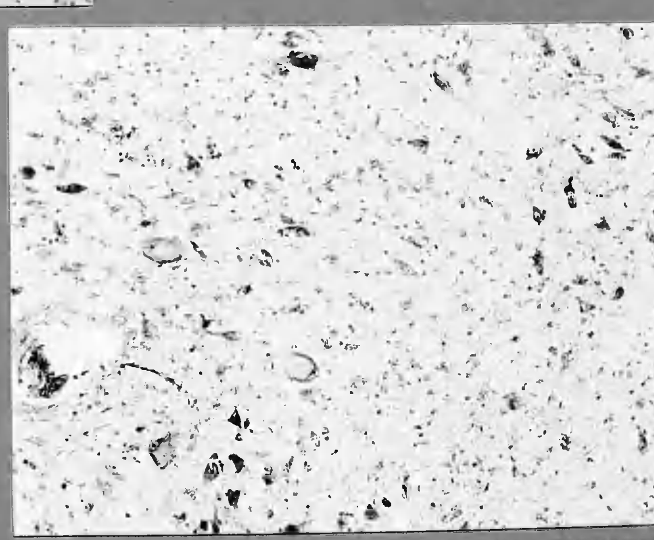


FIG 186

FIG 187 (CASE 33)

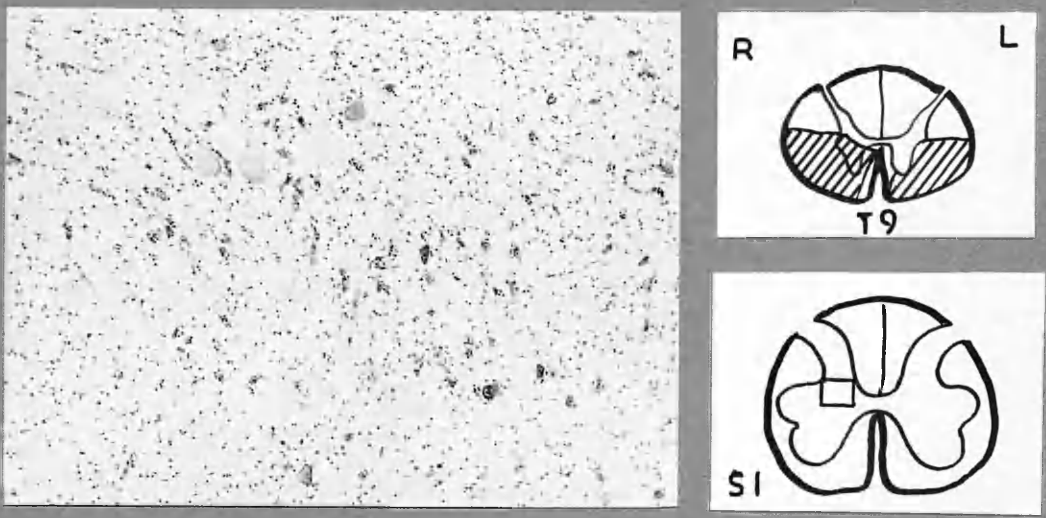
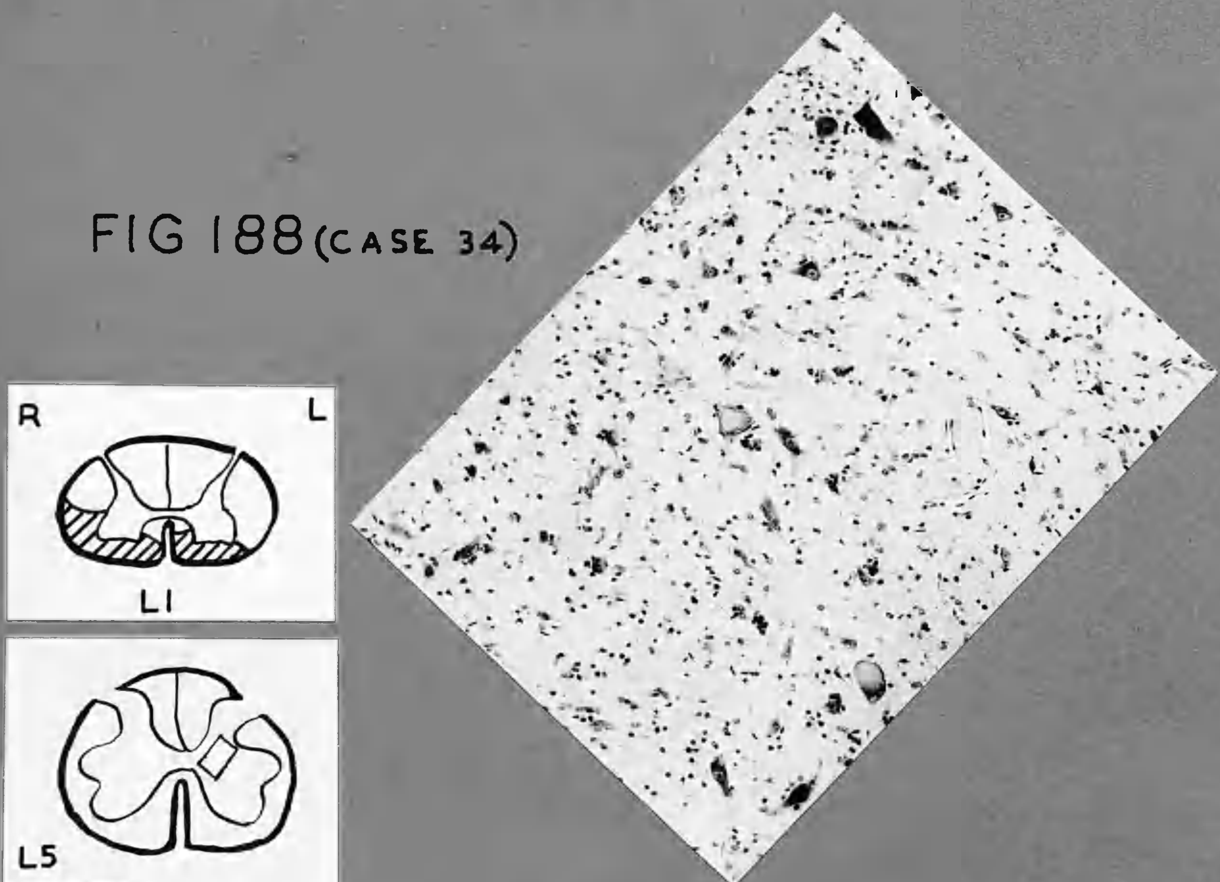


FIG 188 (CASE 34)



region, at the base of the dorsal horn and in the intermediate grey matter. Chromatolytic cells were seen after lesions confined to the periphery of the cord, e.g. case 23: Figs.182 and 183 (39 days). In the unilateral cases a very few abnormal cells were seen in this region on both sides of the cord. In only one case were any changes seen in the cervical cord; in this case there was slight gliosis on both sides.

Examples of these chromatolytic cells are shown from:-

Case 18: Figs.184, 185 and 186 (66 days)

Case 33: Fig.187 (109 days)

Case 34: Fig.188 (91 days)

Relation of the lateral column to cells at the base of the Dorsal Horn and cells of the Intermediate Grey Matter.

It is concluded that some fibres ascending in the ventro-lateral column, possibly only in its peripheral part, take origin from cells of the base of the dorsal horn and the intermediate grey matter. These fibres are both ipsilateral and contralateral. It has not been proven whether any fibres arising from these cells ascend in the dorso-lateral column or not.

VI. Cells of the Ventral Horn. (Plate 111).

In many of the cases one or more ventral nerve roots were cut or pulled on at operation. Also, in many of these cases, the carcinoma which was the cause of the patient's presence in this series involved peripheral nerves of the lumbo-sacral region. Hence, any changes observed in ventral horn cells of this region might then be the result of degeneration in the ventral roots. It is clear that such cases cannot be utilised for determining if retrograde changes in ventral horn cells occur after a cordotomy. In a few cases, however, no evidence of any involvement of any nerve of lumbo-sacral origin could be found.

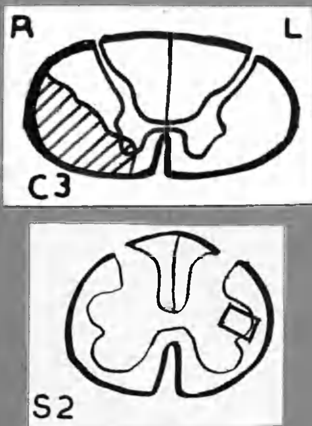
a) Normal Cells.

The characteristics and the distribution of the cells of the ventral horn are so well known that no further observations on the normal will be given here.

b) Axonal Reactions to cells.

Chromatolysis is easily recognised in these cells. This was the only definite stage of retrograde cell change that was seen.

The cases that could be used - there being no



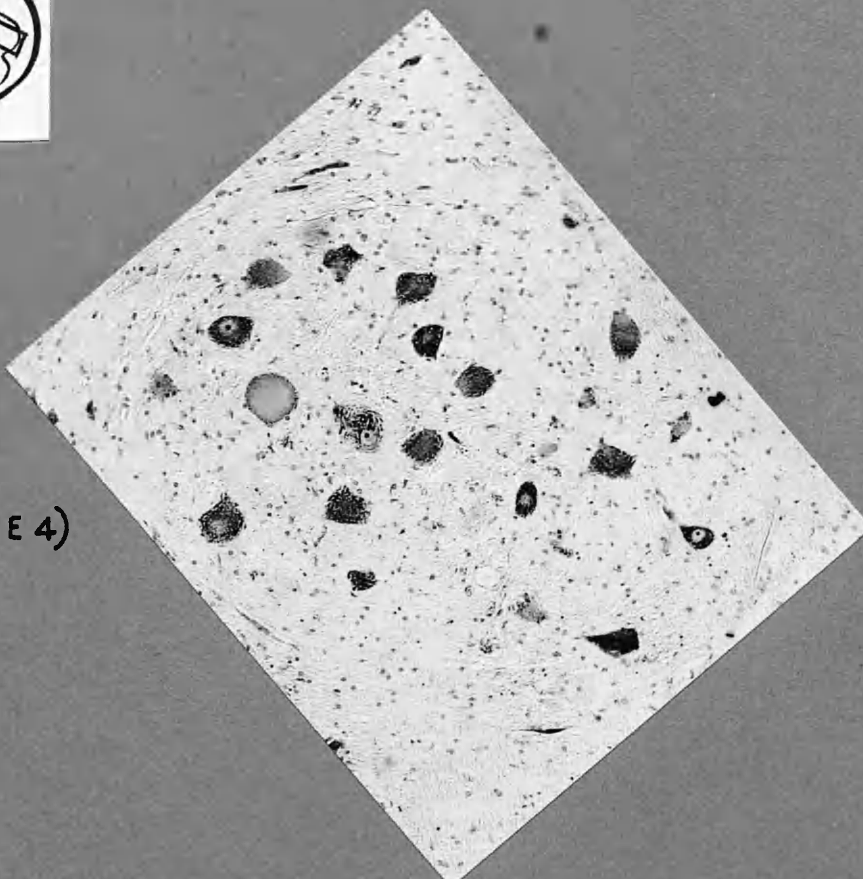


FIG 189 (CASE 4)

damage to the nerves - were 1, 2, 4, 5 and 7. In all these cases a few ventral horn cells showed chromatolysis; these changes were bilateral, but mostly contralateral.

Case 1 has not been included in Table 3, as the complete examination of serial sections of the cord has not been completed.

In case 4: Fig.189 (34 days) a few chromatolytic cells are present in the fourth lumbar segment and first and second sacral segments. These cells are present in both the lateral and the medial groups of ventral horn cells, most of them being on the side contralateral to the lesion.

In case 5 a very few chromatolytic cells are present in the second lumbar segment on the side contralateral to the lesion. In the other 3 cases a very few chromatolytic cells are present in the first and second sacral segments on the side contralateral to the lesion. In all these cases one or two chromatolytic cells are present in the same segment on the ipsilateral side.

Relation of Ascending lateral column fibres to cells of the Ventral Horn.

It is concluded that some fibres ascending in the lateral column, arise from cells of the ventral horn of the lumbo-sacral segments. The majority of the fibres are contralateral, some are ipsilateral. Some at least of the fibres run in the ventro-lateral column; whether others run in the dorso-lateral column has not been ascertained.

VII. Cells of the Lateral Horn.

The reservations made in respect of the ventral horn cell changes due to peripheral nerve involvement apply to this group also.

a) Normal cells.

A definite lateral horn is distinguishable only in the thoracic and the upper lumbar segments. In the upper segments the number of cells vary from about 3 to 6, and in the lower segments from about 5 to 16. The cells are small and medium in size, the larger cells being present in the lower segments. The cells tend to be dark staining, and of a somewhat vesicular appearance; the nucleus is excentric, and the Nissl substance peripheral.

b) Axonal Reactions to cells.

In view of the appearances of these cells, chromatolysis is not easy to recognise unless it affects a number of cells.

KEY

C - chromatolysis

L - loss of cells

GH - ghost cells

S - shrunken cells

N - neuronophagia

GL - gliosis

V - vacuolated cells

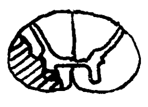
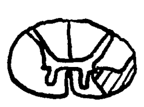
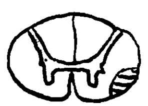
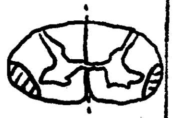
(X) - slight

X? - query

X+ - marked

TABLE 3.

SUMMARY OF RETROGRADE CELL CHANGES.

Case No.	Post Operat. Survival	Lesion	Cells groups showing marked changes.						Cells groups showing some definite changes.						All groups showing only slight changes.																		All groups showing some changes: Peripheral involvement.											
			Cells of Clarkes Column						Cells at apex of Dorsal Horn.						Cells of Substantia Gelatinosa						Cells of Nucleus Proprius of Dorsal Horn.						Cells at base of Dorsal Horn & in the intermediate grey matter.						Cells of Ventral Horn.						Cells of Lateral Horn					
			Lesion C8		T1-T9		T10-L2		Lesion C8		T1-T9		T10-Co		Lesion C8		T1-T9		T10-Co		Lesion C8		T1-T9		T10-Co		Lesion C8		T1-T9		T10-Co		Lesion C8		T1-T9		T10-Co		Lesion C8		T1-T9		T10-Co	
		R L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
2	313	C2 				(L)		L+			C N	C?													C	C N											C	(C)						
4	5	C3 			C L?		C+	(C)		(C)		C										(N)		N	C	C							(C)		C	C		C			C?			
5	81	C3 						L (GH)					C	C?		(GL)		G?												G		C		(C)		C	C?							
7	112	C3 			L? GL	< L? GH GL	L S GL	< L S GL			C?			GL?	(GL)	(GL)	GL?	GL?	GL?	GL?	(C)	(GL)	(C)	(GL)			(GL)	(GL)	GL?	GL?			(C)	(C)	C	(C)	(C) GL?	C GL?			C GL?			
12		C5 C6 													(GL)	(GL)	GL?	GL?			C?				C?								(C)	(C)	C? (L)	C (L)								

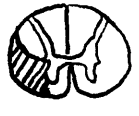
Case No.	Post Operat. Survival	Lesion	Cells of Clarkes Column: LESION CR C8-T9 R	L	T10-L2 R	L	Cells at apex of Dorsal Horn: LESION-T9 R	L	T10-Co R	L	Cells of Substantia Gelatinosa: LESION-T9 R	L	T10-Co R	L	Cells of Nucleus Proprius: LESION T9 R	L	T10-Co R	L	Cells at base of Dorsal Horn: Lesion-T9 R	L	T10-Co R	L	Cells of Ventral Horn: Lesion-T9 R	L	T10-Co R	L	Cells of Lateral Horn: Lesion-T9 R	L	T10-Co R	L
8	112	T3 	L?	L?			GL	GL	GL	C	GL?	GL?	GL?	GL	GL	GL	C				GL?	GL?			C L?	C L?		GL		

TABLE 3 CONT.

SUMMARY OF RETROGRADE CELL CHANGES.

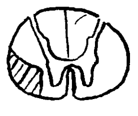
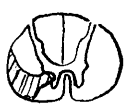
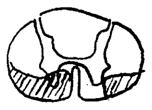
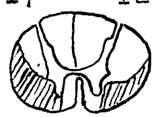
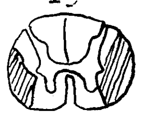
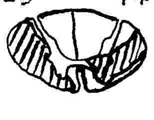
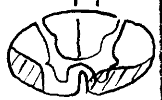
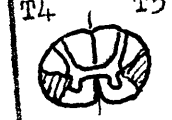
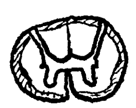
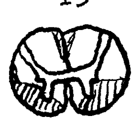
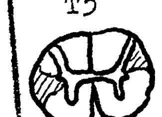
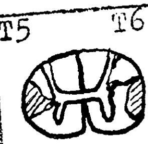
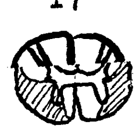
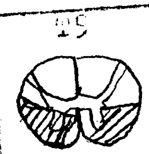
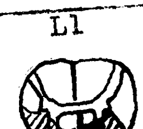
Case No.	Post Operat. Survival	Lesion R	Lesion L	Cells groups showing marked changes.				Cells groups showing some definite changes.				All groups showing only slight changes.												All groups showing some changes: Peripheral involvement.							
				Cells of Clarkes Column				Cells at apex of Dorsal Horn				Cells of Substantia Gelatinosa				Cells of Nucleus Proprius of Dorsal Horn.				Cells at base of Dorsal Horn & in the intermediate grey matter.				Cells of Ventral Horn.				Cells of Lateral Horn.			
				Lesion or C8 -T9		T10 - L2		Lesion-T9		T10 - Co		Lesion-T9		T10 - Co		Lesion-T9		T10 - Co		Lesion-T9		T10 - Co		Lesion-T9		T10 - Co		Lesion-T9		T10 - Co	
				R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
9	23	T5 		C L? S	L?	C L S	C? L?											C	C					C L		(C) L?	C L				
11	116	T6 		C		C L S	C L?					GH						C	C							C ·<	C				C?
13	159	T1 		L GL	L GL	(C) L+ >	(C) L							GL	GL			C GL	C N GL?							C	C				
14	170(R) 102(L)	T7 	T2	L < GL	L GL	L > GH GL	L GH GL			C	C	GL)						C	C			C GL	(C) GL			L?	C GL				
15	53	T3 				L?	L?			C S?	C S?					C			C GH	N			C			V	V				
17	390	T3 	T4	L > GL	L GL	L GH GL	L GH GL					L	L					(C)	C								C				
18	66	T4 		L GH GL	L GH GL	L S GL	L S GL			C+	C	GL?	GL?	GL	GL			C		N GL	GL	C N GL	N GL	GL?	GL?		C				

TABLE 3 CONT.

SUMMARY OF RETROGRADE CELL CHANGES.

Case No.	Post Operat. Survival	Lesion R L	Cells groups showing marked changes. Cells of Clarkes Column: Lesion or C8 -T9 R	L	T10 - L2 R	L	Cells groups showing some definite changes. Cells at apex of Dorsal Horn: Lesion-T9 R	L	T10 - Co R	L	All groups showing only slight changes. Cells of Substantia Gelatinosa: Lesion-T9 R	L	T10 - Co R	L	Cells of Nucleus Proprius of Dorsal Horn. Lesion-T9 R	L	T10 - Co R	L	Cells at base of Dorsal Horn & in the intermediate grey matter. Lesion-T9 R	L	T10 - Co R	L	All groups showing some changes: Peripheral involvement. Cells of Ventral Horn. Lesion-T9 R	L	T10 - Co R	L	Cells of Lateral Horn. Lesion-T9 R	L	T10 - Co R	L
19	23	T4 T5 	C	C	C	C			C	C					C		C	C								c				
22	24	T5 	C L >	C L?	C GL <	C GL	GL				GL?	GL?							C?			N	C				C			
23	39	T5 	C L S <	C L S	C L	C L											(C)				C	C	C L	C L	C	(C)				
25	141	T5 	L N GL >	L N GL	L GL? >	L? GL	GL	GL	C N GL		(GL)	(GL)	(GL)	(GL)	GL	GL	N	N			GL	GL	GL?	GL?	C	C				
26	154	T5 	L+ S >	L+ S	L+ S >	C L+ S				c							C						S?		C	C				
27	42	T5 T6 	L+ S N	L+ S N	C? L+ GL	L+ GL			(C)		GL	GL	GL	GL			(C) L+	GL			GL				(C) (GL)	(C) (GL)				
30	23	T7 	C L? GL	L? N GL	C L GH	C L GH			C N		GL?	GL?	GL	GL				C	N	N+		C		C GL	C >	C	N?	C		
31	280	T7 	L GL	L GL	GL	GL	L?		L?	L?	L (GL)	L (GL)	L GL	L? GL	L?	L?	L?	L?	GL	GL		GL	GL?	GL?	(C)	C	GL	GL	GL	GL
33	109	T9 	L S	L S	L S	L S	C		C	C	(GL)	(GL)	(GL)	C (GL)		C	C	C	C		C L?	C GL?	N	C N	C	C			C?	
34	91	L1 			6	C			C	C							C	C				C		N	C	C N				

In a few cases there are one or two cells which are chromatolytic, in a very large number of sections of the cord. There are so few that no conclusions can be drawn regarding them.

Summary.

A summary of the total evidence of the cells of origin of the ascending fibres in the lateral columns is presented in tabular form as Table 3. Typical examples of changes in all the cell groups have been given in this chapter.

The Table has been divided into four parts in accordance with the frequency of cell changes in certain groups of cells; marked changes, some definite changes, only slight changes, some changes - frequent peripheral nerve involvement. There is consistent evidence relating to cells of Clarke's column. The cell bodies appear to be sensitive to injury of their axons, and many become chromatolytic and disappear within 40 days of the lesion. Fibres arising from cells of this group ascend the cord in the ventro-lateral column as well as in the dorso-lateral column. The course of most of the fibres is ipsilateral to their cells of origin, but a few have a contralateral course. Some of the contralateral fibres probably ascend in the ventrolateral column; it has not been determined if some contralateral fibres also ascend in the contralateral column or not. Some of the fibres ascend in the peripheral layers of the column. Some of the fibres reach the lateral column in the same segment as their cells of origin.

The evidence of the origin of the fibres of the lateral column, other than those from Clarke's column is still rather inadequate. The changes in these other groups appear to occur in a few cells over a longer range of periods of survival, and at no time does any group show such extensive incontrovertible indication of axon damage. When definite changes have been seen, definite conclusions that there is axon damage may be drawn, but when no changes are seen no conclusion as to whether the axon is injured or not can be drawn. This has been discussed in Chapter VII.

It has been shown that fibres arising from apical cells and fibres arising from cells of the nucleus proprius of the dorsal horn ascend in the dorso-lateral and in the ventro-lateral columns. Most of the fibres from the apical cells ascend on the contralateral side, and a few on the ipsilateral side. The fibres from the cells of the nucleus proprius are both ipsilateral and contralateral.

It has also been shown that fibres arise from cells at the base of the dorsal horn and in the intermediate grey matter and ascend on both sides of the cord, in the ventro-lateral column. It has not been determined if any fibres from these cells ascend in the dorso-lateral column or not. Some fibres arise from ventral horn cells of the lumbo-sacral segments and ascend in the lateral column, most probably in the ventral part. Most of these ascend on the contra-lateral side.

No conclusions have been drawn regarding ascending fibres and the cells of the lateral horn.

In view of the paucity of cell changes in the groups other than Clarke's column and the apical cells, no conclusions can be drawn as to the proportion of lateral column fibres arising from these cells. Not all the fibres ascending in the lateral column go to the cerebellum. It is not possible to say definitely which of the fibres arising from which cells go to the cerebellum. But in view of the very large number of cells in Clarke's column which degenerate, and the large number of lateral column fibres which go to the cerebellum, it may be deduced that many of these fibres arise from Clarke's column cells.

CHAPTER XII

CONCLUSIONS.

It now remains to present the conclusions drawn from this investigation of the spino-cerebellar tracts in man.

The usual manner of dividing the spino-cerebellar into two distinct tracts - the dorsal and the ventral - does not give a true representation of the facts. I have been forced to conclude that the following manner of considering the spino-cerebellar tract is one which more closely accords with the facts.

The long spino-cerebellar fibres might best be considered as being in three groups. It is, however, not suggested that the usual conception of two parts of the spino-cerebellar tract should be replaced by a conception of three spino-cerebellar tracts. This would not fit the facts for the following reason. There is a general tendency for the ventral fibres to move dorsally in the spinal cord. Rostral to the upper part of the third cervical segment, there is a complete intermingling of the majority of the spino-cerebellar fibres; thus at these levels it would be impossible to pin-point any fibre and say where it originated and where it lay at more caudal levels. The fibres that enter the cerebellum via the restiform body are intermingled, and come from all levels of the cord. Only a few fibres enter the cerebellum via the brachium conjunctivum. These fibres are not those of the "ventral spino-cerebellar tract" of other workers, but appear to lie deeper to a ventro-lateral group of fibres in the cord. However, for descriptive purposes in the cord it is convenient to discuss fibres occupying the dorso-lateral column and two groups of fibres occupying the ventro-lateral column. These terms are not synonymous with the terms "dorsal spino-cerebellar tract" and "ventral spino-cerebellar tract" of other workers.

The region of the cord on the periphery between the dorsal horn and a line running transversely through the central canal is almost entirely occupied by spino-cerebellar fibres. Most of the fibres of this region arise from cells of Clarke's column; they are mostly ipsilateral (to their cells of origin) some may be contralateral. Some fibres arise from the apical cells of the dorsal horn and from the cells of the nucleus proprius. It is likely that most - though not all - of the fibres arising from the apical cells run contralateral to their cells of origin, and that the fibres arising from the nucleus proprius run both contralaterally and ipsilaterally. Which part of the column is occupied by the fibres from the different cell groups has not been determined. Many of the fibres in this dorso-lateral group are of large calibre. Some of fibres move dorsally as they ascend the cord. The fibres which enter the cord at different levels and which shift dorsally all come to be intermingled in the dorso-lateral column, and there is no lamination of fibres derived from different segmental levels.

Some fibres of this group are already situated in the dorso-lateral zone as low as the first lumbar segment; more fibres are added throughout the thoracic cord, many more arising in the more caudal segments than in the upper thoracic segments. No lesion confined to the dorsal sector of the cord in the cervical region has been examined, so it is not possible to say definitely whether any fibres of the dorso-lateral group arise at this level or not.

In the fourth and third cervical segments the dorso-lateral fibres move ventrally; they become separated from the dorsal horn by the lateral cortico-spinal tract, which in these segments reaches the surface of the cord. In their more ventral position, they form a compact mass of fibres with those of the ventro-lateral column. These dorsal fibres then return to their more dorsal position abutting against the dorsal horn at the first cervical segment. In the medulla, they enter the restiform body, most of them passing the descending nucleus of the fifth nerve on its lateral aspect. As they enter the cerebellum, they at first occupy an area immediately caudal to the anterior lobules of the anterior lobe, dorsal to the dentate nucleus. The distribution of the fibres will be considered later, together with the rest of the spino-cerebellar fibres.

The ascending fibres of the ventro-lateral column are intermingled with fibres of other ascending systems, such as the spino-reticular, spino-tectal and spino-thalamic. It has not been possible to separate completely which fibres of the various systems arise from which groups of cells. It appears that there are two groups of spino-cerebellar fibres in the quadrant of the cord, a peripheral or lateral group, and a deeper group. Many of the fibres of the peripheral group arise from cells of Clarke's column: most of them arise ipsilaterally, but some arise contralaterally. Fibres of the whole ventro-lateral ascending system arise from apical cells of the dorsal horn, mostly, though not entirely, ipsilaterally; from cells of the nucleus proprius both ipsilaterally and contralaterally; from cells at the base of the dorsal horn and the intermediate grey matter; and from cells of the ventral horn, mainly though not entirely, contralaterally.

Some ascending fibres of the ventrolateral column are already present as low as the first lumbar segment. Fibres are added throughout the thoracic cord, and there is some evidence that a few fibres also arise in the cervical cord. Some of these fibres reach the lateral column in the same segment as their cells of origin. During their course in the cord the fibres move dorsolaterally. There is no lamination of fibres in this peripheral group. In the deeper and more medial group, however, there is a certain degree of dorso-lateral, ventro-medial lamination of fibres, those from the most caudal segments lying dorso-laterally to those from the more rostral segments. The size of the fibres in the ventro-lateral column varies from large to very fine. There are more large fibres in the peripheral zone and more fine fibres in the medial zone. The majority of the spino-cerebellar fibres lie in the peripheral zone.

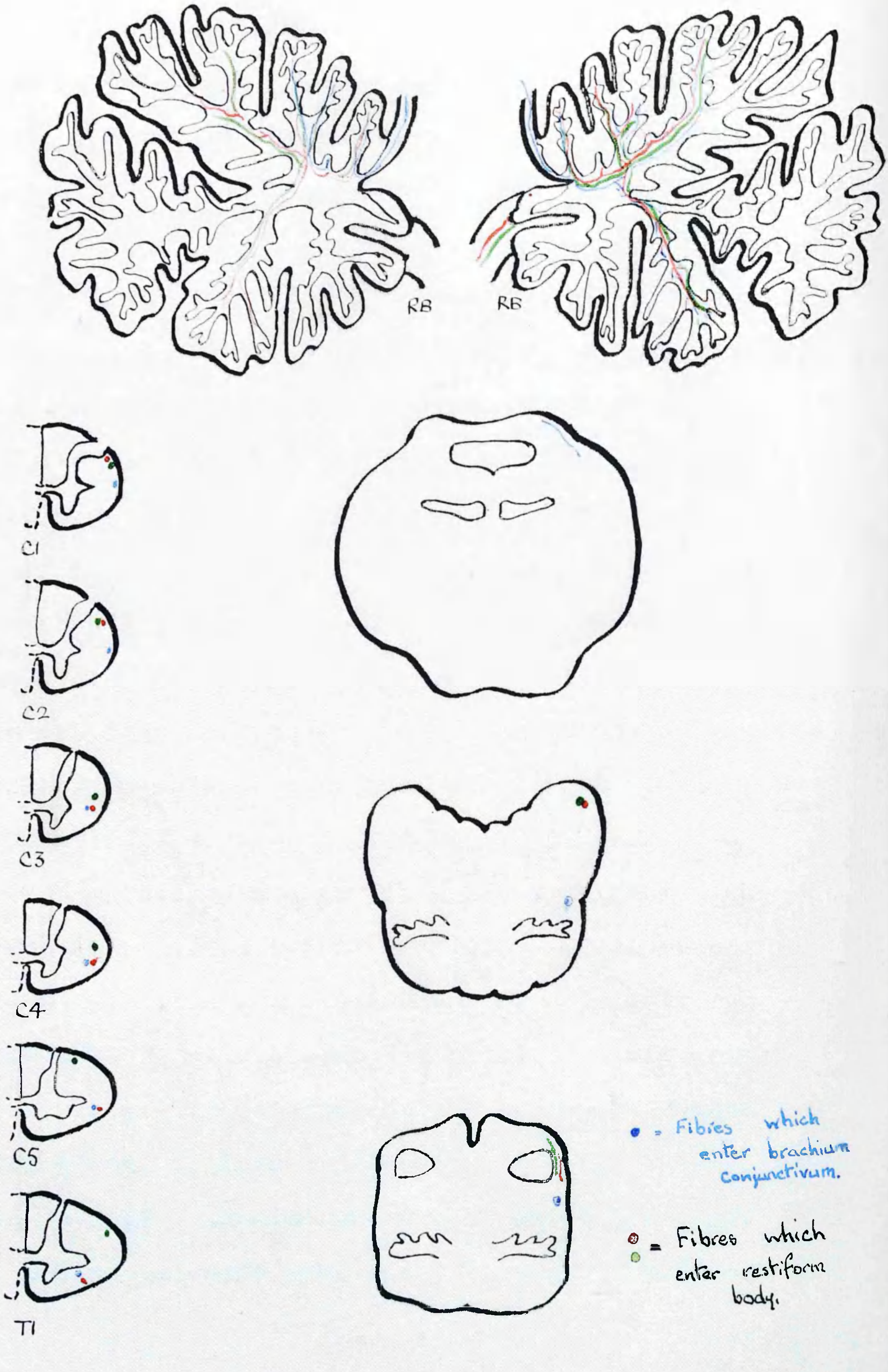
In the lower thoracic segments, most of the peripherally lying ventro-lateral fibres move dorsally into the dorso-lateral column. At other levels of the cord the fibres of the ventro-lateral column, lying ventral to a line through the central canal, remain in this column until the fourth cervical segment. In the fourth and third cervical segments some fibres of the ventro-lateral column move more medially, forming a compact mass with the fibres of the dorso-lateral column. In the second and first cervical segments many of the fibres move dorsally within two segments to reach the most dorsal zone of the dorso-lateral column, intermingling completely with the fibres which ascended the cord in the dorso-lateral column. Many of the fibres of larger calibre in the ventro-lateral column migrate back in this manner. In the medulla these fibres from the ventro-lateral column of the cord are completely intermingled with the dorso-lateral fibres in the zone immediately ventral to the spinal nucleus of the fifth nerve. Thus at this level nearly all the spino-cerebellar fibres are in that position usually attributed to only the dorsal and spino-cerebellar tract. Ventral to these fibres are some remaining ascending fibres from the ventro-lateral column, which reach the restiform body at a slightly more rostral level: they then mingle with the other spino-cerebellar fibres within the restiform body. A small bundle of the fibres from the ventro-lateral column remains dorsal to the olive. Only a few of these are spino-cerebellar; the others are spino-reticular, spino-tectal and spino-thalamic. In the pons these fibres pass obliquely dorsally, so that they come to lie in the dorsal aspect of the pons. As they ascend, a few fibres pass into the cerebellum via the brachium pontis. The remaining spino-cerebellar fibres pass dorsally and caudally into the brachium conjunctivum. As these fibres enter the cerebellum they lie ventro-medial to the fibres which enter by the restiform body. Thus, the fibres entering the cerebellum via different peduncles come to intermingle.

The fibres which entered the cerebellum by the restiform body, lie ventral to the anterior part of the anterior lobe, turn sharply medially to run at right angles to the medial plane of the vermis. They are at first packed compactly into a mass, oval in cross section, and then they gradually spread out along the base of the anterior lobules of the anterior lobe. In the most lateral part of their course in the cerebellum, a large bundle leaves the main mass and passes dorso-caudally to enter the most lateral part of the pyramis and medial part of the biventral lobule. Some of the fibres in the folia run laterally and medially so that they terminate in the lateral parts of the biventral lobule and more medial parts of the pyramis. At the level where this bundle enters the pyramis, a very few fibres leave the main groups and enter the white matter of the anterior lobe. Further medially numerous fibres leave the group and pass into the lingula, the central lobule and the culmen; in the culmen most fibres enter the most anterior part. Some few fibres also go the declive, mostly to its rostral part, and a few fibres enter the folium and the tuber. Some of these fibres spread out to terminate in the hemispheres.

Numerous fibres continue to enter the most anterior lobule of the anterior lobe. Fewer fibres pass into the most medial part of the anterior lobe, than into the more lateral part. A number of the fibres cross to the contralateral side.

The pattern of distribution of the fibres is the same on the contralateral as the ipsilateral side, though there are fewer contralateral fibres.

The fibres which enter the cerebellum by way of the brachium conjunctivum are also distributed in the anterior lobe. Their distribution is approximately the same as that of the fibres entering the cerebellum by the restiform body; but they do not extend as far laterally as the restiform body fibres; and also a larger proportion of the fibres go to the lingula than to the other lobules of the anterior lobe. A small number of fibres also go to the declive, especially to its rostral aspect, and a few fibres go to the folia and tober. A small proportion of these fibres cross in the superior medullary velum and are distributed mainly to the contralateral lingula with a smaller number going to the central lobule and the culmen. It has not been decided if some of the fibres entering by the



RB
RB
C1
C2
C3
C4
C5
T1
= Fibres which enter brachium conjunctivum.
= Fibres which enter restiform body.

brachium conjunctivum go to the pyramis or not. If any do, they must be few, and mainly ipsilateral. A few fibres go into the fastigial nucleus, but whether they actually end there or not has not been decided. No fibres from either the restiform body group nor the conjunctivum group have been definitely traced to other nuclei of the cerebellum.

No fibres of either group have been traced to the uvula or the nodulus.

No somatotopic localisation of any fibres of the spino-cerebellar fibres in the cerebellum has been found. The distribution of the fibres has been the same regardless of the rostro-caudal or the dorso-ventral site of the lesion. In all cases the bulk of the fibres have been found to project to the anterior lobe, in particular to its rostro-medial part, and to the pyramis and medial part of the biventral lobule.

The course and distribution of the spino-cerebellar fibres, as described above, is shown in the diagram on the opposite page.

CHAPTER XIII

DISCUSSION.

My main purpose in this thesis has been to present new facts on the anatomy of the spino-cerebellar tracts in man. Hence, a detailed comparison of the facts shown here and the observations of earlier workers, most of whom worked on animals, will not be given. Some aspects of the findings and discrepancies between the facts as I have found them, and the facts reported by others, however, do demand further consideration.

It was pointed out on page 26 that the spino-cerebellar tract is universally considered as consisting of two distinct parts - the dorsal and the ventral spino-cerebellar tracts. The work which I have presented here has led me to regard this view of the spino-cerebellar tract as untenable. My views on a truer conception of this tract have been summarized in Chapter XII. There are considerable differences in the two views. The essential difference resides in the concept of the ventral fibres of the spino-cerebellar system. According to other workers, these fibres pursue a course in the cord independent of the dorsal fibres. Further, they are held to enter the cerebellum by way of the brachium conjunctivum. In my view, most of the fibres ascending the cord in the peripheral part of the ventro-lateral column pass dorsally and join those of the dorso-lateral column. In the second cervical segment the fibres from the ventro-lateral and dorso-lateral columns are mingled together, and they all enter the cerebellum by way of the restiform body. Thus, the tract which other workers call the ventral (or indirect) spino-cerebellar tract in fact loses its identity in the most cranial segments of the cord; and it does not enter the cerebellum via the brachium conjunctivum, but via the restiform body. There are, however, some ventral fibres which enter the cerebellum via the brachium conjunctivum. These fibres, it is true, do come from the ventro-lateral part of the cord; but they lie deep to those usually designated as the ventral spino-cerebellar tract. They are finer fibres than those of the other two groups, and they are few in number.

It might be asked why other workers have not found these facts. It seems to me that the reasons are the following. The majority of observations have been made on animals and not on man. It is obvious that it is unjustified either to apply such observations to man or to apply findings from man to other species.

All those who worked on man (except Collier and Buzzard) reported their findings on only one, or rarely, two cases. In order to learn the facts about the origin and termination of the tract, one case may be useful. But to learn about the relationship of the fibres from different parts of the body to one another in the spinal cord, several cases are necessary. It has been seen in Chapter VIII that the relationships described here could be worked out only on material consisting of several cases: the material used to work out the course of the fibres as described here consisted of thirty-four cases. It is clear that a large lesion will conceal the different courses of fibres which might be shown up by small lesions. Thus a lesion involving both the dorso-lateral and ventro-lateral columns necessarily masks the changing course of most of the ventro-lateral spino-cerebellar fibres, owing to the concomitant degeneration of fibres of the dorso-lateral column.

In no case, in man, has there ever been made a detailed study of ascending degeneration of the lateral column, in which the lesion was confined to the ventro-lateral zone. It may be noted here, that in animals, also, studies of ascending degeneration after only ventro-lateral lesions are rare. It is true that in the case reported by Gardner and Cuneo and that reported by Rasmussen and Peyton, the lesion did mainly involve the ventro-lateral column. But unfortunately these workers failed to examine every cervical segment: one or two levels are shown as typical of 'the cervical cord'. It will be remembered that the major shift of ventro-lateral column fibres to join the dorso-lateral column occurs in the upper two cervical segments. Any one examining only the lower cervical region will see the picture of two separate and contiguous groups of spino-cerebellar fibres, which is illustrated in every text-book of neuro-anatomy.

A further reason why this dorsal shift of the ventro-lateral peripheral mass of ascending fibres has not been noted is the following. In dogs and monkeys it was known that fibres move dorsally from the ventral part of the dorso-lateral column as they ascend. Any transference of fibres from more ventral regions of the peripheral part of the cord was not recognised as such, but was thought to be merely a part of the shifting of position within the dorso-lateral group of fibres. None of these workers observed the definite shift of the fibres of the ventro-lateral quadrant into the dorso-lateral quadrant in the second and first cervical segments. And it is this intermingling of the fibres of the so-called ventral spino-cerebellar tract with the fibres of the so-called dorsal spino-cerebellar tract which - if it had been observed - would have cast doubt on the validity of the current conception of the whole system.

It is to be recorded however, that Foerster and Gagel did observe this pattern of degeneration of the ascending fibres. They described these fibres which shifted from the ventro-lateral to the dorso-lateral column as "aberrant fibres"; it could not be determined by these workers whether these fibres went to the cerebellum or not.

In this discussion of the reasons for the conception of two clearly separate tracts, we have not considered the views of Schafer and Bruce. They, alone and together, clearly stated their conception of the dorsal and the ventral spino-cerebellar tracts in monkeys as merely components of one and the same tract. Some earlier workers had also noted that some ventral quadrant fibres enter the restiform body, both in man (Barbacci, Rossolimo) and in animals (Kohnstamm, Tschermak). In view of the evidence produced here it is surprising that the observations of all these workers never received more recognition. One reason for this neglect might be that their observations were unsupported by any adequate series of illustrations; the conclusions were merely stated.

A transference of fibres from the ventral zone of degeneration into the restiform body has been observed in this series of cases. This has probably been practically completely unnoticed in other human material, because so few cases have been studied. Schäfer and Bruce recorded a similar finding in monkeys.

Occasionally workers have observed, both in man and in animals, that some fibres leave the ventral group and enter the brachium pontis. In this series of cases a few fibres taking this course was observed. Other workers have failed to see these fibres, doubtless owing to their being few and to the fact that the brachium pontis is very large; at most only very few fibres are likely to be found in any one section.

It is difficult to see why there is a definite separation of spino-cerebellar fibres, arising from Clarke's column cells, into two groups in the cord, for the greater part of their course, and then a complete intermingling of these fibres in the upper cervical segments. The underlying reasons for this temporary separation may perhaps be found rather in electrophysiological work than in anatomical studies.

Little evidence has been produced to show that any spino-cerebellar fibres arise from the upper limbs. The cases showing cell changes in the cervical region are too few, and the changes too scanty, to provide definite conclusions. The fact that cervical lesions cause more profuse degeneration in these tracts than thoracic lesions does suggest that fibres continue to join the tract in the cervical cord.

My evidence on the distribution of the spino-cerebellar fibres within the cerebellum has been presented in Chapter X, and the general conclusions were given in Chapter XII. It has already been pointed out in Chapter II that there is only inadequate knowledge concerning this subject in man.

It is perhaps justified to state that the work reported here is the only systematic study of the human cerebellum planned to find out the distribution of the spino-cerebellar fibres - as far as I know. It is also the first investigation where serial sections were made of this part of the brain. In this series, the cerebella of twenty cases were examined, and of these twenty, twelve were examined in serial section. Also, this seems to be the first series in which the actual evidence has been presented in the form of photographs.

This work of tracing the degenerate fibres throughout such a complicated organ as the cerebellum was helped considerably by the making of the coloured maps (shown on Plates 11-24). Without such maps, it would have been most difficult to recognise which lobulus was being examined. This applies less to the vermis; and this is doubtless one of the reasons why most fibres have previously been traced to the mid-vermis only.

All those who studied the termination of the spino-cerebellar tract in man, with the exception of four workers, made their observations on only one case. The exceptions are Flechsig, whose work was done on the embryo, Hoche who studied two cases, and Collier and Buzzard, who analysed twenty cases of different cord lesions; the evidence they presented consisted of drawings of one case; it cannot be determined from their paper how many cases were studied, their views were given as general statements, but they appear to have been derived from this one case.

All those who studied material from man have presented findings which vary in some respects from each other. The only observation common to all, is that fibres of the "dorsal" spino-cerebellar tract go to some part of the anterior lobe. Some workers think they run only to the vermis, while others have found fibres projecting also to more lateral regions. Fibres are varyingly described as going also to the nodulus and uvula, also the the whole of the rest of the vermis, or to be distributed to the whole vermis and also the lateral lobes. In so far as it was mentioned, the fibres were found to be distributed mainly ipsilaterally to their course in the cord. The "ventral" tract has been described, by workers on human material, as going to the contralateral superior vermis, to the ipsilateral lingula, or to the superior vermis and the flocculus, the side being unstated.

It is necessary to recapitulate briefly the findings from my series of cases. The fibres entering the cerebellum by the restiform body go to the anterior lobe and to the pyramis; a very few go to the declive, the folium and the tuber. The distribution of these fibres to these regions was five ipsilateral to one contralateral. No fibres were found going to other parts of the vermis. The fibres entering the cerebellum by the brachium conjunctivum go to the anterior lobe, the majority going to the lingula; about one in ten cross to the contralateral side. Some fibres may run to the pyramis, but this remains unproven.

The discrepancies between my findings and those of previous workers may be attributed to the following causes.

When the cerebellum is sectioned in the sagittal plane, the impression gained of the distribution of the fibres varies considerably according to the plane of section. For example, a section taken in the most medial plane of the cerebellum would show some fibres in the anterior lobe, and practically none elsewhere in the vermis. But a section taken slightly more laterally on the side of entrance of the fibres, would present a picture of much more abundant degeneration. This is due to the fact that the most medial strip of the vermis receives fewer fibres than more lateral zones. In either of these two planes of section there may be no or almost no fibres in the pyramis. But if a section is taken further laterally, through the lateral border of the vermis, then a large number of fibres will be seen entering the pyramis, and only a few entering the anterior lobe. This may account for some of the variable findings. Further, when sections are cut in the horizontal plane, another reason for false findings is early established. When horizontal slices are cut caudal to the main mass of the central white matter of the cerebellum, there is no continuous white matter to keep the folia in continuity. It is therefore very easy to lose pieces during the technical processes of dehydration and embedding; and so the most caudal part of the cerebellum is not examined.

These observations are sufficient to explain most of the differences between the evidence from my cases and the observations of other workers. But some workers have found a much more extensive distribution of degenerating fibres in the vermis than has been found in the present series. As no photographs were given by previous workers, it is impossible to assess the evidence described. It would appear surprising if there is a more extensive projection of fibres in the vermis, in particular to the uvula the nodulus and the flocculus, than was observed in any of the cases reported here.

No criticism is intended of earlier work, which has laid the foundations of our knowledge, but it is necessary to point out the difficulty involved in assessing the significance of findings stated but not supported by actual evidence. Yet it is these statements which have become the authority for the conception of the spino-cerebellar tract.

It now remains to consider my findings regarding the cells of origin of the tract in relation to previous work. The most striking observation made here is that some of the fibres lying in the ventro-lateral region of the cord arise from cells of Clarke's column both of the same, and, to a lesser extent, of the opposite side. No such observations have been made before, in man, although some workers have described similar findings in animals.

It would seem that the main reason why this was not observed before is that mentioned with regard to the mapping of the ascending fibres: the fact that lesions of the ventro-lateral columns are almost always accompanied by lesions of the dorso-lateral column. Any changes found in Clarke's column have then been attributed to damage to the fibres of the dorso-lateral column. Hogg, who studied the development of Clarke's column in man, found that most of the fibres leaving the nucleus passed to the dorsal part of the lateral column. Only a very few fibres were sometimes seen to pass to the more ventral part. In view of the consistent findings in this series of changes in the nucleus after lesions limited to the ventro-lateral columns, it is surprising that Hogg did not find more fibres going to the ventral part of the lateral column. It is possible that myelination studies in man, with more extensive examination of segments at different levels of the cord, would reveal findings in keeping with those made in degeneration studies. In monkeys, Schäfer and Bruce made similar observations to those which I have made in man; they also found chromatolysis of the Clarke's column cells after lesions confined to the ventral quadrant.

With respect to the other cell groups showing reactive changes after cord lesions, little evidence has been obtained from the present series to show which of the ascending fibre systems arise from which group of cells. It is only possible to say that some fibres of the dorso-lateral column and of the ventro-lateral column arise from the cells at the apex and in the nucleus proprius of the dorsal horn. But whether these fibres lie in the dorsal or the ventral part of the two columns has not been decided; nor could it be decided whether they go to the cerebellum or not. It has been shown that some fibres arise from cells at the base of the dorsal horn and in the intermediate grey matter; but it could not be determined also in this case which group of fibres originated in these cells.

Other workers have also found this difficulty in determining which fibres arise from which group of cells. Foerster and Gagel assumed that the spino-thalamic tract arises from cells of the dorsal horn; but they had even less evidence than that presented here, as a basis for their conclusions. Kuru drew more detailed conclusions from far less evidence. He allocated the different groups of ventro-lateral fibres to different cell groups on the basis of linking cell loss in certain segments with maximum alteration in certain modalities of sensation in the same segments. It is very doubtful whether any of his deductions are valid. His method of sensory testing has been criticised on clinical grounds. And in view of the very definite poverty in cell changes found in this series, outside Clarke's column, it is questionable whether his observation of abundant cell changes, found in two cases, was not based on a too liberal interpretation of certain cell appearances as pathological.

From animal work a correlation between certain ventral horn cells and fibres of the ventro-lateral column was to be expected in man. Bing, from his case of poliomyelitis affecting Clarke's column cells and ventral horn cells, deduced that the 'ventral' spino-cerebellar tract arises from ventral horn cells, in man. His conclusions may be correct, and in view of the observations made here, and summarised in Chapter XII, some fibres of the ventro-lateral column probably do arise from ventral horn cells. But it must also be mentioned that in Bing's case some of the ventro-lateral column degeneration may have resulted from the involvement of Clarke's column cells. It is notable that the difficulty in determining which cells of the cord give rise to each of the lateral column ascending fibres is found in animal work as much as in human work. From the time of Edinger many observers have traced fibres from cells of the dorsal horn and intermediate grey matter into the lateral column. But the interpretation of such findings has been entirely subjective; and incidentally, it is always complicated by the workers' conception of what "Gowers' tract" actually is. It has been shown that many fibres of the ventro-lateral column arise from Clarke's column. Certain cell groups also giving rise to fibres in the ventro-lateral column have been determined. But the final decision as to whether any of the spino-cerebellar fibres arise from these other cell groups as well as from Clarke's column must wait for evidence obtained from cases with lesions of the grey matter of the cord, and from cases with lesions of the cerebellar peduncles.

From the series of cases reported here, no evidence has been obtained of any somatotopic localisation of spino-cerebellar fibres, either in the cord or in the cerebellum. The only fibres showing some variation in their site in the cord, associated with the level of origin, have been found to belong not to the spino-cerebellar, but to the spino-thalamic or spino-tectal systems. No other worker on human material has recorded any somatotopic localisation, although it has been described in animals.

Strong (1929), in the opening chapter of the Association for Research in Nervous and Mental Disease publication 'The Cerebellum' wrote:-

"We do not know the source and nature of many of the impulses projected upon the cerebellum by its various afferent paths; we do not know accurately the areal projections of these various afferent paths upon the cerebellar cortex; we do not know many important details as to the distribution of the cerebellar outflow. Consequently we do not know how far there is topographic representation, how far there is a blending or non-blending of different forms and combinations of activity....."

Towards a filling of some of these gaps in our knowledge, this thesis is presented.

CHAPTER XIV.

SUMMARY.

I. Observations made on certain histological techniques employed to demonstrate degeneration of nerve fibres in the central nervous system are reported.

A. The Marchi method: The following observations are made:

a) Large blocks of tissue can be investigated if they are sufficiently thin, and if certain other precautions are taken.

b) The precautions which have been found to be necessary to avoid artefact formation are discussed.

c) Certain criteria by which the staining signifying genuine degeneration can be distinguished from artefact staining are discussed. The different forms of artefact staining are illustrated.

d) The length of the period of survival during which the Marchi method is applicable, in human tissue, is discussed.

e) The effect of prolonged storage of material in formol saline is discussed, and the value of the Marchi method on such material is illustrated.

f) The occurrence of degenerating fibres, as shown by the Marchi method, in control material, without operative lesions, is discussed.

B. The Gros Bielschowsky silver impregnation method is discussed. Certain new observations on obtaining consistently good preparations with this technique are presented.

II. A method by which maps were made of slices of the cerebellum, cut in different planes, is described. These maps were used to trace the termination of the spino-cerebellar tracts in the cerebellum. A series of these maps is appended.

III. The spinal cords and brains from 34 patients who had the operation of ventro-lateral cordotomy, were utilised to demonstrate the ascending degeneration in the lateral columns.

The following conclusions are drawn: The usual conception of separate dorsal and ventral spino-cerebellar tracts is misleading. Fibres of the ventral spino-cerebellar tract enter the cerebellum in the restiform body along with the fibres of the dorsal spino-cerebellar tract. Only a small proportion of the fibres from the ventro-lateral column of the cord enter the cerebellum by the brachium conjunctivum. Many fibres ascend in the ventro-lateral column of the cord until the level of the third cervical segment, and then transfer into the dorso-lateral column, becoming intermingled with the fibres already there. This transference of fibres in the upper cervical segments has not been noticed before as examination of all three upper cervical segments has not usually been undertaken. Certain changes in the relations of the fibres of the dorso-lateral column, also, in the upper cervical segments, have been described. The fibres of the dorso-lateral column are in juxtaposition with the dorsal horn at the fifth and at the second cervical segments, but are separated from the dorsal horn by the crossed cortico-spinal tract, which comes to the surface of the cord in the third and fourth cervical segments. Minor alterations in the course of the fibres, in the different parts of the lateral column, during their ascent, are also analysed. Many of the fibres of the ventro-lateral column arise from the cells of Clarke's column.

Other groups of cells showing changes are discussed.

The termination of the fibres in the cerebellum has been studied. The majority of the fibres project to the rostral part of the anterior lobe and to the lateral part of the pyramis, on both sides. More of the fibres have been found to end ipsilateral to their course in the cord than contralateral to it. The details of the distribution of the fibres, in relation to the varied topography of the lesions have been studied.

It has been found that fibres project to the same areas of the cerebellum, whether the lesion involves the ventro-lateral column or the dorso-lateral column, and whether it was made at the first lumbar segment or at the first cervical segment, or at any level between these two.

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BIBLIOGRAPHY

ADRIAN, E.D. (1943) Brain, 66, 289.

ANDERSON, R.F. (1943) J. comp. Neurol., 79, 415.

AUERBACH, L. (1890) Virchows Arch. 121, 199.

BARBACCI, O. (1891). Riv. sper. Freniat., 17, 35.

BARKER, L.F. (1901) The Nervous System and its constituent neurones. D. Appleton & Co., N. York.

BASTIAN, C.H. (1867), Med. Chir. Trans. 50, 499.

VON BECHTEREW, W. (1885), Neurol. Zbl. 15, 337. Ibid. 337.

BECK, G.M. (1927), Brain, 50, 60.

BECK, A. & BIKELES, G. (1912) Pflug. Arch. ges. Physiol., 143, 283. Ibid. 296.

BING, R. (1907). Die Bedentung der Spino-cerebellaren Systeme. J.F. Bergmann, Wiesbaden.

BOUCHARD, C. (1866). Arch. gén. Méd. VI^{e} serie, tome 7, 272, 441, 561.

BRODAL, A. & JANSEN, J. (1941). Anat. Anz. 91, 185.

BRUCE, A. (1898). Brain, 25, 757.

BRUCE, N. (1910). Quart. exper. Physiol. 3, 391.

BRUNS, L. (1893). Arch. Psychiat. Nerveukr., 25, 757.

BUCY, P.C., (1927). J. comp. Neurol. 43, 221.
(1928) Ibid. 45, 129.

CADWALADER, W.B. & SWEET, J.E. (1912). J. Amer. med. Ass., LVIII. 1490.

CARREA, R.M.E. & GRUNDFEST., H. (1954). J. Neurophysiol. 17, 208.

CHANG, H.T. (1951). J. comp. Neurol. 95, 43.

CHANG, H.T. & RUCH, T.C. (1944). J. Anat., (London) 83, 303.

CLARKE, J.L. (1951) Philos. Trans. 141, 607.
(1859) Ibid. 149, 437.
(1863) Ibid. 152, 911.

COLLIER, J. & BUZZARD, E.F. (1903). Brain, 26, 557.

COOPER, S. & SHERRINGTON, C.S. (1940). Brain, 63, 123.

COMBS, C.M. (1954). J. Neurophysiol. 17, 123.

DOW, R.S. (1939). J. Neurophysiol. 2, 543.
(1942). Biol. Rev., 17, 179.

DOW, R.S. & ANDERSON, R. (1943). J. comp. Neurol. 79, 415.

DUNCAN, D. (1930). J. comp. Neurol. 51, 197.

(1931). Arch. Neurol. Psychiat. (Chicago). 25, 327.

VON DYDYNSKI, L. (1903). Neurol. Zbl. 22, 898.

EDINGER, L. (1889). Anat. Anz. 4, 121.
(1911). Vorlesungen über den Ban der Nervösen Zentralorgane des Menschen und der Tiere.
Vogel. Leipzig.

FERRARO, A. & BARRERA, S.E. (1935). Brain, 58, 174.

FLECHSIG, P. (1876) Die Leitungsbahnen im Gehirn und Rückenmark des Menschen.
Engelmann, Leipzig.

FOERSTER, O. (1913) Berl. Klin. Wschr. 1, 32.
(1927) Arch. Psychiat. Nervenkr., 81, 707.

FOERSTER, O. & GAGEL, O. (1927) Neurol. Zbl. 47, 139.
(1932) Neurol. Psychiat., 138, 1.

FOVILLE, M. (1844) Traité Complet de L'Anatomie, de la physiologie et de la pathologie du systemè nerveux cérébrospinal.
Fortin, Masson et Cie, Paris.

GARDNER, E. & CUNEO, H.M. (1945) Arch. Neurol. Psychiat. (Chicago). 53, 423.

GASKELL, W.H. (1886). J. Phyziol. 7, 1.

VAN GEHUCHTEN, A. (1906) Anatomie du Systemè nerveux de l'homme. A. Uystpruyst - Dreudonné, Louvain.

GEIST, F.D. (1933) Arch. Neurol. Psychiat. (Chicago). 29, 88.

GLEES, P. (1943). Brain, 66, 29.

GLEES P. & CLARK, W.E. le GROS, (1941). J. Anat. (London) 75, 295.

GOLDSTEIN, K. (1910). Neurol. Zbl. 29, 898.

GRUNDFEST, H. & CAMPBELL, B. (1942). J. Neurophysiol. 5, 276.

GOWERS, W.R. (1878) Clinical Society's Transactions 11, 24 (Read 1877).
(1880) The diagnosis of diseases of the spinal cord. J. & A. Churchill, London.
(1886) Lancet, i, 1153.

HADDEN, W.B. & SHERRINGTON, C.S. (1889) Brain, ii, 323.

HARE, W.T. & HINSEY, J.C. (1940). J. comp. Neurol. 73,489.

HAMILTON, D.J. (1897) Brain, 20, 180.

HOCHE, A. (1896) Arch. Psychiat. Nervenkr. 28, 510.

HOGG, I.D. (1944) J. comp. Neurol., 81, 69.

HORRAX, G. (1915) Anat. Rec., 9, 307.

HORSLEY, V.H. & THIELE, F.H. (1901) Brain, 24, 519.

INGVAR, S. (1918) Folia neuro-biol., Lpz. 11, 105.

KEENE, L. & HEWER, E.E. (1931) J. Anat. (London). 60, 1.

KOHNSTAMM, O. (1900). Neurol. Zbl. 19, 242.

KURU, M. (1938). Gann 32, 1.

LANGWORTHY, O.R. (1930). Contr. Embryol. Carneg. Inst. 21, 37.

LARSELL, O. (1947). J. comp. Neurol. 87, 85.

LASLETT, E.E. & WARRINGTON, W.B. (1899) Brain, 22, 586.

LEWANDOWSKY, M. (1904) Leitungsbahren des Truncus Cerebri. Fischer, Jena.

LÖWENTHAL, N. (1884) Rev. méd. Suisse rom. 4, 54.
(1885) Des Dégénérations secondaires de la Moelle épinière consécutives aux Lésions experimentales médullaires et corticales. Thèse de Genève.

LJUBISCHIN, A. (1912) Neurol. Zbl. 21, 151.

MACNALTY, A.S. & HORSLEY, V. (1909) Brain, 32, 237.

MAY, W. PAGE (1906) Brain, 29, 742.

MARGULIÉS, A. (1897) Mschr. Psychiat. Neurol. 1, 277.

* VON MONAKOW, C. (1883) Arch. Psychiat. Nervenkr. 14, 1.

METTLER, F.A. (1932) Stain Technol. 1, 95.

METTLER, F.A. & HANADA, R.E. (1942) Stain Technol. 17, 111.

MORIN, F., SCHWARTZ, H.G. & O'LEARY, J.L. (1951) Acta Psychiat. Kbh. 26, 371.

MOTT, F. (1888) J. Anat. & Physiol. 22, 479.
Ibid. (1890) Brain, 13, 433.
" (1892) Brain, 15, 215.
" (1895) Brain, 18, 1.

NAUTA, W.S.H. & GYGAX, P.A. (1951) Stain Tech. 26, 5.

DE NEEF, C. (1901) Névraxe. 2, 71.

OTT, I. & SMITH, R.M. (1879) Amer. J. med. Sci., 78, 438.

PASS, I.J. (1931) Proc. Soc. Exper. Biol. Med. 29, 230.
Ibid. (1933) Arch. Neurol. Psychiat. (Chicago) 30, 1025.

PATRICK, H.T. (1893) Arch. Psychiat. Nervenkr. 25, 831.
(1896) J. nerv. ment. Dis. 21, 86.

PELLIZI, G.B. (1897) Arch. ital. Biol. 24, 89.

POIRIER, L.T., AYOTTE, R.A. & GAUTHIER (1954) Stain Tech. 29, 711.

PROBST, M. (1900) Arch. Psychiat. Nervenkr. 33, 1.

QUENSEL, F. (1898) Neurol. Zbl. 17, 482.

RASMUSSEN, A.T. & PEYTON, W.T. (1941) Surgery, 10, 699.

ROMANES, G.T. (1941) J. Anat. London. 76, 112.

Ibid. (1946) Ibid. 80, 117.

ROSSOLIMO. G.J. (1898) Neurol. Zbl. 17, 935.

ROTHMANN, M. (1900) Neurol. Zbl. 19, 16.

RUSSELL, J.S. RISIEN. (1898) Brain, 21, 145.

SCHÄFER, E.A. (1899) Proc. Physiol. Soc. in J. Physiol. XXIV, XXII-XXIV.
Ibid. (1908) in Quain's Anatomy. Longman, Green & Co., London.

SCHÄFER, E.A. & BRUCE, N. (1907) Proc. Physiol. Soc. in J. Physiol. 35, XLIX.

SCHAFFER K. (1895) Neurol. Zbl. 14, 386.

SCHIMERT, J. (1939) Z. Anat. Entw. Gesch. 109, 665.

SCHÜLLER, A. (1910) Wien. med. Wschr. 60, 2292.

SCHWARTZ, H.G. & O'LEARY, J.L. (1941) Surg. 9, 183.

SHERRINGTON, C.S. (1889) J. Physiol. 5, 429.
(1890) Philos. Trans. 181, 33.
(1895) J. Physiol. 14, 255.

SHERRINGTON, C.S. & LASLETT, E.E. (1903) J. Physiol. 29, 188.

SINGER, J. (1887) S.B. Akad. Wiss. Wien. Abth. 3, 95.

SMITH, M.C. (1951) J. Neurol. Neurosurg. & Psychiat. 14, 222.

SNIDER, R.S. & STOWELL (1944) J. Neurophysiol. 7, 331.

SPILLER, W.S. (1905) J. Nerv. & Ment. Dis. 32, 318.
Ibid. (1905) Univ. Pa. med. Bull. 18, 147.

SPILLER, W.G. & MARTIN, E. (1912) J. Amer. med. Ass. LVIII, 1489.

STILLING B. (1859) Neue Untersuchungen ueber den Bau des Rückenmarks. Hotop. Cassel.

STRONG, O. (1929) The Cerebellum. Res. Publ. Ass. nerv. ment. Dis. 6, 3.
Ibid. (1936) Bull. neurol. Inst. N.Y. 5, 378.

STRONG O. & ELWYN, A. (1948) Human Neuroanatomy. The Williams & Wilkins Company, Baltimore.

VON SOLDER, F. (1897), Neurol. Zb. 16, 308.

STEWART, P. (1901). Brain, 14, 222.

SWANK, R.L. & DAVENPORT, H.A. (1934) Stain Tech. 9, 11.
Ibid. 129.
(1935) Ibid. 10, 45.
Ibid. 87.

TESTUT, L. (1893) Traité d'anatomie humaine, Octave Doin. Paris.

TOOTH, H.H. (1885) St. Barts' Hosp. Rep. 21, 135.
(1887) Ibid. 21, 141.
(1889) The Gulstonian Lectures on Secondary degeneration of the Spinal Cord. J. & A. Churchill, London.
(1892) Brain, 15, 317.

THIELE, F.H. & HORSLEY, V. (1901) Brain, 24, 519.

THOMAS, André. (1897) Le cervelet e'tude anatomique, clinique, et. physiologue. G. Steinheil. Paris.

TSCHERMAK, A. (1898) Arch. Anat. Physiol. Lpz. 291.

TÜRCK, L. (1853) S.B. Akad. Wiss, Wien. II, 93.

WALKER, E.A. (1940) Arch. Neurol. Psychiat. Chicago, 43, 284.

VON WALLENBURG, A. (1900) Anat. Auz. 18, 81.

WESTPHAL, C. (1880). Arch. Psychiat. Nervenkr. 10, 788.

VON WOROSCHILOFF, - (1874, published 1875) Arbeiten aus. der Physiologischen austalt zu Leipzig. 9, 99.

YOSS, R.E. (1952) J. comp. Neurol. 97, 5.
(1953) Ibid. 99, 613.

* **MARINESCO, G. (1898). Rev. Neurol. 6, 463.**