

THE STRUCTURE OF THE SPINAL GANGLIA AND OF THE SPINAL NERVES

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FIFTEEN FIGURES

The application to the spinal ganglion of the reduced silver method of Cajal has brought to light many new facts (Cajal, '05) and the renewed interest in this subject has found expression in a number of investigations including that of Dogiel ('08). The present paper is concerned, in part, with a confirmation of these newer observations and in part with observations which, though touched upon by Dogiel and Cajal, escaped serious consideration by either of them.

For this work the largest spinal ganglia (L VI, VII, S I) in large dogs were subjected to the pyridine-silver (modified (Cajal) technique, an account of which has already been published (Ranson, '11). Pieces of fresh nerve are placed for two days in absolute alcohol containing 1 per cent of concentrated ammonia; washed one to three minutes in distilled water; placed in pyridine for twenty-four hours, after which they are washed in many changes of distilled water for twenty-four hours. They are then placed in the dark for three days in a 2 per cent aqueous solution of silver nitrate at 35° C.; then rinsed in distilled water and placed for one day in a 4 per cent solution of pyrogallie acid in 5 per cent formalin. Sections are cut in paraffin and after mounting are ready for examination. With fresh pure chemicals, absolutely clean utensils, and a reasonably constant temperature this method can be relied upon to give uniform results.

¹ The work upon which this paper is based was done in the Anatomische Anstalt, Freiburg i. Br. My thanks are due to Professors Wiedersheim and Keibel, through whose courtesy it was possible for me to carry on the investigation.

The ganglia were cut into sections 18μ thick. It is difficult to make use of thicker sections because the silver method, unlike the intra-vitam use of methylene blue, brings out all the nerve elements so that very thick sections are confusing. On the other hand it is difficult except in thick sections to follow the axons to their bifurcation.

Types of spinal ganglion cells according to external form

1. *The simple unipolar cell.* From the body of a cell of this type arises a single axon, which after a longer or shorter, straight or convoluted course divides dichotomously into a thin fiber directed toward the spinal cord and a much thicker fiber running into the nerve. These represent, according to my observations, the great majority of the cells in the spinal ganglia of the dog. In sections 18μ thick it is only in a small proportion of the axons that the entire course from cell body to bifurcation can be seen. For the most part it is possible to follow the axons for only a limited distance before they leave the level of the section. Many axons can be seen dividing but these can rarely be followed back to their cells of origin. Nevertheless this connection is so well established that it needs no confirmation.

In the case of (a) the large cells, the axon is usually much convoluted in the immediate vicinity of the cell and within its connective tissue capsule, but in some cases the coil is wanting. In other cases the axon is very short and divides almost immediately after leaving the cell. These axons acquire a myelin sheath and stain by the pyridine silver method a light yellow.

(b) All of the small cells and some of the medium sized ones present a different picture (fig. 1). The axon (whose thickness varies with the diameter of the cell) is thin and stains a dark brown or black. These axons seldom make complicated coils about the cells, but run more or less directly toward the central fiber bundles of the ganglia. Here these fibers can be seen in large numbers dividing in the manner of a *T* or *Y* into a very fine centrally directed fiber and a somewhat thicker one running toward the nerve (fig. 2). These branches together with others

of similar origin and appearance form bundles of fine black fibers which can be followed into the dorsal root on the one side and into the peripheral nerve on the other. These axons are devoid of a myelin sheath (or according to Dogiel, some of them may present a thin and interrupted coat of myelin similar to that which is seen on some sympathetic fibers).

The axons in fig. 1 show about the average amount of coiling; but while in many cases they are almost straight, in a few the winding is as pronounced as that of the axon of any large cell. It is of interest to compare the bifurcation of these fibers with that of the medullated axons (fig. 2). These latter branch at a node of Ranvier and show a marked constriction both of the main stem and the two branches at the point of bifurcation. In none of the dividing non-medullated fibers is such a constriction to be seen. Instead there is a broad triangular area at the point of the bifurcation. These fibers differ then from the medullated in their small size, in the intensity with which they stain with silver, in the absence of a surrounding unstained ring of myelin, and in the manner of their bifurcation.

The description which is here given of the small cells and their axons is in no sense new. Dogiel in 1897 gave a very satisfactory account of them, which was confirmed by Cajal ('07) and later again by Dogiel ('08, p. 33). Dogiel found on some of these fibers very fine myelin sheaths which disappeared and reappeared from stretch to stretch along the fiber. It is strange that neither author gave any further consideration to these axons, apparently overlooking the fact that they outnumber the medullated fibers by as much as the small cells outnumber the large. We will return to the significance of these observations in another part of this paper.

2. *Cells whose axons have collaterals ending in end bulbs.* Dogiel's type II, Cajal's type VI. The peculiarity of these cells lies in the fact that the axon gives off fine collaterals, which after a course usually of no great length, end in characteristic swellings, which according to their location may be divided into three sub-groups: (a) In the majority of the cases the collaterals are given off from the axon before it has left the connective tissue capsule

which surrounds its cell of origin. The collateral is usually short and directed toward the surface of the cell but may be long and coiled in its course. It ends in a bulb which lies upon the surface of the cell from the axon of which it arose (fig. 3). The terminal swelling may be very large in proportion to the size of the collateral, and in some cases the latter increases in thickness as it approaches the end-bulbs. These bulbs take only a light stain with silver, appearing bright yellow. They lie upon the surface of the cell beneath the connective tissue capsule and produce as a rule a depression of the cell surface. (b) Sometimes the collateral is given off from the axon at some distance from its cell of origin—and piercing the connective tissue capsule of another cell terminates in an end bulb which lies upon the surface of this second cell (fig. 4). (c) Still other collaterals run in the connective tissue of the ganglion and end there in bulbs surrounded by a special capsule. Sometimes two or three such bulbs lie together in a felt-work of fine fibers and the whole mass is surrounded by a capsule.

Huber ('96) was the first to describe these structures but saw only those that fall under subhead (a). Both Cajal and v. Lenhossék considered that some of these fibers were fine dendritic branches arising directly from the cell body. On this point my observations agree with those of Dogiel for in every case where the origin could be determined they arose as collaterals from axons and never as fine dendrites. According to Cajal and Dogiel the axons of cells of this group, after having given off the collaterals just described, end by dividing after the manner of a *T* or *Y* into central and peripheral fibers.

3. The axon of a cell of this type splits up into a number of branches which with or without further branching are finally reassembled into a single axon. In sections 18μ thick it is not possible to see in their entirety such complicated structures of this sort as were seen by Dogiel in his thicker sections and whole mounts; but the simpler forms are often included within a single section. A relatively common arrangement is seen in fig. 5. The axon divides into two fibers which may or may not be of equal size and which soon reunite. A somewhat more compli-

cated form is shown in fig. 6. Here the axon breaks up into a number of fibers which unite with each other to form a plexus out of which a single axon is again formed. Sections through much more complicated networks formed by splitting axons can often be seen.

4. In another variety, closely related to those just described, the axon arises from the cell by two or more roots, each of which has the appearance of an axon and forms a conical expansion at the point of origin from the cell. Each of these roots may branch repeatedly. These branches then reunite with each other forming a more or less complicated network, out of which a single axon arises (fig. 7).

Groups 3 and 4 are closely related in that the cells of the latter differ from those of the former only in the fact that the splitting involves the initial portion of the axon. In both cases it is rare to find a myelin sheath on the fine fibers forming the plexus. These two groups correspond to Dogiel's types v and vi taken collectively, but the basis of separation into the two groups is different. It is quite bewildering to read Dogiel's description of types v and vi with their subvarieties and try to determine what the basis of classification of his seven subvarieties into these two major groups might have been. For this reason it has seemed best to adopt as a basis of classification the more obvious and apparently more fundamental difference in the origin of the axon by a single or by a number of roots.

According to Dogiel the axons of both types, after exhibiting their peculiar plexiform arrangements course as single axons for some distance and finally divide in the manner of a *T* or *Y* into central and peripheral fibers, a point which could not be verified in the relatively thin sections with which I worked. It was, however, chiefly the origin of the axon from several roots, the splitting of the axon or its roots, and the formation of plexuses in its course which most needed confirmation; the final division of the axon as described by Dogiel agrees so well with our former knowledge of the ganglion that it may safely be accepted. The cells included in groups 3 and 4 are fully as numerous as those in group 2; and if one might be permitted to make a very rough

estimate they might be said to represent together about 3 per cent of the total number in the spinal ganglia of the dog. In the horse, according to v. Lenhossék, they are very much more numerous.

5. Cajal's 'fenestrated' cells are characterized by the presence of excavations in their substance. These are most commonly found in the neighborhood of the origin of the axon, where they often cause a U-shaped mass of protoplasm to be raised from the surface of the cell. The axon usually arises from the summit of such a loop. Fig. 8 shows a simple cell of this kind and fig. 9 a more complicated one. These excavations are filled with small cells, 'subcapsular or satellite cells.' It is only in the poorer of the pyridine silver preparations, however, that these satellite cells are stained. Dogiel was unable to find the fenestrated cells in his preparations—and concluded that Cajal had seen and wrongly interpreted certain cells of our type iv.

Indeed it seems that among his fenestrated cells Cajal has figured and described some which more properly belong with the cells of the preceding variety. There is, however, a group to which the term 'fenestrated' properly applies, such as those seen in figs. 8 and 9. In these the network is formed by protoplasmic loops, while in figs. 5, 6 and 7 the axon is itself broken up to form the network. In the fenestrated cells the axon is usually smaller than the protoplasmic loops from which it arises, while in the other varieties the size of the fibers forming the network is always smaller than that of the axon and depends upon the number of such fibers into which the axon has been split.

In addition to the cells of the varieties just enumerated, one bipolar and two multipolar cells were seen in the sections of the spinal ganglia of the dog. Fig. 10 represents a multipolar cell with short, club-shaped processes, and fig. 11 a cell of Dogiel's type xi, which, according to his more complete pictures, possesses many medullated processes which divide repeatedly, breaking up into fine branches with expanded ends.

According to Nageotte ('07) the fibers ending in end bulbs resemble those seen in large numbers in transplanted ganglia and are therefore to be regarded as being the product of regenerative

activity in the neurone. Cajal ('07) accepts this interpretation and Bielschowsky ('08) extends it to the fenestrated cells and to the cells whose axons have plexuses intercalated in their course. On this hypothesis one would expect to see an increase in the number of such cells after the division of the associated nerve. With this in mind the left sciatic nerve was cut in four dogs and after one month the associated spinal ganglia were prepared by the pyridine silver technique. The results of these experiments were entirely negative. There was no increase in the number of fine fibers ending in end bulbs nor were any other of the peculiar cell types seen in the normal ganglia increased in number. Since the division of the axons might be expected to be as efficient as any stimulus in producing regenerative changes in the neurone, these experiments, so far as they go, speak against the interpretation of these new cell types as the expression of a slow regeneration constantly going on in the normal ganglia. Other experiments are in progress with the purpose of making a more complete test of the hypothesis of Nageotte.

The axons of the small cells

In concluding his section on the cerebro-spinal ganglia in 'Plasma und Zelle,' Heidenhain ('11) says:

Es würde gewiss für die Physiologie von grosser Bedeutung sein wenn wir behaupten könnten, das wir mit der Anatomie der cerebrospinalen Ganglien im reinen sind. Dies ist jedoch nicht der Fall. Erstlich ist der Ursprung der erwähnten afferenten sympathischen Fasern leider nicht näher bekannt Und zweitens befindet sich nach den Zählungen von Gaule und Lewin, ebenso von Bühler in den Ganglien eine ausserordentliche Ueberzahl von Zellen deren Fortsätze wir noch nicht kennen.

It is with this second problem that we wish now to deal. The numerical excess of spinal ganglion cells over medullated afferent fibers is well established as table 1 shows, although in most cases it is not so great as that found by Gaule and Lewin in the 32d spinal nerve of the rabbit.

Hatai ('02) by a separate enumeration of the large and small cells of the (iv C, iv T and ii L) spinal ganglia of the white rat,.

TABLE I
Ratio of spinal ganglion cells to dorsal root fibers

AUTHOR	ANIMAL	NERVE	NUMBER OF GANGLION CELLS	NUMBER OF MEDULLATED AFFERENT NERVE FIBERS
Gaule and Lewin ('96).....	Rabbit	I Coc.	20,361	3,173
Hatai ('02).....	White rat	VI C	12,200	4,227
Hatai ('02).....	White rat	II L	9,442	1,644
Ranson ('08).....	White rat	II C	7,721	2,472

showed that the small cells constitute about 60 per cent of the total number, while Warrington and Griffith ('04) working with the II C. spinal ganglion of the cat estimated the small cells as constituting 70 per cent of the total number. Now we have shown in a former paragraph that the axons of these small cells are non-medullated and it is therefore clear that they could not be taken into consideration in the enumeration of the afferent fibers represented in table 1 based as it was in every case upon a differential myelin sheath stain. It is to these non-medullated fibers, the axons of the small spinal ganglion cells, that we are to look for the explanation of the discrepancy between the number of spinal ganglion cells and *medullated afferent fibers*. If a count of the *afferent axons* were made, the number would probably closely approximate that of the spinal ganglion cells.

We have shown in fig. 1 how these non-medullated fibers arise from the small cells, in fig. 2 how they divide dichotomously into a thin fiber directed toward the dorsal root and a slightly thicker one directed toward the nerve. These branches unite themselves into bundles of fine black fibers which course longitudinally through the ganglion—along with the medullated fibers having an analogous origin from the large cells. These bundles of non-medullated fibers can be followed into the dorsal root to which they give an appearance wholly different from that of the ventral root. Similar bundles of non-medullated fibers can be followed into the nerve. Fig. 12 shows the point of union of the ventral and dorsal roots to form the mixed nerve. It can be seen at a glance that the composition of the dorsal root (*a*), as it streams out of the spinal ganglion to unite with the ventral root (*b*) differs

markedly from the latter because of the bundles of fine black fibers which it contains. One can see this contrast in a striking way where the bundles from the two roots decussate as fibers from the ventral root run into the dorsal ramus (*d*) and others from the dorsal root into the ventral ramus (*c*). Fig. 13 represents a portion of this decussation under higher magnification. In the center is a pure bundle of medullated fibers derived from the ventral root, while the fibers taking the other direction are derived from the dorsal root, and of these some are medullated but more are non-medullated.

It has not been possible to show that no non-medullated fibers run into the nerve from the ventral root, but if present they are in very small number. The majority of such fibers seen in the nerve can be directly traced into the spinal ganglion. Nor has the contribution of the ramus communicans to the non-medullated fibers of the nerve been investigated, but even this must be small compared to the enormous numbers coming through the dorsal root.

As to what ultimately becomes of these fibers, there are as yet no observations. That the central branches of the non-medullated axons enter the spinal cord, there can be no doubt, but their distribution within it has not yet been investigated. That their peripheral branches run for long distances in the nerve has been shown in a previous paper. They have been demonstrated in the sciatic nerve of man, dogs, cats, rabbits and rats (Ranson, '11). Figs. 14 and 15 have been drawn with the aid of a camera lucida from adjacent sections of the same human sciatic nerve, the one (fig. 14) prepared according to the Pal-Weigert technique and the other (fig. 15) by the Cajal silver method. The magnification is the same in both instances. Great care was exercised not to decolorize any medullated fibers in differentiating the Pal-Weigert preparations and the field from which fig. 14 was drawn was chosen because it exhibited the maximum number of small medullated fibers. In the Cajal preparation (fig. 15) the colorless rings represent the myelin sheaths, within which are lightly stained axons. In the interspaces between these medullated fibers are enormous numbers of small black axons directly imbedded

in the connective tissue from which they are only separated by a thin neurilemma. The number of axons medullated and non-medullated which can be seen in the Cajal preparation far exceeds the number of myelin sheaths demonstrated by the Pal-Weigert method.

In summing up this point it may be said that the small cells of the spinal ganglion exceed in number the large cells, that their axons are non-medullated and divide after the manner of a *T* or *Y* into a central and a peripheral fiber. The former runs into the spinal cord and the latter can be followed for long distances in the spinal nerves, but the ultimate distribution of neither the centrally nor peripherally directed branch has yet been determined.

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PLATE 1

EXPLANATION OF FIGURES

The drawings are, with the exception of figs. 14 and 15, free hand sketches from pyridine silver preparations of the spinal ganglia of dogs. Figs. 14 and 15 are camera lucida tracings from a human sciatic nerve, the section from which fig. 14 was drawn having been prepared by the Pal-Weigert method, and that from which fig. 15 was drawn by the Cajal method.

1 Small and medium sized cells with non-medullated axons. Non-medullated fibers black, medullated fibers gray.

2 Bifurcation of a medullated fiber and four non-medullated fibers. The latter are fine and black with a triangular expansion at the point of bifurcation, the former is large and grey (in the preparation light yellow) with a constriction at the point of bifurcation.

3-4 Collaterals ending in end bulbs.

5-6 Cells whose axons are split to form a plexus.

7 A cell whose axon arises by three roots which form a plexus out of which the axon is formed

8-9 'Fenestrated' cells.

10 Multipolar cell.

11 Cell of Dogiel's type xi.

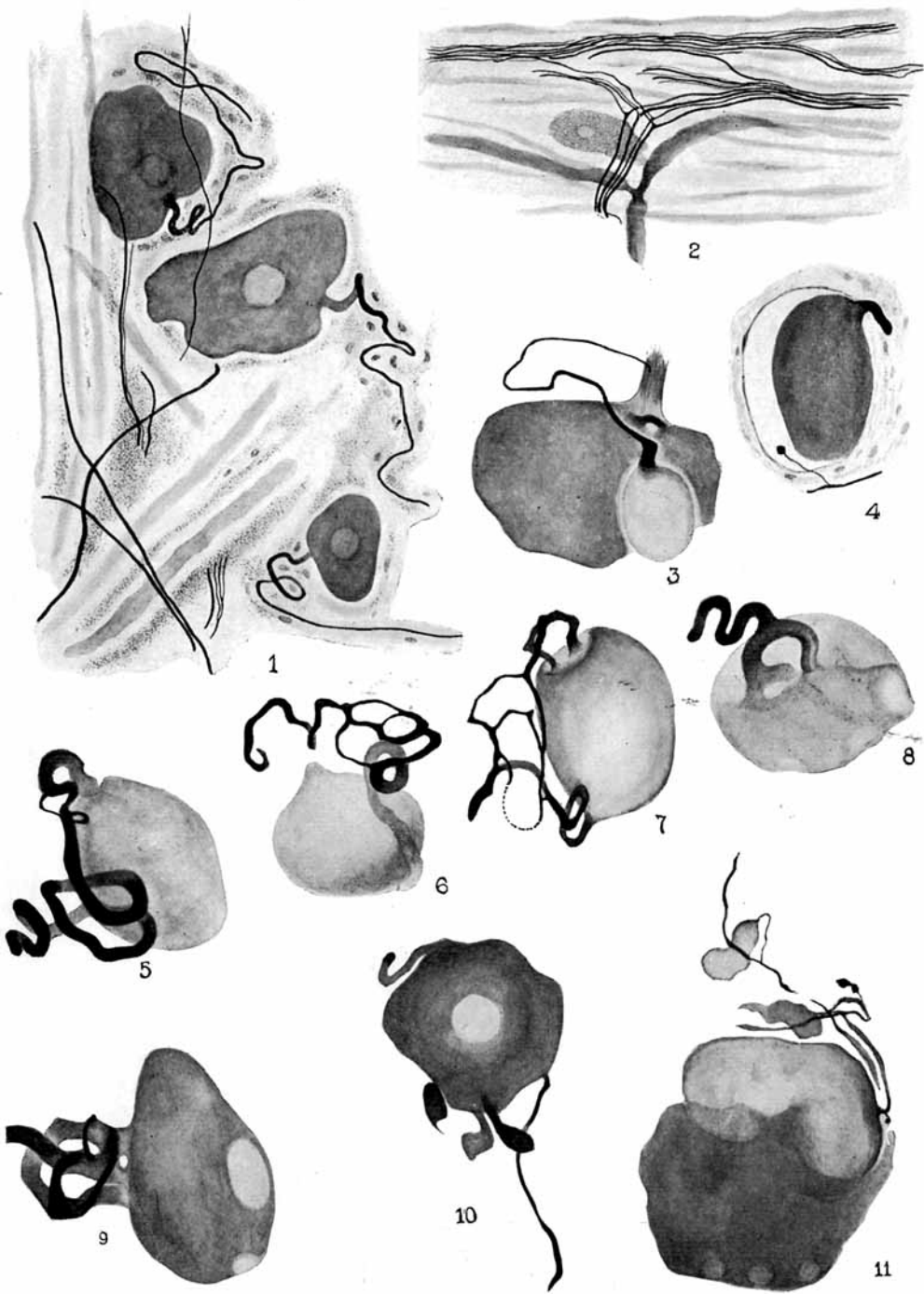


PLATE 2

EXPLANATION OF FIGURES

12 Nerve just distal to spinal ganglion; *a*, dorsal root just outside the ganglion; *b*, ventral root; *c*, ventral ramus of nerve; *d*, dorsal ramus of nerve; *e*, an arrow points to a central bundle of ventral root fibers running into the dorsal ramus.

13 Higher magnification of the central portion of fig. 12. The central bundle is derived from the ventral root and contains only medullated fibers; the fibers passing in the other direction are from the dorsal root. A large part of these are non-medullated.

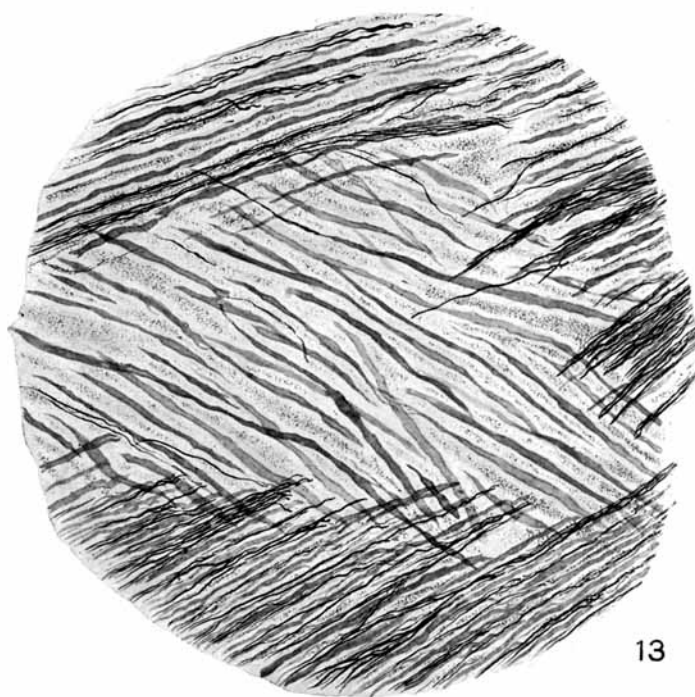
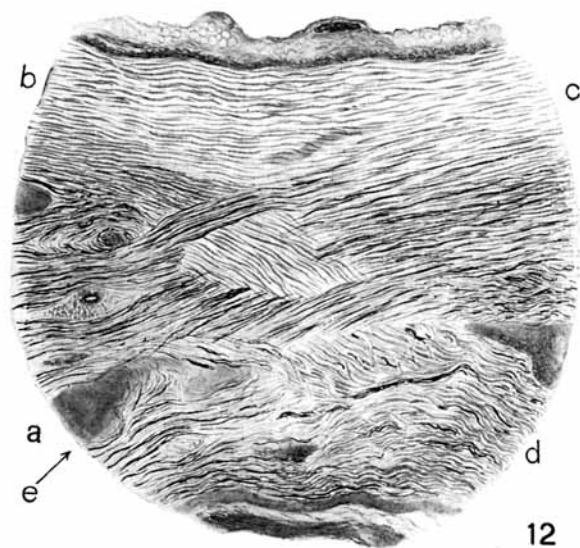
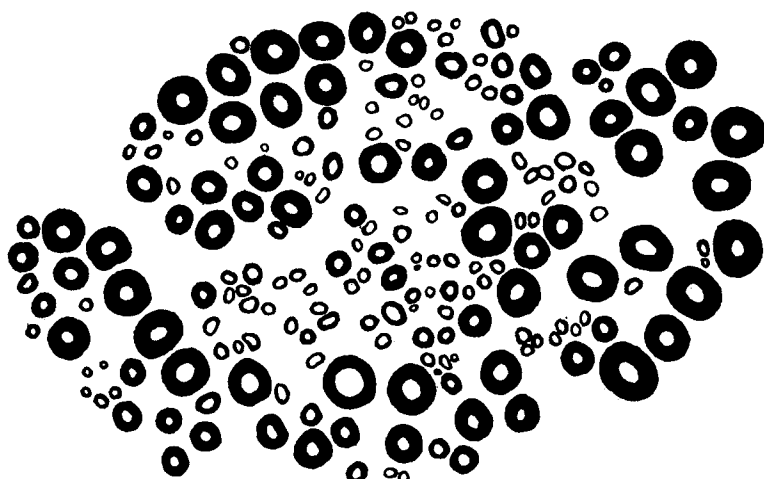


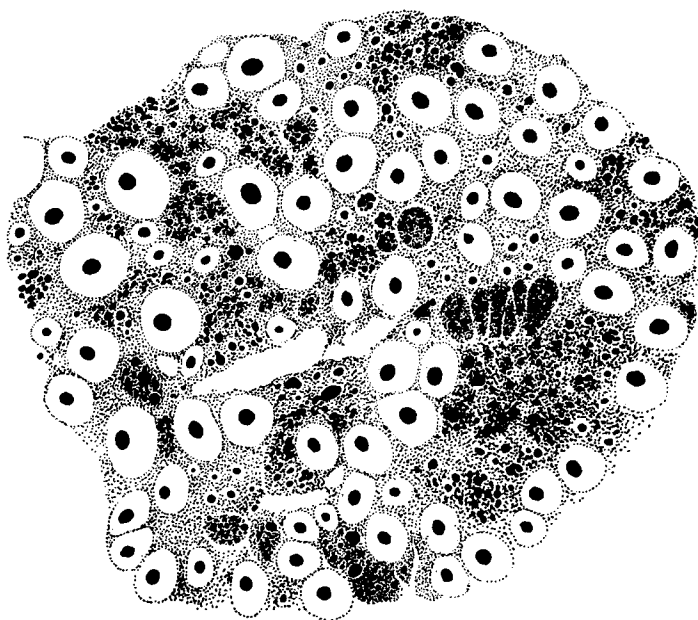
PLATE 3

EXPLANATION OF FIGURES

- 14 Human sciatic nerve in cross section. Myelin sheaths as black rings.
 - 15 From same nerve as fig. 14, axons black, myelin sheaths colorless.
- Non-medullated fibers in the interspaces between the medullated ones.



14



15