J. Anat., Lond. (1964), 98, 1, pp. 17–25
With 5 plates
Printed in Great Britain

Comparative electron-microscopic observations on the connective tissues of a peripheral nerve and a spinal nerve root in the rat

By H. J. GAMBLE

Department of Anatomy, St Mary's Hospital Medical School, London, W. 2

INTRODUCTION

Attempts to tease apart the fibres of a rat's dorsal nerve roots show immediately that they differ from those of a peripheral nerve. The latter separate readily and over lengths of a millimetre or more but the fibres of a root are so soft and fragile that their separation is practically impossible. Clearly some difference in structure, probably involving the quantity or distribution of the endoneurial collagen, must account for this difference in the properties of the fibres concerned.

The connective tissues of peripheral nerve have recently been studied by electron microscopy (e.g. by Causey & Barton, 1959; Thomas, 1963*a*) and the results, in general, confirm those of the classical researches of Key & Retzius (1876) and Ranvier (1878). Nerve roots, by contrast, have been relatively neglected by electron microscopists. Using light microscopy Tarlov (1937) reported that the structure of nerve roots corresponds with that of peripheral nerve, and Laidlaw (1930) had found an essentially similar distribution of collagen and reticulin in the two situations. These findings, however, are of questionable value in view of the inadequacies of the collagen staining techniques available for light microscopy (Harkness, 1961). Collagen may be recognized quite readily in electron microscopy and this technique has therefore been employed to compare collagen distribution in peripheral nerve and in nerve roots with the possibility in mind that differences might account for the dissimilar teasing properties described above.

MATERIALS AND METHODS

Four young adult male albino rats, weighing between 180 and 210 g. were used. From 2 of them tissues for electron microscopy were taken under chloral anaesthesia, and consisted of 3 normal sural nerves and 4 normal sacral dorsal roots. The other 2 were operated on and allowed to survive for 6 and 10 months, when they weighed 280 and 300 g., respectively. At operation (under ether anaesthesia and with aseptic precautions) the cauda equina was approached from the dorsal aspect through small openings made in the sacrum and dural sac and one or more roots divided. Adherent scar tissue made the proximal and distal stumps, although reunited, easy to identify when the animals were killed. In addition to the central stumps of the divided roots, 2 normal roots and 2 sural nerves were taken from the experimental animals. On examination these appeared identical with those taken from the younger animals.

All tissues for electron microscopy were fixed in buffered 1 % osmium tetroxide for 2–4 hr. and stained with 1 % P.T.A. (in 90 % ethanol) during the course of the dehydration which led to imbedding in Araldite. Blocks were sectioned on a Porter–Blum or Huxley microtome, sections mounted on copper grids (some carbon-filmed, but most uncoated) and examined with a Siemens Elmiskop I electron microscope.

RESULTS

Peripheral nerve (sural)

The connective tissues of rat sural nerve are essentially similar to those described in the rabbit by Thomas (1963*a*). They will therefore be described briefly (emphasizing only the differences observed) before turning to consideration of the nerve roots.

Endoneurium. The usual cellular elements are present, viz. capillary endothelial cells and pericytes, fibroblasts, mast cells and Schwann cells. The Schwann cells can be distinguished by their relationship to axons and by the presence of a basement membrane, and the fibroblasts by the absence of both these features. Occasional masses of cytoplasm, sometimes nucleated, and surrounded by a basement membrane but with no enclosed axons were taken to be processes of Schwann cells. The fibroblasts are quite numerous in the interstices between nerve fibres and immediately within the perineurium; their processes may extend for considerable distances between and sometimes around nerve fibres. Mast cells, previously seen by light microscopy (Gamble & Goldby, 1961), are also present (Pl. 1, fig. 2). They are characterised by large (up to 1 μ) inclusions so numerous that the cytoplasm is reduced to narrow strands. Nothing was seen which would support the view that the mast cells are implicated in the elaboration of connective tissue ground substance and, indirectly, of fibrils (Riley, 1959).

Endoneurial collagen fibrils are of small diameter (250–650Å.) and for the most part directed longitudinally. Around the larger myelinated fibres they often form an outer densely packed layer and an inner layer of finer and less regularly oriented fibrils (Pl. 1, fig. 1). These layers seem to correspond with the sheaths of Key & Retzius and of Plenk-Laidlaw as they have been defined by Thomas (1963*a*); they are sometimes incomplete and the inner sheath is seldom identifiable around the smaller nerve fibres. As in rabbit endoneurium (Thomas, 1963*a*) no elastin fibres have been seen but occasional groups of 100 Å. microfibrils are present, scattered among the collagen fibrils.

A feature of the collagen not previously described is the frequent inclusion of bundles of fibrils within what appear to be reduplications of the basement membrane of Schwann cells (Pl. 2, fig. 6*c*). These bundles may indent the surface of the Schwann cell, or become more deeply invaginated to form 'collagen pockets' (Pl. 2, fig. 6*a*, *b*). Occasionally the invagination penetrates the beginning of a mesaxon (Pl. 1, fig. 5) and sometimes it is much deeper so that the bundle of collagen fibres becomes suspended by a double layer of plasma membrane in much the same way as an axon by its mesaxon. The invagination includes the basement membrane which separates the collagen fibres from the plasma membrane, although the layer of basement membrane is not always complete (Pl. 1, fig. 3). What appears to be a further extension of this process is shown in Pl. 2, fig. 7. Here collagen fibres are

found between the basement and plasma membranes of a cell process and five invaginated bundles are suspended by 'mesaxons' which make up to two spiral turns before their layers separate to enclose the bundle. Their relationship to the cytoplasm is identical with that of an axon to the cytoplasm of a Schwann cell and the appearance of the spiral turns is very like that of incipient myelination. In the cell process illustrated no axons are seen, but the presence of a well defined basement membrane makes it probable that it is a process of a Schwann cell.

Nothing like the collagen pockets described above was seen in relation to the Schwann cells of myelinated nerve fibres. The only unusual appearance noted here was the very occasional presence of bleb-like projections of the basement membrane which had no special relationship to collagen fibrils.

Perineurium. The concentric cellular layers of the perineurium are separated in places by collagen fibrils, most of which run longitudinally and are 250–625 Å. in diameter. No elastin nor microfibrils have been seen. Although four cytoplasmic layers can often be identified (Pl. 5, fig. 13), this does not necessarily indicate that four layers of cells are present because the cytoplasmic extensions of single cells may branch. A small nerve containing only 3 myelinated and some 30 unmyelinated axons was found to be covered by a single cytoplasmic layer. Both inner and outer surfaces of the layers are covered by basement membranes, but where they are closely apposed the basement membranes fuse to form a single intervening membrane. Where edge to edge contacts occur within a layer, no basement membranes intervene and the plasma membranes are thickened to form the 'closed contacts' described by Thomas (1963*a*); such contacts have not been seen between successive layers. Elongated mitochondria and flattened nuclei are also characteristic of perineurial cells.

Epineurium. The epineurium consists almost wholly of longitudinally directed collagen fibrils which may be considerably thicker than those found in either perineurium or endoneurium, ranging from 250 to 1000 Å. in diameter (Pl. 5, fig. 13). The usual cellular elements (fibroblasts, vascular endothelial cells, etc.) are present in small numbers but neither elastin nor microfibrils have been seen.

Teased nerve fibres. The electron microscopic examination of sections of teased sural nerve fibres showed that in both myelinated and unmyelinated fibres a covering of collagen fibrils had been retained. Clearly such teased fibres gain some and perhaps most of their tensile strength from this associated collagen.

Dorsal nerve roots (sacral)

As already stated, light microscopy has revealed no significant differences between the connective tissues in nerve roots and peripheral nerves (Laidlaw, 1930; Tarlow, 1937). Mast cells however, are absent from nerve roots central to the ganglion.

Endoneurium. Electron microscopy shows that the collagen fibrils (which are slightly finer than in the sural nerve with a maximum diameter of 550 Å.) run longitudinally and often form no more than a single attenuated layer between adjacent nerve fibres (Pl. 3, fig. 8). Small aggregations may occur and are sometimes found associated with blood vessels or with the inner aspect of the pial covering (Pl. 5, fig. 14), but the proportion of collagen is obviously very much smaller than

in the peripheral nerve. Sheaths of Key & Retzius and of Plenk–Laidlaw cannot be recognized, although fibres running obliquely near the nodes of Ranvier and perhaps around them (Pl. 4, fig. 10) have some resemblance to those of the latter.

'Collagen pockets' are present and show some of the features described in the sural nerve (Pl. 3, fig. 9). They are seen less often, perhaps because unmyelinated fibres are less numerous and the collagen less abundant, and so far they have not been seen in a cell or cell process which contains invaginated axons as well. The cell illustrated in Pl. 3, fig. 9 is probably a Schwann cell because of the presence of the basement membrane, but as basement membranes also surround endothelial cells and pericytes this identification is not certain.

The pial sheath. The pial sheath of nerve roots has essentially the same structure as the perineurium of peripheral nerves as recognized many years ago by Key & Retzius (1876) and Laidlaw (1930). It shows as many as four lamellae in electron micrographs with basement membranes similar to those of perineurial cells (Pl. 5, fig. 14). Collagen fibrils are almost all longitudinally directed and of about the same size as those of the endoneurium. No epineurium covers the individual nerve roots; the dural sac is said to be its equivalent, but has not been investigated.

Regenerated dorsal nerve roots (sacral)

Endoneurium. After 6 months a dorsal root central to the transection contains large numbers of fibroblasts, debris, regenerated nerve fibres (including myelinated fibres ranging from 1·5 to 8 μ in diameter) and a greatly increased quantity of collagen (Pl. 4, figs. 11, 12). Little further change occurs after 10 months except that less debris is present. The collagen may be coarser than in normal roots and consists of fibrils from 250 to 600 Å. in diameter. They run in bundles in all directions occasionally interspersed with microfibrils, but are not organized to form recognizable sheaths around the nerve fibres. No elastin fibres are seen.

Fibroblasts are more numerous than in normal roots and similar in appearance. A few contain distended cisternae in the endoplasmic reticulum and many mitochondria, as might be expected 'under conditions engendering the rapid formation of collagen fibrils' (Chapman, 1962). Very occasionally such fibroblasts contain fine filaments (about 100 Å.) and may lack a clear limiting membrane over parts of their surface. Some cells containing debris in vacuoles within their cytoplasm resemble fibroblasts in all other particulars (Pl. 4, fig. 12) but should perhaps be classified as macrophages. They were seen more often in the 6 months than in the 10 months specimen. In the latter most of the debris was lying free in the tissue. Other cellular constituents (endothelial cells and pericytes) show no unusual features.

Pial envelope. After 6 months' survival the pial envelope is very variable in structure. In some places it is reduced to a single cytoplasmic layer (as in Pl. 5, fig. 15) with swollen nuclei and the outer basement membrane absent. In others the nuclei have their normal flattened form (Pl. 5, fig. 16) but the cytoplasmic extensions enclose large, apparently empty vacuoles. The collagen of the pial envelope is also affected, being much reduced in some areas and more than usually abundant in others. In regions showing marked structural change basement membranes are present only over small and scattered areas.

DISCUSSION

The primary purpose of this work was to investigate the possibility that the different mechanical properties (as shown by teasing) of peripheral nerves and their spinal roots were due to differences in the connective tissue framework. The very small content of endoneurial collagen which has been demonstrated in the root, as compared with a peripheral nerve, shows that this is indeed the case, at least so far as the rat is concerned.

The illustrations published by Hess (1956) show that a similar condition may apply in the rabbit, although he was not primarily concerned with the connective tissues and did not comment on the quantities of collagen present. Similarly Gasser's (1955) electron micrographs of dorsal roots in the cat show very little or no collagen. Although his preparations were not made to demonstrate connective tissues, any considerable quantity of collagen would have been obvious. If this condition is general, it is surprising that it was not observed by Laidlaw (1930) or Tarlov (1937). Laidlaw stated that both 'the longitudinal fibres and the web' (corresponding to the sheaths of Key & Retzius and of Plenk–Laidlaw, respectively) 'are heavier and more prominent' in nerve roots than in perpheral nerve, and Tarlov that the connective tissues of nerve roots correspond with those of peripheral nerves. Tarlov worked mainly with human material; Laidlaw's illustration of a nerve root is from a cat, but he worked also with dog, rabbit, guinea-pig, rat and man, at least so far as the peripheral nerves were concerned. The possibility of species differences clearly cannot be excluded, but it seems more likely that the inadequacy of light microscopy for the quantitative evaluation of the collagen content of nerves accounts for the discrepant observations. Harkness (1961) points out that the specificity of collagen staining is not established and that collagenous tissue does not stain consistently. Positive results require confirmation by other means and a negative result does not preclude the presence of collagen. This difficulty does not apply in electron-micrographs when collagen fibrils can be recognized with confidence.

The presence of endoneurial tubes (presumably the collagenous sheaths of Key & Retzius and of Plenk–Laidlaw) in peripheral nerve has sometimes been emphasized as helping to explain the regenerative powers of peripheral nerve fibres (see, for example, Sanders & Young, 1944). There is also no doubt of the ability of dorsal root fibres to regenerate, at least through the length of the root itself. They were seen to do so by Cajal (1910) and more recent evidence is provided by Nathaniel (1962) and by the present study. The processes of regeneration in nerve roots must begin in the absence of tubular collagenous sheaths and the subsequent increased collagen content does not become organized to produce sheaths in any way comparable with those of normal or degenerated peripheral nerves. The degree of maturation of nerve fibres observed in this work has been achieved therefore, in the absence of 'endoneurial tubes' of collagen. Thomas's work (1963*b*) suggests that a tubular structure, containing proliferated Schwann cells, may be formed by the basement membrane which once surrounded the intact nerve fibre. Such an arrangement could be present in both regenerating peripheral nerves and nerve roots, and responsible for their common powers of regeneration, but more evidence is required

before this can be regarded as more than a speculation. At present it can be said only that organized collagenous sheaths are not essential for the regeneration and maturation of the fibres in nerve roots.

A second result of the present work is the demonstration of 'collagen pockets' in the Schwann cells of unmyelinated axons and in other basement membrane-covered cells which are probably also Schwann cells but lack the axons which would confirm their identity. Several bundles of collagen may be invaginated into a single cell of the latter type, each bundle being attached to the cell surface by a spiralling 'mesaxon'. This condition may be visualized as arising by individual growth or elongation of the 'mesaxons' but not from a rotation of the cell around the several bundles: a similar mechanism may, of course, be involved in the formation of myelin.

A close contact between endoneurial collagen and the basement membrane of Schwann cells is an inevitable consequence of the ensheathing of the nerve fibres by collagen. It has been described in some detail, especially in regenerating nerves, by Causey & Barton (1959; 1961), Causey (1962), and Barton (1962). These contacts have been put forward as evidence for collagen formation by Schwann cells, supported by the supposition that endoneurial fibroblasts are too few to perform this function. Thomas (1963*a*), however, thinks that endoneurial fibroblasts may be much more numerous than previously reported (Causey & Barton, 1959). The present demonstration of particularly intimate and in some places highly organized contacts between collagen fibrils and cells which are not fibroblasts, might be taken as further evidence for a formative relationship but is not, of course, conclusive. There is no reason at all for supposing that collagen fibrils outside the basement membrane of Schwann cells are not formed by fibroblasts and the situation of those within the basement membrane could have been acquired secondarily after their formation.

The finding of bundles of collagen fibrils deeply invaginated into Schwann cells and attached to the cell surface by mesaxon-like prolongations of the surface membrane is also relevant to this question. It shows that Schwann cells or their processes are capable of engulfing not only axons, but other elongated structures of suitable dimensions and orientation. This is a function performed only once by the Schwann cells of myelinated nerve fibres where invaginated collagen bundles have never been seen; it is repeated many times by the Schwann cells of unmyelinated fibres, and, by such a cell, is occasionally directed at collagen fibre bundles. It is possible that the Schwann cells of myelinated and unmyelinated fibres are of two different types as suggested by Antoni (1920) and recently by Barton (1962), only the latter having the general potentiality for engulfing either axons or collagen. On the other hand, there is some evidence that the behaviour of the Schwann cell in forming or not forming a myelin sheath is dependent on the nature of the axon with which it becomes associated (Simpson & Young, 1945). However this may be, the similarity between the relationship of axons and, occasionally, collagen to Schwann cells, suggests that the situation of the collagen, like that of the axon, is secondary and not evidence of formation by the Schwann cell.

The present work has also confirmed that the perineurium of peripheral nerves and the pial coverings of nerve roots are essentially similar in structure. This was first pointed out by Key & Retzius (1876) and the lamellar form of perineurium,

where fibrillar and cellular layers alternate, was described by Ranvier in 1878 and received confirmation by Thomas (1963*a*).

It has been demonstrated in a number of investigations that the connective tissue sheaths of peripheral nerves form an effective barrier to the diffusion of certain ions (see, for example, Huxley & Stampfli, 1951) and certain drugs capable of blocking nerve impulse conduction (Crescitelli, 1951). There has been dispute over the site of the barrier, the perineurium being favoured by Huxley & Stampfli, by Krnjević (1954) and by Thomas (1963*a*). If the diffusion barrier is indeed located in the perineurium it might be expected that the pial covering of nerve roots, similarly constructed, would possess similar properties. There is reason to doubt if this is so. Many works concerned with spinal and epidural analgesia stress the importance of avoiding the injection of an intended dose of epidural analgesic into the subarachnoid space where effects are obtained far more rapidly and with smaller doses. Lee (1959, p. 268) explained this by saying that 'the nerve roots within the dura have no epineurial sheaths and are therefore easily affected by doses of analgesic brought into contact with them' and recommended very much larger doses for epidural than for intradural injection. All this clearly implies that the nerve root fibres are more quickly and effectively penetrated by the analgesic via the pial covering than are peripheral nerves through their perineurial and epineurial coverings. Since the perineurium and pial coverings are so similar, this suggests that the effective barrier may be the epineurium. Alternatively, perineurium and pia may have different properties so far as their permeability is concerned in spite of their structural similarity.

SUMMARY

1. The connective tissues of a peripheral nerve (sural nerve) and of sacral dorsal nerve roots of the rat have been compared using the techniques of electron microscopy.

2. Except that mast cells are present in the endoneurium of peripheral nerve and absent from that of nerve roots, the cellular elements are essentially similar in the two structures and conform closely with the pattern recently dscribed in the peripheral nerve of rabbit.

3. Endoneurial collagen is very scanty in the nerve roots and is not organized as sheaths around the nerve fibres; this is in marked contrast with the distribution of the abundant collagen of peripheral nerve.

4. Collagen fibrils of the endoneurium of peripheral nerve (especially) and of nerve roots may be found in peculiarly intimate relationships with the cytoplasmic and basement membranes of the Schwann cells of unmyelinated nerve fibres. On occasion this relationship closely resembles those found between Schwann cells and unmyelinated and newly myelinating axons.

5. Six and ten months after transection of nerve roots, endoneurial collagen is greatly increased in quantity but its distribution is random and it does not form recognisable sheaths around the regenerated nerve fibres. Fibroblasts and Schwann cells are more numerous than in normal roots but there is no evidence of change in pericytes nor in vascular endothelial cells. Debris is present in macrophages and lying free in the interstitial spaces. The flattened cells of the pial covering apparently

react locally to injury, with loss of basement membrane and the formation of vacuoles within their cytoplasm.

6. The significance of the findings has been discussed.

Thanks are due to the Wellcome Trust for providing the electron microscope and to the Dowager Countess Eleanor Peel Trust for the microtomes.

I wish to thank Dr M. Kidd and Miss Rosemary Eames for advice and help with electron microscopy, Prof. F. Goldby for helpful criticism of the manuscript and Mr R. J. Fant for photography.

REFERENCES

ANTONI, N. R. E. (1920). *Ueber Rückenmarkstumoren und Neurofibrome.* München: J. F. Bergmann.

BARTON, A. A. (1962). An electron microscope study of the degeneration and regeneration of nerve. *Brain*, **85**, 799–808.

CAJAL, S. R. Y (1910). Observations sobre la regeneración de la porción intramedular de las raíces sensitivas. *Trab. Lab. Invest. biol. Univ. Madr.* t. 8, fasc. 4.

CAUSEY, G. (1962). The structure and function of the supporting cells of the nervous system. In *The Scientific Basis of Medicine Annual Review*, pp. 294–304. University of London: The Athlone Press.

CAUSEY, G. & BARTON, A. A. (1959). The cellular content of the endoneurium of peripheral nerve. *Brain.* **82**, 594–598.

CAUSEY, G. & BARTON, A. A. (1961). An electron microscopic examination of degenerating and regenerating peripheral nerve. In *Cytology of Nervous Tissue.* Proc. Anat. Soc., November 1961. London: Taylor and Francis.

CHAPMAN, J. A. (1962). Fibroblasts and collagen. *Brit. med. Bull.* **18**, 233–237.

CRESCITELLI, F. (1951). Nerve sheath as a barrier to the action of certain substances. *Amer. J. Physiol.* **166**, 229–250.

GAMBLE, H. J. & GOLDBY, S. (1961). Mast cells in peripheral nerve trunks. *Nature, Lond.*, **189**, 766–767.

GASSER, H. S. (1955). Properties of dorsal root unmedullated fibres on the two sides of the ganglion. *J. gen. Physiol.* **38**, 709–728.

HARKNESS, R. D. (1961). Biological functions of collagen. *Biol. Rev.* **36**, 399–463.

HESS, A. (1956). The fine structure and morphological organization of non-myelinated nerve fibres. *Proc. Roy. Soc.* B, **144**, 496–506.

HUXLEY, A. F. & STAMPFLI, R. (1951). Effect of potassium and sodium on resting and action potentials of single myelinated nerve fibres. *J. Physiol.* **112**, 496–508.

KEY, A. & RETZIUS, G. (1876). *Studien in der Anatomie des Nervensystems und des Bindegewebes.* Stockholm: Samson and Wallin.

KRNJEVIĆ, K. (1954). The connective tissue of frog sciatic nerve. *Quart. J. exp. Physiol.* **39**, 55–72.

LAIDLAW, G. (1930). Silver staining of the endoneurial fibres of the cerebro-spinal nerves. *Amer. J. Path.* **6**, 435–444.

LEE, J. A. (1959). *A Synopsis of Anaesthesia.* Bristol: John Wright.

NATHANIEL, E. J. H. (1962). Fibrillogenesis by reactive Schwann cells in regenerating dorsal roots. In *Electron Microscopy*, ed. S. S. Breese. New York and London: Academic Press.

RANVIER, M. L. (1878). *Leçons sur l'histologie du système nerveux.* Paris: F. Savy.

RILEY, J. F. (1959). *The Mast Cells.* Edinburgh and London: E. and S. Livingstone, Ltd.

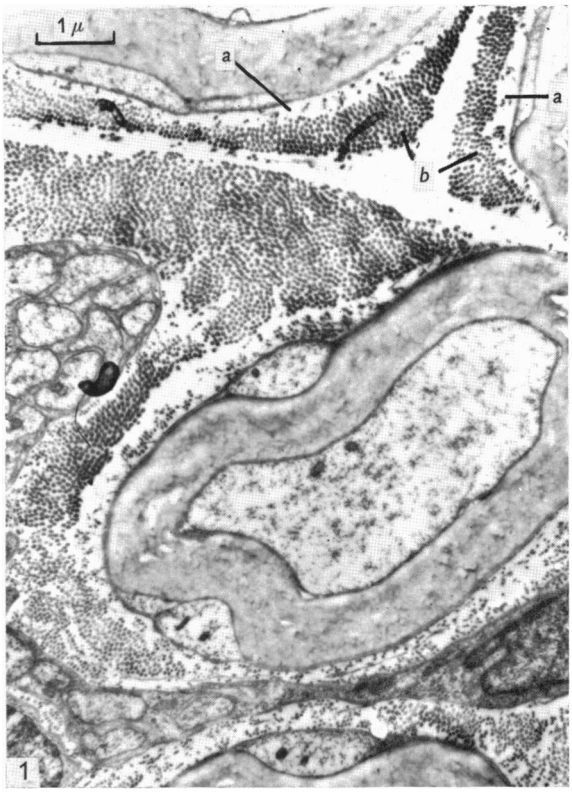
SANDERS, F. K. & YOUNG, J. Z. (1944). The role of the peripheral stump in the control of fibre diameter in regenerating nerves. *J. Physiol.* **103**, 119–136.

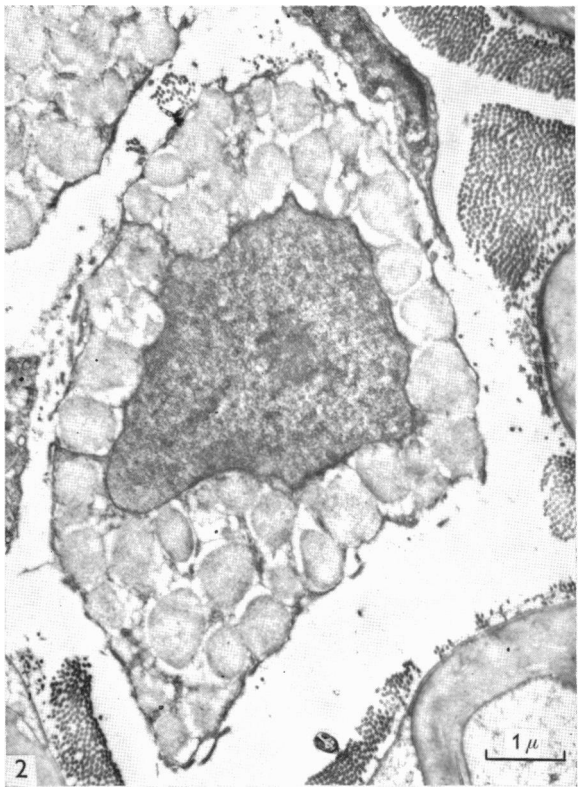
SIMPSON, S. A. & YOUNG, J. Z. (1945). Regeneration of fibre diameter after cross-unions of visceral and somatic nerves. *J. Anat., Lond.*, **79**, 48–65.

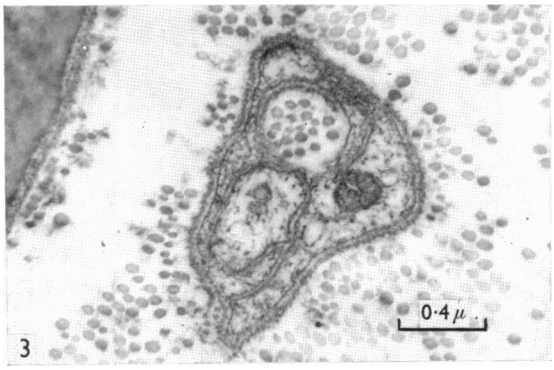
TARLOV, I. M. (1937). Structure of the nerve roots. I. Nature of the junction between the central and the peripheral nervous system. *Arch. Neurol. Psychiat.* **37**, 555–583.

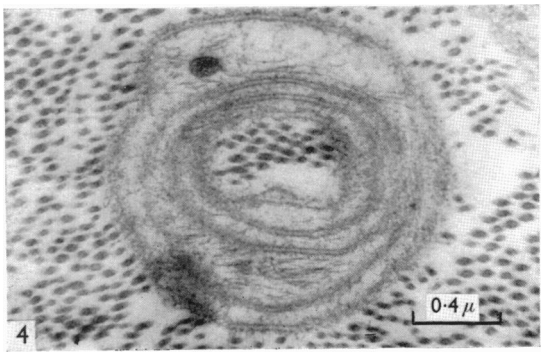
THOMAS, P. K. (1963*a*). The connective tissue of peripheral nerve: an electron microscope study. *J. Anat., Lond.*, **97**, 35–44.

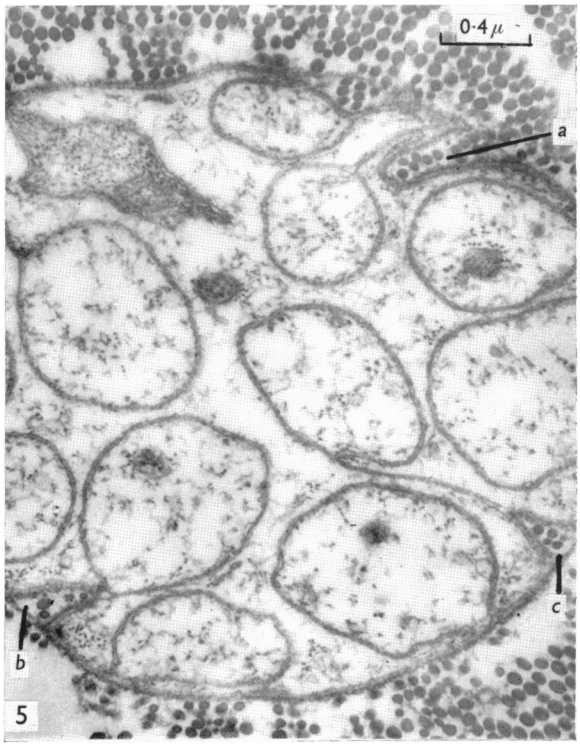
THOMAS, P. K. (1963*b*). The fate of the endoneurial tube during Wallerian degeneration. *J. Anat., Lond.*, **97** 476.

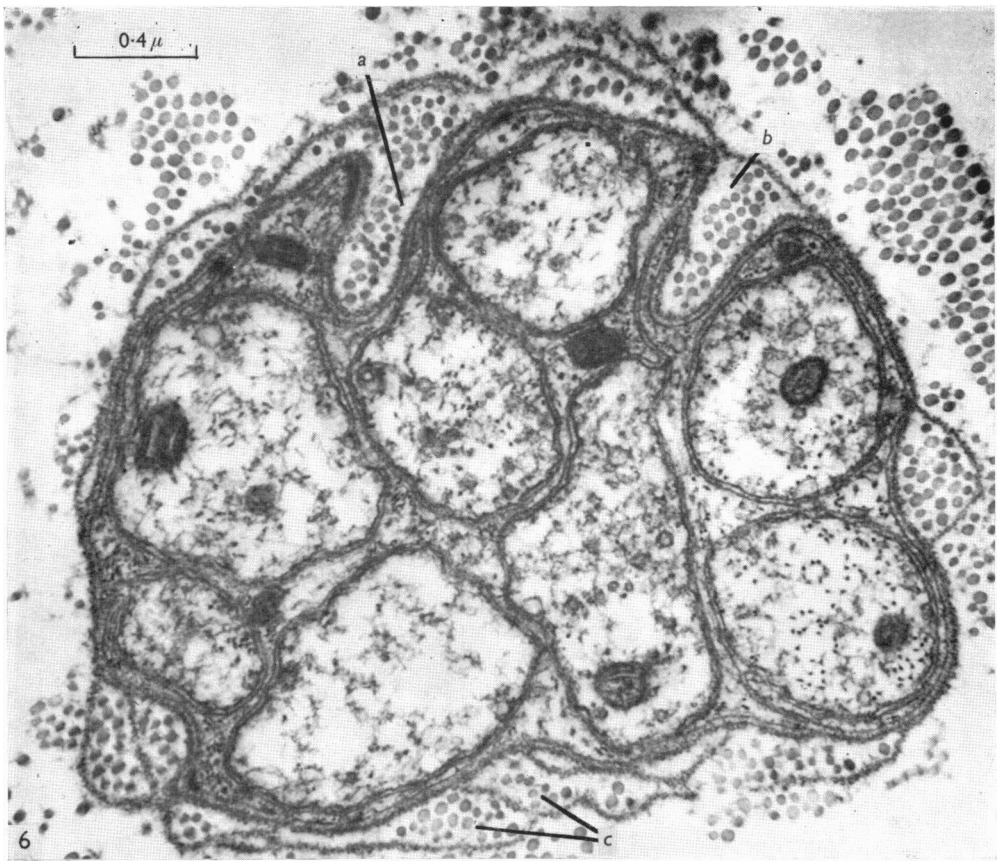

1 μ
a
a
b
1

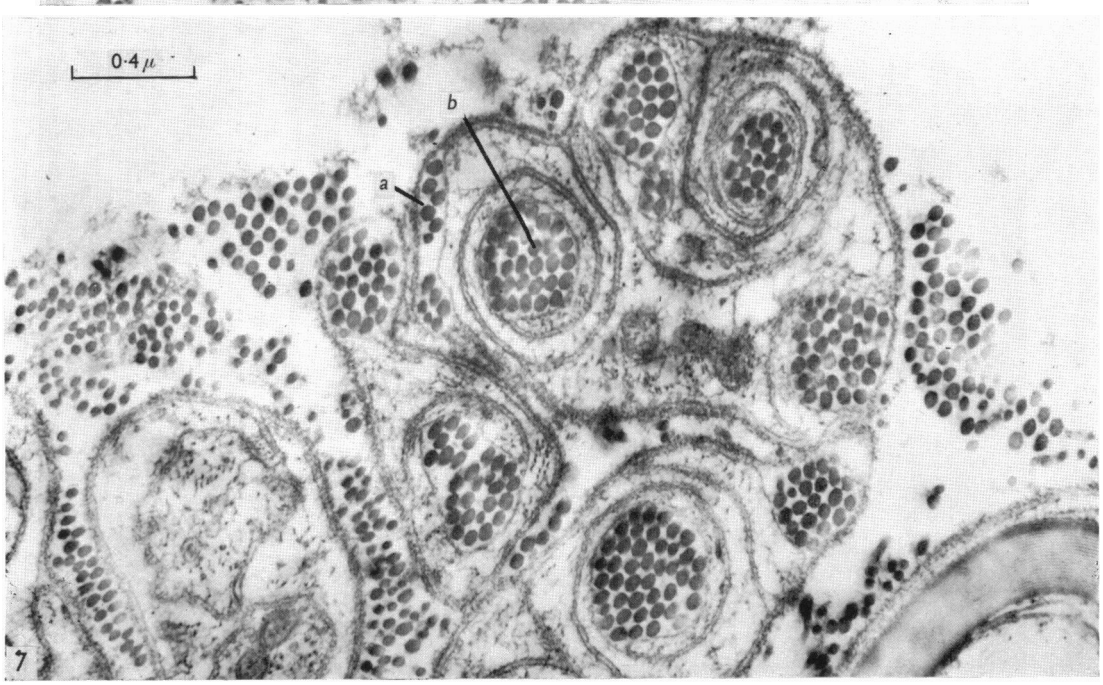

1 μ
2

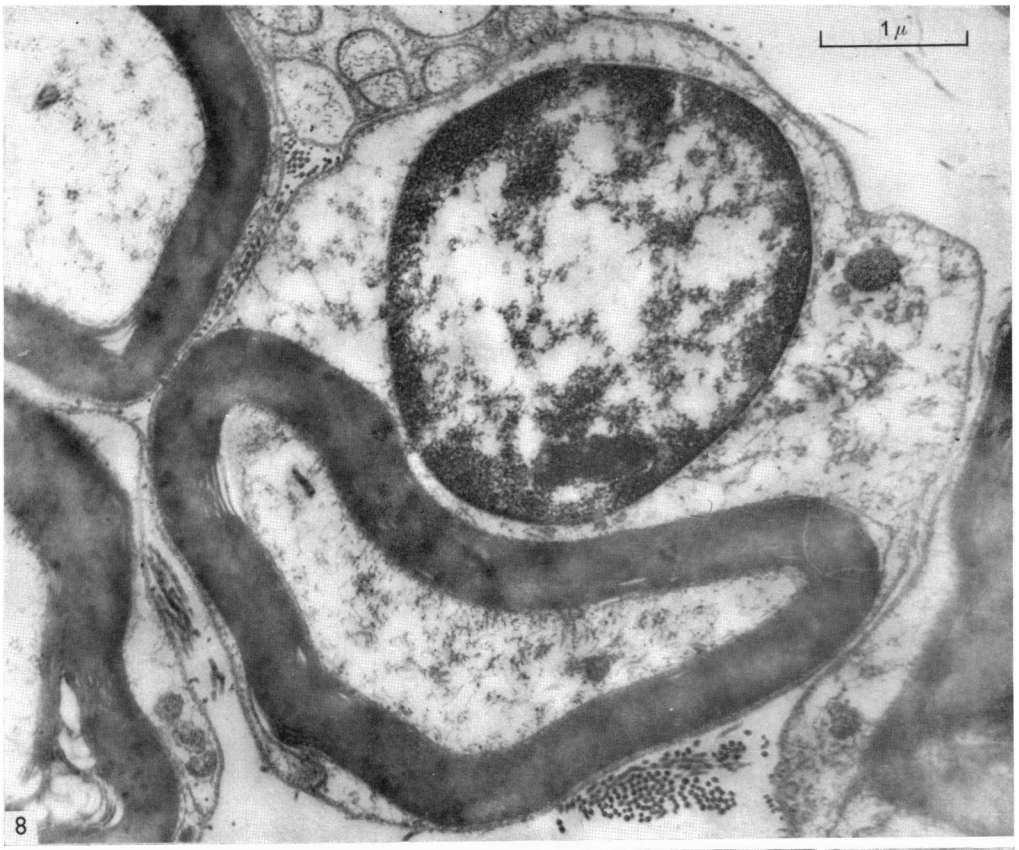

0·4 μ
3

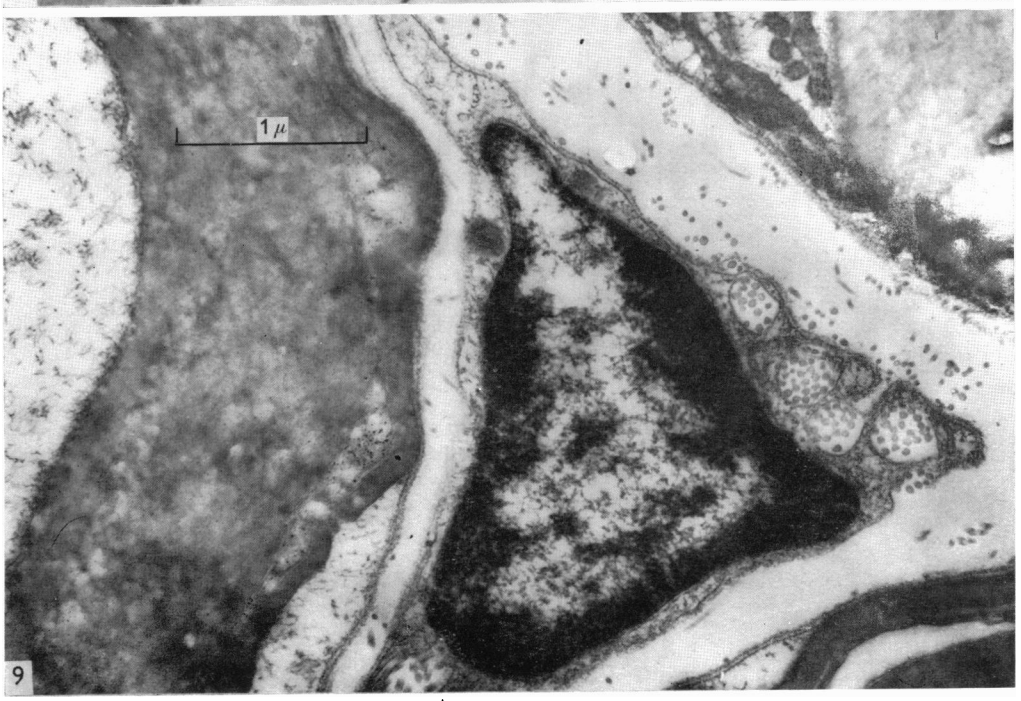

0·4 μ
4


0·4 μ
a
b
c
5

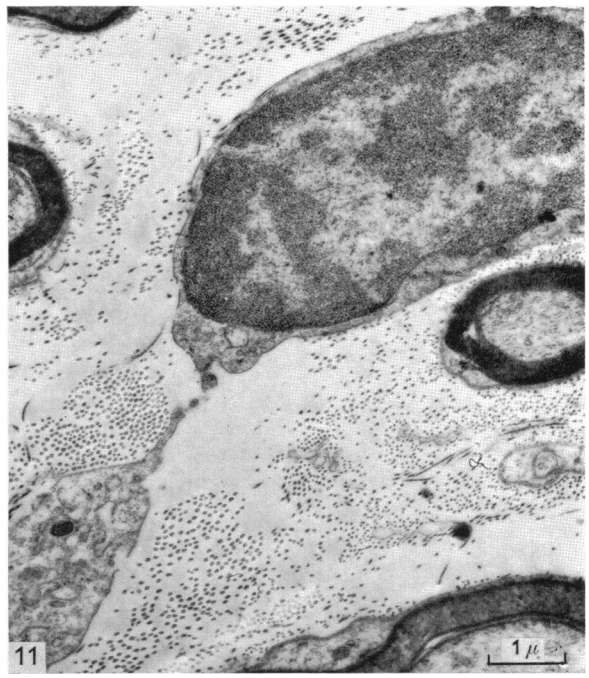

0·4 μ
a
b
c
6

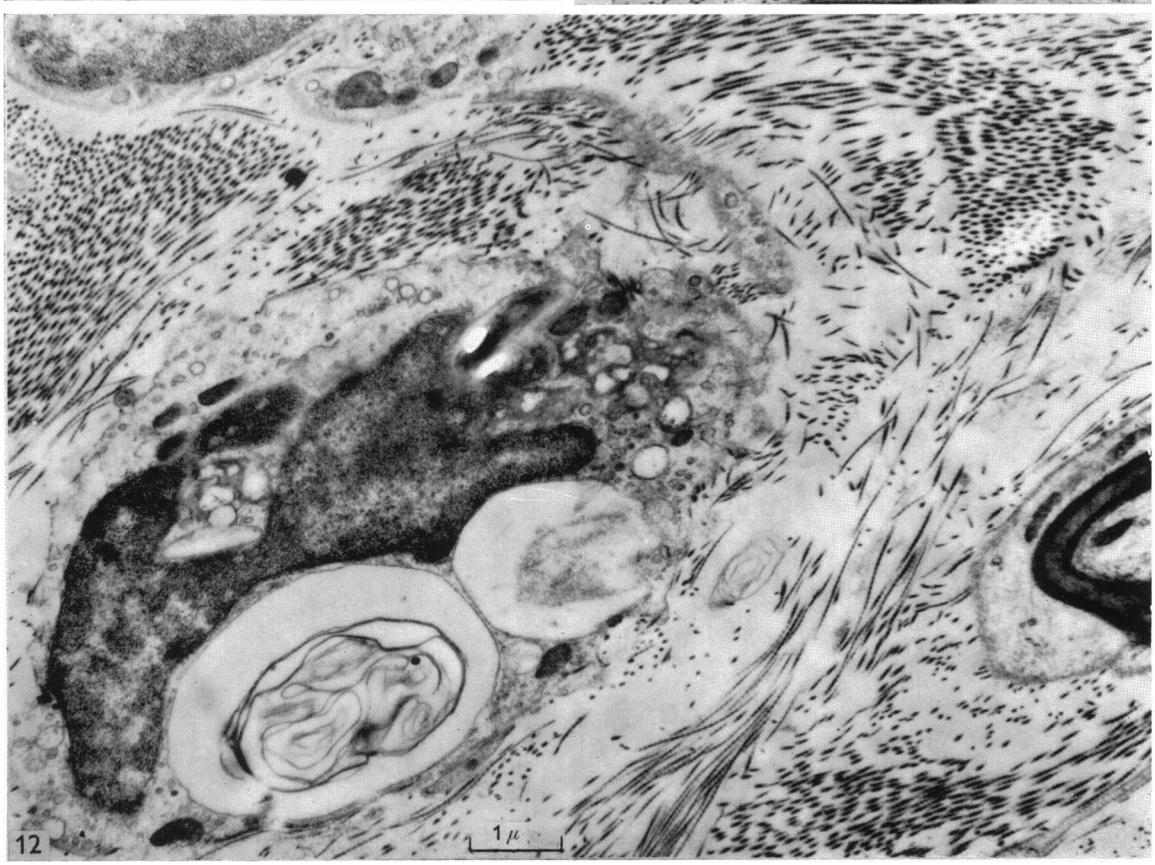

0·4 μ
b
a
7

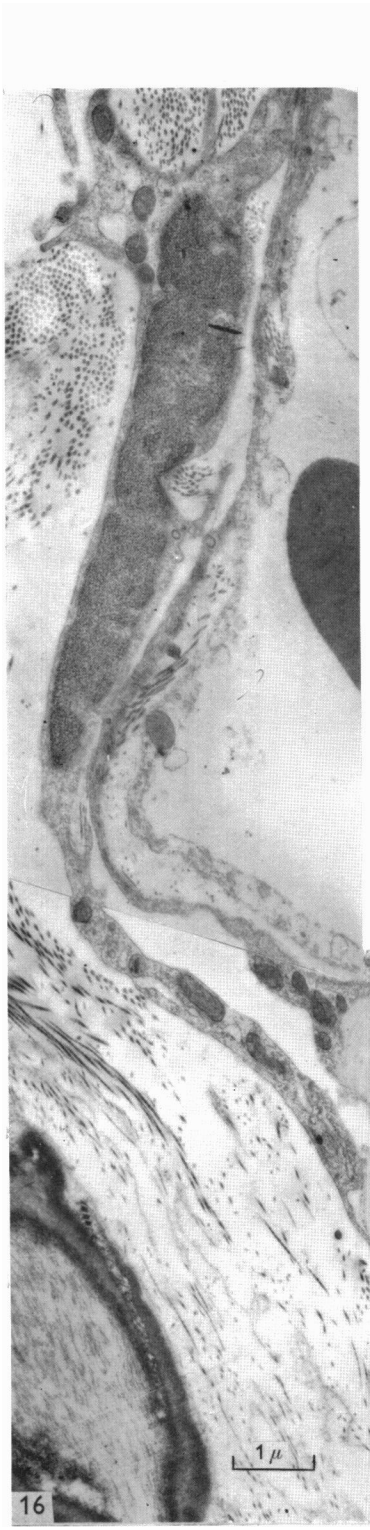

1 μ
8

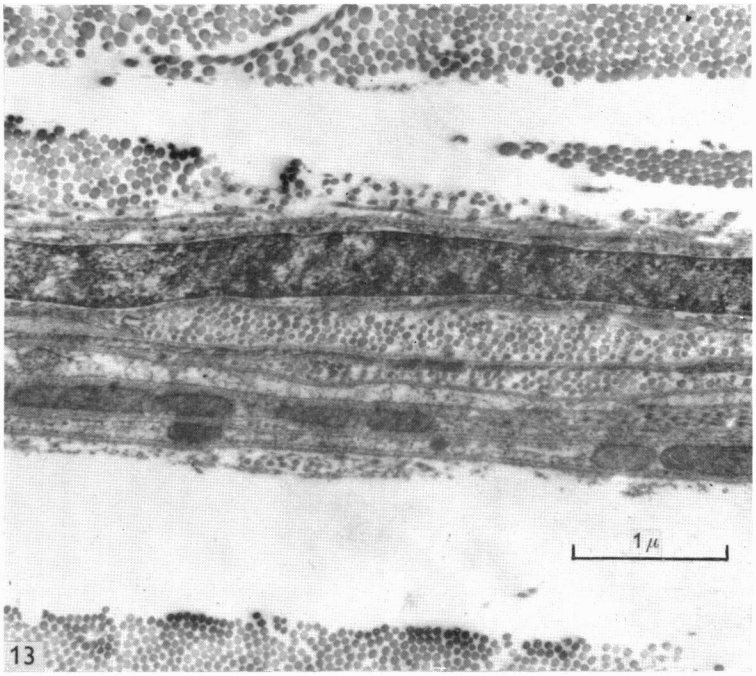

1 μ
9

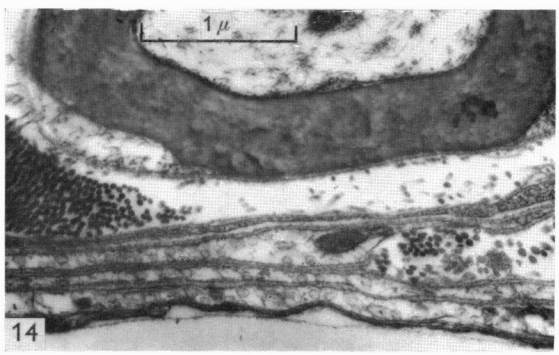

1 μ
10

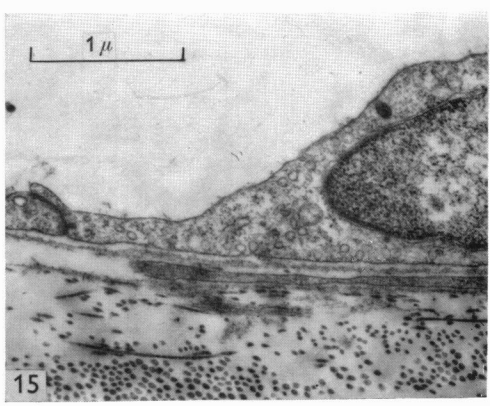

1 μ
11


1 μ
12


1 μ
16


1 μ
13


1 μ
14


1 μ
15

EXPLANATION OF PLATES

PLATE 1

Fig. 1. Sural nerve showing abundance of endoneurial collagen and its subdivision into (*a*) inner and (*b*) outer sheaths around large myelinated nerve fibres.

Fig. 2. Sural nerve showing an endoneurial mast cell.

Fig. 3. Sural nerve showing a Schwann cell process containing an unmyelinated axon and also a 'pocket' of collagen, suspended by a 'mesaxon' and partly surrounded by basement membrane.

Fig. 4. Regenerated dorsal nerve root showing cell process (probably of a Schwann cell) containing a 'pocket' of collagen suspended by a 'mesaxon' which makes more than two loose spirals around it.

Fig. 5. Sural nerve showing a bundle of unmyelinated nerve fibres. Pockets of collagen are related to the Schwann cell, indenting its surface at (*a*) and lying between duplications of its basement membrane at the parietal attachments of 'mesaxons' at (*b*) and (*c*).

PLATE 2

Fig. 6. Sural nerve showing a bundle of unmyelinated nerve fibres. Pockets of collagen are related to the Schwann cell, indenting its surface at (*a*), similarly indenting the surface at (*b*), but trapped there by duplication of the basement membrane, and trapped by reduplication of the basement membrane, at (*c*).

Fig. 7. Sural nerve showing pockets of collagen intimately related to a process of a probable Schwann cell. Collagen fibrils lie between the basement and cytoplasmic membranes at (*a*); cytoplasmic membrane forms a spiralling 'mesaxon' whose two layers split to enclose a bundle of collagen fibrils at (*b*).

PLATE 3

Fig. 8. Sacral dorsal root (normal) showing myelinated and unmyelinated nerve fibres. Collagen is generally scanty but a small aggregation is seen.

Fig. 9. Sacral dorsal root (normal) showing 'pockets' of collagen related to a probable Schwann cell.

PLATE 4

Fig. 10. Sacral dorsal root (normal) showing a node of Ranvier on a small nerve fibre lying adjacent to the pial covering. Endoneurial collagen fibrils lying close to the fibre are fine and run in all directions.

Fig. 11. Sacral dorsal root (6 months after transection) showing a fibroblast, remyelinated nerve fibres and much endoneurial collagen.

Fig. 12. Sacral dorsal root (6 months after transection) showing parts of a fibroblast and of a remyelinated nerve fibre, a macrophage containing debris and much endoneurial collagen.

PLATE 5

Fig. 13. Sural nerve showing lamellae of perineurium separating epineurium (top) from endoneurium.

Fig. 14. Sacral dorsal root (normal) showing lamellae of pia mater.

Fig. 15. Sacral dorsal root (6 months after transection) showing contact between pial cells in a region where the pial covering is reduced to a single cellular layer.

Fig. 16. Sacral dorsal root (6 months after transection) showing large vacuoles in or between cytoplasmic processes of pial cells; the processes largely lack basement membrane.