Surgical Disorders of the Peripheral Nerves

SURGICAL DISORDERS OF THE PERIPHERAL NERVES

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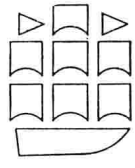
SECOND EDITION



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Preface to the First Edition

OF the various disorders of the peripheral nerves that excite the interest of surgeons, injuries eclipse all the rest put together. The commonest cause of injury is an open wound, particularly that produced by a missile; thus surgery of the peripheral nerves is a child of war, and it was born a century ago.

The first organized investigation of nerve injuries was undertaken during the American Civil War, at the instigation of W. A. Hammond, Surgeon General to the Federal Armies. Work began in May 1863 at an army hospital in Turner's Lane, Philadelphia, with Silas Weir Mitchell in charge. After fifteen months he and his co-workers published a little book that is the foundation stone of our knowledge of nerve injuries. Another and a more complete work appeared in 1872.[1] Weir Mitchell was a man of such remarkable ability and versatility that he would undoubtedly have made valuable observations on such patients as came to him in the ordinary course of military hospital practice; but the foresight of his chief provided him with opportunities that would otherwise have been lost.

In Britain, a policy of concentration was adopted, though not immediately, during the First World War and throughout the Second World War.

The wound that injures a nerve often damages neighbouring structures—bones, joints, blood vessels and tendons—and it is, therefore, desirable that the surgeon choosing (or in times of war ordered) to devote himself particularly to the surgery of peripheral nerves should have a wide range of skills. Moreover, reconstructive operations are sometimes necessary if a nerve cannot be mended or fails to recover satisfactorily after repair.[2]

As in the management of traumatic paraplegia—in which diverse skills are also required—the organization should be such that the patient is never in doubt about who is looking after him. And as in some other disorders of the locomotor system a precise programme of treatment is all-important: the man who draws it up is the one to whom the patient knows he belongs. Moreover, the commitment has no time limit. Ideally, the arrangements should be immune from disruption by administrative machinery. In Britain, during the Second World War, great pains were taken to ensure that this was so; and despite the hazards of war and the dictates of geography, continuity of treatment and supervision was very good, as is evident from the Medical Research Council's Special Report published in 1954.

The necessity for this segregation, this concentration of cases, is recognized increasingly. It is in the patients' interests; it also facilitates advances in understanding and technique, and encourages the co-operation of scientists. For example, during the decade that included the First World War two anatomists, Huber in the United States and Stopford in Britain, applied themselves to the study of nerve injuries with most fruitful results. During the Second World War the collaboration of clinicians and laboratory workers was extremely close. At Oxford I had the inestimable privilege of working

[1] Weir Mitchell wrote with unusual felicity. It is perhaps worth mentioning that he published eight slender volumes of verse. A selection from them was published in London by Macmillan in 1901; William Holmes gave me a copy, which I treasure.

[2] No attempt has been made to describe the many reconstructive operations that may be required, though a few are mentioned. There are two reasons for this. Reconstructive surgery is best dealt with in relation to all forms of peripheral paralysis; and to cover the subject adequately would involve making this book much too long.

with J. Z. Young, P. B. Medawar, William Holmes, F. K. Sanders, and Ernst Gutmann. And since then I have been blessed by equally close association with Hubert Sissons and his colleagues in the Department of Morbid Anatomy of the Institute of Orthopaedics.

There is one field of enquiry in which neither animal experiment nor access to a large number of patients is of much use; the study of disturbances of sensibility, more particularly cutaneous sensibility. It is no accident that the renowned investigations of Head, Trotter and Davies, Boring, Woollard and Weddell were done in times of peace. It is a leisurely occupation. Animal experiments, such as Sarah Tower's, have helped a little; but man alone, and an intelligent man at that, can describe the manifold sensations experienced after injury to a nerve and during regeneration. Moreover, the injuries themselves must be deliberately inflicted, with great precision, and the subject has to be a fully informed member of the experimental team. What is so astonishing is that in spite of the devoted efforts of many workers the riddle of sensibility is still not yet solved.

It may be said that this is rather the province of the physiologist and the anatomist. In methodology this is true enough, but the problem is intensely practical. In addition to the victims of nerve injury, there are some 15 million lepers in the world, most of whom suffer from disabling disorders of sensibility, the origin of which is in the peripheral nerves.

Causalgia is rare even in times of war, but what in Chapter 9 are described, for want of a better term, as irritative nerve lesions are always with us and there is as yet no rational basis for their treatment.

There are grounds for disquiet in this small, but absorbing and often rewarding field of surgery. We live in an age of unparalleled technological advance. A surgeon selects such new weapons as may help him to help his patients. But in some centres of endeavour established, proven and reliable techniques are being jettisoned in favour of what is novel. 'For all the Athenians . . . spent their time in nothing else, but either to tell, or to hear some new thing' (*Acts*, 17.21). And the old is sometimes abandoned when it is palpably better for the patient. This is noticeable in some of the recent work on nerve homografts.

There is a way of disciplining this ardour, this enthusiasm, which is too valuable to be censured. It is by using one of the most weighty weapons of contemporary research, the controlled clinical trial. Surgeons, by nature inventive, by temperament emotionally attached to their brain-children, find this more rigorous than do almost all other clinical experimenters. Yet the clinical trial is necessary. Its morality has been questioned. Today it is the other way round; it is often immoral not to embark on a trial. But the cost to the investigator must be counted. In many fields of work the duration of the trial may be 10 years; surgery of the peripheral nervous system is one of them. There are three reasons for this protracted ordeal. The first is that the inflow of patients is usually slow, though this can be remedied by a number of centres joining in a common investigation. The second is that the necessary period of observation after the performance of this or that operation is measured by years rather than months. The third is that comparisons are being made not between life and death, as was the case with tuberculous meningitis before and after the advent of streptomycin, but between methods of treatment that are more or less efficacious. It is a matter of finding out which is the better. In this I am obliged to confess negligence; opportunities that lay within our grasp have been missed. Now, in what seems to be a belated penitential exercise, I am involved in a clinical trial, in a field unrelated to the peripheral nervous system. From first to last it requires 10 years of unremitting effort on the part of a considerable number of people who are prepared to work to a common programme. It is costly too. The reward is unspectacular, but peculiarly satisfying: at the finish, certainty of knowledge that can be translated

with complete assurance into action that benefits patients. This should be good enough. The technique of the clinical trial has been perfected. The problem is finding the people with sufficient self-discipline to use it.

For the management of damaged peripheral nerves the surgeon must arm himself with three weapons: detailed knowledge of the anatomy of the limbs; the special skills —and the patience—of the neurologist; and, in operative surgery, a delicacy of touch that lies between those of the neurosurgeon and of the otologist. I learned the second from George Riddoch and the third from Hugh Cairns. This book is dedicated to their memory; they were the best friends a man could wish for.

I am indebted to other friends. P. K. Thomas read the first, second and fourth chapters, and he supplied the best of the illustrations they contain. D. Lloyd Griffiths read the chapter on neurovascular injuries, and Hubert Sissons the one on nerve tumours. I am deeply grateful to all three for criticisms and suggestions—which I hastened to accept. My greatest debt is to John Crawford Adams who read all the other chapters; he brought to them the erudition and the superb command of our language which, over many years, have contributed so largely to the eminence of the British edition of the *Journal of Bone and Joint Surgery*. I cannot thank him adequately.

For over 20 years my partner in this work has been D. M. Brooks. He brought to it an innate wisdom which for me has been indispensable; and the elegance of his operative technique is of an order that I have never been able to achieve.

The most time-consuming labour was studying the records of some 2,000 patients. Under the guidance of Dr Ian Sutherland I designed an analysis card. The soul-destroying job of completing them was undertaken by Miss Ingrid Schoeberl, with endless patience and great accuracy. I scanned every dossier and card myself. After the information had been transferred to standard punch cards the analyses were made with a counter sorter that Dr Sutherland placed at my disposal at the Medical Research Council's Statistical Research and Services Unit. This work was costly, and would hardly have been possible but for a grant from the Institute of Orthopaedics, which I gratefully acknowledge, as I do the constant help of Mrs Mary Glen Haig, Medical Records Officer at the Royal National Orthopaedic Hospital.

Someone with the mind of an accountant could ferret out some statistical discrepancies. Although our notes have always been good, not every dossier contained all the information one was seeking. The gaps are small. Every set of figures is accurate in relation to the topic under consideration; they show what happened.

It has been my good fortune to work with a succession of able and enthusiastic junior colleagues. The consequence has been a steady stream of published papers on various aspects of disorders of the peripheral nerves. All this work has been incorporated in this book. But this formal acknowledgment is as nothing compared with what I owe them for constant mental invigoration, for transfusion of ideas. In working through our records, which were necessarily more their work than mine, I could not but recall with gratitude some words of Weir Mitchell's. 'No labour has been spared in making these clinical histories as perfect and full as possible. Those only who have devoted themselves to similar studies will be able to appreciate the amount of time and care which has been thus expended. We indulge the hope that we shall leave on record a very faithful clinical study of nerve injuries, and that we shall have done something at least towards lessening the inevitable calamities of warfare.'

I take the liberty here of mentioning three by name. W. Bremner Highet joined us at the outbreak of the Second World War. This talented young New Zealander was awarded the Jacksonian Prize by the Royal College of Surgeons of England for an essay on nerve injuries. The closure of the Mediterranean Sea left only the Cape route for the evacuation of men injured in the fighting in the Desert War. As a result of the shortage of transport

shipping many of them piled up in South Africa. Highet was chosen to look after those who had suffered nerve injury. He was sent by sea; the ship was torpedoed and there were no survivors.

Ludwig Guttmann had come to Oxford from Foerster. He placed his master's and his own profound knowledge of peripheral nerve injuries at our disposal. His research work was superb. Guttmann (now Sir Ludwig) was soon to achieve worldwide renown when he set about establishing a spinal injuries centre at Stoke Mandeville.

Graham Weddell was and is a versatile anatomist. As a pupil of Woollard's he applied himself particularly to the problems of cutaneous sensibility. He also developed electromyography as a clinical weapon, and thus we were able to exploit this diagnostic aid at a time when the machines that today are commonplace did not exist.

In wartime we took our own photographs; their quality was only passable. Later, at the Institute of Orthopaedics, I was to benefit from the skill of Robert Whitley, that great master of medical photography. I thank him most warmly. Almost all of the line drawings and histograms are the work of Robin Callander of the Department of Medical Illustration and Photography in the University of Glasgow. I pay tribute not only to his skill as a draughtsman, but to his uncanny grasp of exactly what is required.

A number of illustrations, many of them my own, but a fair number from the works of others, have been reproduced from books and published papers. The generosity of many friends has been a great encouragement. I am grateful to editors and publishers for so willingly according me permission to reproduce pictorial material of great value. I acknowledge my indebtedness to: The Controller of Her Majesty's Stationery Office: The Association of British Members of the Swiss Alpine Club: *Bibliotheca Anatomica: Brain: British Journal of Surgery: British Medical Journal: British Surgical Practice: Canadian Medical Association Journals: The Hand: Journal of the American Medical Association: Journal of Anatomy:* The American and British Editors of the *Journal of Bone and Joint Surgery: Journal of Neurology, Neurosurgery and Psychiatry: Journal of Neurosurgery: Journal of Physiology:* E. and S. Livingstone, Edinburgh: *Physiotherapy: Plastic and Reconstructive Surgery: Revue de Chirurgie Orthopédique:* W. B. Saunders and Company, Philadelphia and London: *Surgery Gynecology and Obstetrics:* The Williams and Wilkins Company, Baltimore.

I am deeply grateful to my wife, to Mrs Helen Bamber and to Mrs Valerie Webster for their arduous and painstaking labour in preparing the typescript. I am no less appreciative of Miss Una Grant's devotion in checking and listing the (perhaps too numerous) references and preparing the index of authors.

None of the imperfections found in this book can be laid at the door of the publishers, Churchill Livingstone; they took endless trouble with it, and for this, and for their patience, they have my warmest thanks.

Stanmore, 1972 H. J. SEDDON

Contents

1. The Structure of a Peripheral Nerve

NERVE FIBRES

THE ESSENTIAL ELEMENTS of a peripheral nerve—its conducting fibres—are extraordinary in being cell processes that are mostly of immense length. In man the volume of the axon, without its myelin sheath, may be more than 200 times that of the cell body. The axon necessarily depends almost entirely on a local blood supply; yet severed from the cell body it degenerates, and robbed of its proper peripheral connection it fails to attain its proper size (Aitken, Sharman and Young, 1947).

An average cutaneous nerve may contain 10,000 fibres. The largest unmyelinated fibres, which predominate, may be about 1 μ in diameter, whereas the largest myelinated fibres are 20 times the size. There is an even greater range, about 1:100, of conduction velocities, the rate being greatest in the largest fibres. Nerve fibres in the periphery of a limb are smaller than those supplying the proximal parts; and it is possible that the longest fibres taper towards the end of their course (Young, 1950). It has been suggested (Sunderland and Ray, 1947) that the size of fibres in a nerve may have a bearing on its suitability for employment as a graft. There is no doubt that a large fibre growing into a very small Schwann tube cannot inflate it more than a little (Simpson and Young, 1945); but in the conditions that obtain clinically this is unlikely to be significant, because the differences in diameter are far less than those in the reported experiments, in which the proximal part of a somatic nerve was joined to the distal end of an autonomic nerve composed entirely of unmyelinated fibres.

Although we speak of fibres and although the axon appears fibrillar in stained preparations, the axoplasm behaves like a viscous liquid. The giant nerve fibres of some invertebrates show this property to a remarkable degree. When the worm *Myxicola* contracts the diameter of a cylinder of axoplasm trebles, and its length is reduced accordingly (Nicol and Young, 1946; Nicol, 1948). For surgeons this property of fluidity is of some interest. There is as yet nothing to indicate that when regeneration begins the outflow of axoplasm is any more purposive than a stream of molten lava making its way down the gullies on the slope of a volcano: with one proviso, that the streams of axoplasm have a particular affinity for the surfaces of Schwann cells, to which they adhere (Abercrombie, Johnson and Thomas, 1949).

All peripheral nerve fibres are enclosed by *Schwann cells*. There is one for each segment—the part between two nodes of Ranvier—in a myelinated fibre. In man the Schwann cells of unmyelinated fibres are remarkable. Whereas in some other species a number of nerve fibres are invaginated into the cytoplasm of the Schwann cell, in man the Schwann cell has pseudopodia—almost tentacles—which reach out to embrace neighbouring unmyelinated fibres. Thus one may find a number of fibres, each with its investment of Schwann cytoplasm (Fig. **1**, 1), but without any apparent connection with the main body of the relevant Schwann cell. Yet this is no more than a crude simplification of a remarkably complex arrangement (Eames and Gamble, 1970).

Both types of axon are invaginated into the cytoplasm of the Schwann cell and this gives rise to the formation of the *mesaxon*, which is clearly demonstrable electron-microscopically (Fig. **1**, 1).

Outside the Schwann cells is the *basement membrane* (Figs **1**, 1; **2**, 4 and **2**, 6, pp. 2, 11 and 13). In the case of unmyelinated fibres it encloses all that are embedded in the cytoplasm of one Schwann cell, in myelinated fibres it encloses only one with its investing Schwann cells. Thus a Schwann tube, to which reference will frequently be made, consists of a column of Schwann cells contained in a basement membrane. The membrane is continuous; the cells, however intimate their ramifications, are not—they do not form a syncytium.

The *myelin sheath* is the distinctive feature of

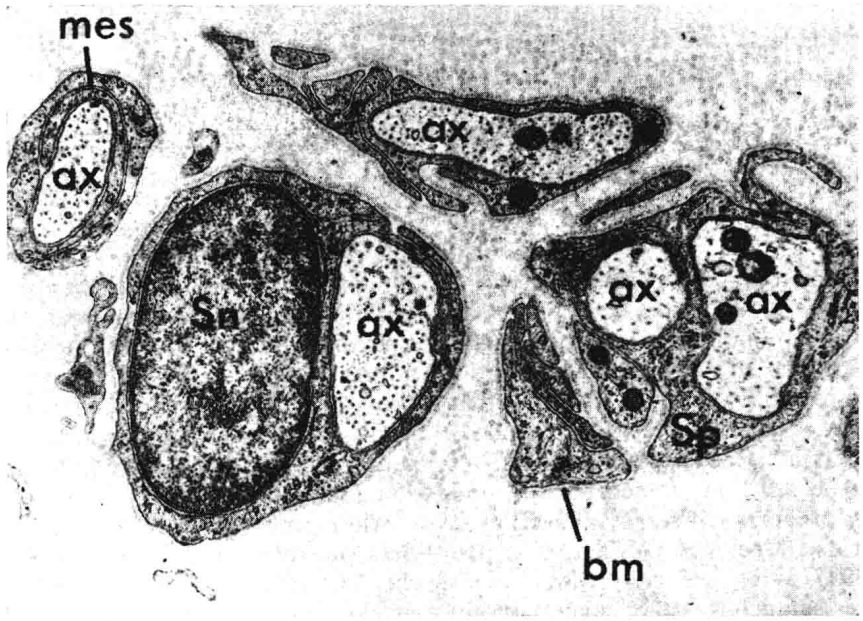

FIG. 1, 1. Electron-micrograph (×19,000) of a group of unmyelinated axons: human sural nerve.

ax	axon	bm	basement membrane
Sn	Schwann-cell nucleus	mes	mesaxon
Sp	Schwann-cell process		

(Courtesy of Dr A. J. Aguayo)

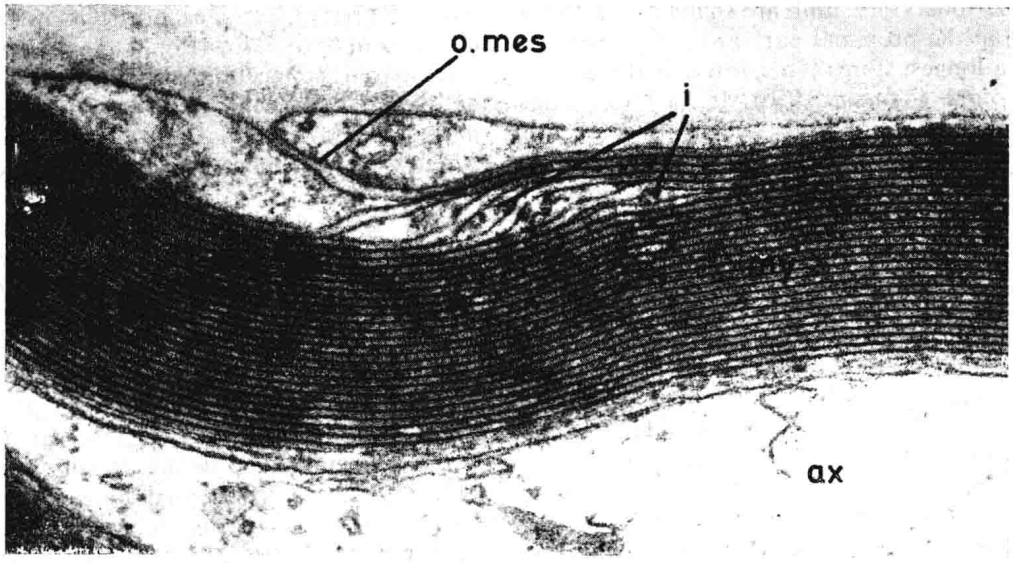

FIG. 1, 2. Electron-micrograph (×84,000) of a portion of a transverse section through a small myelinated nerve fibre. The myelin sheath displays a partial Schmidt-Lantermann incisure.

o. mes	outer mesaxon
my	myelin
i	Schmidt-Lantermann incisure
ax	axon

the large nerve fibres. Here the Schwann cells envelop only one axon. The myelin is derived from the mesaxon becoming wrapped spirally round the axon; obliteration of the intervening cytoplasmic layers producing the appearance of compact lamination (Fig. **1**, 2). There are also periodic funnel-shaped clefts in the myelin sheath, the incisures of Schmidt-Lantermann, where the lamellae are separated by cytoplasm (Figs **1**, 2 and **1**, 3).

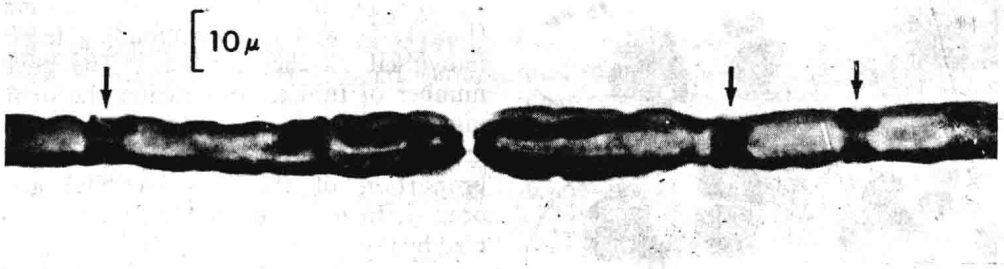

FIG. **1**, 3. Single myelinated nerve fibre showing one node of Ranvier and Schmidt-Lantermann incisures (arrows). Stain: osmium tetroxide. (Courtesy of Mr P. S. Spencer.)

The *nodes of Ranvier* (Fig. **1**, 3) demarcate the myelin segment. They represent the junctions between adjacent Schwann cells which have come into close contact with the axon membrane at the nodes. The basement membrane and collagenous ensheathment of the Schwann cell dip in at the nodes.

The distance between nodes is greater in the larger fibres, but the correlation is not strict. The internodal length is largely determined by the amount of longitudinal growth that has occurred after myelination. At birth the internodal length in large fibres is about 230 μ. In nerves supplying the forearm it increases fourfold by the eighteenth year: in nerves to the leg, the same; in nerves to the jaw only two-and-a-half times (Shepherd, Sholl and Vizoso, 1949; Vizoso, 1950). The jaw grows far less longitudinally than the distal segment of the upper or lower limb.

THE SUPPORTING TISSUES

The *endoneurium* is the supporting tissue of the individual fibre, a fibrocytic stroma composed of two layers of collagen. It forms the endoneurial tube, closely investing the Schwann basement membrane, but separating from it when degeneration occurs. The nerve fibres with their related endoneurium form aggregations variously called bundles, fasciculi or funiculi (the last is preferred) which are enclosed by a much larger, cellular and collagenous envelope, the *perineurium* (Fig. **1**, 4). This tube is composed of mesothelial cells in which are embedded 7 to 15 collagenous lamellae, the fibres being arranged longitudinally, circularly and obliquely (Sunderland, 1965). It has a smooth inner surface lined by flat polygonal mesothelial cells, and there are collagenous condensations dipping into the funiculus, so forming the intrafunicular septa. The nerve fibres are slack inside the perineurium; thus in longitudinal sections they present a wavy appearance.

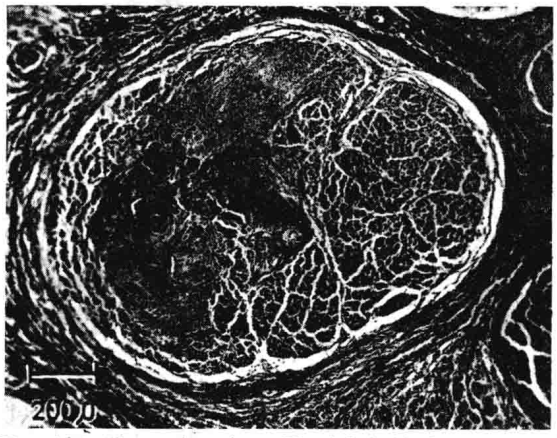

FIG. **1**, 4. The perineurium. The left half of its contents is abnormal, and this is referred to on page 272 (Fig. **15**, 26). On the right the pattern of the funiculus is normal, whereas on the left there is endoneurial fibrosis.

The funiculi are held together by a variable amount of collagenous connective tissue with a

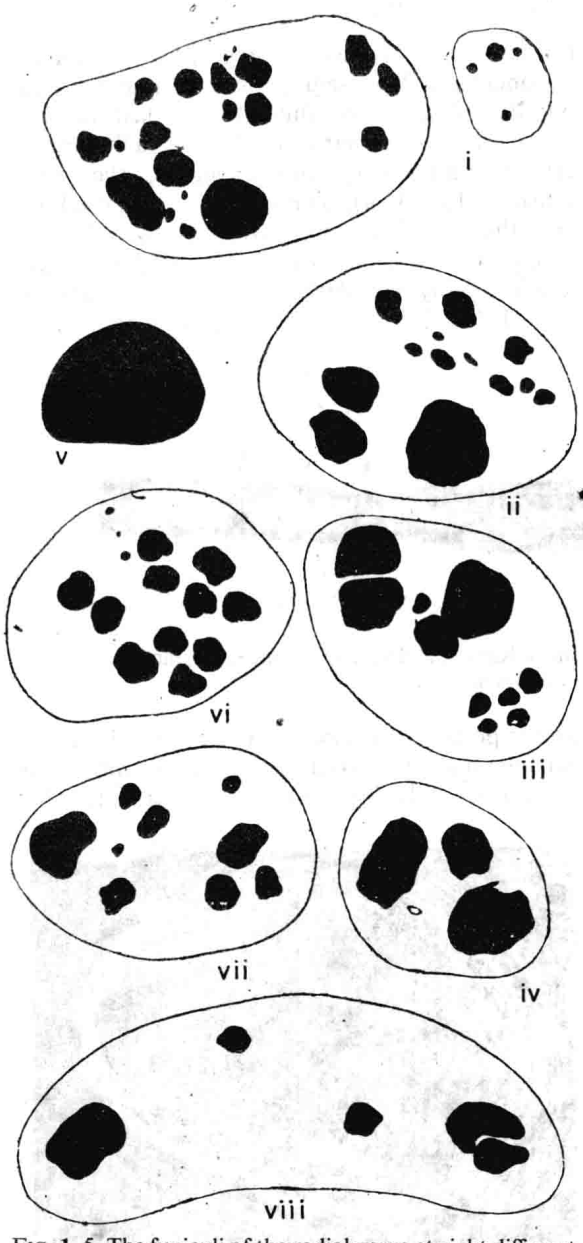

FIG. 1, 5. The funiculi of the radial nerve at eight different levels. (Reproduced by kind permission from Sunderland, S., 1945, *Brain*, **68**, 243.)

little fat here and there; and enclosed by the outermost envelope, the *epineurium*, which is composed mainly of longitudinally disposed collagen fibres, fibrocytes and some elastin fibres (Thomas, 1963). Here again, the funiculi lie slack within the epineurium and, as surgeons are aware, they pout out when a nerve is transected. So there is double protection for the nerve fibres against stretching; inside the funiculi, and inside the nerve sheath, the epineurium.

Fluid injected beneath the epineurium passes easily proximally and distally and between the funiculi. Within a funiculus there is also fairly free passage. This is particularly significant in connection with the damage resulting from the intraneural injection of drugs (p. 135).

The amount of packing between the funiculi varies enormously as between one nerve and another, in different reaches of the same nerve (Fig. **1**, 5), and at corresponding levels in an individual on the two sides. The greater the number of funiculi the greater the quantity of interfunicular tissue; or, put another way, the greater the number of funiculi the smaller the proportion of the cross-sectional area they occupy. In most nerves the greatest area occupied by the funiculi is about 50 per cent—and the smallest can be as low as 16 per cent (Sunderland and Bradley, 1949).

The tensile strength and elasticity of a nerve are determined by the supporting stroma. The greater the number of funiculi and, therefore, the greater the amount of interfunicular tissue, the stronger the nerve (Sunderland and Bradley, 1961*a*). In spinal nerve roots the connective tissue is relatively scanty and poorly organized (Gamble, 1964), and in traction injuries of the brachial plexus (Chap. 11) the spinal roots are notoriously susceptible to damage. Sunderland and Bradley (1961*b*) found that in them it was the nerve fibres that ruptured first. That the nerve fibres and Schwann cells contribute little to the tensile strength of a nerve is suggested by the demonstration (Sunderland and Bradley, 1961*c*) that in this respect there is no difference between the proximal and the degenerated distal segment of a severed nerve.

The elasticity of nerve has recently acquired a new practical significance. It has long been known from experience of leg-lengthening operations that with care nerves can be elongated without suffering damage. Sunderland (1968, p. 63) gives precise details about the elasticity of human nerves, the important fact being its great variability which ranges from six to 22 per cent. The autologous grafting operation recommended by Millesi seems to be based on the supposition that

in a sutured nerve the property of elasticity is best forgotten. This is discussed on p. 299.

INTRANEURAL PLEXUSES

From what has just been described it is evident that the internal topography of a peripheral nerve is plexiform; it changes from one level to another.

This subject has been studied since the early years of this century by a variety of methods:

1. Anatomical: dissection and histological examination (Bardeen, 1906; Stoffel, 1913, 1915; Langley and Hashimoto, 1917; Sunderland, 1945*a*; Sunderland and Ray, 1948).

2. Animal experiment: observing the distribution of Wallerian degeneration after partial section of a nerve (McKinley, 1921; Kilvington, 1940).

3. Very localized electrical stimulation (Langley and Hashimoto, 1917; McKinley, 1921).

4. Observation of the consequences of partial nerve injury (Sherren, 1908; Déjerine, Déjerine and Mouzon, 1915).

The most authoritative review, with an account of his own anatomical observations, is Sunderland's (1968).

The important practical conclusions are these:

1. The funicular pattern is inconstant, as between one subject and another, and as between right and left nerve trunks in the same subject.

2. The funicular pattern changes throughout the length of a nerve: the longest reach of any nerve showing a constant pattern is 15 mm, though individual funiculi may pursue considerably longer courses, especially where they are about to branch away from the main trunk. The average length of constant pattern is much less, only a few millimetres.

3. Not only is there communication between one funiculus and its neighbours but the number and size of the funiculi varies widely; and, as would be expected, the greater the number of them, the smaller their size.

The teleological explanation is simple enough. The grouping of neurons in the spinal cord and posterior root ganglia has to be translated into the appropriate innervation of muscles, skin and other tissues: for the limbs this is achieved first to some extent in the brachial and lumbosacral plexuses; but more delicate transpositions are required throughout the distribution of each nerve trunk. Yet there is an inescapable impression that this intermingling of nerve fibres and funiculi is rather overdone, and we are obliged to conclude that much of it is fortuitous, as is suggested by the inconstancies referred to above.

The clinical importance of the intraneural plexuses is considerable. In 1908 Sherren pointed out that one-third of a nerve trunk could be divided without producing any clinically detectable deficit. This is true enough—in certain situations, such as the ulnar nerve in the upper third of the arm. I have seen a patient with the ulnar nerve half severed at this level who showed no more than slight weakness of *all* the muscles of ulnar innervation and a trifling and *uniform* depression of cutaneous sensibility. The intermingling of the damaged fibres with the normal ones was just about complete by the time they reached the periphery. But because a branch of a nerve runs a well-defined course within it for some centimetres proximal to the point of separation, partial section of a nerve at this level and in the relevant sector has well-localized and easily recognizable consequences, that is, loss of function within the distribution of the branch.

The shifting funicular pattern makes it inevitable that any repair of a nerve in which the gap is considerable must be followed by confused re-innervation, however carefully the operation is done; the sizable cross-sectional area presented by the supporting connective tissue adds to the confusion and, worse, to wastage of axonal sprouts, some of which wander blindly in between the funiculi and lose themselves.

The separate course run by branches within a nerve, just above their points of departure, adds greatly to the effectiveness of surgical mobilization of a nerve; an indispensable feature of secondary suture. The distances over which important branches may be stripped from nerve trunks are given on page 269.

BLOOD VESSELS

That a peripheral nerve is less susceptible to ischaemia than voluntary muscle is proved by observations on patients with Volkmann's ischaemia in which sudden infarction, occurring in a previously healthy limb, deprives all

tissues in the affected part of their blood supply. The nerves suffer less than the muscles (p. 94). Moreover, the apparent impunity with which nerves can be partially devascularized in the course of surgical mobilization has encouraged the notion that their blood supply is relatively unimportant. Yet this remarkable tolerance has a limit which, even if ill-defined, is entitled to some respect.

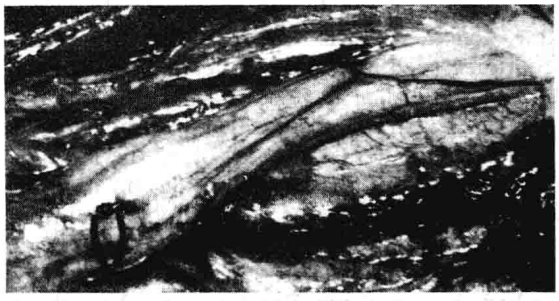

FIG. 1, 6. Proximal stump of a severed nerve: guide suture, but not the end-bulb, visible on left. To show the ascending and descending branches of a collateral vessel.

Systematic studies of the blood supply of nerves, and of the effects of devascularization on regeneration have been carried out by a number of workers (see references in Sunderland, 1945*b*).

The blood vessels supplying a nerve always run in a web of connective tissue that Smith (1966) calls the *mesoneurium* because it resembles the mesentery. In certain situations arteriae nervorum join the nerve and may be up to 1 mm in diameter; the veins may run with the arteries or separately. Their length does not exceed 2·5 cm. Both arteries and veins exhibit some tortuosity, which helps to maintain the blood supply in situations where movement is often rapid, sudden and extensive. At some points, either in the mesoneurium or on the surface of the nerve (Fig. 1, 6), there are longitudinal anastomoses, so ample that in certain sites—the median nerve in the upper arm, for example—hardly any collateral vessels join the nerve. Within the nerve, longitudinally disposed vessels are conspicuous beneath the epineurium and also between the funiculi (Fig. 1, 7). Sometimes, when the proximal stump of a severed nerve is transected in preparation for secondary suture, a small artery within the substance of the nerve will spurt vigorously. Arterioles may be found even inside funiculi and, finally, there is a rectangular mesh of capillaries. It is doubtful whether there are any true end-arteries.

FIG. 1, 7. Injected normal nerve. The large vessels anastomose freely. The significance of the large round or oval shadows is unknown. Dr Werner Nobel, who made these preparations and to whom I am indebted for this photograph, doubts whether they are extravasations. (Reproduced by kind permission from the proceedings of *5th Europ. Conf. Microcirculation, Gothenburg*, 1968. *Bibl. anat.*, **10**, 316.)

The result is that a nerve can be freed from its bed over a considerable length without jeopardizing its blood supply (Adams, 1943; Bentley and Schlapp, 1943). The longitudinally disposed blood vessels maintain it, although

when the collaterals are severed they grow into the nerve again quite rapidly (Blunt and Stratton, 1956). A caveat is necessary here. Of the longitudinally disposed vessels those that descend are larger than those that ascend. Hence if both parts of a severed nerve are mobilized the nerve immediately distal to the point of transection may become ischaemic. Evidence of this, in the form of collagenization extending over perhaps a centimetre, has been found many times in sections of distal stumps resected at operation. Whatever the inferences from animal experiment (Bacsich and Wyburn, 1945*b*), mobilization of a severed human nerve retards regeneration (Nicholson and Seddon, 1957); and in the cases we reported the mobilization was largely confined to the proximal part of the nerve, that is to say, the part best able to withstand partial devascularization. There is an even greater risk of distal ischaemia if the injury has severed the accompanying main artery, because re-establishment of the circulation in the distal part of the nerve depends on the opening up of a roundabout collateral circulation. Striking examples of extensive peripheral ischaemia are shown in Figures **6**, 8B (p. 97), and **15**, 33 (p. 278).

The practical points emerging from these considerations are:

1. When mobilizing a nerve care should be taken to avoid, if possible, severance of major nutrient vessels, such as the one joining the sciatic nerve in the gluteal region, or the one running with the median nerve in the forearm.

2. Because some of the longitudinal anastomoses are situated in the mesoneurium, a millimetre or two wide of the epineurium, it is wise to conserve them by cutting the tissues surrounding the nerve so that a fringe of mesoneurium remains attached to it (Sunderland, 1945*d*). The mobilization should be no more than is essential.

3. If there is any choice the proximal rather than the distal stump of a severed nerve should be mobilized.

4. If the main artery as well as a nerve has been cut across there is a possibility of severe ischaemia of the stump of the distal segment. In such cases secondary rather than primary suture is preferable; after a few weeks the extent of the distal ischaemic changes will be easily recognizable as dense intraneural collagenization, and the resection can be planned accordingly.

MOTOR NERVES

At its termination a nerve fibre supplying voluntary muscle connects with a number of end-plates, and the ensemble is called a motor unit. In limb muscles there may be several hundred muscle fibres in one motor unit. An impulse causes simultaneous contraction of all the muscle fibres with which the one nerve fibre is connected, and this produces a characteristic electrical disturbance (Chap. 4). It is unlikely that the diameter of a motor nerve fibre is related to the number of end-plates it controls (Young, 1950). The muscle fibres comprising one motor unit interdigitate, an overlapping that explains why a number of motor-unit action-potentials can be picked up, on moderate contraction, by one concentric needle electrode (p. 61). This arrangement facilitates smooth muscle action.

The sudomotor, pilomotor and cutaneous vasomotor fibres are derived from the autonomic system; they are all unmyelinated, they run in the cutaneous sensory nerves and have much the same distribution. This permits an objective assessment to be made of the state of cutaneous innervation, particularly by observing sweat secretion (p. 45).

SENSORY NERVES

As was dramatically demonstrated at a Ciba Foundation Symposium (1966) the topics of tactile, heat, and pain sensibility, although the subject of intensive and continuing investigation by many distinguished physiologists and anatomists, still pose questions of bewildering complexity. There is no lack of elaborate receptors of which the Pacinian corpuscle is the most imposing, though some sensory nerve fibres appear to have none at all. The problem is deciding which does what, and also what happens when one modality such as the perception of heat merges into another, pain. Certain facts, besides the anatomically striking specialization of receptors, demand explanation on the basis of 'sensory units' comparable with motor units. The most obvious of these clinically is the almost constant pattern of sensory loss, as between one

modality and another, after interruption of a cutaneous nerve. Tower (1940) went some way towards showing that in the admittedly unique surface of the cornea there are areas of innervation forming the peripheral expansions of 'sensory units'; the unit, somewhat like a motor unit, consisting of a central cell body, its axon and a considerable number of endings in a circumscribed but relatively large area, perhaps as much as 200 mm^2. The areas of contiguous sensory units overlap. On this hypothesis (Fig. 3, 6, p. 40) the areas supplied by cutaneous pain units are much larger than the units subserving touch; and at the finger-tips, where two-point discrimination (p. 53) may be 4 mm or less, the tactile unit areas are smaller than, say, in the thigh, where two-point discrimination is far less accurate. Unfortunately, some consequences of interruption of a cutaneous nerve (p. 39) cannot be explained on a purely anatomical, specific sensory-unit basis, and indeed the whole concept of the specificity of the forms of cutaneous sensibility has been questioned (Weddell, 1961; Weddell and Miller, 1962).

But there is no getting round the fact that we perceived specific sensations and testing based on them is an important aspect of clinical examination. It will be considered in Chapter 3.

2. Degeneration and Regeneration

ONE OF THE great attractions of work on nerve injuries is the ease with which they can be studied experimentally in animals. But this has its pitfalls; it does not follow that the results of experiment can always be taken as a guide to clinical practice.

Kline, Hayes and Morse (1964) produced identical gaps in nerves—excision of a 1-cm segment, which left a gap of 2 to 3 cm—in dogs, rhesus monkeys, baboons and chimpanzees. The results were far from uniform both in the amount of connective tissue proliferation and the effectiveness of axonal regeneration. Bridging of the gap by outgrowing nerve fibres was poor in the baboon and still worse in the chimpanzee. In other experiments nerves were crushed, or divided and sutured. The chimpanzee's behaviour was poor in comparison with that of the other animals.

If the range of species were extended by putting the favourite animal for experiments of this sort, the rabbit, at one end and man at the other, the differences in capacity for regeneration would almost certainly be even more pronounced.

There are two other points: on the basis of experiments on small animals some workers, such as Gutmann and Holubar (1951), are so confident that the capacity for regeneration of spinal neurons is virtually unlimited that they boldly propose the clinical employment of operations designed to keep the cell bodies in a state of intense activity. Yet much clinical evidence (p. 312) suggests that in the human adult there is a limit to the quantity of axoplasm that, say, an anterior horn cell can synthesize. Differences in size of cell body (if this is relevant) as between a large and a small mammal are not great: they are less than the differences in size between cells of the same kind—for example, anterior horn cells—in one species. A human lumbar or upper sacral motor neuron is an astounding structure: it is very long, and the volume of axoplasm is 200 to 300 times that of the cytoplasm of the cell body. But a neuron with an exceptionally long axon does not have an outsize cell body. Recovery after repair of a proximal lesion of the sciatic nerve is always poor at the periphery. While it is true that retrogressive changes at the periphery—in the distal part of the nerve and in muscle—are fairly pronounced by the time regenerating fibres should arrive there, the picture, as will be explained later (p. 242), is rather that of axonal exhaustion. Nerve fibres capable of functioning do not reach the periphery. Hence, in considering the effectiveness of regeneration, the size of the animal can hardly be ignored. Another factor, as will appear later (pp. 296 and 305), is age. In a child—who has the added advantage of short limbs—recovery is far better than in the adult.

Thus, in the account that follows, the selection of evidence from animal experiment is influenced by its relevance to clinical practice.

It is not possible to make a sharp distinction between the process of degeneration and that of regeneration, because, almost from the first, the one is a preparation for the other.

DEGENERATION OF NERVE

When a nerve is cut across, its stumps separate more or less and the gap is filled with blood clot. The proximal end of the nerve swells because of the oedema and the non-specific cellular response that occurs in any recently damaged tissue. There is always retrograde degeneration, its extent depending on the kind of injury. It is slight after a cut with a sharp instrument, it may extend over 1 to 3 cm after the great commotion produced by a high-velocity projectile (p. 71). Thus the Wallerian degeneration that takes place throughout the whole length of the distal part of the nerve also occurs at the end of the proximal part (Fig. **2**, 1). As a result of the initial inflammatory reaction, collagen is deposited in the end-bulb or neuroma that forms (Fig **2**, 2), and the funiculi lose their mobility. The epineurium is fixed to them and it becomes much thicker than normal, this thickening extending some way proximal to the end-bulb. Scarring—collagenization—also occurs within the funiculi. The Schwann cells