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ORIGINAL ARTICLES

PERIPHERAL NERVE INJURIES.*

By H. J. SEDDON, D.M., M.A., F.R.C.S.Eng.,
Nuffield Professor of Orthopædic Surgery, University of Oxford.

ALTHOUGH the interest of clinicians in peripheral nerve injuries seems to wax in wartime and wane when peace comes, the peripheral nervous system has few rivals in the fascination it has exerted over the minds of workers in many fields of medical science. Yet although the most remarkable advances in knowledge have been made, the clinical application of them has been tardy, perhaps because the field is so vast and, it must be admitted, almost beyond the comprehension of one man. During the last war Otfried Foerster in Breslau attempted a kind of synthesis of this work in relation to the injuries of warfare, with the result that his work is of outstanding and abiding merit.

Thanks to the foresight of the Medical Research Council and the Ministry of Health, there is some hope of similar work being done by workers in this country, though it will not be the work of any one man but of the co-ordinated teams in the five peripheral nerve injury centres. And it is encouraging to find that much recent work, at first apparently only of theoretical interest, has proved relevant in the interpretation of clinical phenomena. It is not possible, in the time at my disposal, to review the whole field, and I shall confine my remarks to the investigations with which I am immediately concerned, those taking place at Oxford, and even here some sort of selection must be made. Much of

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this work is as yet uncompleted and by no means ready for publication.

Classification of Nerve Injuries.

We had not been going for very long before we found it necessary to extricate ourselves from the confusion in current terminology. It became evident that nerve injuries were of three main types, or various combinations of them. The names we used at first were "division," "lesion in continuity" and "transient block." Later, Professor Henry Cohen of Liverpool suggested more high-sounding but undoubtedly more accurate names, that

TABLE

Ætiology of Nerve Lesions.

Neurotmesis	*Axonotmesis*	*Neuvapraxia*
1. Open wounds	1. Open wounds	1. Open wounds
2. Direct blunt injuries	2. Direct blunt injuries	2. Direct blunt injuries
3. Traction.	3. Traction	3. Traction
	4. Compression, sudden or prolonged	4. Compression sudden or intermittent
	5. Friction (? a combination of 3 and 4 as in traumatic ulnar neuritis)	
	6. Freezing	5. Freezing
4. Local chemical poisoning	7. Local chemical poisoning (*e.g.* injection of sulphapyridine)	6. Certain drugs
	8. Experimental crushing	7. Experimental compression

we have since adopted (Seddon, 1942, *British Medical Journal* *2*, 237). The accompanying table gives some idea of how these three types of injury may be produced.

The diversity in ætiology shows how fruitless it is to classify injuries to nerves according to the kind of violence inflicted, since the same injury may, in different circumstances, produce different lesions, and indeed a single injury to a limb may produce all three types of lesion in the three main nerve trunks. A classification should give a picture of the morbid

FIG. 1.

Neurotmesis due to traction. The whole of the nerve is replaced by dense fibrous tissue and only a few disorganised bundles (N) are visible at each end of the excised segment. The fissure on the lower margin is the result of an exploratory incision at the point of greatest density. (Permission of British Journal of Surgery).

state, both gross and histological; it should give an indication of the disturbance of function resulting from this state—the disturbance manifest clinically as the symptoms and signs of the disorder—and, lastly, it should give some notion of the kind of recovery to be expected. Neurotmesis (τμῆσις a 'cutting') should be given a wider application than the term 'division' since the nerve as a nerve may be divided and yet appear to be in continuity. As Fig. 1 shows, a traction lesion may produce such intense intraneural scarring that recovery is quite impossible, as impossible as if the nerve had been severed by a bomb splinter; the injection of a chemical may have precisely the same effect. Yet in neither case is the nerve divided in the anatomical sense. Axonotmesis is a break in the nerve fibres with preservation of more or less of the supporting structures; it is like the breaking of the metallic filaments in a cable with preservation of the insulating material. There is no significant gap at the point of interruption, and regeneration occurs not only spontaneously but along the old channels, with the result that ultimate function is usually excellent.

Clinically, it is impossible to distinguish between neurotmesis and axonotmesis since in each case the paralysis is complete. The nerve trunk below the lesion is completely degenerate; the muscles waste and show the reaction of degeneration; there is paralysis of sweat glands and blood vessels; and complete loss of sensibility within the cutaneous area supplied exclusively by the damaged nerve (the autonomous zone).

(For the moment we will leave neurapraxia, since it has little in common with the other two types of injury).

The Distinction Between Neurotmesis and Axonotmesis.

It is, however, of the utmost importance that we should find some means of distinguishing between neurotmesis and axonotmesis since spontaneous recovery is almost unknown after the first type of injury, whereas it is invariable after the second.

(1) From *clinical experience* it is often possible to make a shrewd guess as to the nature of a lesion. In a case where a closed fracture of the humerus has produced complete radial

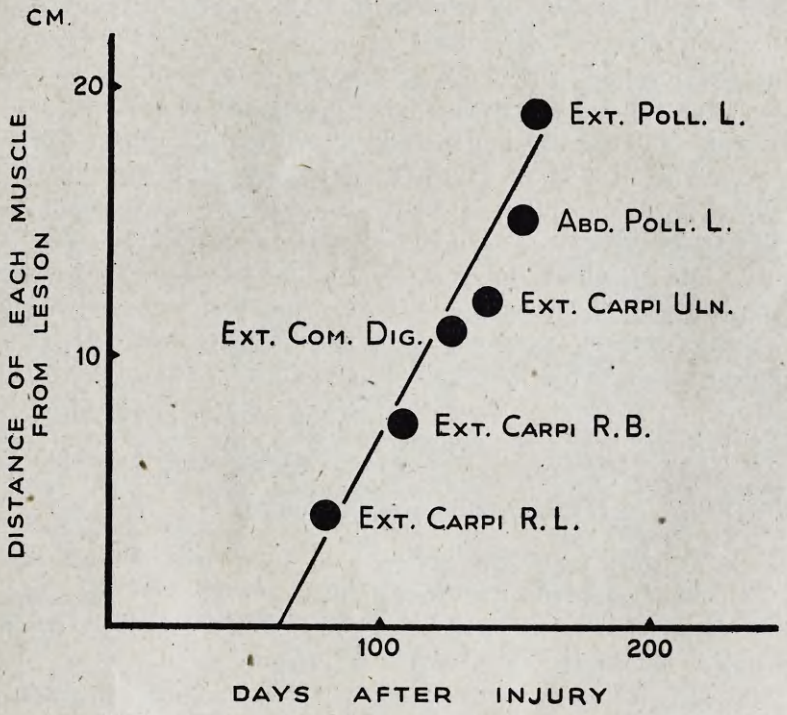
paralysis, in nine cases out of ten the nerve lesion is an axonotmesis and spontaneous recovery will follow; on the other hand, a gunshot wound of the arm may well have divided the nerve. One would not, therefore, explore with the same alacrity in the first case as in the second. Clearly, then, the surgeon must be guided by events; he must wait for a certain time to see whether spontaneous recovery will occur. If the humerus is fractured, or if there is a wound, he must wait anyway, since exploration should not be performed until there is firm union of the fracture, a good range of movement in the neighbouring joints, and sound healing of the wound. Very often he has the answer by the time the plaster is finally removed, for he may find that some of the previously paralysed muscles are working. But it is not always so, and he must then decide for how long it is proper to wait. In the past various times have been given; they had this in common, that they were all arbitrary.

(2) *The rate of regeneration.* A proper estimate can only be made if we know something about the rate of regeneration of nerves, especially motor nerves. It has been possible to work out the rate of regeneration by a method based on serial re-innervation of muscles, and for this purpose we have used cases of axonotmesis and of neurotmesis after suture. It is necesary to know the level of the lesion, the point of entry of motor nerves into the muscles they supply, and the interval between injury or suture and the first appearance of voluntary contraction in each muscle. The level of injury was noted as accurately as possible, and there was no difficulty whatever when an open operation had to be performed; the points of entry of motor nerves were determined from observations made in the dissecting room; and the appearance of voluntary contraction was observed in specially selected cases that could be kept under close observation and seen at frequent intervals. When all the data had been collected it was possible to construct a graph such as is shown in Fig. 2, and a line drawn through the points gives a fairly good indication of the rate of regeneration of functionally mature motor fibres. Although a straight line seems to be a good fit in many cases, we now have unmistakable evidence that regeneration does not

in fact proceed at a uniform rate. Like other growth processes, it is fast at first, then slows down as the process approaches completion. However, over considerable periods the rate is more or less uniform and of the order of 1·5 mm. a day.

How are we to apply this information in a case of fracture of the humerus with a break at, say, 12 cm. above the epicondyle and complete radial paralysis due, presumably, to a lesion of the nerve at the same level? The nerve to the brachioradialis enters the muscle 2 cm. above the external

FIG. 2.



A graph showing how rates of regeneration may be calculated. A straight line gives a good fit and a rate of 1·92 mm. per diem. A case of low radial axonotmesis.

epicondyle and during regeneration the axons have, therefore, to travel abont 100 mm. before any voluntary contraction can take place. If all went well they would do this in 70 days. But we must make allowance for regeneration that may be a little slower than normal and there is a period of

delay at the level of the lesion and at the muscle itself; nerve fibres do not begin to regenerate immediately after the injury or suture, nor does voluntary contraction begin immediately on their arrival in a muscle. At present we have no precise knowledge of the duration of this two-fold latent period; all we know is that it is generally longer after suture than after axonotmesis. In the latter it is probably wise to add 40 or 50 days; thus in the case under consideration one would expect a flicker in the brachioradialis at 120-150 days. Its non-appearance would be an indication for exploration of the nerve. It is clear that the correct time-interval between injury and exploration is derived from knowledge of the level of the lesion and of the point of entry of the nerve of supply into the most proximal muscle in the paralysed group. There can be no fixed period for waiting. Nevertheless, where the distance is considerable it may be unwise to wait for the whole of the calculated time. In a high lesion of the tibial division of the sciatic nerve it would take nearly a year for the fibres to grow down as far as the most proximal muscle, the gastrocnemius. If at the end of this time there was no recovery, and exploration revealed complete division, another year would be required after suture before any return of power in the calf muscle could be expected. Meanwhile irreversible degenerative changes would have occurred at the periphery, perhaps of such severity as to preclude good recovery. In such a case early exploration is indicated.

(3) *Naked eye appearances at operation.* When the decision to explore has been taken, the state of the nerve often provides a complete answer; if it is divided, repair should be carried out forthwith. However, the nerve may appear to be in continuity, and will then be found to present one of four appearances (Fig. 3):—

(*a*) The nerve looks and feels normal, or there is perhaps a slight thickening of the sheath. Unless it is a traction lesion (the pathology of this type of injury is so involved that we cannot properly consider it on this occasion), recovery will almost certainly occur.

(*b*) The nerve shows a smooth spindle-shaped swelling, little

firmer than normal, the well-known fusiform neuroma. Here again spontaneous recovery is to be expected though it is often slower than in cases where the nerve shows no gross lesion.

(*c*) The nerve is narrowed or swollen, but the most striking feature is the presence of scar tissue within its substance which is sometimes such as to make the line of dissection quite artificial. These are the really difficult cases, for it is clear that if there is, in fact, nothing but scar tissue at the site of damage, the nerve, in spite of the apparent continuity, is indeed divided and must be sutured.

(*d*) A lateral neuroma may be found. This is an indication (if paralysis is complete) that certain fibres have suffered neurotmesis, while those in the apparently normal part of the nerve have probably suffered axonotmesis; the swelling is exactly analogous to the neuroma that forms on the central stump of a divided nerve and the glioma that forms at the periphery, though the two may be so close together as to form a single lateral bulge. There is unfortunately no time to discuss the treatment of these interesting lesions, though it may be said that in general resection is not often indicated.

(4) *Electrical Stimulation.* Whatever the naked eye appearance (apart from complete division) the nerve should be stimulated with bipolar faradism, and in many cases of axonotmesis it will be found that although the paralysis is clinically complete, contraction occurs in one or more of the muscles innervated from the peripheral trunk. This is because faradic excitability of a nerve usually returns some weeks before voluntary contraction is possible. A positive response is an almost certain guarantee of spontaneous recovery. Although this finding means that the operation is of no value so far as recovery is concerned, it is still a diagnostic necessity since the clinician cannot discover this state of affairs until the nerve has been exposed. But a negative response does not carry quite the same weight. For reasons already given, the exploration may have been carried out at a time before regenerating motor fibres could have reached the most proximal muscles, and a positive

response cannot be obtained until motor fibres have not only arrived, but arrived in fair number. If there were some means of detecting *sensory* fibres in the peripheral trunk, reliable information should be obtainable at any stage; this is possible in certain cases. We have found that, if there is not too much scar tissue at the site of the lesion, no great difficulty is experienced in exposing a nerve trunk under local anæsthesia. If one uses 0.5 per cent. procaine with 1-200,000 adrenalin and avoids injecting the nerve trunk direct (it is much more difficult to hit a nerve trunk than to miss it), the exposure may be made without interfering at all seriously with conductivity in the nerve. It is remarkable to find how easily an anæsthetised nerve may be freed without producing pain, provided that the operator exercises great gentleness, and provided that the patient is not mentally unsuitable for local anæsthesia. To detect the presence of sensory fibres, electrodes are applied below the level of the lesion; a very weak faradic current must be used. It is wise to apply the electrodes first to the normal nerve, and increase the current from zero until the patient feels a distinct but not unpleasant tingling in the distribution of the nerve. They are then moved to the periphery, and the patient is then asked to describe his sensations. A positive answer is usually as follows: "I can feel the tingling as I did before, but it is very much fainter." By this means it has even been possible to determine the distance to which sensory fibres have travelled, for there is a sudden cessation of response the moment one reaches the completely degenerate zone of the peripheral trunk. If there is no response to a small current a strong one should not be used, for, by spreading to surrounding tissues, it will almost always produce some kind of sensation. If by this means no indication of conduction is obtained, resection and suture must be considered.

(5) *Trial Incision of the Nerve.*—A lesion that fails to show any sign of conductivity will undoubtedly be fibrotic, and it is justifiable to make a small incision at the point of greatest density. If it reveals fibrous tissue for more than half the thickness of the nerve trunk, no hesitation need be felt in proceeding to resection.

These, then, are the chief ways, admittedly crude, by which one attempts to distinguish between neurotmesis and axono-

tmesis in the early days after a nerve injury. But as recovery proceeds—spontaneously in the cases of axonotmesis, after surture when the nerve has been divided—more subtle differences become apparent and they are bound up with the course of events at the site of the lesion. When a divided nerve fibre begins to regenerate, the central end sends out many sprouts, sometimes twenty or more, and if one of them makes contact with the central end of any column of Schwann cells in the peripheral stump, it grows down the column, spinning out a fibre behind it. Most of the sprouts are abortive, but we know that at least two may travel all the way to the periphery and make good connection with end-organs. This is how axon reflexes are produced after peripheral nerve injury. (Duel and Balance). Not only may one central fibre establish connection with more than one Schwann column in the peripheral stump, but axonal sprouts may and frequently do get into the wrong kind of tube (motor into sensory; pain into touch; heat into pain, etc.), and one central fibre may supply new fibres to two or more Schwann columns in the periphery. And if a considerable segment of nerve has been excised prior to suture, the funicular patterns at the central and peripheral surfaces are so incongruous that the confusion is enormous. Foerster regarded it with such cynical despair that he said that, where a fairly generous resection has preceded suture, the result would not be made any worse by rotation of the stumps through 90 or 180 degrees. Hence there is a double source of confusion at the suture line. This is why the results of suture of mixed nerves, especially secondary suture, are always imperfect, and it is difficult to see how they could be otherwise. A motor axon growing down a Schwann tube connected with a sensory end-organ is an axon wasted. A touch fibre which normally innervated the tip of the thumb growing into a Schwann column connected with a touch-ending in the index finger, although not wasted, is misdirected; I have seen several patients where the confusion was such that a stimulus applied to one digit was referred by the patient to another and a long period of re-education was required to remedy this confusion. In the median area especially, one finds evidence of the imperfection of sensory regeneration in poor

two-point discrimination, inability to appreciate the quality of surfaces, or to distinguish small articles, such as screws and coins. In the hand this is a very serious disability. On the motor side, a similar effect is seen in the interossei, after suture of the ulnar nerve; I have seen only one case (primary suture of the nerve in a child) in which dissociated movements of the interossei were regained. The radial nerve, being predominantly motor and subserving functions that are not intrinsically delicate, gives excellent results in suture, but even here there is a considerale interval between the appearance of voluntary power and the return of dissociated and synergic movements.

The picture after axonotmesis is much brighter. On the sensory side recovery is often perfect, not only when judged by ordinary tests for return of sensibility to pain and touch, but two-point discrimination is restored to normal and with it the ability to identify small objects or the character of surfaces. In some cases I have found excellent two-point discrimination in the palm at a time when the tips of the fingers were still anæsthetic; the finer grades of perception follow close behind restoration of gross sensibility. And when muscles are regaining their power after axonotmesis, synergic and dissociated movements often return before muscle power is normal. These phenomena are in striking contrast with those observed in recovery after suture of a nerve, and one cannot escape the conclusion that the regenerating fibres must have got back into their old paths, without branching wildly at the site of the lesion. One cannot explain the inferior recovery after suture on the grounds of delay. We know that the quality of recovery is worse the longer one has to wait after the infliction of the injury before repairing the nerve; irreversible changes occur in end-organs, muscle and skin and there is deleterious shrinkage of the peripheral stump. But I have compared a number of cases of high axonotmesis with cases of low primary suture in which the recovery after suture was well ahead of that after axonotmesis and yet the final result was more favourable in the latter. The really significant difference is at the site of damage.

I have described the recovery seen after pure axonotmesis, a lesion in which only the axons have suffered, their supporting structures remaining almost intact. This is a lesion that can

be produced experimentally, and is often seen as a result of blunt injury to a nerve in man. But there are cases in which the intraneural damage is not so specific; and, indeed, in producing the experimental lesion a little roughness may result in a breaking up of some of the bundles just beneath the epineurium. One must, therefore, be prepared to include in this group a certain number of cases in which the damage is not uniformly axonal; yet regeneration is spontaneous and of excellent quality since confusion during regeneration can never be very great. But in nerves subserving highly developed functions, the median and ulnar for example, delicate clinical tests sometimes reveal imperfect recovery. Recently I saw a medical officer who served in both wars and who in 1915 was wounded just below the right axilla. He suffered a complete median palsy with gross muscle wasting and loss of sensibility in the distribution of the median nerve. Exploration showed that the nerve was in continuity, and in the course of twenty months he made a remarkable spontaneous recovery. Nevertheless, he told me that his hand had never been really good for delicate work, and he found it impossible to hold small screws accurately when doing carpentry. When I examined him, 27 years after the original injury, all ordinary tests indicated that recovery had been very good. But two-point discrimination on the tips of his index and middle fingers was 8 mm. instead of the normal 2, and his appreciation of the size of coins and of the character of surfaces was imperfect. Clearly then, he had never regained the density of cutaneous innervation necessary for the finest grades of tactile discrimination. Either some fibres got into the wrong channels or their growth had been blocked by scar tissue at the site of the lesion. Here was a case of axonotmesis which fell short of the strict definition, and this is not an uncommon finding after gunshot wounds. This is why it is necessary in defining this type of lesion to say that *more or less* of the supporting structures of the nerve is preserved, since not all cases conform strictly to the behaviour exhibited by the purely axonal lesion.

NEURAPRAXIA.

This condition, in its most dramatic form, is familiar to

all who have seen cases of nerve injury resulting from gunshot wounds. The story is that immediately after receipt of the injury the victim felt that the whole limb had been shot away or that it was completely paralysed. And, indeed, complete paralysis of an extremity is not uncommonly seen for a short period immediately following the injury. However, power returns within hours, days, or a week or two, leaving the patient either with normal power or with complete paralysis confined to one of the main nerves. The same relatively transient paralysis is sometimes seen after the application of a tourniquet or, less commonly, an Esmarch bandage; it is the type of paralysis associated with pressure from crutches; it may be caused by a fracture, and a mild traction injury is sometimes responsible.

The clinical features of neurapraxia cannot be described with the same precision as those of neurotmesis and axonotmesis which, as has been explained, conform to an anatomical pattern. It is rare for neurapraxia to produce complete interruption of a nerve; the lesion is essentially a partial one, and as all the main nerves of a limb may be affected the clinical picture is often exceedingly confusing. Nevertheless, there are certain features of the condition that enable one to make a diagnosis with fair confidence.

Motor changes.

(a) The paralysis may be and often is complete; it is said that muscle tone is sometimes retained but this is an observation that I have been unable to confirm. A few muscles may escape, or there may be generalised weakness such as occurs after partial neurotmesis or partial axonotmesis.

(b) Muscle wasting is slight, generally no more than can be accounted for by disuse or injury to other structures.

(c) The electrical reactions are normal. When a nerve has been completely divided the paralysed muscles retain their faradic excitability for about two weeks, but it is then quickly lost. By contrast, the responses in neurapraxia remain unchanged, which is proof that the nerve has not degenerated.

Sensory changes.

(a) The patient frequently complains of parœsthesiæ; aching in the limb, shooting pains and—most commonly—tingling, not unlike that experienced when a leg "goes to sleep."

(b) The changes in cutaneous sensibility discovered on examination are almost invariably less extensive than the motor changes; often one finds no detectable difference by the ordinary tests for touch and pain sensibility, although the patient may outline an area, such as that supplied by the superficial radial, in which he feels the characteristic tingling. There may, however, be a gross disturbance of deep sensibility, and the two forms often lost over a very wide area are postural sense and vibration sense. Here the contrast with the true degenerative lesion is especially striking, since in neurotmesis or axonotmesis the extent of loss of deep sensibility is always very much smaller than that of cutaneous loss.

Sympathetic changes.

The only changes that we have investigated in detail have been in the activity of sweat glands. Sweating may be quite unaffected; one sometimes finds it depressed over a wide area, but only for a short time. There is rarely any correspondence, such as is found in degenerative nerve lesions, with whatever changes in cutaneous sensibility may be present.

This curious combination of findings makes it quite impossible to explain the lesion on ordinary anatomical grounds and this, in a negative way, is of help in arriving at the diagnosis.

But by far the most striking feature of neurapraxia is the way in which recovery occurs. In a mild case the paralysis may last only a few hours; but it may persist for days, weeks, or even two or three months. Nevertheless, when recovery occurs, it always does so with a rapidity far exceeding that seen after even the most benign degenerative lesion. Furthermore, there is no anatomical march of recovery such as is seen after a lesion with axonal degeneration. The paralysis often disappears within a few days, though it may have been present for a month or more, and recovery may proceed irregularly, or with equal rapidity, throughout the affected zone. It is like the wearing off of a local anæsthetic.

Unfortunately, we know far less about this condition than we do about neurotmesis and axonotmesis. All one can say is that the injury somehow interrupts conduction without breaking the axons and so causing peripheral degeneration. The most striking evidence of this is the retention of normal electrical excitability of the muscles. In some cases conduction itself is not wholly abolished. We have found that if a concentric needle electrode is inserted into a muscle supplied by a nerve that has suffered neurapraxia, motor units can sometimes be demonstrated by the cathode-ray oscilloscope when the patient attempts to contract the muscle. There is no visible movement, but each attempted movement is accompanied by electrical outburst which indicates clearly that something is getting through, though not in such a manner as to produce a manifest contraction. On one occasion I had the opportunity of stimulating a nerve exposed during the course of an operation on a patient who showed signs of ulnar neurapraxia. Clinically, motor paralysis was complete, yet it was possible to get a moderately brisk contraction in the affected muscles on faradic stimulation of the nerve central to the lesion. Unfortunately, there was no justification for exposing the nerve below the lesion (it was a potentially infected wound), and one was left to surmise that the response on distal stimulation would probably have been much more brisk. The motor fibres, therefore, are interrupted in such a way as to produce temporary but complete paralysis, although evidence is accumulating that impulses can be transmitted somehow, which may explain why certain observers have remarked on the retention of muscle tone. The sensory fibres, apart from those concerned with deep sensibility, are not affected to anything like the the same extent.

During the last two decades great attention has been paid to nerve fibre types and it has been shown by Gasser and and Erlanger, and by others, that there is a correlation between fibre size, function, the character of the action potential wave, and the rate of conduction of impulses. There are three main groups of fibres, A, B and C. Group A, which is made up of the large fibres, includes those supplying voluntary muscle and those responsible for deep (proprioceptive) sensibility. The vulnerability of fibres of different sizes to various agents,

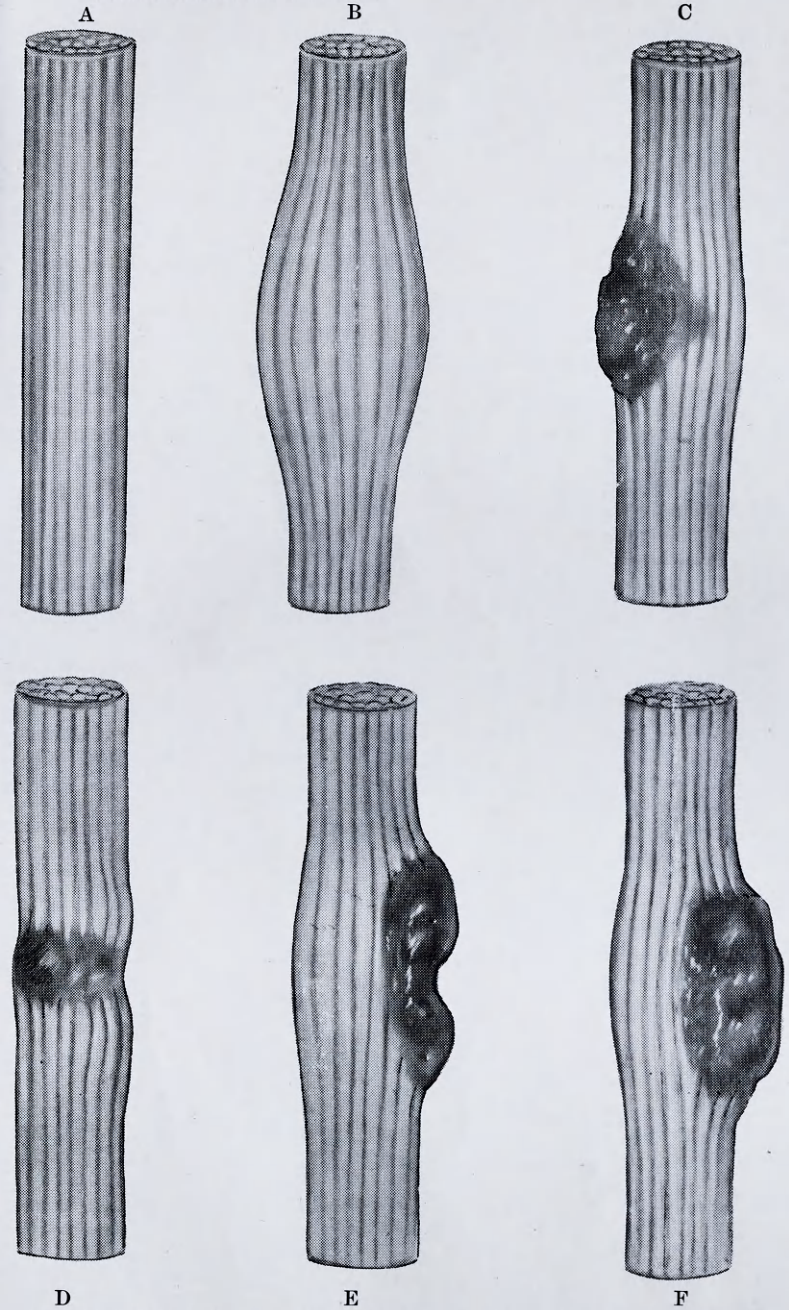
FIG. 3.

Diagrammatic picture of lesions exposed at operation in which the diagnosis of exonotmesis must be considered.

(a) nerve appears normal ; almost certainly a pure axonotmesis.

(b) fusiform neuroma with fairly uniform swelling of all bundles ; probably axonotmesis.

(c) scar tissue invading part of the nerve ; some bundles undoubtedly ruptured. Lesion is a mixture of axono- and neurotmesis.



(d) scar tissue involving the whole of the nerve : a little spontaneous regeneration may occur, but the quality will be poor. The lesion is predominantly a neurotmesis ; resection and suture are indicated.

(e) A typical partial neurotmesis with lateral neuroma and glioma.

(f) The same, but the swellings are confluent.

cold, local anæsthetics, compression and poisons, is not uniform. In clinical practice the selective action of local anæsthesia is perhaps the best known. Here we have an example of selective action by mechanical trauma, the larger fibres suffering most. The nature of the damage is still unknown, though it may be revealed by work now in progress.

In conclusion, one may say that most cases of nerve injury (but not ischæmic lesions or irritative lesions and perhaps not traction lesions) may be explained by reference to the conditions described as neurotmesis, axonotmesis, and neurapraxia. In practice, many difficulties will be encountered; since combinations of the three, either among themselves or with normally conducting fibres, are by no means uncommon. To describe these partial and mixed lesions would require a lecture even longer than this one; but those who are interested may be glad to know that W. B. Highet, who has been working at Oxford since these investigations began, is publishing a paper shortly in which the more common mixed lesions will be described in detail.