THE PATTERN OF CUTANEOUS INNERVATION IN RELATION TO CUTANEOUS SENSIBILITY

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THE purpose of this paper is to present histological findings which indicate the fundamental pattern of cutaneous innervation in vertebrates, as illustrated by an elasmobranch fish, the rabbit, the rhesus monkey, and Man. These findings are compared with clinical observations on Man and discussed in the light of Head's theory of protopathic and epicritic sensibility.

MATERIAL AND METHODS

Histological. Whole preparations of considerable areas of skin from the flank of an elasmobranch fish, *Acanthias vulgaris*, were impregnated with silver by a modified Bielschowsky-Gros method. This was carried out by Dr P. Glees of the Department of Human Anatomy, Oxford, to whom I am much indebted for the loan of preparations.

Whole preparations of skin from the ears of albino rabbits were stained with methylene blue by the technique of local injection (Weddell *et al.* 1940). Minor modifications have been introduced, following the observation that the most complete and uniform staining over a wide area resulted from the vaso-dilatation following cervical sympathetic neurectomy. To produce the same effect, a local anaesthetic (1 % procaine hydrochloride) was dissolved in a concentration of 0·015 % methylene blue in normal saline solution. This is found to give consistent staining over wide areas in about half an hour, and it is possible by this method to stain nerves uniformly throughout the skin of the dorsal or ventral surface of the ear.

Nerves in the skin of the forearm and finger-pad of the monkey were stained in a similar manner.

In Man unexpected difficulties were encountered in obtaining consistent and uniform staining. This was found to be due in part to the rapid concentration and excretion of the dye by the sweat glands, and in part to the thickness of the skin. The addition of atropine sulphate to the injected solution delays the excretion, and to some extent the concentration, of the dye by the sweat glands. In most cases good results can be obtained when the concentration of the dye is increased to 0·03 % in normal saline solution containing procaine hydrochloride 1 % and atropine sulphate 1/10th grain per 100 c.c.

Clinical. The areas of sensory loss of touch, pain, cold and warmth were mapped out in patients suffering from peripheral nerve injuries which included root lesions, plexus lesions, and nerve trunk lesions. The test objects used were von Frey hairs for touch, sharp needles for pain, and plane copper discs, 1 cm. in diameter, which could be maintained at constant temperatures, for warmth and cold.

Experimental. The dorsal nerve at the base of the ear in albino rabbits was resected in ten cases and partially sectioned in four cases. The partial section was performed under direct vision through a dissecting microscope by a single cut with iridectomy scissors. Approximately one-quarter of the trunk was divided. Care was taken to avoid damaging vessels running in the connective tissue sheath surrounding the nerve. Various intervals, ranging from 12 hr. to 4 days, were allowed for nerve degeneration in the case of total resection; 2 days were allowed to elapse following partial nerve section.

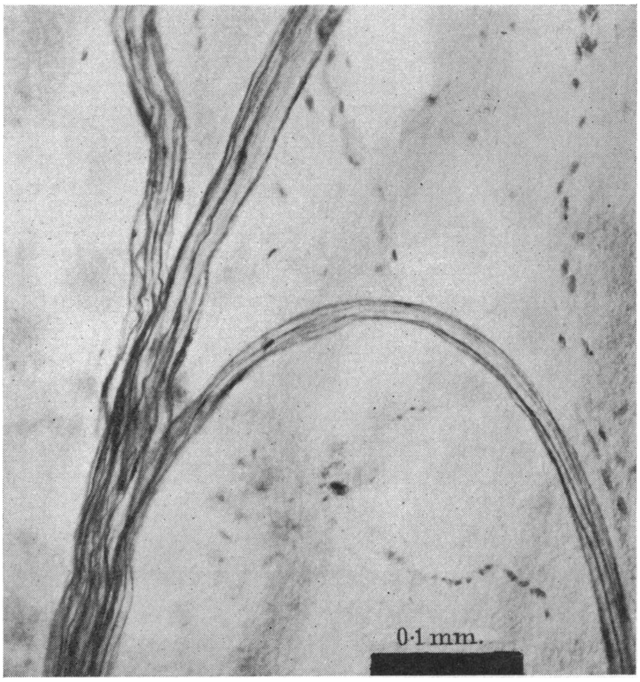
In Man the radial nerve was blocked in the lower third of the forearm in a normal subject who is experienced in the perception of sensory stimuli, by the infiltration of 2 % novocain containing 1 in 20,000 adrenalin. The areas of loss of pain and touch sensibility were mapped out. The same nerve was similarly blocked on a subsequent occasion in the lower third of the arm and the areas of loss of pain and touch sensibility again mapped out. The test objects used were sharp needles and von Frey hairs. The nerve blocks and sensory tests were carried out by Dr L. Guttmann, to whom I am much indebted.

Attempts were made to see stained nerve fibres and endings in the intact human skin by direct vision through a microscope. A 16 mm. objective fitted with an oil-immersion dipping cone and oblique illumination were used. The source of illumination was a low-voltage filament lamp, light from which was concentrated into a circle 1 mm. in diameter by a carefully corrected optical system.

HISTOLOGICAL OBSERVATIONS

In *Acanthias vulgaris* there is a cutaneous nerve plexus disposed in two main layers through the thickness of the skin. Single fibres travelling in the deeper nerve trunks, when traced peripherally, are seen to change direction and enter the cutaneous nerve plexus in which they dichotomize repeatedly as they approach the skin surface. The terminal ramifications of a single fibre become evenly distributed over a wide, approximately circular, area. The final branches of the fibres which were followed were found to end freely beneath and between the cells of the basal layer of the epidermis. Neighbouring fibres undergo a similar dichotomization through the cutaneous nerve plexus, and the terminal ramifications of any one fibre are always evenly interlocked with those of surrounding fibres. The method of distribution of the terminal ramifications may be compared with the branching and interlacings of a cultivated vine.

In the ear of the rabbit the cutaneous nerve trunks are arranged in a pattern which can be seen macroscopically after staining with methylene blue; they follow the venous pattern closely. A large nerve trunk enters the root of the ear, lying on the lateral side of the main dorsal vein. This soon gives rise to large branches which pass up the margins of the ear. The central nerve trunk continues towards the apex of the ear, giving off lateral branches at intervals. These pass towards the margins of the ear and divide into ascending and descending trunks which inosculate with other trunks derived in a similar manner. The pattern is complicated at various points by the formation of intermediate arcades and inosculations which occur between the marginal and central trunks (Text-fig. 1). In the marginal nerve trunks and intermediate



Text-fig. 1. Photomicrograph showing change in direction of nerve fibres derived from a main nerve trunk in skin from the dorsum of the ear of the rabbit. Methylene blue preparation.

arcades the nerve fibres pass in both directions, some fibres passing distally and others returning proximally towards their terminations. No nerve fibres within the nerve trunks were actually seen to dichotomize, but it is possible that this may occur occasionally. The central nerve trunk is composed of a number of fasciculi. Fibres occasionally leave one fasciculus to join another, in which they may continue distally or return proximally before leaving the main nerve trunk (Text-fig. 2). In other words, not every fibre in the main nerve trunk is necessarily passing in a distal direction; on the contrary, some may be running a recurrent course. In this connexion it has been noticed on several occasions that stimulation of the distal, as well as of the proximal ends, of the blue severed nerve trunks seen in the subcutaneous tissue after the removal of skin stained with methylene blue gave rise to nociceptive reactions in lightly anaesthetized animals. These reactions take place frequently when the distal end of the central nerve trunk is stimulated beyond the point where it has given rise to the marginal nerve trunks, but only occasionally if stimulated before it has given rise to these trunks.

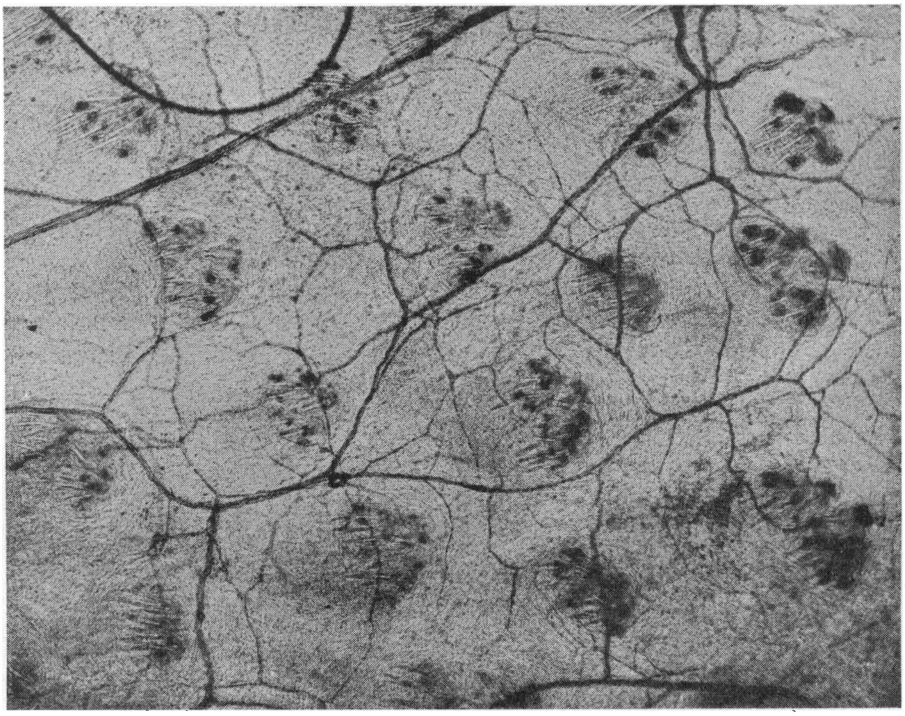
It will be observed from this general account that there is no question that the nerve fibres of a main trunk or of its branches approach from one direction, and in approximately parallel formation, the area of skin which they are destined to supply, and then deploy in an even pencil of fibres over the area.

Text-fig. 2. Photomicrograph showing a nerve fibre passing from one fasciculus to another in the main nerve trunk of the dorsal nerve in the ear of the rabbit and running a recurrent course. Methylene blue preparation.

On the contrary, to use a botanical simile, the pattern of innervation resembles the reticulate venation seen in certain types of leaves in contrast to the parallel venation seen in others.

Nerve bundles from the main nerve trunks give rise to branches which pass up from the subcutaneous layers towards the skin surface and distribute fibres to the cutaneous nerve plexus (Pl. 1, fig. 1). The latter is disposed in two main layers through the thickness of the skin. On entering the plexus, the fibres undergo repeated dichotomization. The cutaneous nerve plexus is formed by the inosculation of the two layers of dichotomizing nerve fibres arranged in meshwork patterns which enclose polygonal areas of approximately hexagonal shape (Text-fig. 3). Hair follicles lie for the most part at the centre of the superficial polygonal areas enclosed by the nerve-fibre meshwork. The terminal nerve-fibre ramifications which supply the hairs approach them in several directions from the periphery.

In the case of the rabbit, there are two modes of nerve-fibre termination. Some fibres end around the hair follicles and innervate the hairs; others end in nerve nets immediately beneath the epidermis. From these nets, fine beaded endings arise which are disposed below and between the cells of the deeper layers of the epithelium. The branches of an individual fibre traced throughout



Text-fig. 3. Photomicrograph showing the neural topography in the skin from dorsum of the ear of the rabbit. Methylene blue preparation. ×47.

its ramifications in the cutaneous plexus bear endings of only one variety. Beneath the epidermis, fibres can be seen arising from nerve bundles, and in some cases from the deeper layer of the cutaneous nerve plexus, forming nerve nets around the larger blood vessels. Fine fibres leave the nets and ramify in the walls of the vessels, and the capillary blood vessels in the subcutaneous areolar tissue at the base of the dorsum of the ear are accompanied by fine beaded nerve fibres derived from similar nerve nets.

After total resection of the dorsal ear nerve, the fibres supplying the hair follicles and giving rise to the subepidermal nerve nets are found to be undergoing degenerative changes. All such fibres in the skin from the centre of the dorsum of the ear were found to exhibit histological evidence of degeneration at the end of 2 days; these changes were clearly evident in the nerve trunks and at the fibre terminations.

After partial section of the dorsal ear nerve the degenerating fibres stand out in contrast to the normal fibres. In one instance it was possible to trace a single degenerating fibre to its termination around hair follicles. This fibre was found to run through the main and subsidiary nerve bundles without branching, although it changed its direction several times. Dichotomization began as soon as the fibre entered the deep layer of the cutaneous plexus. The branches continued to multiply through the plexus and were distributed over a wide, approximately circular, area, the greatest diameter of which was 1 cm. The number of hair-follicle groups supplied by branches from this single fibre was in the neighbourhood of three hundred, and a group of hair follicles may contain up to ten hairs. The terminal ramifications of every main fibre so traced was found to remain independent of those from other fibres. It is important to note that each hair follicle group is supplied by branches from at least two main nerve fibres (Pl. 1, fig. 2). This also applies to the individual hairs. The nerve fibres leaving the superficial plexus usually break up into a number of branches on their way to the hairs, so that a single hair may be innervated by as many as fifteen terminal ramifications. After partial dorsal nerve section, degenerating nerve fibres can be seen over the whole extent of the dorsum of the ear of the rabbit. The plan of innervation of the skin of the ear of the rabbit is summarized in Text-fig. 4.

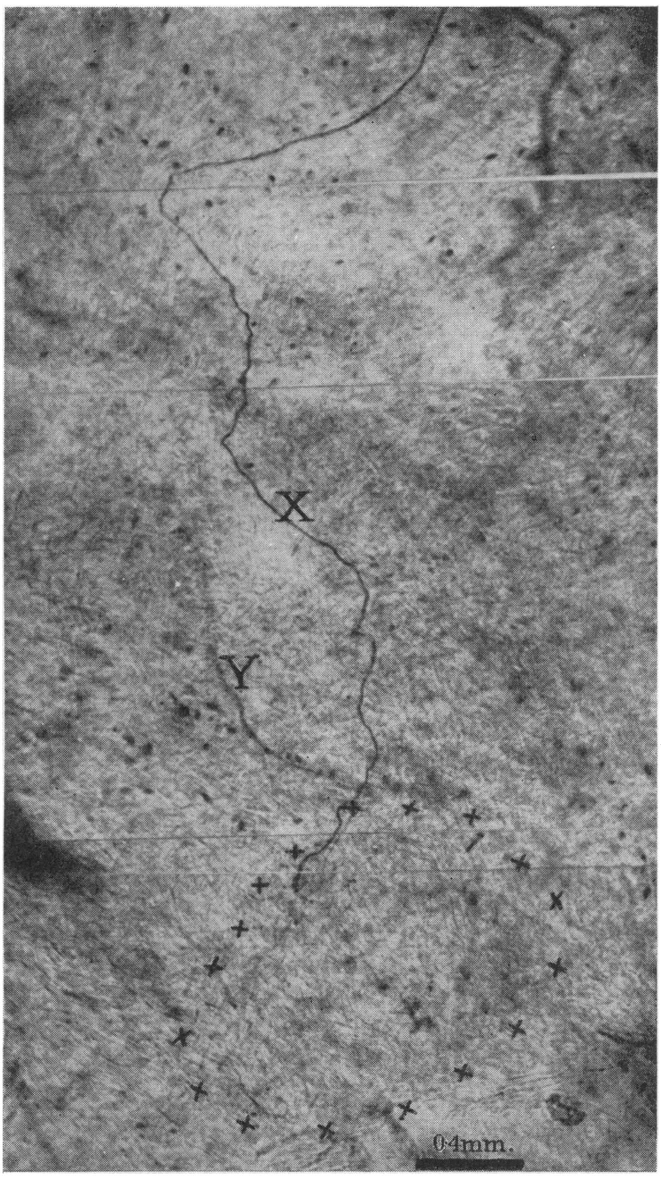
In skin taken from the pad of the thumb of a rhesus monkey there was found to be a cutaneous nerve plexus disposed in two main layers. Its pattern is, in general, similar to that seen in skin from the ear of the rabbit. Arising from the superficial layer are fibres of which each bears one or more endings. The endings borne by a single fibre arising from the cutaneous nerve plexus are always of the same type. The following types of ending have been identified: Meissner's corpuscles, Merkel's discs, Krause's end-bulbs, and fibres giving rise to nerve nets situated immediately beneath the epidermis. Fine terminal fibres arise from the net and end beneath and between the cells of the deep layer of the epidermis, and the endings derived from the nerve nets can be seen to lie in the same optical plane (4 mm. dry objective) as the cells of the deep layers of the epidermis (Text-fig. 6) The nerve nets from a single fibre are distributed over an approximately circular area. The nerve fibres from which they arise remain single and unbranched as far as they can be traced through the cutaneous nerve plexus. The nerve net derived from any one fibre is interlocked with those arising from neighbouring single unbranched fibres (Text-fig. 5). There is in no instance any visible fusion between the interlocked ramifications of nerve nets derived from separate fibres; on the other hand, there is continuity between the branches of the nerve net derived from a single nerve fibre. The area of skin covered by a net arising from a single nerve fibre in the thumb of the rhesus monkey is approximately 1·5 mm. in diameter.

HISTOLOGICAL OBSERVATIONS IN MAN

Direct observation. Direct observation of nerve fibres and endings in the intact, vitally stained skin of the human arm and hand proved unsatisfactory for two reasons. It was found extremely difficult to keep the arm and hand

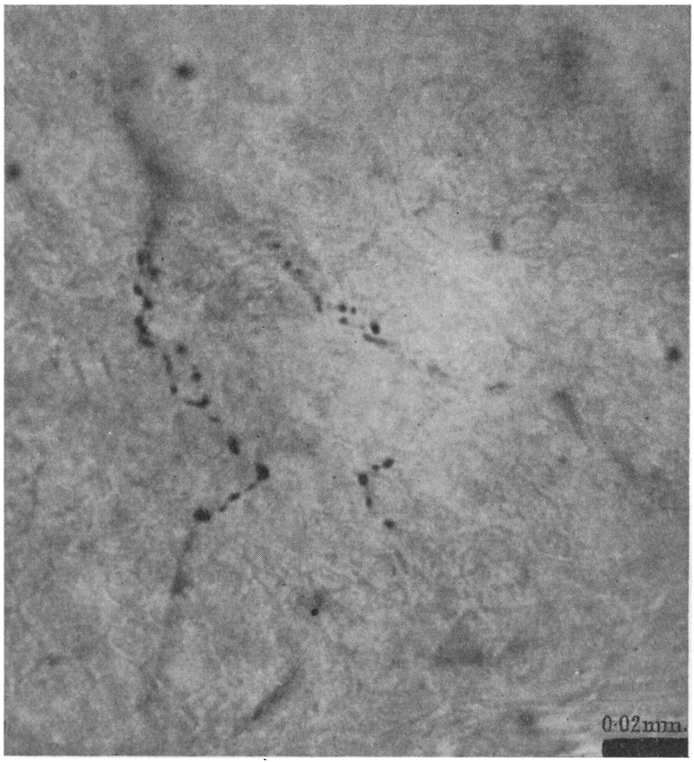
Text-fig. 4. A line drawing summarizing the general pattern of the distribution of the nerve fibres in skin from the dorsum of the ear of the rabbit. A, main nerve trunk; B, marginal trunk; fibres are passing in both directions; C, nerve fibres inosculating; D, intermediate arcade; E, nerve fibre which has run a recurrent course in the main nerve trunk; F, showing a mode of innervation of a unit area of skin; G, hair follicle group; H shows innervation of a hair follicle group by two fibres arising from subsidiary nerve bundles and passing through the cutaneous nerve plexus.

sufficiently still under the microscope for detailed observations to be made, and it was not found possible to see the details of any structure situated more deeply below the surface of the skin than the capillary loops in the dermal



Text-fig. 5. Photomicrograph showing a fine nerve fibre *X* emerging from the cutaneous nerve plexus from the pad of the thumb of a monkey and giving rise to a superficial nerve net. The area over which the nerve net is distributed is outlined by the ink crosses. It is 1·5 mm. in diameter. An interlocking nerve net is derived from the nerve fibre marked *Y*. Methylene blue preparation.

papillae. Half an hour after the injection of the dye into the skin of the forearm of a normal human subject (G. W.) fine blue nerve fibres arranged like a spireme were seen around some of the capillary loops in the dermal papillae, but it was not possible to trace the course of the fibres owing to the greater thickness of the interpapillary skin. Fine blue dots could also be seen over the whole stained area lying just beneath the surface layers of the epidermis, but, again, their connexions could not be traced. The dots were, however,



Text-fig. 6. Fine beaded endings lying between the cells of the deep layer of the epidermis derived from a superficial nerve net in the pad of the thumb of a monkey. Methylene blue preparation.

similar in all respects to the beaded terminals derived from superficial nerve nets seen immediately beneath the epidermis in cleared specimens of skin. The ducts of the sweat glands could be seen as blue coiled tubes passing through the surface layers of the epithelium. They were dark in colour, particularly if the injected dye solution contained neither local anaesthetic nor atropine, and they could then be seen intermittently discharging drops of blue fluid on to the skin surface. After discharging the fluid the ducts became pale.

Biopsy material. The skin to be described from the first subject was taken some years ago during work done in collaboration with the late Prof. H. H. Woollard. A cold spot had previously been mapped out on the skin of the forearm (H. H. W.) by the method described by Woollard (1935). A full thickness of skin 0·5 cm. square which included the cold spot was removed and stained supravitally with methylene blue. Histological examination showed a cutaneous nerve plexus resembling that seen in the monkey. Close beneath the surface ink mark which indicated the position of the cold spot, two groups of endings resembling Krause's end-bulbs were seen to be borne upon terminal ramifications of thick nerve fibres arising from the superficial layer of the cutaneous plexus. The two groups of endings were 0·3 cm. apart. It was not possible to ascertain whether they were borne on branches of the same fibre or on independent fibres; they were, however, derived from fibres which could be traced for some distance through the superficial layers of the cutaneous nerve plexus and which themselves gave rise to further branches. Owing to the limited size of the preparation the latter could not be traced to their peripheral destinations. The endings resembling Krause's end-bulbs were situated approximately 1 mm. below the surface of the skin. Meissner's corpuscles, hair sheath endings, nerve fibres passing to blood vessels, and nerve fibres which gave rise to more superficially placed nerve nets, were seen to arise from nerve fibres which ran an independent course within the cutaneous plexus. The map of the neural topography underlying the cold spot (Pl. 2) illustrates these findings. This map was made by placing together a number of photomicrographs which followed the course of the nerve fibres to their endings through varying optical planes.

Skin from a second subject was stained and removed from the forearm of a patient (J. A.) attending the skin department of the Radcliffe Infirmary, Oxford, for psoriasis elsewhere on the body. This piece of skin measured 1 by 0·5 cm. A similar cutaneous nerve plexus was seen in it. From the plexus fibres arose which ended around hair follicles, other fibres giving rise to Meissner's corpuscles, and still other fibres to superficially placed nerve nets situated beneath the epidermis. No other types of organized ending were seen. The endings derived from the nerve nets were particularly well stained and could be seen as a carpet of beaded terminals lying between and beneath the cells of the deep layers of the epidermis.

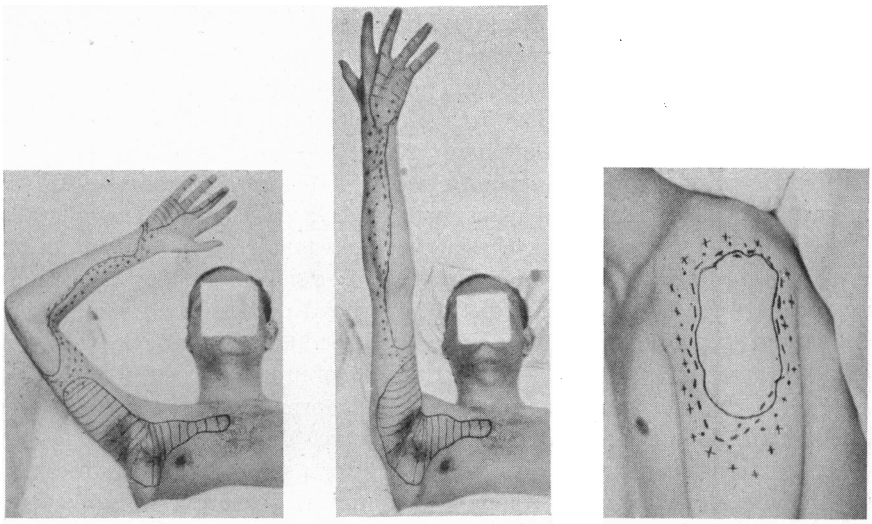
In order to determine the neurohistology of skin from which only one modality of sensation could be aroused, the pattern of sensory loss was outlined in a patient (Pte At.) with a sciatic nerve lesion. The area from which pain could not be aroused was smaller than that from which touch could not be aroused, and this in turn was smaller than the areas over which temperature sensibility had been lost. A piece of skin 2 by 3 cm. was stained and removed from a zone in part of which pain only could be aroused and in part of which both touch and pain could be evoked. In the area from which pain alone could be aroused fine nerve fibres were seen giving rise to superficial nerve nets; no thick nerve fibres or organized endings were seen. On the other hand, in the area of skin in which both pain and touch could be aroused, the cutaneous nerve plexus was seen together with thick nerve fibres ending around hairs and thinner fibres giving rise to superficial nerve nets.

The pattern of sensory loss was also outlined in a patient (Pte C.) in which a tube pedicle had been raised on the lateral aspect of the abdominal wall. The pedicle had been constructed so that its long axis was approximately in the line of the ninth rib; it stretched beyond the costal margin to within 2 cm. of the midline, and was 4 cm. in width. Sensation in the skin was normal one-third of the way from its lateral attachment, beyond which there was a zone 1·5 cm. in width across the pedicle in which pain only could be aroused. Over the rest of the pedicle there was complete loss of all forms of sensation. A piece of skin approximately 1 cm. square was stained and removed from the zone in which pain only could be evoked. Only fine nerve fibres and superficial nerve nets giving rise to beaded endings were found on histological examination.

A further case was examined (Pte A.) who had a partial interruption of the ulnar nerve and transverse fractures of the radius and ulna in the lower third of the forearm. There was paralysis of the small muscles of the hand normally supplied by the ulnar nerve, and impaired sensibility over the usual area of distribution of its cutaneous branches. The patient stated that he could not feel the test objects so clearly or so strongly throughout the affected area as compared with the same area on the opposite hand. It was hoped that in skin from such a case the neurohistology might be somewhat simplified, as had occurred in the rabbit after partial section of the dorsal ear nerve. Skin was therefore stained and removed from the centre of the affected area on the dorsum of the hand. This piece of skin was 3 cm. square, but not of full thickness owing to the fact that it was shaved off by a razor. In a central area of the skin approximately 1·5 cm. square the staining was good and the outline of the cutaneous nerve plexus could be seen. In one limited field a single well-stained nerve fibre was seen among other unstained and presumably degenerated fibres of the cutaneous nerve plexus. After leaving the plexus this fibre was traced to its terminal ramifications in a nerve net situated immediately beneath the epithelium and covering an approximately circular area of 0·75 cm. in greatest diameter. There were no interlocking nerve nets in this area, presumably owing to the degeneration of the immediately adjacent fibres. Arising from the superficial nerve plexus, and at some distance from the position of origin of the fibre giving rise to the nerve net, was a single isolated Meissner's corpuscle borne upon a thick nerve fibre.

CLINICAL OBSERVATIONS

Nerve-root lesions. Two cases of nerve-root lesions were examined. The first case was that of a doctor (Dr M.) who had a laminectomy performed by Prof. Hugh Cairns. An 8 g. neurofibroma was removed from the lower cervical and upper dorsal region of the spinal canal. During the course of the operation it was found necessary to divide the first right posterior thoracic root intrathecally before the tumour could be removed. Eight days after the operation, a sensory examination of the skin over the right upper extremity was carried out by Dr L. Guttmann. The area of sensory loss involved the skin over the whole medial half of the lower third of the arm, and skin over the medial half of the whole of the forearm. The areas of sensory loss for the four primary modalities of sensation were found to be almost completely superimposed in a concentric manner. The area of loss of touch sensibility was the smallest, being closely followed by that for pain. The area over which the sensation of



a *b* *c*

Text-fig. 7 *a* and *b*. Photographs showing pattern of sensory loss following section of the first posterior thoracic nerve root.

——— Touch; - - - - - Pain; 40° F. ...... Cold; 120° F. + + + + Warmth; Diminished sensibility.

Text-fig. 7 *c*. Photograph showing pattern of sensory loss following section of the fifth cervical posterior nerve root.

——— Touch; - - - - - Pain; 40° F. ...... Cold; 120° F. + + + + Warmth.

cold (40° F.) was lost was larger than that for pain, but smaller than that for warmth (120° F.). There was a slight diminution of sensibility to all forms of sensation over the second and third thoracic segments (Text-fig. 7 *a* and *b*).

The second case was that of a patient (T. A.) who had a laminectomy performed by Prof. Hugh Cairns for the removal of a 20 g. neurofibroma situated both extra- and intra-durally in the lower cervical region. It was again found necessary to section a posterior nerve root before the tumour could be removed, and in this instance the fifth left posterior cervical root was cut. Twelve days after the operation sensory examination of the skin was carried out by Dr L. Guttmann. The area of sensory loss involved the outer aspect of the upper half of the arm. The pattern of sensory loss was similar to that in the case previously described (Text-fig. 7 *c*).

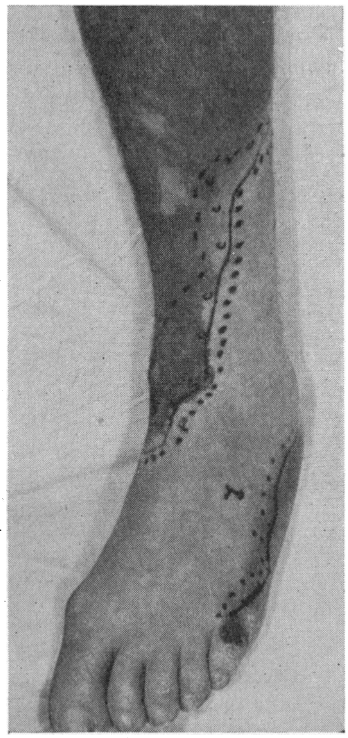
Nerve trunk lesions. A patient (Pte J. S.) was wounded by an explosive bullet in the left buttock. This resulted in a compound comminuted trans-trochanteric fracture of the neck of the left femur and injury to the sciatic nerve. Five months later the wound had healed and the patient had complete loss of sensation over the usual area of distribution of the common peroneal nerve. There was also complete paralysis of the muscles normally supplied by the nerve. The pattern of loss of the four primary modalities of sensation was similar to that usually found in such lesions. The area from which pain could not be aroused was the least extensive, being concentrically superimposed by an area in which touch sensibility had been lost. The areas from which cold and warmth could not be aroused were still larger and superimposed upon the area of loss of touch sensibility. The area of greatest loss was that for warmth sensibility. A sweating test (Guttmann, 1937) was carried out, and the area of anhydrosis was found to correspond closely to that of sensory loss. In only one position were points of sweat seen within the area of complete sensory loss (Text-fig. 8). There was hypoaesthesia over the whole area of skin supplied by the tibial nerve, and hyperalgesia along the outer side of the foot at the line of junction between the territories of the superficial peroneal and sural nerves. The patient was operated on by Prof. H. J. Seddon. The sciatic nerve was found to be embedded in a dense scar at the site of injury. A neurolysis showed that the tibial nerve was intact and appeared normal, whilst there was complete interruption of the common peroneal nerve.

The pattern of sensory loss was found to be of a similar type in four cases of median nerve lesion, two of which were found at operation to be complete interruptions, in eight cases of ulnar nerve lesion, four of which were complete interruptions, and in eight cases of sciatic nerve lesion, three of which were found at operation to be completely interrupted.

Brachial plexus lesions. A patient (Pte B.) met with a motor-cycle accident in which he sustained what was probably a traction injury of the brachial plexus, involving the fifth, sixth and seventh cervical roots. There was motor loss which involved the triceps, deltoid, brachialis and supinator muscles. The pectoral muscles were weak. The areas of sensory loss comprised one over the lateral aspect of the upper part of the arm, and one on the back of the centre of the forearm. The areas of complete sensory loss were surrounded by areas of partial sensory loss. The patterns of loss of the four primary modalities of sensation were not concentrically superimposed. On the contrary, they overlapped each other excentrically. The area of loss of pain in this case was larger than that for touch in both positions, and the loss of both cold and warmth sensibility was still larger, the area of loss of warmth sensibility being the most extensive. The area of anhydrosis did not correspond in outline with any of the other areas of sensory loss.

Four other brachial plexus lesions were examined. The outlines of the areas of sensory loss for pain and touch were found to cross each other at various points in all cases. In three cases of radial nerve lesions, known to be complete interruptions, the patterns of sensory loss were of a similar nature for all modalities of sensation.

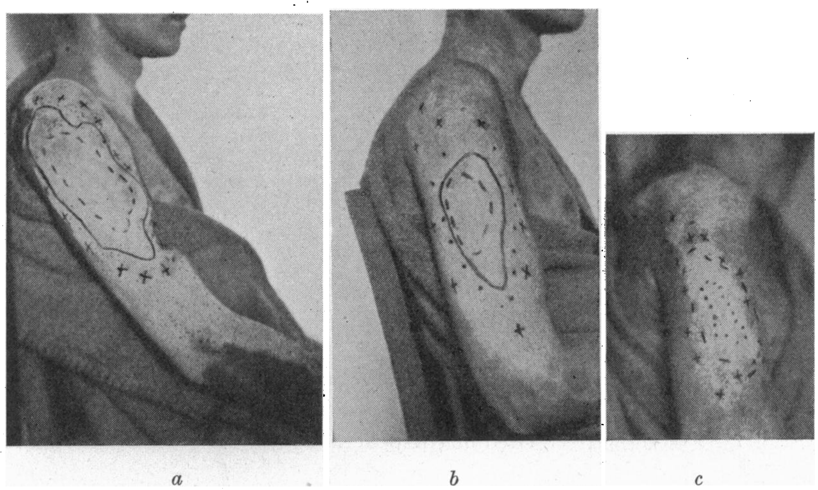
This series of cases serves to illustrate the relationship between the outlines of patterns of sensory loss for the four primary modalities commonly found in nerve root, plexus, and trunk lesions respectively. It is not suggested, however, that every case of nerve injury can be fitted into one of the three types of pattern described, for patterns of an intermediate type will be likely to occur after lesions at junctional regions between nerve plexuses and nerve roots and trunks respectively. The matter is further complicated by the fact that in some peripheral nerve trunks there is a tendency for the nerve fibres to continue their plexiform arrangement.



Text-fig. 8. Photograph showing area of sudomotor and sensory loss following a lesion of the common peroneal nerve. The arrow indicates points of sweat within the anaesthetic and analgesic area. ...... Pain; ——— Touch; 120° F. - - - - - Warmth; 40° F. ccccc Cold; + + + + Border of hyperalgesia.

Pattern of recovery of sensibility after complete peripheral nerve lesions. A patient (Dr K. S.) was examined who had had an acute inflammatory lesion of unknown aetiology involving the fifth and sixth cervical roots in the upper part of the lateral cord of the brachial plexus. The skin sensation was examined by Dr L. Guttmann 10 days after the onset of the lesion. There was loss of sensation over the upper and outer part of the arm. The area of analgesia was the smallest, being overlaid by an area of loss of touch, this in turn being overlaid by areas of loss of cold and warmth sensibility. A sweating test showed that the area of sensory loss was surrounded by an area of anhydrosis. The interval before recovery commenced (2 months) indicated that the lesion had completely interrupted the nerve fibres. During the course of recovery of sensation, the areas of sensory loss and anhydrosis were found to shrink in size. It may be emphasized that the value of the sweating test lies in the fact that it is objective in nature, and the close correspondence between the pattern of sudomotor and sensory loss in nerve lesions and during regeneration of nerve fibres has been noted previously (Guttmann, 1940). The pattern of sensory and sudomotor recovery in this case is illustrated by Text-fig. 9 *a–c*. The tests were performed at intervals of 3 and 5 months from the date of onset of the lesion.

A second patient (Sgt. A. H.) received a machine-gun bullet wound which completely severed the median nerve at the level of his right wrist. The nerve was sutured. Two months after the injury the areas of sensory and sudomotor loss were those typical of complete median nerve lesions at this level. The sweating test clearly indicated the overlap of fibres from the ulnar nerve into the median area which is commonly seen. One month later the areas of sensory loss and anhydrosis were found to have shrunk in size on the palm. In the thumb, index and middle fingers, the lines of recovery were advancing from the sides, and this advance was more marked at the base of the fingers



Text-fig. 9*a*. Photograph showing area of sensory loss after an inflammatory lesion involving the fifth and sixth cervical roots in the upper part of the lateral cord of the brachial plexus.
- - - - - Pain; ———— Touch; 120° F. + + + + Warmth.

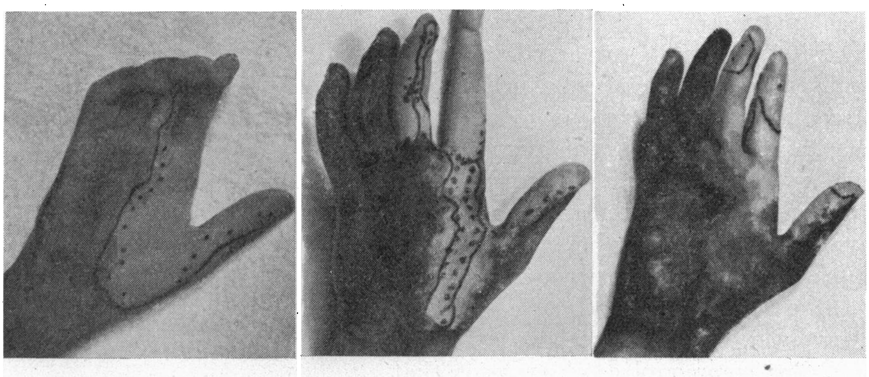
Text-fig. 9*b*. Same case, 3 months later.
- - - - - Pain; ———— Touch; 40° F. . . . . . . Cold; 120° F. + + + + Warmth.

Text-fig. 9*c*. Same case, 5 months later.
. . . . . .Pain; 40° F. - - - - - Cold; 120° F. + + + + Warmth.

and thumb. Two months later the only areas of complete sensory loss remaining were over the tip of the thumb, over part of the index finger, and over a small portion of the middle finger. The area of anhydrosis was rather larger (see Text-fig. 10 *a–c*).

These cases illustrate the fact that the recovery of cutaneous sensation may take the form of a circumferential shrinkage of the area of sensory loss rather than an advancing line of recovery commencing at the proximal border of the affected area.

Nerve-block experiments. Nerve-block experiments were carried out in order to determine whether there is any change in the limen of two-point discrimination or ability to localize stimuli in areas of partial sensory loss. The radial nerve was blocked by novocain 2 % and adrenalin 1 part in 20,000 in the lower third of the forearm in a normal subject (G. W.) experienced in the perception of sensory stimuli. The areas of loss of pain and touch sensibility were mapped out. The outline of the area of loss of pain sensibility was everywhere within that of the loss of touch sensibility. The borders of sensory loss between the ulnar nerve and the radial nerve on the dorsum of the hand, those between the median and radial nerves on the thenar eminence and thumb, and those in the web between the thumb and the forefinger, were not sharp. Two borders were outlined in these regions; the first by asking the subject to state when he first felt the test object, the second by asking him to state when the sensations aroused by the test object appeared normal. Both



a b c

Text-fig. 10*a*. Shows the area of sensory sudomotor loss 2 months after complete median nerve lesion at the level of wrist.

———— Touch; .... Pain.

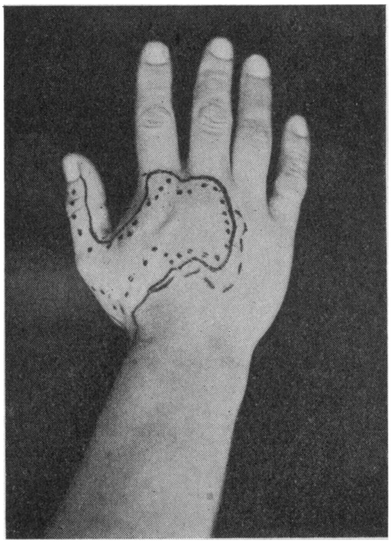
Text-fig. 10*b*. Same case, 1 month later.

Text-fig. 10*c*. Same case, 2 months later.

borders were difficult to define, but the sensation within the intermediate zone was uniformly diminished. Further testing showed that two-point discrimination for touch and pain and the ability to appreciate the pattern of figures traced upon the skin were lost in the area, and localization was also impaired (Text-fig. 11). The radial nerve was subsequently blocked in the lower third of the arm and a similar area of sensory loss was found to have been produced; it was concluded from this second observation that the radial nerve had been completely interrupted by the anaesthetic.

CORRELATION BETWEEN THE HISTOLOGICAL AND CLINICAL FINDINGS

The pattern of innervation in the skin of the rabbit's ear is such that, in general, each unit area is evenly innervated by fibres approaching it from all directions. This is brought about by the scattering of the nerve bundles beneath the skin and the dichotomization of the nerve fibres as they pass through the cutaneous nerve plexus to give rise to endings dispersed over approximately circular areas and evenly interlocked with endings derived from neighbouring fibres. There is histological evidence of the existence of a similar cutaneous nerve plexus in Man. The clinical finding that partial interruption of a main nerve trunk can give rise to a diminution of sensibility throughout its area of supply, and the finding with regard to the pattern of sensory and sudomotor recovery following certain nerve lesions, suggest that the cutaneous nerve trunks, on approaching the skin, rapidly disperse and ramify over wide areas before giving rise to a cutaneous nerve plexus, as in the case of the rabbit. For example, as the main trunk of the axillary nerve approaches the centre of the area of skin which it supplies, it appears that it then breaks up into bundles which travel throughout the area so as to approach their terminations from all parts of the periphery; that is to say, many of the fibres which innervate the central area of skin have the farthest distance to travel. In the case of the median nerve at the level of the wrist the same principle seems to be involved, but not in such an extensive form. The commonplace observation that small incisions through the skin are not accompanied by extensive areas of surrounding sensory loss also supports this conclusion.



Text-fig. 11. Photograph showing area of sensory loss following a radial nerve block in the lower third of the arm. ——— Touch; ...... Pain; - - - - - Boundary of the area within which there was hypoalgesia and hypoaesthesia.

The histological finding that, in areas of skin in which pain alone could be aroused, only fine nerve fibres giving rise to superficial nerve nets could be found, confirms a previous conclusion that such nerve nets subserve the sensation of pain (Woollard *et al.* 1940). It is further shown that the size of the superficial nerve nets varies in different parts of the body. On the back of the hand in Man, the net derived from a single fibre covers an approximately circular area which is 0·75 cm. in greatest diameter. This distance is approximately the same as the limen of two-point discrimination for pain in this region. The diameter of the nerve net from a single fibre in the skin of the pad of the thumb of the monkey is only 1·5 mm. in diameter. This approximates to, but is in fact rather less than, the limen of two-point discrimination in this region in Man.

In areas of partial sensory loss, such as those found between the radial, and ulnar and median nerves after blocking the radial nerve, the powers of discrimination for two points and 'figure-writing' are lacking. Localization is also defective. Histologically, in an area of skin supplied by a partially interrupted nerve there are isolated endings such as single nerve nets and single Meissner's corpuscles, in contrast to the number of endings and close interlocking normally present.

It thus appears that the powers of localization and discrimination are dependent at least to some extent on the number of nerve fibres supplying unit areas; in other words, they certainly involve a factor of spatial summation.

The patterns of sensory loss following the nerve-root lesions described are similar to those described by Foerster (1936) and are such that the area from which pain cannot be aroused is larger than that from which touch cannot be aroused. It is suggested that this can be explained by the large amount of overlap normally present between the territories of adjacent nerve roots, and the smaller area supplied by the terminal ramifications of fibres subserving touch as compared with those subserving pain. A change in the pattern of sensory loss occurs in lesions extending through the brachial plexus until in the more peripheral interruptions of the median and ulnar nerves the area from which pain cannot be aroused is smaller than that from which touch cannot be evoked. The relatively small amount of overlap which occurs between these nerves compared with that between nerve roots, and the size and nature of the interlock of the terminal ramifications of fibres subserving pain and touch, presumably account for this change in pattern.

DISCUSSION

Evidence has been brought forward which indicates that as the cutaneous nerve fibres approach the skin they dichotomize and interlock with one another in the form of a cutaneous nerve plexus. This occurs in such diverse types as an elasmobranch fish, the rabbit, the monkey, and Man. The cutaneous nerve plexuses have been noted by a number of workers. Martinez (1934) mentions a cutaneous nerve plexus in connexion with free nerve endings, but it is not clear whether he is describing superficial nerve nets or the underlying cutaneous nerve plexus. Tamponi (1938) mentions that the nerve fibres supplying hair follicles are derived from a plexus of nerve fibres. Woollard (1936*b*) has described the cutaneous nerve plexus in the skin of the rabbit's ear. His general description accords well with the present observations, but the areas of skin examined were comparatively small.

In the elasmobranch fish only one system of cutaneous nerve fibres was observed, in the rabbit two systems of fibres, one set innervating the hairs and the other giving rise to superficially placed nerve nets. In the monkey and in Man there are still further sets of fibres and types of ending. There is evidence that in Man there are specific nerve fibres and endings which subserve the four primary modalities of sensation in the skin (Strughold & Karbe, 1925; Bazett, 1935; Woollard, 1935, 1936*a*; Woollard *et al.* 1940). There is no histological evidence that any unit area of skin or cutaneous organ such as a hair is innervated by two sets of fibres or endings of different histological type, subserving each of the four primary modalities of sensation. On the contrary, evidence has now been brought forward that each unit area of skin or separate hair is innervated by more than one nerve fibre of the same type whose endings interlock with each other. In fact, each unit area of skin is innervated by a number of fibres which approach the area from all directions. Head's (1908) theory of protopathic and epicritic systems of nerve fibres was built on findings which were qualitative rather than quantitative in nature. His work was repeated by many other observers, the most detailed and elaborate studies being those of Trotter & Davies (1909), Boring (1916) and Lanier (1935). These workers approached the problem from a quantitative rather than a qualitative point of view, and disagreed with the findings of Head. Boring based a theory of cutaneous innervation on the dual innervation of each sensory spot, which fits in well with the present findings, but stated that the recovery of sensation did not follow the course of the nerve. He was, however, unaware of the nature of the pattern of cutaneous innervation. The findings of Trotter & Davies, Boring, Lanier, and other workers, that in general all forms of sensibility tend to reappear together after nerve division and suture, and that at first all returning sensation is diminished and then gradually approaches normal, can be interpreted in the light of the present histological observation. For it is now clear that each unit area of skin is supplied by nerve fibres approaching from more than one direction, the fibres having the farthest distance to travel presumably taking the longest time to re-establish functional connexions. The statement by Head that temperature of the epicritic type could only be aroused by large applicators at least the size of a sixpence is probably related to the histological finding that there are multiple endings which resemble Krause's end-bulbs borne upon two nerve fibres situated about 0·3 cm. apart in the skin in the proximity of a cold spot. The finding that the fibres giving rise to these end-bulbs also give rise to other branches within the cutaneous nerve plexus suggests that there are probably multiple groups of Krause's end-bulbs dispersed over relatively wide areas subserving each single cold spot.

It has been shown that in the normal skin there is a close interlocking between nerve endings, and that the size of the terminal ramifications of a single nerve fibre varies in different parts of the body. In the case of pain, the size of the ending is directly related to the limen of two-point discrimination. This confirms a suggestion made by Woollard *et al.* (1940) and a statement by von Frey (1899) that every nerve ending is distinct from every other nerve ending and that it is not possible to distinguish distances of sensation on the skin smaller than the distance between two nerve endings. The increase in the limen of two-point discrimination in areas of partial sensory loss, and the tendency towards poor localization, can be correlated with the histological findings of poverty of endings and the absence of interlock between the endings.

It has been shown by Weddell & Harpman (1940) that the nerve endings which probably subserve pain in the periosteum are in the nature of nerve nets, but that there is not the same intimate interlocking between the nets compared with that seen in the skin. Localization of pin-prick is also poor in periosteum and there is occasionally false reference.

The work of Kredel & Evans (1933) with regard to the recovery of sensation in various types of skin graft is interesting in the present connexion. They stated that the nerve fibres innervating pedicle grafts of full thickness whose polarity had been reversed during transplantation are re-innervated from above and to some extent from the sides, and that the direction of re-innervation bears no relation to the direction of the original nerve fibres in the flap. From this they concluded that the nerve fibres which re-innervate pedicle flaps do not follow the course of the old neurilemma sheaths, but form new pathways. The pattern of cutaneous innervation demonstrated in this paper indicates however that it is not necessary to draw such a conclusion.

In a previous paper (Woollard *et al.* 1940) it was suggested that the findings of Foerster (1925, 1927) that stimulation of the distal stump of a completely divided cutaneous nerve often gave rise to sensations travelling centrally in neighbouring cutaneous nerves was due to the passage of an impulse across closely interlocked endings. It is now clear that such an interpretation was unnecessary since the explanation must lie in the recurrent course occasionally taken by nerve fibres in nerve trunks. The findings of Foerster (1929) that stimulation of the distal end of a completely divided ulnar nerve at the wrist gave rise to pain referred to the fourth digit some months after the nerve section, and a similar observation in another case of a divided median nerve at the wrist, are explained on the basis of fibres passing from the median to the ulnar nerve across the communication which commonly occurs in this region, and running a recurrent course. In this connexion it can be stated that stimulation of the distal stumps of a number of completely divided nerves under local anaesthesia in Man by Prof. H. J. Seddon has so far elicited no sensation, but in no case has there been a known anatomical communication with neighbouring nerves in close proximity to the point of stimulation. With regard to the fact that nerve fibres have been seen to pursue a recurrent course within main nerve trunks, it is interesting to note that living nerve fibres growing into the tail of the frog tadpole have been seen to retrace their steps and run a recurrent course parallel to distally growing nerve fibres (Speidel, 1933).

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SUMMARY

1. The cutaneous nerve plexuses in skin from *Acanthias vulgaris*, the rabbit, the rhesus monkey and Man are constructed on a similar pattern.

2. Only one type of nerve ending was seen in skin from *Acanthias vulgaris*, two types were seen in skin from the ear of the rabbit, and multiple types in skin from the monkey and Man.

3. The pattern of cutaneous innervation in skin from the ear of the rabbit has been demonstrated. It is such that in general each unit area is evenly innervated by fibres approaching it from all directions.

4. A single nerve fibre in the dorsal nerve at the base of the ear of the rabbit breaks up into terminal ramifications which are distributed to approximately three hundred hair-follicle groups.

5. The terminal ramifications of a single nerve fibre distributed to hair follicles in the ear of the rabbit cover an approximately circular area of 1 cm. in greatest diameter.

6. Each hair-follicle group and each hair is innervated by at least two separate nerve fibres whose terminal ramifications are evenly interlocked with each other.

7. After section of approximately one quarter of the dorsal ear nerve in the rabbit, degenerating nerve fibres can be seen throughout the whole extent of the skin of the dorsum of the ear.

8. The size of a single superficial nerve net in skin from the pad of the thumb of the monkey covers an approximately circular area of 1·5 mm. in greatest diameter. It is closely interlocked with neighbouring nerve nets.

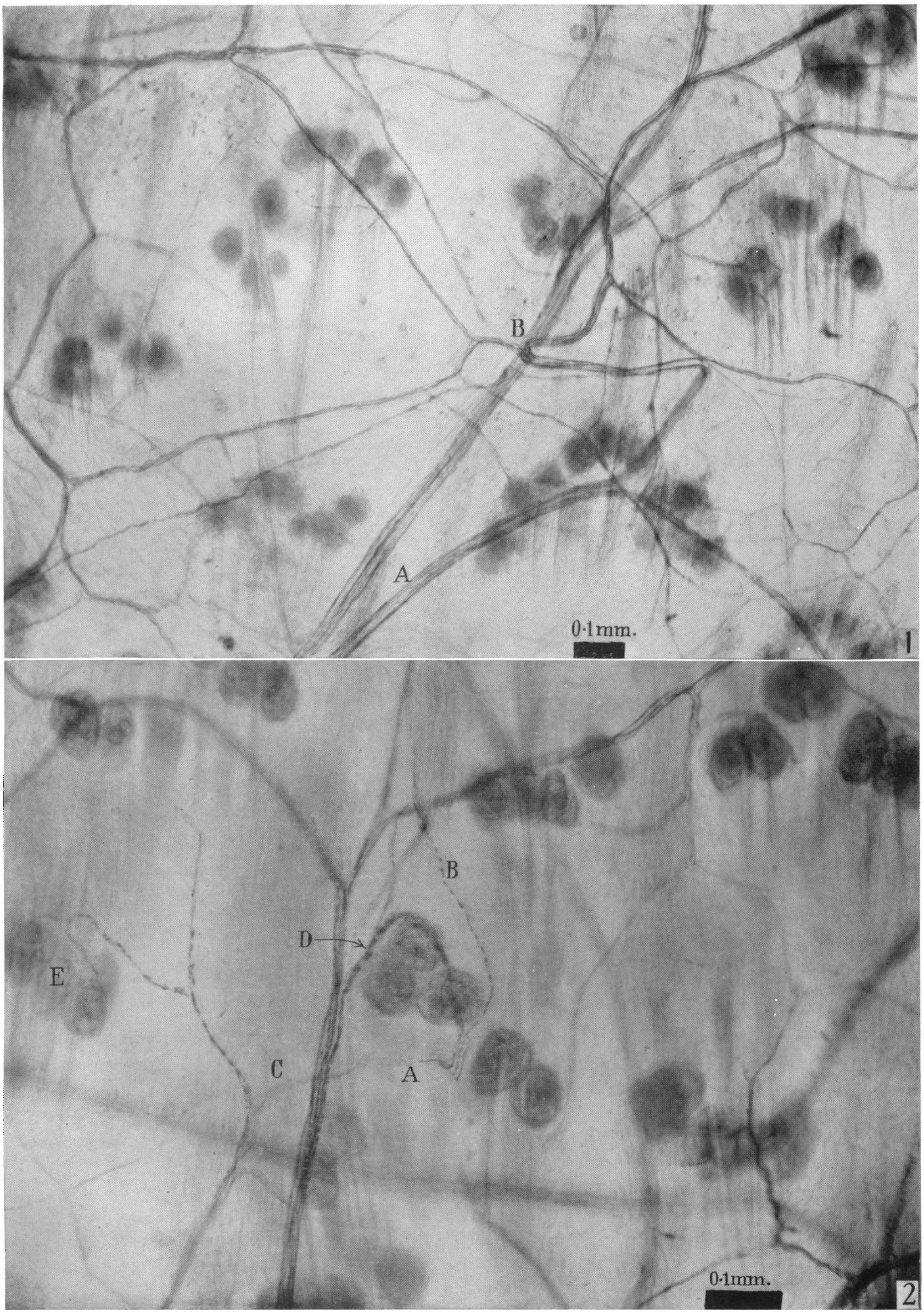
9. Multiple groups of Krause's end-bulbs are found beneath each cold spot in the skin of the human forearm. They are situated about 1 mm. from the skin surface and are borne on widely separated nerve fibres.

10. A single isolated superficial nerve net in a hypoalgesic area of skin from the dorsum of the hand in Man covers an approximately circular area of 0·75 cm. in greatest diameter. This distance corresponds to the limen of two-point discrimination for pain in a similar normal area.

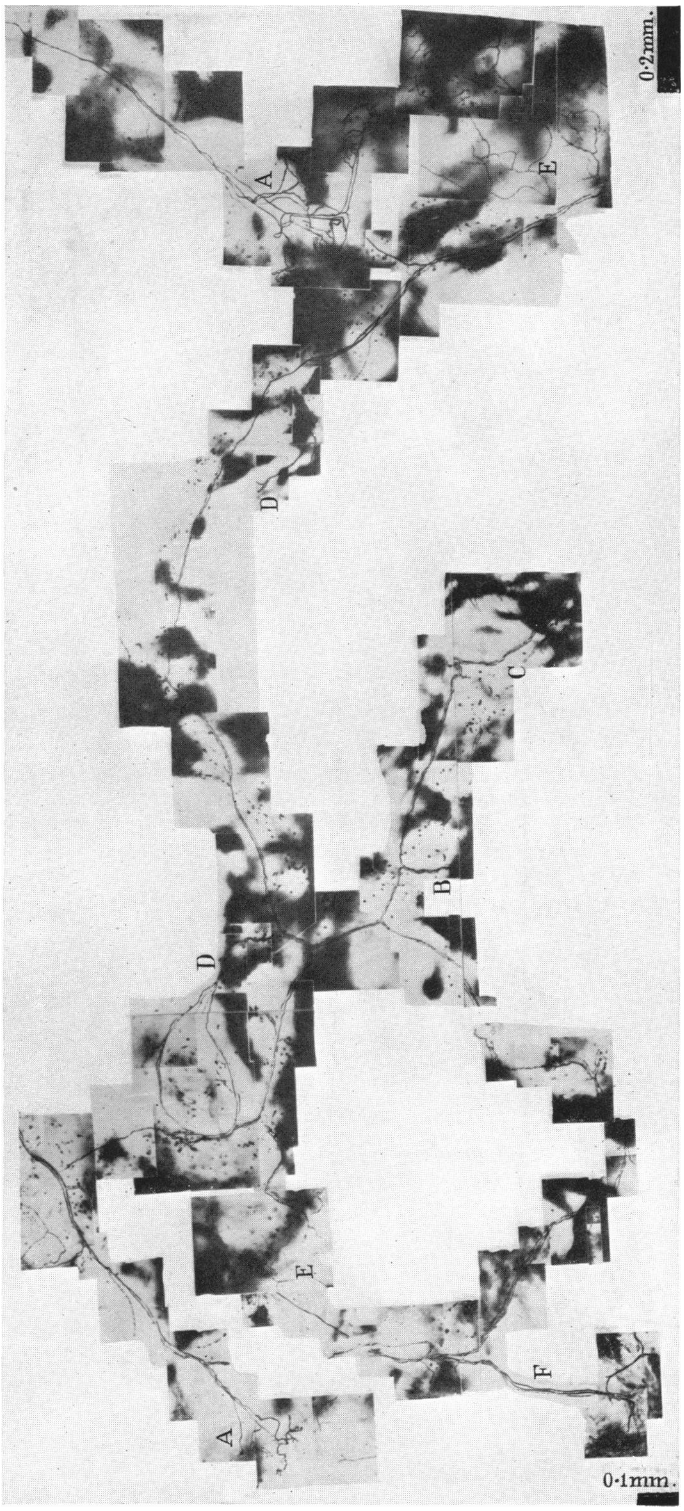
11. The pattern of sensory loss after certain nerve root, nerve plexus and nerve trunk lesions in Man has been described.

12. The pattern of sensory recovery after certain complete nerve trunk interruptions has been described.

13. The clinical findings have been correlated with the histological findings and discussed.



WEDDELL—PATTERN OF CUTANEOUS INNERVATION



WEDDELL—PATTERN OF CUTANEOUS INNERVATION

EXPLANATION OF PLATES 1 AND 2

(All figures are photomicrographs from methylene blue preparations)

Plate 1

Fig. 1. A subsidiary nerve bundle A is seen to be ending in the deep layer of the cutaneous nerve plexus. The nerve fibres are beginning to undergo dichotomization at B. Preparation from the skin of the dorsum of the ear of the rabbit.

Fig. 2. Shows a single hair being innervated by both normal and degenerating nerve fibres, 2 days after partial section of the dorsal nerve in the ear of the rabbit. A, hair; B, degenerating nerve fibre; C, normal nerve fibre; D, both normal and degenerating nerve fibres; E, hair-follicle group.

Plate 2

This shows the neural topography in the neighbourhood of a cold spot in the skin from the forearm of a human subject. The photograph was retouched for the purpose of reproduction. A, groups of endings resembling Krause's end-bulbs; B, nerve fibres passing to Meissner's corpuscles; C, nerve fibres passing to capillary blood-vessels; D, nerve fibres passing to innervate hair follicles; E, superficial nerve nets; F, fibre proceeding from the subcutaneous tissue to join the cutaneous nerve plexus.

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