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# Innervation of the tylotrich–touch dome complexes in rat skin: changing patterns during postnatal development

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ABSTRACT

The tylotrich–touch dome complexes of the rat were studied in detail at thoracic level, with two objectives: to follow the pattern of innervation of the individual complexes from birth to maturity and to determine the extent of overlap of the segmental nerves supplying them. Techniques included light and electron microscopy and histological observations following section of intercostal nerves. The touch domes were nearly always supplied from a single stem axon; as expected, their terminals increased in number in association with the differentiation of target Merkel cells from the epidermis. In general, they were supplied from the nearest segmental nerves. The tylotrich follicles were each supplied by several stem fibres. The number of palisade terminals applied to the epithelial root sheaths reached a maximum during the 2nd and 3rd postnatal weeks and declined during the following 2 wk. This overshoot can be regarded as another example of hyperinnervation found in the juvenile peripheral nervous system. During the period of decline, the stem fibres extended their territory, resulting in considerable overlap of the territories of the segmental nerves. By the beginning of the 8th week, overlap was relatively scanty, with an irregular distribution.

*Key words*: Cutaneous nerves; neural development; dermatomes.

## INTRODUCTION

The dermatomes are the cutaneous territories of the spinal nerves. The dermatomes exhibit a regular banded pattern extending from the dorsal to the ventral midline and there is general agreement that the nerve distributions overlap across dermatomal boundaries. In clinical studies, dermatomes have been mapped from the distribution of skin lesions in cases of herpes zoster (Head & Campbell, 1900); from maps of 'remaining sensibility' following section of posterior nerve roots (Foerster, 1933), and following nerve root compression by prolapsed intervertebral discs (Keegan & Garrett, 1948). These investigations indicate that the cutaneous distributions of each nerve are intense along the middle of the dermatome, and slight towards the upper and lower margins, which overlap with their neighbours to the extent of half a spinal segment. Electrophysiological studies have been performed by recording posterior nerve root potentials during stimulation of the skin, both in human subjects (Liguori et al. 1992) and in laboratory animals (Kuhn, 1953; Fletcher & Kitchell, 1966). These studies have concentrated on the lumbar and sacral dermatomes, in part because of the relative convenience of the longer nerve roots concerned. They indicate a greater degree of overlap for the hindlimbs than the clinical observations indicate for the trunk. A significant behavioural study on monkeys was performed by Kirk & Denny-Brown (1970), who concluded that the apparent size of a dermatome, on sensory testing, was affected by ongoing events in the posterior grey horn of the spinal cord. For example, a thoracic dermatome seemed to expand to twice its original size within minutes if inhibitory internuncial neurons were blocked by administration of strychnine. Expansion would be possible only if the requisite anatomical foundation were in place within the skin. However, anatomical studies of dermatomal overlap are remarkably scarce. For example, not a single histological assessment seems to have been performed in a laboratory animal following section of one or more spinal nerves. The only histological study of any kind seems to be that of Kinnman (1987), who injected horseradish peroxidase into the 10th thoracic spinal ganglion of rats and found labelled cutaneous

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axons of uncertain destination, extending into the adjacent halves of the territories of the 9th and 11th intercostal nerves. A drawback with injection experiments is that all relevant neurons may not be labelled throughout their full extent.

The present work was undertaken in order to assess the size of thoracic dermatomes in the rat by means of selective section of intercostal nerves followed by silver impregnation of tissue sections. The observations recorded here are confined to the most obvious sensory landmarks, namely the tylotrich follicle-touch dome complexes. In order to obtain baseline information, the innervation of the complexes was observed during the early postnatal weeks before the experiments were commenced.

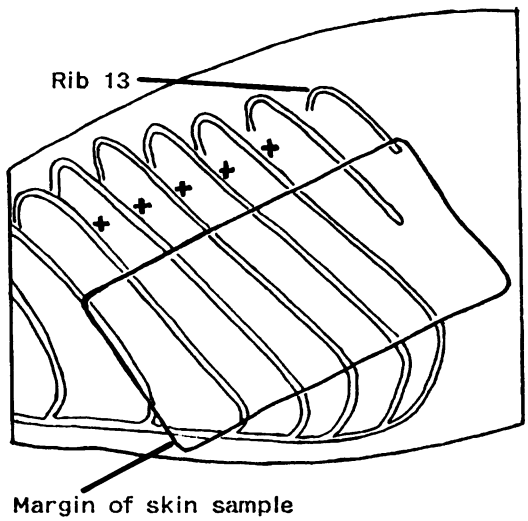


Fig. 1. Experimental procedure. +, sites of intercostal nerve section.

## MATERIALS AND METHODS

### *Control material*

*Light microscopy.* Control material was obtained from rats ranging in age from 7 to 100 d, following killing by chloroform overdose. Skin pieces were placed in paraformaldehyde fixative and frozen sections were impregnated with silver (see later).

*Electron microscopy.* Under intraperitoneal chloral hydrate anaesthesia (0.3 g/kg), the fur on one side of the thorax of 37 rats was removed with the aid of a depilatory cream. Full thickness of 2 $mm^2$ skin pieces were placed in phosphate-buffered glutaraldehyde fixative. In rats more than 3 wk old, silk sutures were first inserted immediately caudal to touch domes; the sutures aided in the identification and orientation of the tylotrich follicles during sectioning. All of the material was fixed in glutaraldehyde, postfixed in $OsO_4$, dehydrated in acetone, and embedded in Epon 812. Serial semithin sections (stained with Azure II in 1% methylene blue) were taken at right angles to the slope of the follicles, until the palisade nerve endings were located under cover of the sebaceous glands. Ultrathin sections were then taken onto formvar-coated slot grids and routinely stained for electron microscopy. At a magnification × 10000, palisade terminals, enclosed by Schwann cells, were identified with ease around the perimeter of the root sheath epithelium, and were enumerated.

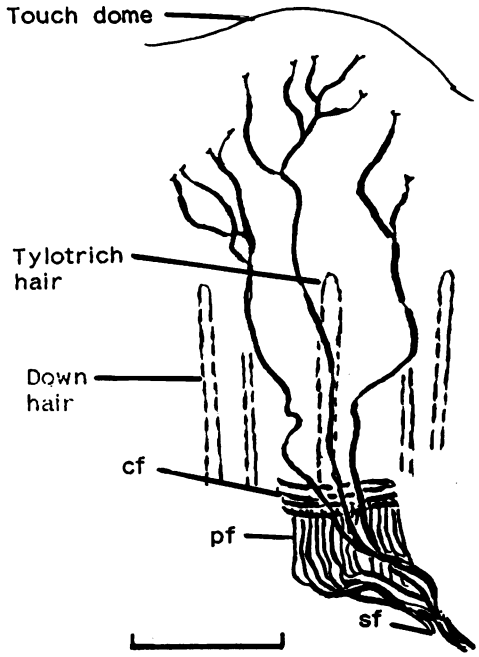


Fig. 2. Camera lucida tracing of the nerve supply to a tylotrich–touch dome complex. This is a vertical section viewed from behind. sf, stem fibres; cf, circumferential fibres; pf, palisade fibres. Bar, 200 μm.

### *Experimental material*

Following a variety of pilot experiments, it was decided that a set of 5 intercostal nerves should be sectioned in order to assess the extent of pre-existing overlap of the nearest intact nerves into their collective territory. Rats 7–50 d old were anaesthetised with intraperitoneal chloral hydrate. A skin incision was made alongside the left erector spinae muscle. The latissimus dorsi muscle was then incised in order to expose the underlying rib cage. Intercostal nerves 7–11 were exposed by teasing the external and internal intercostal muscles. Care was taken to avoid puncture of the parietal pleura underlying the nerves, which were lifted onto a curved forceps and severed (Fig. 1). The wound was closed by means of silk sutures. After 48 h survival, the animals were killed with chloroform and the skin of the left thorax was exposed by means of a depilatory cream. The line of the 9th intercostal

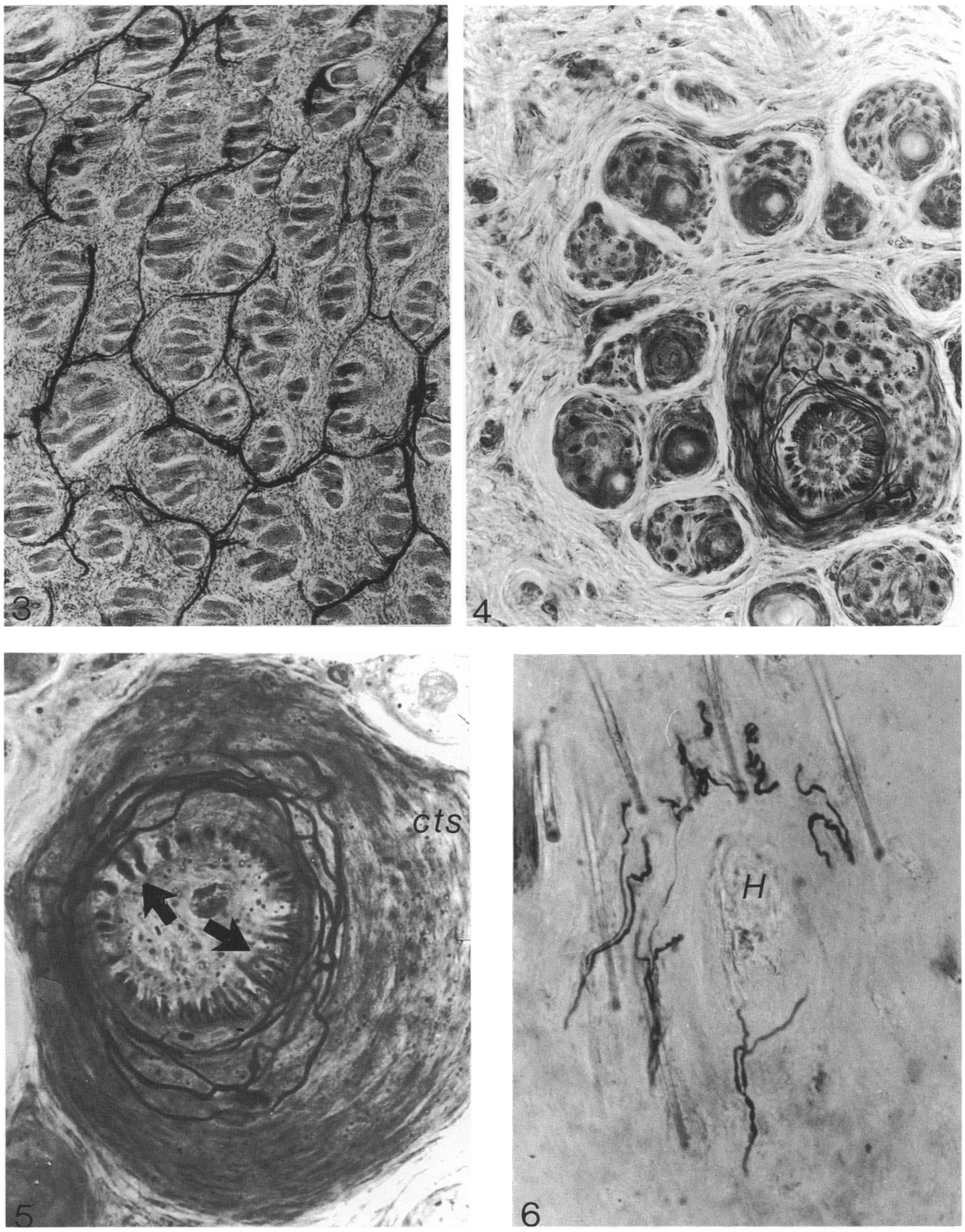


Fig. 3. Section through the deepest level of the dermis of a 21 d old rat; right side of picture is posterior. Groups of hair follicles occupy the interstices of the cutaneous nerve plexus. × 40.

Fig. 4. Section through the middle level of the dermis on d 21; right side is posterior. The large tylotrich follicle (lower right) is surrounded by down hair follicles. × 140.

Fig. 5. Section at same level and orientation as Figure 4; d 21; right side is posterior. The epithelial root sheath is surrounded by palisade terminals (arrows). *cts*, connective tissue sheath. × 300.

Fig. 6. Superficial section, d 21; top of picture is posterior. Several axonal branches are ascending to supply a touch dome. *H*, tylotrich hair. Several down hairs can be seen. × 300.

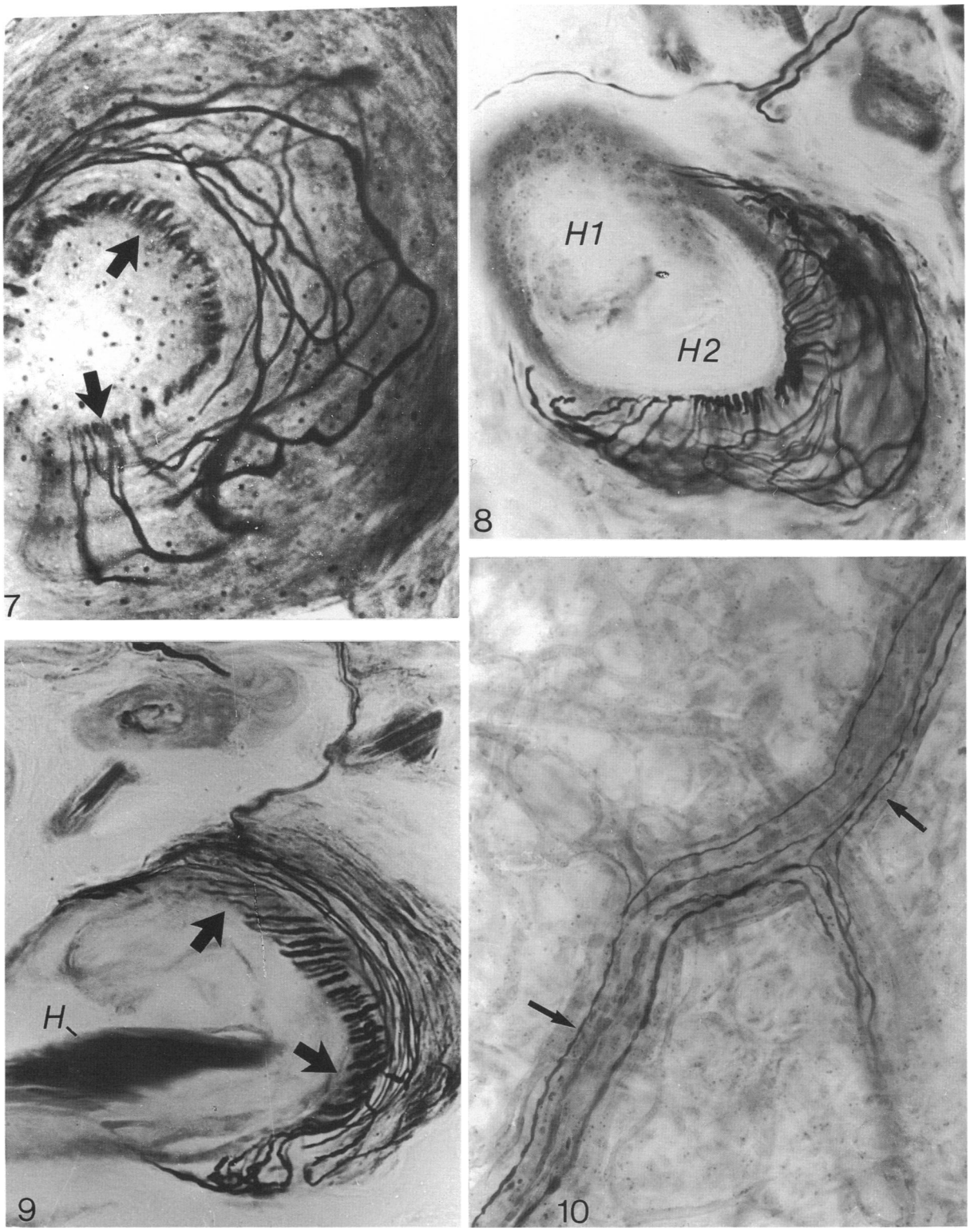


Fig. 7. Section at same level and orientation as Figure 4; d 28. Palisade terminals (arrows) surround the epithelial root sheath of a tylotrich follicle. Circumferential nerve fibres abound within the connective tissue sheath. × 500.

Fig. 8. Tylotrich follicle, d 40; right side is posterior. Palisade terminals are absent from the anterior aspect (left) of the epithelial root sheath. *H1*, original tylotrich hair; *H2*, replacement hair of the second pelage. × 250.

Fig. 9. Tylotrich follicle, d 90. Palisade terminals (arrows), are confined to the posterior (right) aspect of the epithelial root sheath. *H*, tylotrich hair. × 250.

Fig. 10. Partially depleted cutaneous nerve plexus following intercostal nerve section. Arrows indicate intact nerve fibres. × 200.

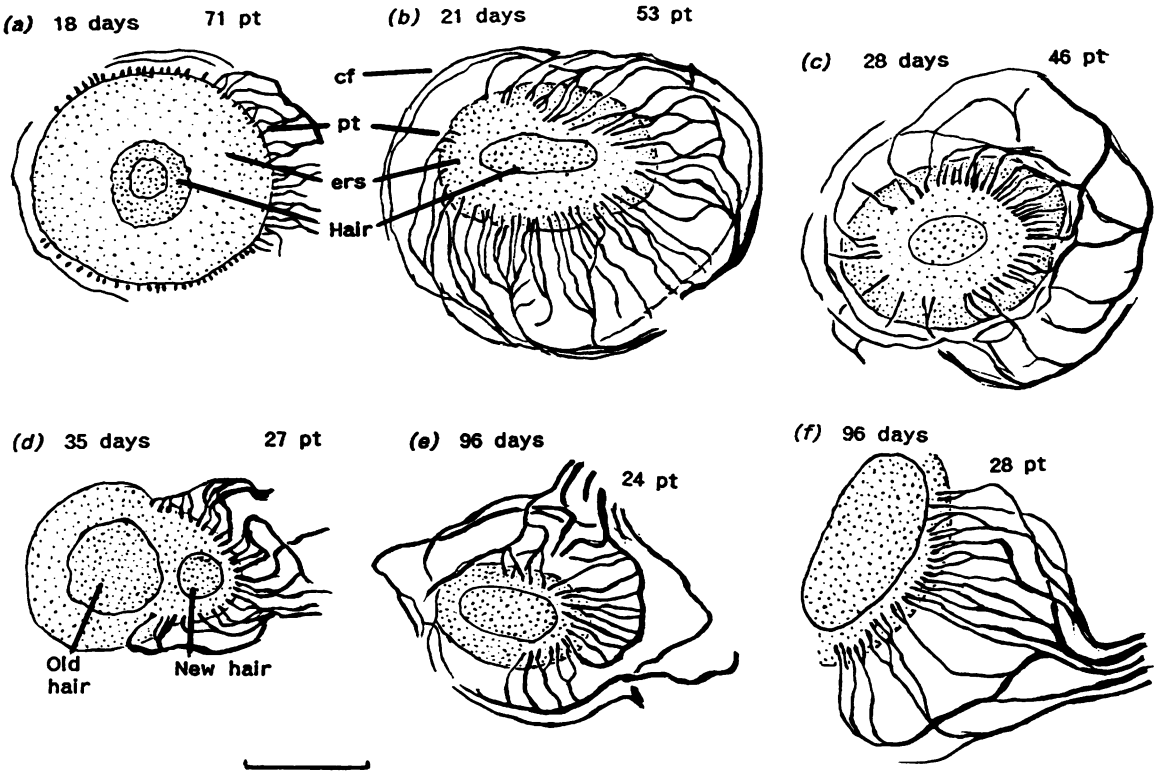


Fig. 11 (*a–f*). Camera lucida tracings of tangential sections of tylotrich follicles taken at the level of innervation at different ages (including 2 at 96 d). Right sides are posterior. cf, circumferential fibres; ers, epithelial root sheath; pt, palisade terminals. Bar, 100 μm.

nerve was identified, the xiphoid process of the sternum serving as a landmark. A rectangle of skin extending from the 6th to the 13th ribs was excised, placed between glass slides, and immersed in 5% paraformaldehyde containing 0.1 M sucrose adjusted to pH 8.0 with anhydrous sodium citrate (after Richardson, 1958). After 4–10 d fixation, frozen sections (30–40 μm) were taken parallel to the skin surface, stored overnight in ethanol containing 5% paraformaldehyde, and rinsed in water before immersion in 10% silver nitrate for 20 min. After passage through 4 paraformaldehyde baths, they were transferred through silver diammine (30 s) into silver carbonate, where they were allowed to develop until mid-brown. Development was stopped in an aqueous sodium sulphite–ammonia mixture (5% of each reagent), after which the sections were toned in 1% $AuCl_3$, rinsed in water and stored in 5% $Na_2S_2O_3$ before being firmly attached to subbed slides (to prevent shrinkage), dehydrated, cleared, and mounted in Entellan (Merck).

## RESULTS

### *Control material*

*Light microscopy.* The pattern of innervation of the tylotrich–touch dome complex is well known (Iggo, 1985; Winkelmann, 1986). Figure 2 illustrates this. It was traced from vertical sections taken parallel to the rib shafts and viewed from behind. The nerve supply is provided by myelinated fibres. The touch dome is supplied from 1 stem axon (occasionally, from 2). This axon branches freely in the superficial part of the dermis and the myelin sheaths end prior to the formation of Merkel cell–neurite complexes in the basal epidermal layer of the dome. The follicular supply is twofold: 1 or 2 stem fibres give rise to a set of circumferential terminals within the connective tissue sheath; and 2–6 stem fibres give rise to a palisade of nerve endings applied to the outer root sheath epithelium. The stem fibres were clearly discernible by the end of the 3rd postnatal week. Their number did not change appreciably in older animals.

Figures 3–10 are all from sections taken in the plane of the skin surface. The deepest sections (Fig. 3) reveal the cutaneous plexus in the base of the dermis; the interstices are occupied by the hair follicles. The innervated region of the follicles is at a more superficial level (Fig. 4). The tylotrich follicle is characterised by thick epithelial and connective tissue sheaths and dense afferent innervation (Figs 5, 7). Sections taken through the most superficial layer of the dermis show the terminal branches of the axon

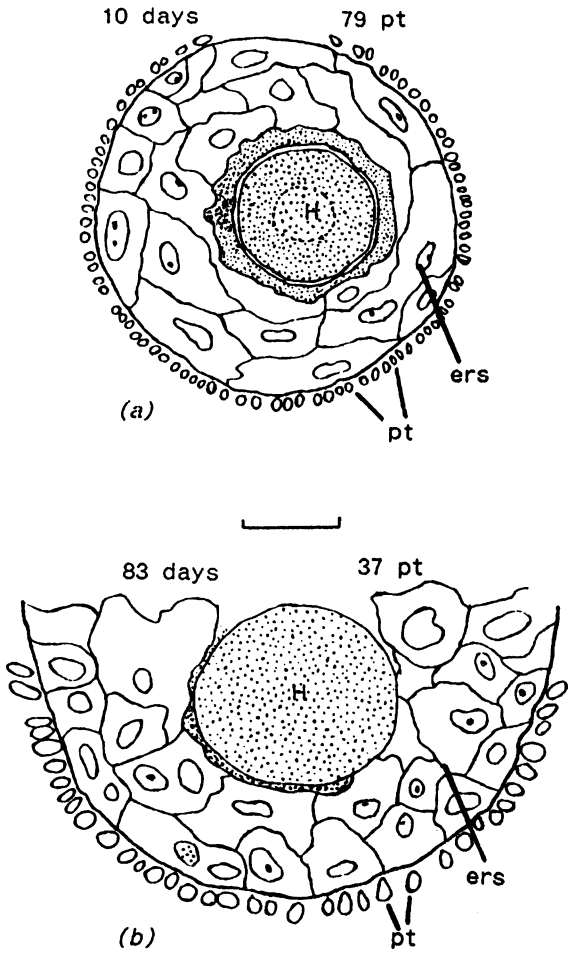


Fig. 12(*a*, *b*). Tracings of electron micrographs of tylotrich follicles transected at the level of innervation. Bottom is posterior. In the older specimen (83 d), palisade terminals (pt) were restricted to the posterior aspect of the outer root sheath (ers). H, tylotrich hair. Bar, 50 μm.

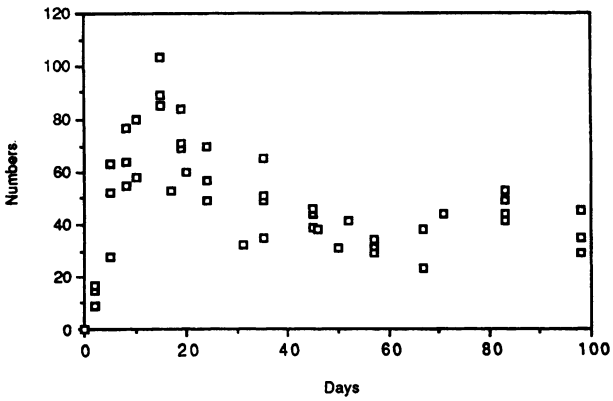


Fig. 13. Numbers of palisade terminals seen in electron micrographs of 46 tylotrich follicles obtained from 27 rats up to 96 d old.

supplying the touch dome (Fig. 6). The number of terminal branches increased progressively during the early postnatal weeks, becoming stable after about 2 months.

The camera lucida tracings in Figure 11 reveal age changes affecting the palisade innervation of the tylotrich follicles. The changes have not been referred to by previous workers. The orientation of 6 follicles is the same as in Figures 5 and 7, the right side of each tracing being the posterior side. Before the 18th day, nerve terminals could not be identified individually because of their fineness. From d 18 to d 30, the terminals surrounded the epithelial sheaths more or less completely. Late in the 5th week, with the onset of a follicular growth wave, the terminals disappeared from the anterior (cranial) aspect of the sheaths, resulting in an overall reduction in palisade fibre numbers (see Fig. 8). The numbers of circumferential terminals also declined. In older animals, following loss of the original hair, terminals were consistently absent from the anterior face of the outer root sheath (see Fig. 9). However, increased obliquity of the follicles rendered precise enumeration of terminals impossible in most older animals.

*Electron microscopy.* In neonates, the primordia of tylotrich follicles were easily identified, in the form of blunt epithelial pegs surrounded by fibroblasts. No axons were found in the immediate vicinity. Small numbers of palisade axons were identified on the surface of the pegs on d 2. As the follicles matured during the following 2 wk, the numbers of axons applied to the epithelial sheaths increased steeply, climaxing in almost total investment of the surface (Fig. 12*a*). During the 6th week and later, terminals were absent from the anterior surface of the epithelial root sheaths (Fig. 12*b*). As shown in Figure 13, maximum values were obtained during the 2nd and 3rd weeks, followed by a gradual decline. The data yielded a highly significant difference ($P < 0.001$ with the Mann–Whitney test) between the mean palisade fibre counts for wk 2–5 ($n = 21$, mean = 64.5, S.D. = 17.8), and those for the older samples ($n = 19$, mean = 38.5, S.D. = 7.8).

### *Experimental material*

Reconstructions following section of intercostal nerves 7–11 are shown in Figure 14. The left half of each of the circles in the reconstructions represents a tylotrich follicle; the right half represents the related touch dome; and the extent of innervation of the two elements is shown in black. (The all-black circles at the left and right ends represent tylotrich–touch dome complexes in the territory of nerves 6 and 12, respectively, cf. Fig. 1.) Numerical details concerning these and a further 8 experiments are included in the Table.

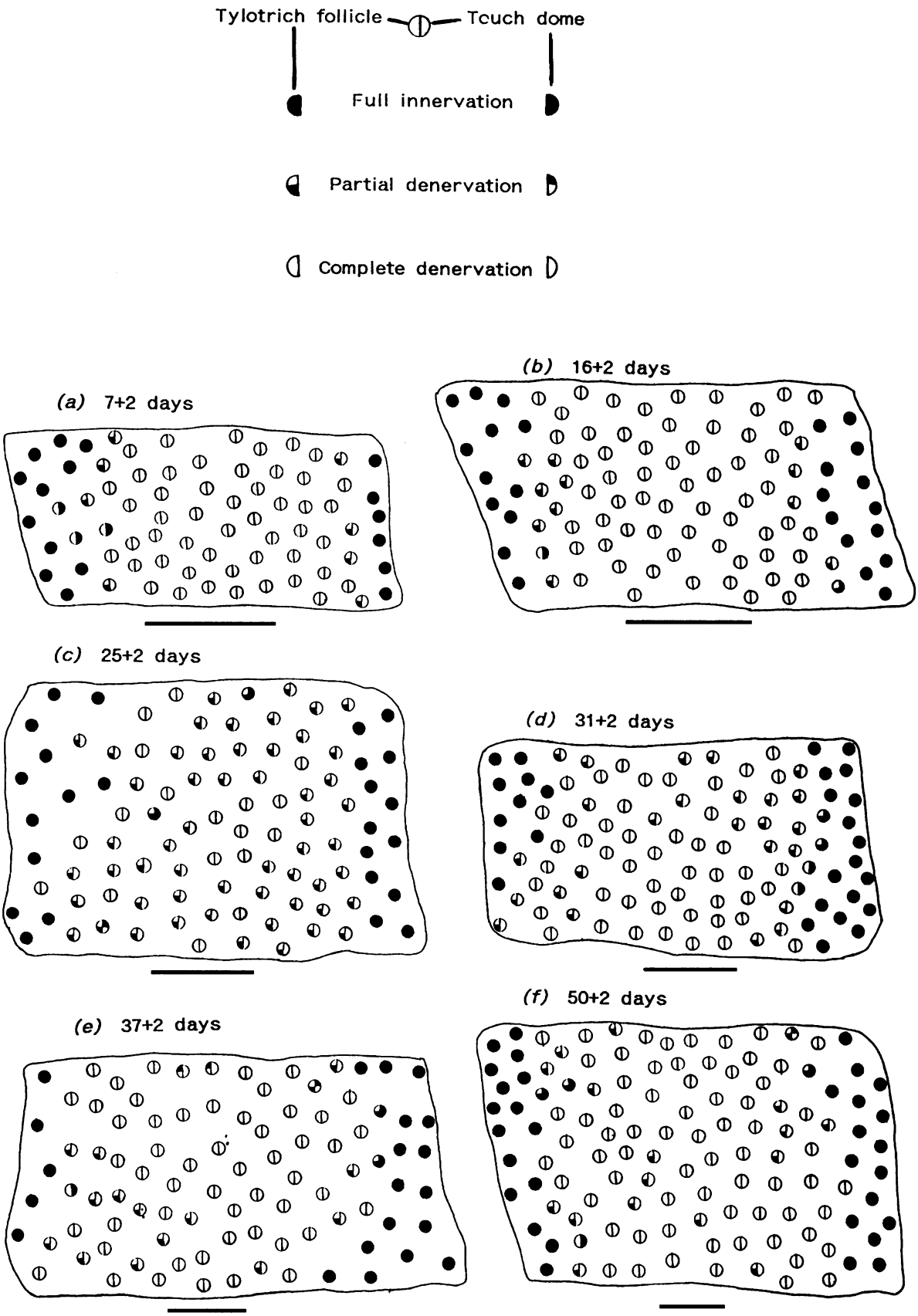


Fig. 14(*a–g*). Reconstructions of tylotrich–touch dome innervation at different ages, 2 d after section of intercostal nerves 7–11. The left half of each of the circles represents a tylotrich follicle; the fight half represents the related touch dome, and the extent of innervation of the two elements is shown in black. Partial denervation of touch domes was rare (lower left in *c*, upper right in *e* and *f*). Other information is included in the Table. Bar, 5 mm. For ease of comparison between younger (therefore, relatively small) and older specimens, the distance between rib 7 and rib 12 was set at an arbitrary value and the areas were adjusted appropriately, as indicated by the scale bars.

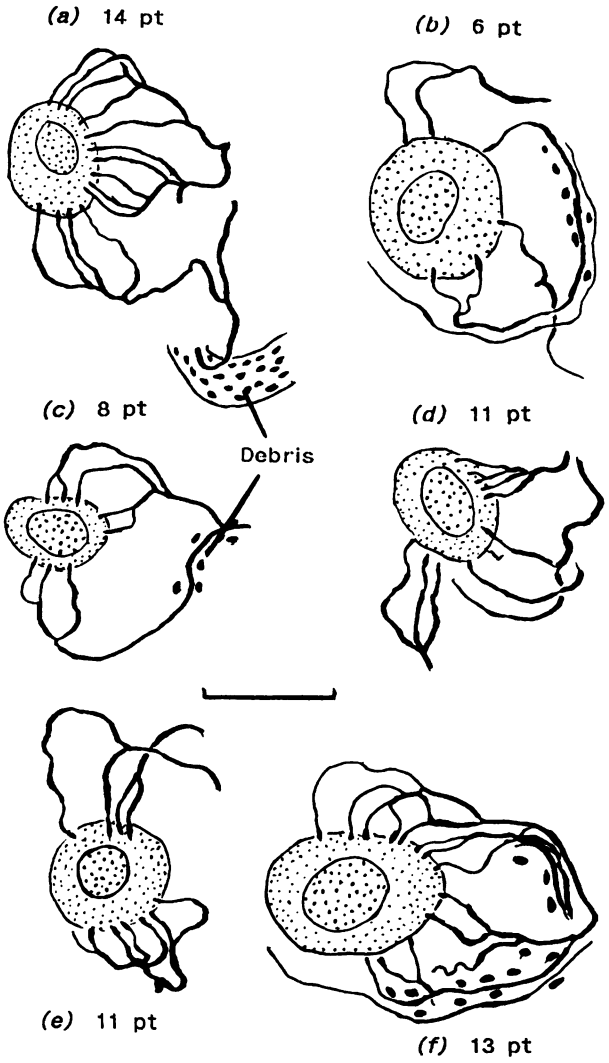


Fig. 15(*a–f*). Camera lucida tracings of partially denervated tylotrich follicles, 2 d after intercostal nerve sections at 23 d. Right sides are posterior. pt, palisade terminals. Bar, 200 μm.

Table 1. *Data from rats killed 2 d after section of intercostal nerves 7–11*

| Age (d) | Ribs 7–12 (mm)* | Denervated tylotrich follicles (*a*) *N* | (*b*) Partial | (*c*) Complete | *b*/*c* ratio† |
|---|---|---|---|---|---|
| 7+2 | 9 | 59 | 8 | 51 | 0.2 |
| 9+2 | 10 | 62 | 3 | 59 | 0.1 |
| 14+2 | 11 | 74 | 13 | 61 | 0.2 |
| 16+2 | 12 | 74 | 12 | 62 | 0.1 |
| 19+2 | 11 | 64 | 4 | 60 | 0.1 |
| 23+2 | 15 | 64 | 35 | 29 | 1.2 |
| 25+2 | 15 | 74 | 56 | 18 | 3.1 |
| 31+2 | 16 | 75 | 27 | 48 | 0.6 |
| 33+2 | 16 | 58 | 30 | 28 | 1.1 |
| 35+2 | 17 | 50 | 16 | 34 | 0.5 |
| 37+2 | 18 | 72 | 19 | 53 | 0.4 |
| 40+2 | 19 | 41 | 12 | 29 | 0.4 |
| 45+2 | 20 | 53 | 13 | 40 | 0.3 |
| 50+2 | 20 | 90 | 20 | 70 | 0.3 |

* Distance between shaft of ribs 7 and 12; † column (*b*)/(*c*).

The pattern of residual innervation of the touch domes did not seem to change appreciably over the time period. Virtually all of the domes within the territory of the 5 severed nerves lost their nerve supply.

The pattern of follicular innervation did change. In animals killed during the 2nd or 3rd weeks, the results resembled those obtained for touch domes. The territory of the severed nerves tended to be almost completely deserted. Typically, a single file of partially denervated tylotrichs separated fully innervated from fully denervated regions. During the 4th week the picture changed, with the appearance of partially denervated tylotrichs scattered across the territory of the sectioned nerves. Partially denervated follicles were characterised by two or all of the following features (Fig. 15): (1) a reduced number of palisade terminals; (2) patches of innervation of epithelial sheaths alternating with patches of denervation; (3) persistence of degenerating ellipsoids among the myelinated fibres approaching the sheaths. During the 4th week, the dermal plexus in the territory of the sectioned nerves contained numerous myelinated axons showing no evidence of degeneration (Fig. 10); they were branches of the 6th and 12th intercostal nerves, and the largest ones supplied tylotrich follicles located up to 7 or 8 mm away. During the 6th and 7th weeks, there were fewer partially denervated tylotrichs; most of those remaining were close to the rostral and caudal borders, the others were scattered across the denervated zone. Myelinated axons in the dermal plexus of the denervated zone were correspondingly scarce.

In the Table, the extent of overlap of intact follicular nerves into vacated skin is expressed as the ratio of partially denervated to completely denervated tylotrichs. The Table includes the ratio from each of the 6 maps illustrated, together with that from 8 other, similar experiments. The ratio was low until the end of the 3rd week. It exceeded unity in 2 samples taken in the 4th week and in 1 taken at the end of the 5th week. Low values were again recorded during the 6th, 7th, and early 8th weeks.

## DISCUSSION

### *Tylotrich–touch dome complexes*

The primordia of touch domes and of tylotrich follicles are present at birth in rats. A cutaneous nerve

plexus is also present. The touch domes become innervated during the first few days after birth, as noted by English et al. (1980). In the present material, innervation of tylotrich follicles by palisade fibres commenced on d 2, attained peak values during wk 2 and 3, and showed an overall decline towards adult values during wk 4–6 (Fig. 13).

The very large populations of palisade fibres during wk 2 and 3 are reminiscent of the state of hyperinnervation that occurs in the somatic and autonomic parts of the peripheral motor system in young rats. In the somatic motor system, each end plate in skeletal muscle is supplied by more than 1 parent nerve fibre during the first 2 postnatal weeks; after the end of the 3rd week, the plates receive 1 axon apiece (Brown & Booth, 1983). The numbers of motoneurons and of muscle fibres are already determined, and the phenomenon is based upon the sharing of end plates among relatively large motor units in young animals. In the autonomic system, hyperinnervation of submandibular ganglion cells by preganglionic fibres begins before birth and is most intense during the 2nd and 3rd postnatal weeks; during the following 3 wk, the number of preganglionic fibres is gradually reduced to adult levels (Lichtman, 1977).

In the somatic sensory system, there is a dearth of quantitative information about target tissue innervation in general, and about sensory epithelia in particular. The only postnatal study pertinent to the present findings seems to be that of FitzGerald (1961). This author studied the thick epidermis of the domestic pig's snout, which contains intraepithelial nerve fibres. He found that the number of axons entering this epidermis was zero at birth, rose to a peak during the 6th postnatal week, and then declined, by half, to adult values.

Why should the epidermis and large hair follicles of juvenile animals be so densely innervated? A need for additional sensory acuity is not obvious, and the explanation may lie elsewhere. The well known experiments on the mystachial vibrissae of rats and mice may be relevant (van der Loos & Woolsey, 1973). The 5 rows of vibrissae on each side of the upper lip are matched by 5 rows of barrel-shaped patches in the cortex of the parietal lobes of the brain. Destruction of individual vibrissae within the first week after birth results in disappearance of the corresponding cytoarchitectonic units from the cortex. A trophic factor is believed to be taken up by the follicular nerve endings from the epithelial sheaths of the vibrissae, transported along the 1st and 2nd order sensory neurons, and delivered by thalamocortical neurons to the developing parietal cortex, where the trophic factor influences the organization of cortical cell columns. Nerve growth factor (NGF) may be involved, since it is present in follicular and epidermal epithelia (Ribeiro-da-Silva & Kenigsberg, 1991). The innervation of autonomic ganglia has a quantitative relationship to the amount of NGF present in the ganglion cells (Ester et al. 1985). NGF is also necessary for the normal development of spinal ganglion cells. Hypothetically, the hyperinnervation provided to juvenile cutaneous epithelia could provide a safety margin, ensuring adequate uptake of trophic factor(s) for provision of cortical cell columns dedicated to these sense organs.

There was no clear evidence of hyperinnervation of developing touch domes. Their development is known to be a lengthy process. During the 1st postnatal week, the epidermis of the trunk is uniformly hyperplastic. A striking feature of each prospective dome region is full penetration of the epidermis by branches of an axon running behind the tylotrich follicle (FitzGerald, 1966). Early in the 2nd week, the branches withdraw to the basal layer where they become applied to Merkel cells. Merkel cells begin to differentiate from the epidermis just before birth; adult numbers are not attained before the 7th week (Nurse & Diamond, 1984). The significance of intraepithelial dome axons during the 1st postnatal week is enigmatic; this phase can be repeated in adults if the epidermis is rendered hyperplastic by physical or chemical methods (FitzGerald et al. 1975).

### *Overlap of segmental nerves*

Interpretation of the experimental series involving section of intercostal nerves 7–11, required the assumption that the mode of distribution of each of the lowest 7 intercostal nerves was the same. There was no reason to believe otherwise, since the distribution of the most caudal fibres of the 6th nerve was a virtual mirror-image of that of the most cranial fibres of the 12th throughout the series. It was also assumed that the patterns of surviving fibres were revealed by the procedures. They could not have been provoked, since a growth response in the form of collateral sprouting has a latent period well in excess of 2 d (Jackson & Diamond, 1984).

For the touch domes, the pattern was simple: almost all were supplied by the nearest available nerves. With the exception of occasional domes having a double nerve supply, there was no overlap. The irregularity of the margins separating innervated from denervated domes reflected the irregular distribution of the domes over the body surface.

For the tylotrich follicles, three phases of neural development could be identified. An *initial phase* was already established at the time of the earliest observation, on postnatal d 9; it persisted until d 21. It was characterised by minimal overlap with (in general terms) a single file of shared innervation along the margins of the denervated zone. A *transitional phase* was under way by d 25, and was also seen on d 27 and d 35. It was characterised by considerable overlap: within the territory of the 5 cut nerves, more than half of the follicles exhibited shared innervation (a partial/complete denervation ratio greater than unity). A *final phase* was seen in 1 33 d sample, and in 5 extending from d 37 to d 52. Overlap into the denervated zone was greatly reduced, although occasional partially denervated follicles were seen near the middle of the zone.

The initial phase coincided with the peak period of hyperinnervation. It has been postulated here that the function of hyperinnervation may be to ensure adequate cortical representation of the tylotrich follicles. It may be that the initial phase, with its relatively clear-cut dermatomal boundaries, is selectively devoted to this function.

How prevalent is hyperinnervation in juvenile somatic sensory epithelia? If its main concern is with cortical representation, as suggested in this paper, then it should first be sought where representation is large — for example, in the digits and oral epithelia, and in the mystachial vibrissae of whiskered animals. In these regions, hyperinnervation may occur at an earlier date: in the case of vibrissae, it may well commence during fetal life.

The transitional phase is marked by the extensive growth of axonal branches within the network provided by the cutaneous plexus. The nerve sections consistently revealed numerous intact terminals of these branches up to 2 intercostal spaces to one side of that containing the nearest intact nerve. This implies a total span of 5 body segments for each of the lower thoracic nerves. The transitional phase involves the withdrawal of some terminals from follicles supplied during the initial phase, with simultaneous branching of stem fibres to create new terminals elsewhere. This feature has a counterpart in the maturing autonomic nervous system of the rat, where many preganglionic fibres supplying the superior cervical ganglion (for example) withdraw while the persistent fibres are extending their synaptic territory (Purves & Lichtman, 1985).

The final phase evidently results from withdrawal of many follicular terminals. Such withdrawal could result from inability of the unipolar neurons concerned to keep pace with the progressive expansion of the body surface, and/or from reduction in the amount of NGF within the target epithelium (or within the neurons themselves). The reconstructions (Fig. 14) indicate that the residual overlap is both extensive and patchy. If this pattern proves to be general for mammalian spinal nerves, it could suffice to provide the neural substrate for the observations of Denny-Brown referred to in the Introduction.

The new observations made about dermatomal overlap are somewhat tentative because the sampling has been quite small. It would be of interest to know whether the changing pattern of overlap seen here may be a feature of cutaneous nerves in general. A relatively simple experimental paradigm could be used to test this possibility in a larger series of experiments, utilising a readily accessible nerve such as the saphenous or lateral cutaneous of the thigh.

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REFERENCES

BROWN MC, BOOTH CM (1983) Postnatal development of the adult pattern of motor axon distribution in rat muscle. *Nature* **304**, 741–742.

EASTER SS, PURVES D, RAKIC P, SPITZER NC (1985) The changing view of neural specificity. *Science* **230**, 507–511.

ENGLISH KB, BURGESS PR, KAVKA-VAN NORMAN (1980) Development of rat Merkel cells. *Journal of Comparative Neurology* **194**, 475–496

FITZGERALD MJT (1961) Developmental changes in epidermal innervation. *Journal of Anatomy* **95**, 495–514.

FITZGERALD MJT (1966) Perinatal changes in epidermal innervation in rat and mouse. *Journal of Comparative Neurology* **126**, 37–42.

FITZGERALD MJT, FOLAN JC, O'BRIEN TM (1975) The innervation of hyperplastic epidermis in the mouse: a light microscopic study. *Journal of Investigative Dermatology* **64**, 169–174.

FLETCHER TF, KITCHELL RL (1966) The lumbar, sacral and coccygeal dermatomes of the dog. *Journal of Comparative Neurology* **128**, 171–180.

FOERSTER O (1933) The dermatomes in man. *Brain* **56**, 1–39.

HEAD H, CAMPBELL AW (1990) The pathology of herpes zoster and its bearing on sensory localisation. *Brain* **23**, 353–523.

IGGO A (1985) Sensory receptors in the skin of mammals and their sensory functions. *Review of Neurology* **141**, 599–613.

JACKSON PC, DIAMOND J (1984) Temporal and spatial constraints on the collateral sprouting of low-threshold mechanosensory nerves in the skin of rats. *Journal of Comparative Neurology* **226**, 336–345.

KEEGAN JJ, GARRETT FD (1948) The segmental distribution of the cutaneous nerves in the limbs of man. *Anatomical Record* **102**, 409–437.

KINNMAN E (1987) Collateral sprouting of sensory axons in the hairy skin of the trunk: a morphological study in adult rats. *Brain Research* **414**, 485–489.

KIRK EJ, DENNY-BROWN D (1970) Functional variation in dermatomes in the macaque monkey following dorsal root lesions. *Journal of Comparative Neurology* **139**, 307–320.

KUHN RA (1953) Organization of tactile dermatomes in cat and monkey. *Journal of Neurophysiology* **16**, 169–182.

LICHTMAN JW (1977) The reorganization of synaptic connections in the rat submandibular ganglion during post-natal development. *Journal of Physiology* **273**, 155–177.

LIGUORI R, KRARUP C, TROJABORG W (1992) Determination of the segmental sensory and motor innervation of the lumbosacral spinal nerves. *Brain* **115**, 915–934.

NURSE CA, DIAMOND J (1984) A fluorescent microscopic study of the development of rat touch domes and their Merkel cells. *Neuroscience* **11**, 509–520.

PURVES D, LICHTMAN JW (1985) *Principles of Neural Development*, pp. 275–280. Massachussetts: Sinauer Associates.

RIBEIRO-DA-SILVA A, KENIGSBERG RL, CUELLO AC (1991) Light and electron microscopic distribution of nerve growth factor receptor-like immunoreactivity in the skin of the rat lower lip. *Neuroscience* **43**, 631–646.

RICHARDSON KC (1958) Comparison of nerve structure in the autonomic ground plexus of intestinal muscle as shown by electronmicroscopy and by silver impregnation. *Journal of Anatomy* **92**, 641.

VAN DER LOOS H, WOOLSEY TA (1973) Somatosensory cortex: structural alterations following early injury to sense organs. *Science* **179**, 395–398.

WINKELMANN RK (1986) Sensory receptors of the skin. In *Spinal Afferent Processing* (ed. T. L. Yaksh), pp. 19–58. New York: Plenum Press.