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Degeneration patterns of postganglionic fibers following sympathectomy

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Summary. In cats the time course of degeneration following lumbal sympathectomy was studied in the ramus communicans griseus (rcg) and in the nerves to the triceps surae muscle using light and electron microscopic methods.

The left lumbar sympathetic trunk including its rami communicantes was removed from L2 to S1 using a lateral approach. The animals were sacrificed between 2 and 48 days after the sympathectomy. Tissue samples were taken (a) one cm proximal to the entrance of the rcg into the spinal nerve, and (b) one cm proximal to the entrance of the nerve into the muscle belly.

In the rcg signs of degeneration can already be recognized in the myelinated as well as in the unmyelinated axons 48 h after sympathectomy. The degenerative processes in the axons reach their peak activity at about 4 days p.o. They end a week later. Signs of the reactions of the Schwann cells and of the endoneural cells can first be seen 2 days p.o. They are most pronounced around the 8th day p.o., and last at least up to the third week. Thereafter the cicatrization processes settled to a rather steady state (total observation period 7 weeks).

In the muscle nerves the first signs of an axonal degeneration of the sympathetic fibers can be recognized 4 days after surgery. The signs of axonal degeneration are most striking about 8 days p.o. They have more or less disappeared another week later. The reactions of the Schwann cells also start on the fourth day but outlast the degenerative processes by some 8 days. Thus the degenerative and reactive processes in the rcg precede those in the muscle nerves by 2 days early after surgery and by 6 days 3 weeks later. Seven weeks after surgery, fragments of folded basement lamella and Remak bundles with condensed cytoplasm and numerous flat processes are persisting signs of the degeneration.

In addition to the differences in time course between the proximal and the distal site of observation, it was also noted that both the axonal degeneration and the reactions of the Schwann cells are more pronounced in the rcg than in the muscle nerve. For example there was abundant mitotic activity in the central endoneural and Schwann cells whereas we could not detect such activity in the periphery.

It is concluded that the time course of degeneration and the intensity of the degenerative and reactive processes is, to a considerable extent, determined by the distance between the site of nerve section and the site from which the specimen is taken. Many of the conflicting data in the literature can be explained by this finding.

Key words: Wallerian degeneration – Muscle nerve – Postganglionic nerve fiber – Ramus communicans griseus – Sympathectomy

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Introduction

In several studies on the degeneration pattern of peripheral nervous structures with a high content of unmyelinated axons, such as the nervus ischiadicus of rat and rabbit (Lee 1963; Friede and Martinez 1970), the spinal nerve of the rat (Nathaniel and Pease 1963), the ganglion cervicale superius of the rat (Roth and Richardson 1969; Iwayama 1970), the nervus vagus of the rabbit (Thomas and King 1970) and the anterior mesenteric nerve of the rabbit (Bray et al. 1972), the data on the time course of the degeneration differ considerably. The shortest time in which the unmyelinated axons have totally disappeared has ranged from about 48 h in a crushed nerve (Nathaniel and Pease 1963) to more than 28 days in a transected nerve (Lee 1963). An explanation for this variability may be that the experimental conditions were not comparable (e.g., cutting versus crushing) and that the specimens studied for the degenerations were dissected at varying distances from the locus of nerve section or alteration. Unfortunately, most studies do not give precise data on this point.

The present investigation resolves these discrepancies by showing that both the time course of the degeneration of unmyelinated sympathetic nerve fibers and the morphological features of the degenerating axons and their surrounding tissue are very different at sites close to the nerve section from those seen far distal from the section. These results are a necessary prerequisite for studying the fine afferent innervation of sympathectomized tissue (Andres et al. 1985).

Methods

In 10 cats a complete left sympathectomy was carried out by removing the ganglia L2 to S1 including the rami interganglionares using a lateral retroperitoneal approach. For this purpose the cats were administered initially 10 to

20 mg/kg ketamine HCl i.m. (Ketanest, Parke-Davis). Then the barbiturate methohexital (Brevital sodium, Lilly) was given i.m. in doses of 10 to 15 mg. The criteria for establishing sufficient depth of anesthesia were the persistence of miotic pupils and the absence of flexor reflexes. Following the sympathectomy the temperature of the skin of the ipsilateral hind paw increased. Careful nursing of the animal was performed in the postoperative period. Behavioral observations after recovery from the operation did not reveal any gross abnormalities.

Animals were sacrificed 2 to 48 days after the operation. After anesthesia (with Nembutal 50 mg/kg i.p.) the thorax was opened, a cannula was placed in the thoracic aorta and the right atrium was opened. An initial perfusion with warm Tyrode's solution (37° C) for 30 s was followed by fixation with 2.5% glutaraldehyde and 1.5% formaldehyde in phosphate buffer (pH 7.4) for 35 min, at a perfusion pressure of 180 mmHg (Andres 1964; Karnowsky 1965). Methyleneblue (0.05 g/l) was added to the fixative solution to permit direct visual control of the time course and extent of the perfusion. Using this method it was regularly noted that the sympathectomized side became coloured much more rapidly than the normal one, presumably because of the absence of a vasoconstrictor tone.

After the fixation procedure, a complete dissection from ventral to dorsal of the abdominal cavity and, in particular, of the dorsal abdominal wall was carried out. On the right side the sympathetic trunk including its rami communicantes was carefully freed from its surrounding tissue. On the left side all distal stumps of the rami communicantes were carefully identified. Photographs and drawings of the control and the operated side were done repeatedly during the course of the dissection (Fig. 1).

The data thus obtained show that the course of the sympathetic trunk is remarkably constant from animal to animal. We did observe, though, some variability in the size and position of the ganglia, and also in the course of the rami communicantes grisei to their respective spinal nerves, which are situated one segment lower (for details see Baron et al. 1985, and Jänig 1985).

Material for histological examination was removed from two areas of both sides: (a) from grey rami L5 and L6 just proximal to their entry into the spinal nerves L6 and L7, and (b) from the nerves to the triceps surae muscle about 1 cm proximal to their muscle entrance of both sides. The specimens of the right side served as control. The distance between the two areas was about 15 to 20 cm, depending upon the size of the animal.

The tissue samples were washed in phosphate buffer and postfixed in 4% OsO_4. Thereafter, they were dehydrated in graded ethanol and embedded in araldite. Series of alternate semithin and ultrathin sections were cut with a Reichert OMU3 and a LKB Ultrotom III. The ultrathin sections were double-stained with uranyl acetate and lead citrate and examined with a Philips 300 electron microscope. Semithin sections were preincubated in 1% periodic acid (50° C) for 1 min, followed by staining with Richardson's solution pH 8.6. The fixation of the rami communicantes grisei and of the nerves to the triceps muscles was excellent in all preparations on both sides. Only in such preparations could the changes in morphology be attributed unequivocally to the extirpation of the sympathetic trunk. The material on which the results at various times after sympathectomy are based has been obtained from one (33,

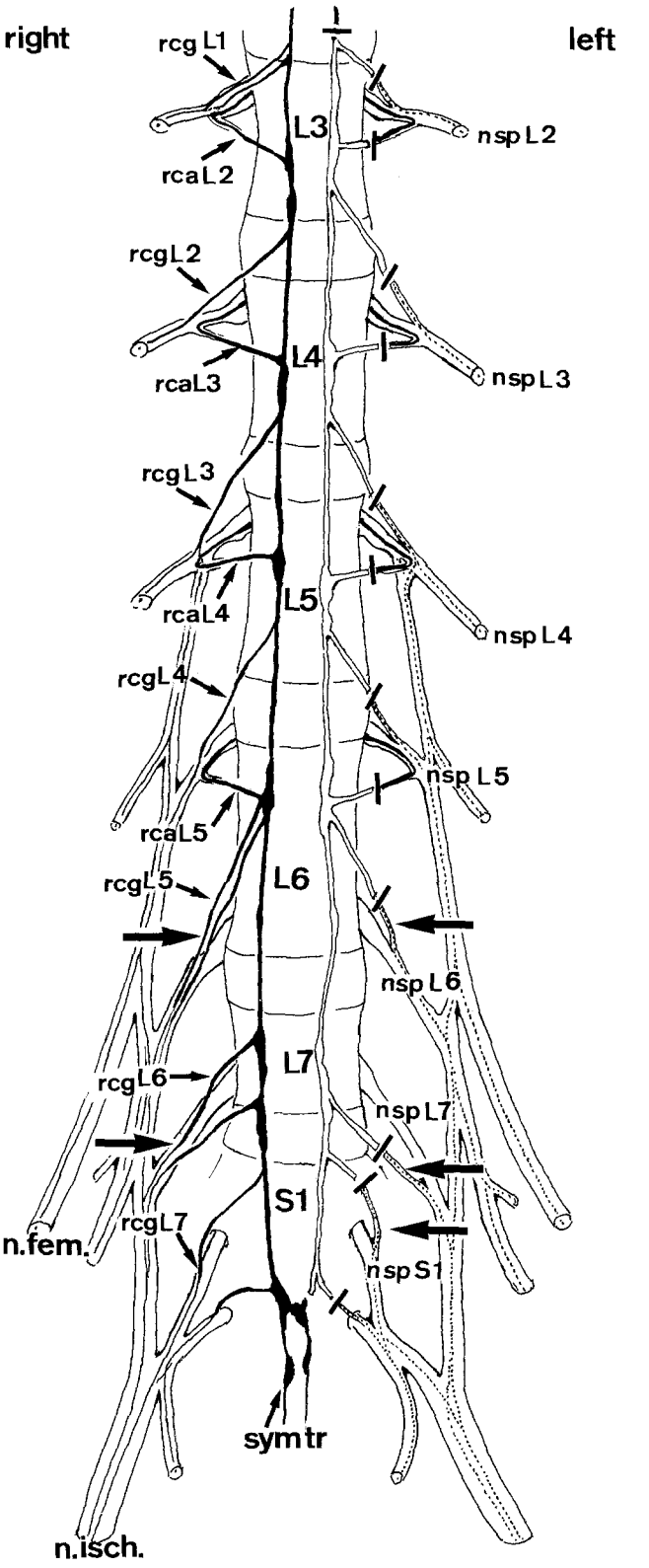

Fig. 1. Schematic drawing of the lumbosacral sympathetic trunks as seen from ventral during the dissection of the perfused animal. On the right side the intact sympathetic chain (*sym.tr.*), its rami communicantes grisei (*rcg*), albi (*rca*) and the spinal nerves (*nsp*) can be recognized. On the left side the removed sympathetic tissue is indicated by *thin lines*. The exact sites of sectioning during the sympathectomy are marked by *short bars*. The *dotted lines* distal to the sections show the course of the *rcg* undergoing Wallerian degeneration. The *arrows* indicate at which sites material has been removed for histological examination

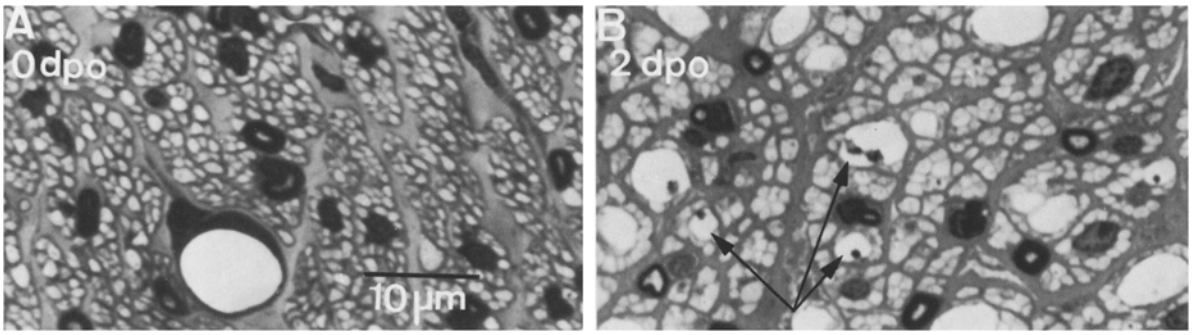

Fig. 2A, B. Histological structure of the rcg under normal conditions (**A**) and two days after sympathectomy (**B**). (*dpo*=days post operationem) ×1,700. The *arrows* in **B** mark axonal swellings with pale axoplasm and osmophilic bodies

48 d) or two animals (2, 4, 8, 14 d). The EM-magnifications in the figures are uniform, with one exception in Fig. 3B1, in order to emphasize the morphological changes in the nuclei and the cytoplasmic organelles of the cells and axons.

Results

Normal ramus communicans griseus

The rami communicantes grisei (rcg) reach the spinal nerves by penetrating the perineural sheath from ventral to dorsal in a semicircular way. As a rule, the sympathetic ramus is accompanied by one or two branches of the neighboring segmental artery. The position and shape of the lumbosacral ganglia show some variability. Occasionally the first sacral ganglia are fused (Fig. 1, see also Baron et al. 1985). Probably, less than 0.6% of the postganglionic axons cross the midline in such ganglia (McLachlan and Jänig 1983).

There are about 35,000 unmyelinated axons in the rcg to L6 and about 42,000 in the rcg to L7. The unmyelinated nerve fibers in the Remak bundles of the rcg are embedded in longitudinal grooves of the Schwann cells. Small bands of cytoplasm separate the axons from each other. The translucent axoplasm contains numerous microtubuli, neurofilaments, mitochondria and components of the axoplasmatic reticulum. These organelles can be seen in axons of all diameters, ranging from 0.5 to 1.8 µm (Fig. 2A).

The rcg from L1 to L7 all contain a considerable proportion of myelinated axons which number up to 25 in the ramus L1, up to 500 in the ramus L6 and from 250 to 900 in the ramus L7. The diameter of these fibers varies between 1.3 and 13 µm. The fine myelinated fibers of about 3 µm are severalfold more numerous than the thick ones (Fig. 2A).

The coarse chromatin pattern in the Schwann cell nuclei concentrates at the nuclear envelope. The shape of the nuclei reflects to a certain extent the deep longitudinal grooves or troughs in which the axons are embedded. Thus, in cross sections the nuclei often exhibit indentations. The length of the nuclei is about 16 µm in the longitudinal direction.

In the cytoplasma close to the Schwann cell nucleus small Golgi complexes, cysternae of the ergastoplasmic reticulum and free ribosomes can be found. Microtubuli and glial filaments are mainly seen in the thin parts of the Schwann cells which enclose the unmyelinated axons.

The rcg are separated from the surrounding tissue by a perineural sheath which has up to six lamellae of perineural cells. The densely-packed collagen fibrils of the endoneural connective tissue run in parallel with the long axis of the rami, giving them tensile strength against stretch or pressure. Fibrocytes, occasional mast cells, and capillaries of the vasa nervorum are further elements of the endoneurium. The amount of amorphous ground substance is negligible in the rcg (Fig. 2A).

Ramus communicans griseus 48 h after sympathectomy

The first sign of degeneration in the unmyelinated axons are vacuoles which under the light microscope appear as empty cavities in the tissue (arrows in Fig. 2B). In the electron micrographs it is seen that they represent enlarged segments of unmyelinated axons devoid of microtubules and neurofilaments but filled with fuzzy material or membrane-bounded cavities (thick arrows in Fig. 7B). Other organelles such as axoplasmic reticulum and mitochondria have broken up to remain as membrane fragments and dense lamellated bodies. In other axons the cytoskeletal structures show cryptiform signs of lytic reactions and a pale axoplasm. Occasionally spiral-shaped convolutions of Schwann cell membranes enclose shrunken axon profiles with desintegrated filamentous structures (small arrow in Fig. 7B). However, the great majority of the unmyelinated axons and all the myelinated ones do not yet show any sign of degeneration 48 h after sympathectomy.

In the Schwann cell cytoplasm, the following reactive changes can be observed at this stage: a less dense appearance of the cytoplasm with a reactive enlargement of the cysternae of the ergastoplasmic and endoplasmic reticulum. The Schwann cell nuclei begin to enlarge, and the dense chromatin pattern at their outer areas loosens up. In cross sections the indentations of the nuclei flatten out to give a more roundish appearance.

The fibrocytes within the endoneural connective tissue react with a broadening of their cytoplasmic cell processes, which at the same time become more translucent.

Ramus communicans griseus 4 days after sympathectomy

Meanwhile a considerable proportion of the unmyelinated axons is completely degenerated. The axoplasmic membrane has disappeared or has fractured. But due to the organelle debris is still lying in the grooves of the Schwann cells, many if not all of these degenerated axons can still be recognized. Other axons are usually swollen, with signs of disintegration of their axoplasmic structures (thin arrows in Fig. 3A1), occasionally they are shrunken. Large lysosomes in the Schwann cell cytoplasm contain vacuoles and

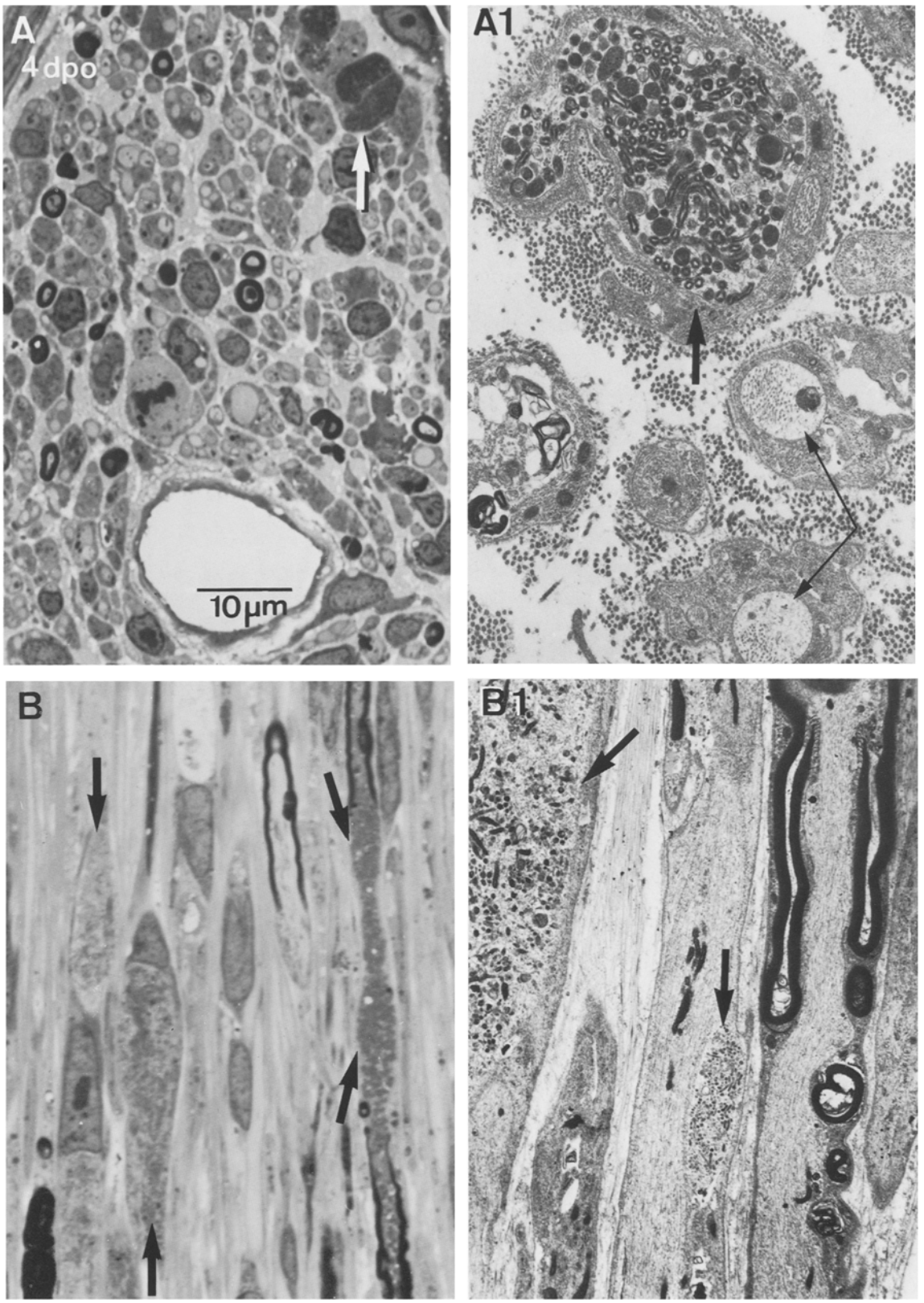

Fig. 3A, B. The left rcg 4 days after sympathectomy in cross (**A**) and longitudinal (**B**) semithin sections. ×1,700. **A1** and **B1** are corresponding electron micrographs to **A** and **B**. *Thick arrows* indicate enlarged axonal profiles of myelinated and unmyelinated axons. *Thin arrows* mark disintegration of cytoskeletal structures in unmyelinated axons. Note mitosis above the capillary in **A**. A1: ×15,000; B1: ×7,500

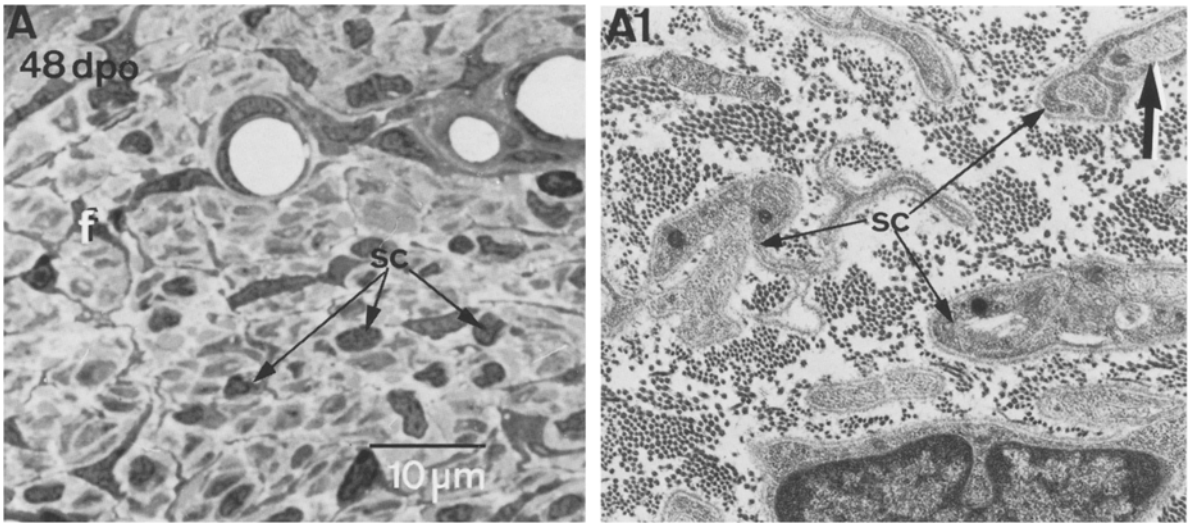

Fig. 4. The left rcg 48 days after sympathectomy. Regenerating axon (*arrow*), fibrocyte (*f*), Schwann cell (*sc*) A: ×1,700; A1: ×15,000

fuzzy material. Within some spindle-like enlargements of these fibers aggregations of mitochondria and lamellated dense bodies are seen (thick arrows in Fig. 3).

The reaction pattern of the myelinated nerve fibers is much more impressive. The nodal segments have widened and contain spindle-shaped axoplasmatic swellings. These are densely filled with mitochondria. The mitochondria show signs of degeneration such as vacuoles, compacting of the matrix and formation of lamellae. In a few cases the axoplasmic swellings are almost exclusively filled with lamellated bodies.

In parts, the myelin sheath still appears intact except for some nodal retractions. But in general the sheaths have disintegrated into globular myelin debris which initially lies in the Schwann cell cytoplasm (Fig. 3B1). Later it is taken up by macrophages (Andres 1963; Thomas and King 1974).

A further remarkable finding four days after sympathectomy is the high rate of mitosis which increases considerably the number of endoneural and Schwann cells of both the myelinated and unmyelinated fibers (Fig. 3A). The volume of the Schwann cell nuclei is now at its maximum. In the pale karyoplasm, the dark-stained nucleoli stand out clearly (compare Fig. 7A–C).

At this time a fine filamentous ground substance has appeared between the originally densely-packed collagen fibrils. It fills the light microscopically empty endoneural space. The endoneural fibrocytes have become considerably enlarged. In their structure they now resemble histiocytes. Processes of these cells penetrate the basement lamina of Remak bundles to participate in removal of axonal debris of degenerating C-fiber axons.

Ramus communicans griseus 8 days after sympathectomy

Eight days after sympathectomy, shadowy remnants of the degenerated unmyelinated axons can still be seen within the bulk of their Schwann cell cytoplasm. The axolemma of these axons is virtually missing (Fig. 7D). In longitudinal and oblique sections the axoplasm of the degenerating axons seems to fuse with the cytoplasm of the Schwann cells. But careful inspection revealed that the membrane of the Schwann cells was always intact.

In Remak bundles which have nearly completely lost their unmyelinated axons, the Schwann cells have formed thin, flat cell extensions which are covered by loosened basal lamina. It seems that the viable Schwann cell cytoplasm no longer fills the basement lamina envelope; consequently it has collapsed and folded up. Sometimes only tubes of folded basement lamina without associated cells occur. Remnants of the destroyed myelinated axons, such as spindle-shaped nodal expansions and myelin debris, are now only occasionally seen (arrow in Fig. 7D).

Judged by the number of cell nuclei, the proliferation of the Schwann cells is now at its maximum. At this time phagosomes can often be seen in the cytoplasm of Schwann cells.

In the endoneural connective tissue the deposition of the fuzzy, fine filamentous ground substance between the collagen fibrils of the endoneural connective tissue is prominent. There is also a remarkable increase in the number of endoneural cells. In addition a considerable reactive expansion of their cytoplasm together with an extraordinary increase of their cell nuclei is observed, so that the cells resemble histiocytes.

Ramus communicans griseus 14 days after sympathectomy

At this time all axonal structures have disappeared in the rcg, and the swollen Schwann cells dominate, with their long interdigitating processes. These processes contain bundles of microfilaments and microtubuli embedded in a pale cytoplasm. Thus they resemble unmyelinated axons and may give the misleading impression that such axons have persisted in the ramus (Fig. 7E).

In semithin sections the texture of the endoneuronal connective tissue with its densely-packed collagen fibrils appears fairly normal, but in electron micrographs the fuzzy ground substance which was described in the preceding stages lies in a condensed pattern between the fibrils. The histiocytes too, are surrounded by the more densely-packed filamentous ground substance. Fragments of basal laminae occur more frequently. The above-average size of the nuclei

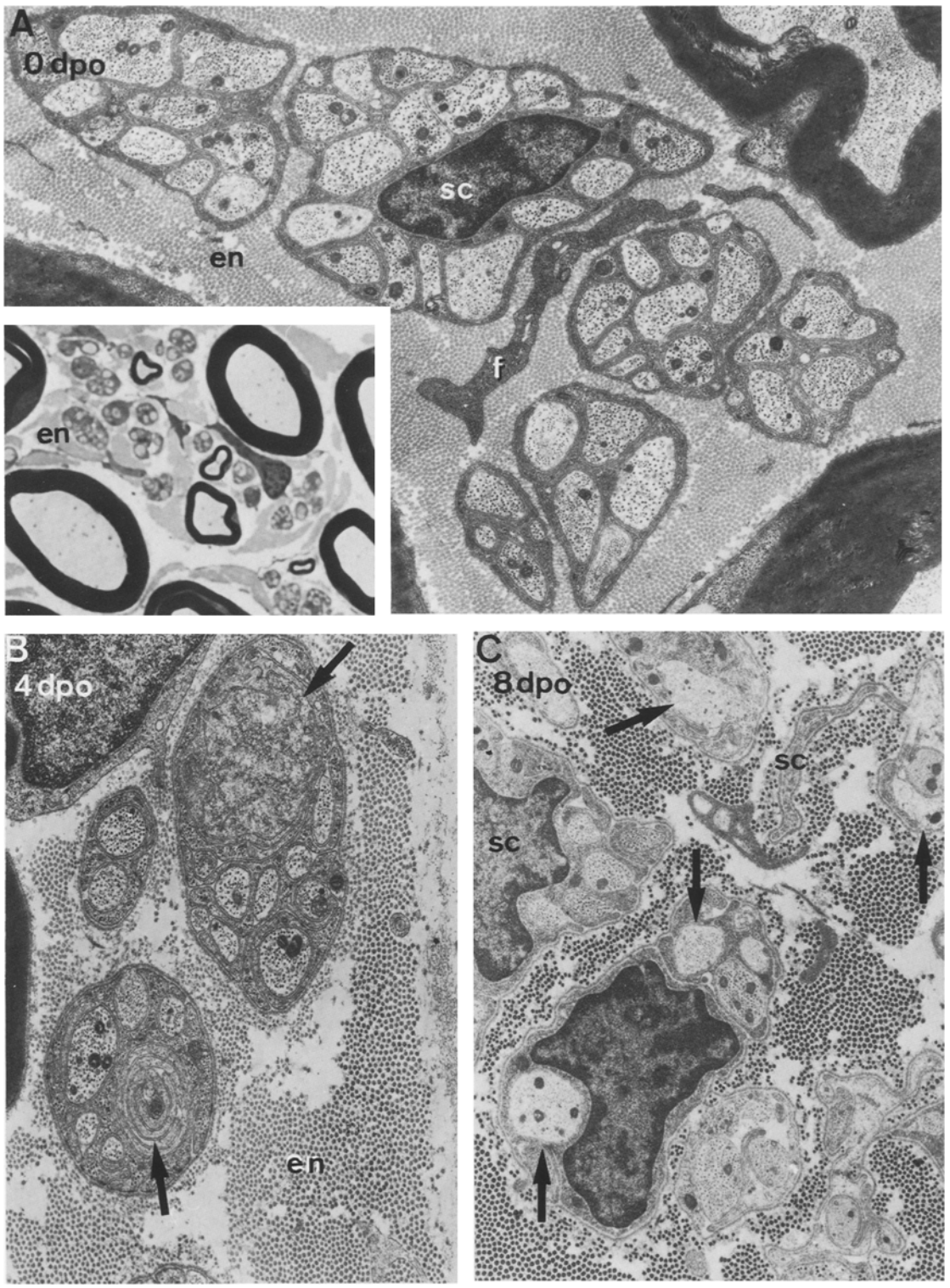

Fig. 5A–C. Time course of axonal degenerations and Schwann cell reactions in peripheral muscle nerve following sympathectomy. **A** C-fiber profiles from the normal right side. *Inset:* Groups of Remak bundles between myelinated axons, ×1,700. **B, C.** Electron micrographs of specimen at the indicated days after sympathectomy (*dpo* = days post operationem); for further explanation see text. Schwann cell (*sc*), endoneural connective tissue (*en*), fibrocyte (*f*). ×15,000

of the endoneural fibrocytes and the strikingly enlarged cisterns of the ergastoplasm in the cell processes are further morphological signs of an increased cellular activity. The number of phagolysosomes seems to be normal in these cells.

Ramus communicans griseus 33 days and 48 days after sympathectomy

There are no obvious differences between the state of degeneration at 33 and 48 days p.o. The rami are now in a state

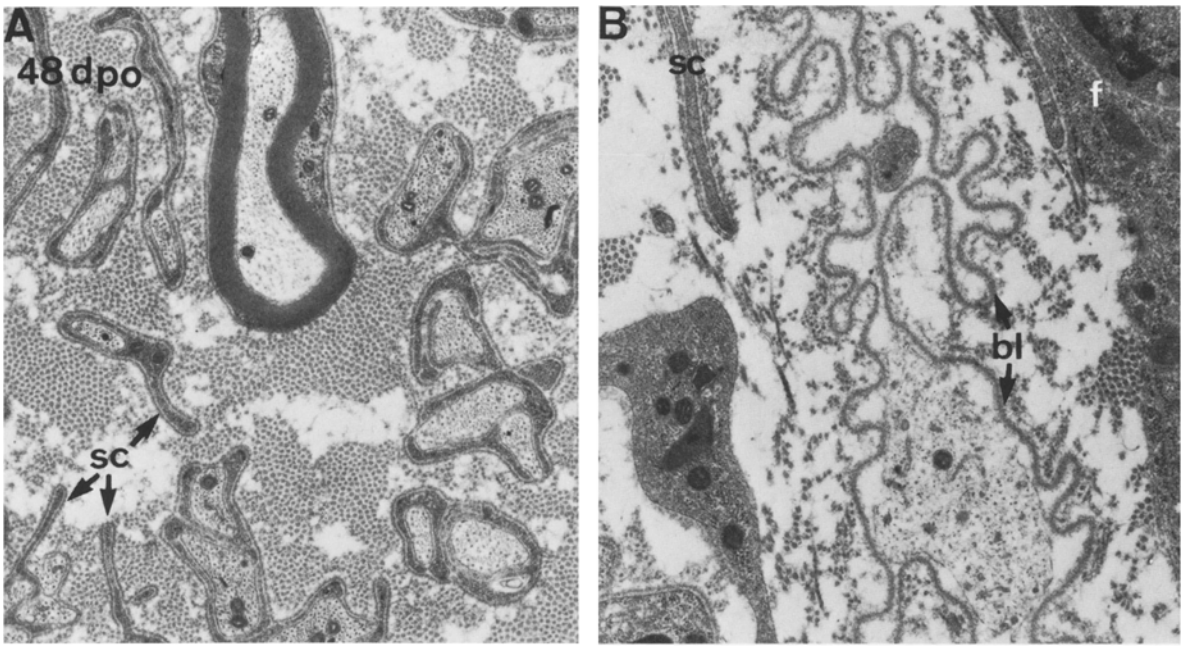

Fig. 6A, B. Left muscle nerve 48 days after sympathectomy. **A** C-fiber profiles within flat Schwann cell processes (*sc*). **B** Basement lamina tube (*bl*) containing cell debris. × 15,000

of cicatrization. Those areas of the Schwann cells which correspond to the "Büngerschen Bändern" show a nucleus with conspicuous condensation of chromatin and darkly-stained, flat cytoplasmic processes (Fig. 4). Some of these processes contain up to 200 regenerating axon sprouts from regenerating afferent fibers. In collagen tissue are enclosed extended remnants of tubes of basal lamina which are extensively folded-up. Histiocytes with elongate processes traverse the endoneural connective tissue (Fig. 4A).

Finally, it is worth noting that throughout the time course of degeneration no changes of the perineural tissue were noted, either in the light or in the electron microscope.

Structure of Remak bundles in normal muscle nerve

In the nerves to triceps surae muscle the Remak bundles lie randomly distributed in the nerve fascicles. They may contain afferent and efferent unmyelinated axons (Andres et al. 1982; Langford and Schmidt 1983a, b). The diameters of the unmyelinated axons range from 0.2 to 1.1 μm, i.e., they are on the average smaller than those of the axons in the rcg. As a rule each of the unmyelinated axons is enclosed by cytoplasmatic extensions of Schwann cells, and in this way they are separated from their neighboring axons (Fig. 5A). However, this separation is not always complete, and from time to time several axons may run together in a single Schwann cell groove. The endoneural connective tissue with its fibrocytes, collagen fibrils matrix of amorphous ground substance and the vasa nervorum is of unconspicuous appearance.

Time course of degeneration in muscle nerves

After 48 h. No signs of degeneration can be detected in the Remak bundles at this time (Fig. 8B). This finding is remarkably different from that reported above for rcg.

After 4 days. A number of structural changes of the Remak bundles can now be recognized. There are at least two types of degenerating axonal profiles (arrows in Fig. 5B). The first type is the most conspicuous (upper arrow in Fig. 5B). It has enlarged axons of up to 2 μm in diameter. These are filled with a flocculent material or with membrane-bounded cavities or disintegrated axoplasmic structures. The second type is characterized by shrunken axons of about 0.2 μm diameter (lower arrow in Fig. 5B). They are filled with nothing but densely packed filaments 10 nm in diameter (arrow in Fig. 8C). These profiles are surrounded by concentrically oriented flat Schwann cell processes, as described in the rcg 2 days p.o. The Schwann cell nuclei are enlarged and exhibit a less dense chromatin pattern. Tongue-like extensions of the Schwann cell cytoplasm protrude without basal lamina into the endoneural connective tissue.

After 8 days. The structural appearance of Remak bundles differs significantly from one bundle to another, depending on the number of degenerating C fibers. A few Remak bundles contain no degenerating axons at all, in others more than half of the axons degenerate; the majority lies between these two extremes. Pale axonal profiles are prominent which are in full course of disintegration of the axoplasmic structures (arrows in Fig. 5C). Neurofilaments and microtubules cannot be identified in such profiles. Other axons, however, are filled with lumps of filaments and osmiophilic bodies. The swelling of the Schwann cell cytoplasm with its lysosomes is most pronounced in those Remak bundles which contain the greatest proportion of degenerating axons (Fig. 8D).

Extensions of the Schwann cells protrude more and more in between the loosened endoneural connective tissue around the Remak bundles. In cross-sections, the Schwann cells have an accentuated ramified appearance. Processes of histiocytes, rich in rough endoplasmic reticulum, Golgi

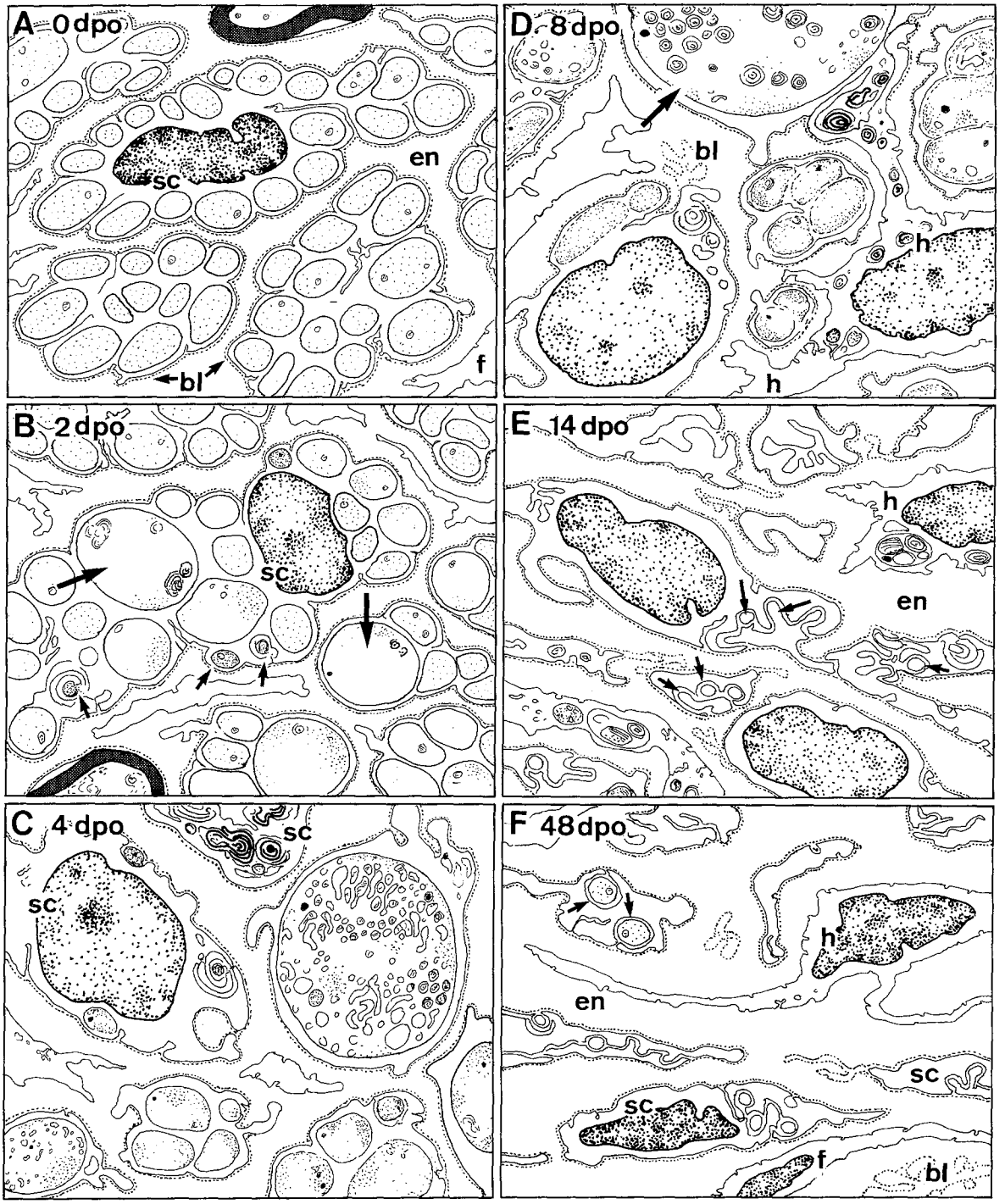

Fig. 7. Pictorial schematic representation of the Wallerian degeneration of sympathetic postganglionic nerve fibers in the rcg following sympathectomy. Emphasis is on the characteristic features of the degenerative and reactive processes typical for the rcg. *Abbreviations* as in the other figures. For magnification of the examples, see scale in **C**

complexes and lysosomal bodies are frequently seen quite near to such reactive Schwann cell cords.

After 14 days. Signs of degenerating axons can be seen in only a few Remak bundles. In correlation to the original axonal composition (only afferent or efferent, or a mixture of afferent and efferent C-fibers) of the Remak bundles the number of persisting axons differs within the Schwann cell cords. Most of the axonal debris has disappeared. Cords of interdigitating Schwann cell processes in parallel stacks mimic axonal profiles of normal Remak bundles (arrows in Fig. 8E). In oblique sections it is sometimes difficult to differentiate between such Schwann cell processes and axons. Additionally, these Schwann cells have an increased number of microtubules and of filamentous structures. There is no change in appearance of the histiocytes as compared to the description 8 days after sympathectomy.

After 33 and after 48 days. By now the ultrastructure of the Remak bundles looks close to normal. The folds and extensions of the Schwann cells remain accentuated (Fig. 6A). As another definite sign of the preceding degen-

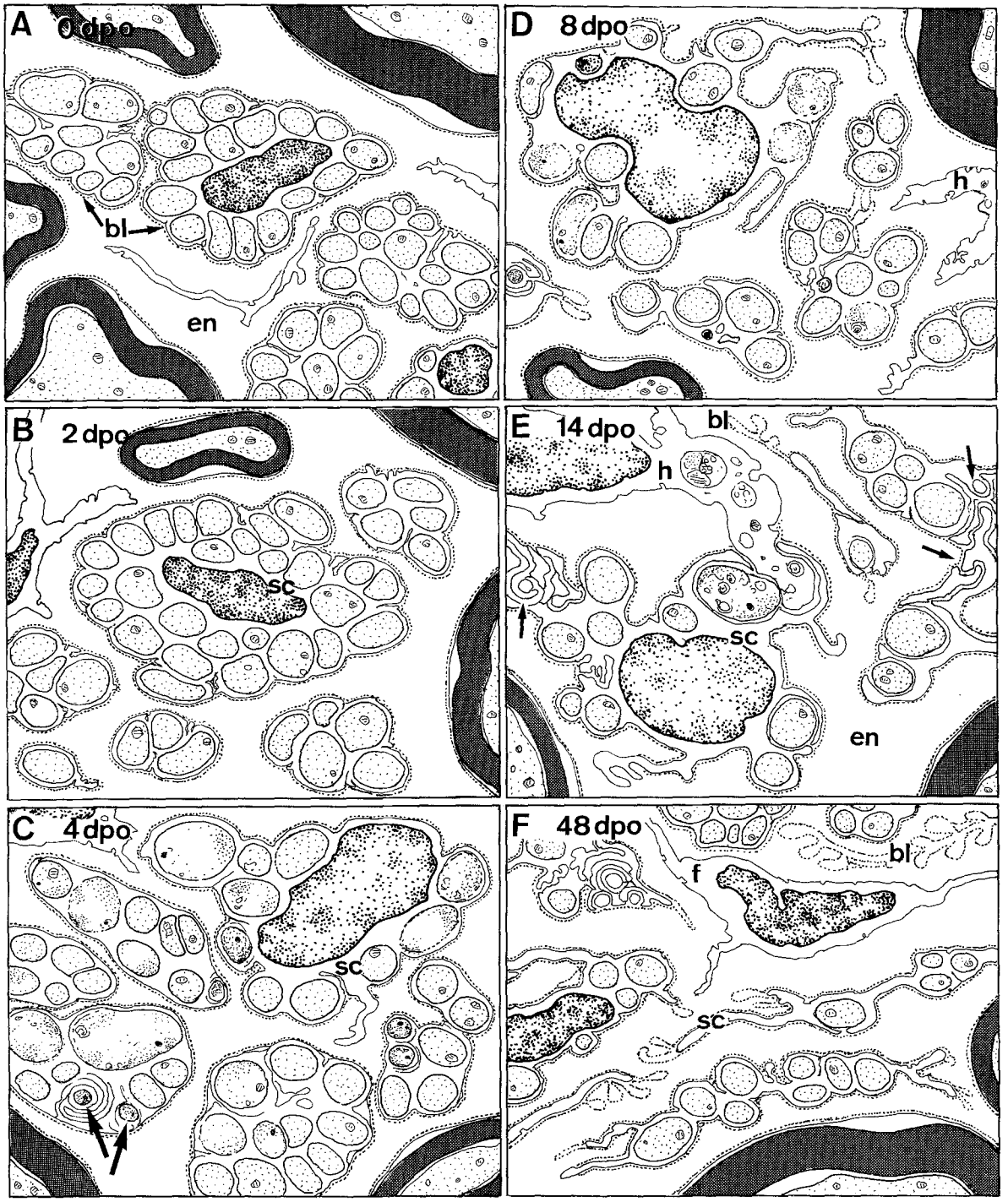

Fig. 8. Pictorial schematic representation of the degeneration of sympathetic postganglionic fibers in the nerves to the triceps surae muscle following sympathectomy. Same arrangement, magnifications and abbreviations as in Fig. 7

eration, folded up empty tubes of basal lamina are seen in the surrounding connective tissue (Fig. 6B). Some tubes contain Schwann cells. These cells are reduced in size because they have lost their axonal profiles. At other sites of the tubes histiocytes still clean up some left-over Schwann cell cytoplasm.

Discussion

The results demonstrate that the postganglionic sympathetic nerve fibers in the rcg degenerate within eight days after extirpation of the lumbal sympathetic trunk. In the peripheral muscle nerves, the degeneration has initially has a delay of two days. The rate of degeneration is also slower. Thus the degeneration ends six days later in the muscle nerves than in the rcg. In addition, it is worth noting that the overall pathological reaction is less pronounced in the periphery (compare Figs. 7, 8).

The onset of decrease in adrenergic transmitter substances in the gastrocnemius muscle after cutting the sciatic nerve starts much earlier (Bareggi et al. 1974). These authors observed that for each cm of the sciatic nerve left

in continuity with the muscle the transmitter decrease started 1.2 h later. Taking these data for our experiments (distance to the muscle 20 cm), the onset of decrease of the transmitter substances ought to start 24 h after sympathectomy. However, at this time no structural signs of degeneration can be recognized in the muscle nerves. The delay of structural degeneration signs for about 3 days may be explained by the fact that the cytoskeletal structures survive for a longer period and the applied technique is not suitable for observing early metabolic events.

The equivocal results concerning the time course of degeneration of unmyelinated axons (Lee 1963; Nathaniel and Pease 1963; Bray et al. 1972; Thomas and King 1974) may be explained by the fact that the distance between the section site of the nerve and the transected specimen varied in all the experiments. On the other hand the dissected nerve segment must be long enough to impede regenerating axonal sprouts from invading the distal nerve stump. In our material we observed some axonal sprouting of myelinated and unmyelinated axons. This finding supports the assumption that the rcg also contain sensory axons which run from the spinal nerves via the sympathetic trunc to the viscera.

The rcg regularly contain myelinated axons. In the lower lumbal portions of the sympathetic trunk they are more numerous than in the thoracic rami (Coggeshall et al. 1976). These authors have shown that most of these myelinated axons have their origin in the ganglia of the sympathetic trunk.

The special degeneration pattern of the myelinated fibers in the rcg should be emphasized. The longitudinal sections revealed that the vacuoles and the spindle-shaped extensions with their great numbers of mitochondria and lamellated osmophilic bodies (Cajal 1928; Nathaniel and Pease 1963; Blümcke et al. 1966; Webster 1962; Martinez and Friede 1970) have their origin in the nodal zone of the myelinated axons. These nodal zones enlarge considerably because the neighboring Schwann cells retract (Andres 1963; Morris et al. 1972). The formation of myelin debris and the initial steps to its removal are brought about by the Schwann cells. Later macrophages ingest the myelin debris (Andres 1963; Thomas and King 1976).

The spindle-shaped extensions of the axoplasm, which are less prominent in the unmyelinated axons, are seen in the proximal parts of the nerve section where special irritation of the axoplasma transport induces these pathological changes (Blümcke et al. 1966). It may be that the degeneration and loss of the microtubuli is the major factor for inducing the alterations (Andres 1963; Hanson and Edström 1978). The dramatic events during degeneration of the myelinated and unmyelinated axons in the rcg are accompanied by a mitotic proliferation of the Schwann cells, which reaches its maximum four days after sympathectomy. In the vagus nerve of the rabbit a comparable mitotic activity has also been observed four days after neurotomy (Rexed and Frederikson 1956). In Remak bundles which have lost a high proportion of postganglionic axons, Schwann cell reactions with mitotic activity are expected to occur. In view of the small numbers of such bundles in peripheral nerves the chance of detecting such mitoses is slight, except perhaps when using colchicin to inhibit this process.

After sympathectomy the Remak bundles in peripheral nerves behave quite differently from those in the rami communicantes grisei. These peripheral bundles obviously contain unmyelinated afferent and efferent nerve fibers in various proportions, as has also been reported for Remak bundles in the phrenic nerve and in the nerves to the knee joint (Langford and Schmidt 1983a, b). If the proportion of efferent fibers is high, the reaction of the Schwann cells is strong, and many phagocytotic and lytic processes can be observed. Again, empty tubes of basal lamina are the only remnants of these Remak bundles.

In those Remak bundles which contain afferent and efferent axons it is easy to discriminate between the autolytic, degenerating postganglionic sympathetic fibers and the intact sensory axons. The comparison between the sympathectomized and the control sides revealed that about 50% of the unmyelinated fibers disappeared in the muscle nerves. Again, these numbers are similar to those obtained in other peripheral somatic nerves (Langford and Schmidt 1983a, b).

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