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THE TEMPORAL COURSE OF THE EFFECTS OF POST-GANGLIONIC AXOTOMY ON THE INFERIOR MESENTERIC GANGLION OF THE CAT

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Some years ago it was observed (Acheson, Lee & Morison, 1942) that cutting the phrenic nerve caused, over a period of 3 weeks, a progressive central block of the transmission of nerve impulses from the respiratory centre to the axons of the cut phrenic nerve. At that time a similar phenomenon was noted in the inferior mesenteric ganglion: section of the hypogastric nerve caused a progressive block of the transmission of preganglionic volleys to the postganglionic axons of the cut hypogastric nerve (Acheson, 1952). This phenomenon was independently discovered in the same site by Brown, McLennan & Pascoe (1952). These authors have aimed their experiments chiefly at the mechanism of the block (Brown & Pascoe, 1954; McLennan, 1954). The present paper reports experiments in which the temporal course of the phenomenon was systematically studied. Campbell, Mark & Gasteiger (1949) and Downman, Eccles & McIntyre (1953) have studied a parallel phenomenon which occurs in motoneurones when ventral roots have been cut and dorsal root axons are stimulated.

METHODS

Cats of either sex weighing from 1·5 to 3·5 kg were anaesthetized by the intraperitoneal injection of pentobarbitone sodium (30–40 mg/kg). With aseptic precautions the abdominal cavity was opened, and the right hypogastric nerve was sectioned about 3 cm away from its ganglion. The left side remained untouched, to be used as a control. In some experiments the colonic nerve from the right inferior mesenteric ganglion was also cut; the results to be reported were not different in the experiments in which the colonic nerves were cut. The abdominal wall was closed, and the animals were allowed to recover. At intervals ranging from 2 to 180 days after the operation, under the same kind of anaesthesia the abdominal viscera were removed. A cannula in the femoral vein was employed whenever intravenous injection of drugs was necessary. The preganglionic trunks of both inferior mesenteric ganglia were dissected and placed together on a single pair of silver electrodes for stimulation, while the hypogastric nerves, after dissection, were laid separately on two symmetrical pairs of silver recording electrodes (Fig. 1). The responses of the two hypogastric nerves to stimulation of the preganglionic trunks by supramaximal rectangular

electrical pulses were recorded simultaneously, after suitable amplification, by a double-beam cathode-ray oscilloscope, and photographed on film. A coat of petroleum jelly was applied to prevent drying of the nerves. By means of additional electrodes, stimuli were applied directly to the hypogastric nerves (Fig. 1). In some instances, separate records were obtained from the preganglionic trunks of the two sides, near the ganglion. The blood supply of the ganglia was not disturbed.

Because of the variable origin of the blood supply to the ganglia, the technique used for close intra-arterial injections of acetylcholine bromide was similar to that of Brown & Pascoe (1954). A cannula was placed in the intestinal end of the inferior mesenteric artery, towards the aorta. During the injections the aorta was clamped below the lowest branch supplying the ganglia. The compound, made up in 0·25 ml. of saline (0·9% NaCl solution), was injected in about 2 sec. The injected fluid momentarily replaced the blood in the zone from which the small ganglionic arteries emerge.

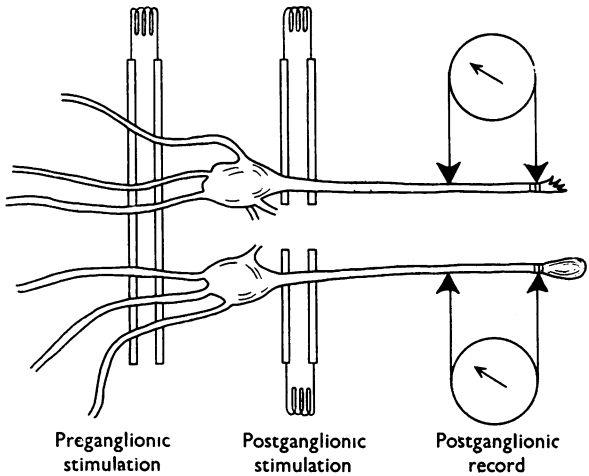

Fig. 1. Diagram of usual arrangements of electrodes on preganglionic and postganglionic trunks of the inferior mesenteric ganglia. The lower (right) hypogastric nerve is depicted with a neuroma resulting from section several days earlier; the left nerve has been cut acutely. Usually each hypogastric nerve was crushed under the distal recording electrode.

RESULTS

The arrangement of electrodes shown in Fig. 1 enabled us to compare the action potentials of the right hypogastric nerve, which will hereinafter be called the cut or previously cut nerve, with those of the control side, to supramaximal preganglionic stimulation. The records are illustrated in Fig. 2. After the stimulus artifact comes a small spike (D_1 of Lloyd, 1937) due mainly to impulses in axons which pass from the preganglionic trunk to the postganglionic without a synapse. This is rather variable in amplitude from animal to animal and, when compared on cut and control sides, was little changed at any time after section of the hypogastric nerve. After a longer latency, a larger and longer-lasting spike (S_2) occurs. This is due almost exclusively to impulses in post-synaptic axons. While S_2 remained fairly constant from

animal to animal on the control side, it changed considerably on the previously cut side according to the number of days elapsed since the nerve was cut.

At short intervals after operation (4 days or less) the responses of the cut side are indistinguishable from those of the control side (Fig. 2, I) when the frequency of stimulation is low (1 c/s or less). As early as 2 days after operation, however, the use of a higher frequency of stimulation (say 10 c/s, which

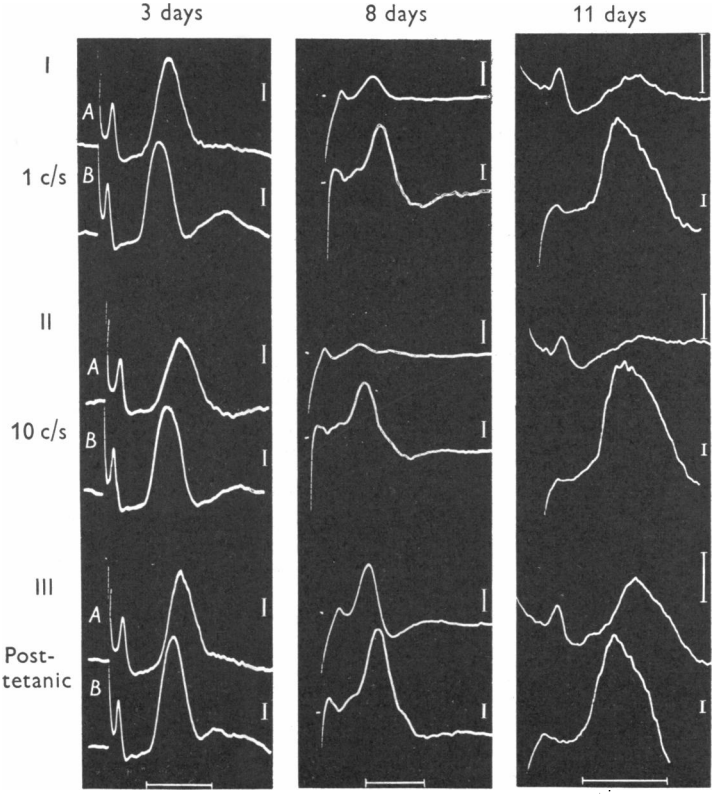

Fig. 2. Action potentials of previously cut (*A*) and control (*B*) hypogastric nerves at different intervals after axotomy: 3, 8 and 11 days. Supramaximal preganglionic stimulation, in the top row at 1 c/s; in the middle row at 10 c/s; and in the bottom row, with a single shock 5 sec after 20 c/s for 5 sec. Vertical calibrations, 50 μV; horizontal calibrations, 25 msec.

has little effect on S_2 of the control) brings out a clear difference in the cut side; S_2 quickly becomes smaller (Fig. 2, II *A*). Brown & Pascoe (1954) noted a similar phenomenon 3 days after axotomy. As the intervals after operation increase, this deficiency increases and is apparent at lower and lower frequencies of stimulation. After 5 days S_2 of the cut side is smaller than that of the control side even at 1 c/s. The magnitude of S_2 obtainable under any of the conditions which were tried (see below) progressively decreases; at

11–14 days only small and quickly fatiguing responses may be elicited (Fig. 2, I). During the 3rd week, practically no S_2 is obtained on the cut side on preganglionic stimulation, although the S_2 of the control side remained normal. In the 4th week, S_2 of the cut side begins a slow recovery. In contrast to our results, Brown & Pascoe (1954) found almost complete block of transmission any time between 3 and 12 weeks after axotomy. In all of our experiments done 28 days or more after axotomy, and in some as early as 21 days, inspection indicated that regrowth of the nerve had progressed beyond the gap produced by axotomy.

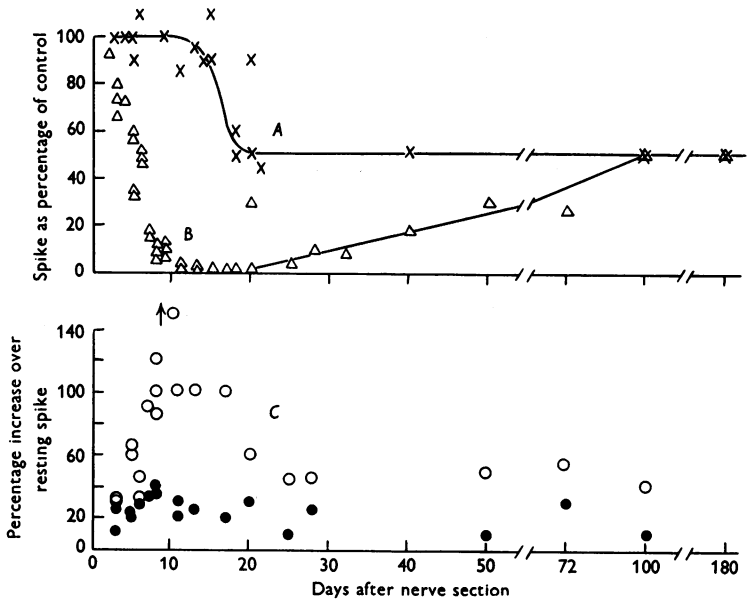

Fig. 3. Temporal course of the changes in the action potentials of the hypogastric nerve resulting from axotomy. Abscissae: days after axotomy. Ordinates for curves *A* and *B*: spike height of previously cut side as percentage of that of control side; *A* (×) supramaximal postganglionic stimulation (10 c/s); *B* (△) supramaximal preganglionic stimulation (10 c/s). Ordinates for curves *C*: height of post-tetanic spike as percentage of that of spike when not tetanized; ○, previously cut side; ●, control side.

Some of these events are depicted in curve *B* of Fig. 3, in which the height of S_2 of the cut side, expressed as per cent of S_2 of the control side (both stimulated at 10 c/s) is plotted against days after the section of the nerve. The swelling and retraction which follow section of the nerve interfere to an unknown degree with the exact comparison of the two S_2 spikes. Each point on this curve represents a single animal.

Post-tetanic enhancement. According to Brown & Pascoe (1954) post-tetanic enhancement was not increased by axotomy. In our experiments, distinct changes in the degree of enhancement could be seen. The interpretation of

these results was, however, rendered more difficult by the changes in the size of the non-tetanized spike on the cut side at different intervals after axotomy. S_2 of the control side is increased in amplitude by less than 40% when tested with a single maximal preganglionic stimulus 5 sec after a 5-sec period of stimulation at 20 c/s (Fig. 2, III*B*, and dots in Fig. 3*C*). On the cut side, the percentage increase of S_2 relative to the non-tetanized S_2 of this side rises progressively during the first 2 weeks after axotomy (Fig. 2, III*A*, and circles in Fig. 3*C*). Since, however, the non-tetanized S_2 is progressively diminishing during this period, the post-tetanic S_2 of the cut side is always less than that of the control side. Hence the tetanus increases but little the failing ability of the ganglion to transmit the preganglionic volley to the postganglionic axons. As the end of the 2nd week approaches, S_2 of the cut side becomes so small relative to the noise that its measurement is very inaccurate. During the 3rd week, little or no response can be obtained even during the post-tetanic period. In each of five observations after the 3rd week, post-tetanic enhancement on the cut side exceeded that on the control side when each was expressed as percentage of its resting S_2 (Fig. 3*C*).

Eserine. Brown & Pascoe (1954) and McLennan (1954) discussed the hypothesis that the block of transmission across the ganglion may result from a failure of cholinesterase to destroy the acetylcholine released by preganglionic volleys. They stated that eserine did not increase transmission in the axotomized ganglion. They also noted that tubocurarine did not increase transmission, as would be expected if block were due to an excess of acetylcholine. Our experiments reported in this section and the next confirm and extend their findings. In doses of 0·1 and 0·4 mg/kg eserine sulphate injected intravenously during supramaximal preganglionic stimulation at 0·5 c/s did not affect S_2 on the control side. On the cut side, these doses decreased S_2 on the 8th and 9th days after axotomy and did not increase the barely recognizable S_2 on the 13th, 17th, and 20th days.

Sensitivity to ganglion-blocking agents. Transmission became tenfold more sensitive to block by tetraethylammonium bromide or atropine sulphate at the end of the 1st week after axotomy and later showed recovery to normal. The following procedure was adopted to test sensitivity. During continuous preganglionic stimulation at a frequency of 0·5 c/s, intravenous injections of increasing doses of one of these two compounds were made at 5–10 min intervals. The initial dose was 0·05 or 0·1 mg/kg, and the other doses used were 0·2, 0·5, 1·0, 2, and sometimes 4 mg/kg.

When S_2 decreased in amplitude after one of these injections, complete recovery had not occurred when the next higher dose was given. On the control side, 1 or 2 mg/kg of either compound reduced S_2 to one-third or less of its original size. A similar degree of diminution of S_2 on the previously cut side was produced by one half of the dose of tetraethylammonium which

blocked the control when tested 3 days after axotomy, and by one-tenth of the dose 7 and 8 days after axotomy. Atropine had a similar effect in less than one-half of the dose 6 days, and in one-tenth of the dose 8 days after axotomy. In experiments after 72 and 100 days, the sensitivity of the axotomized ganglion to tetraethylammonium was similar to that of the control.

Sensitivity to stimulation by intra-arterial acetylcholine. Brown & Pascoe (1954) found the axotomized ganglion to be less sensitive than normal but still able to give a small response to stimulation by acetylcholine. Fig. 4 illustrates the responses we obtained on the previously cut (upper records)

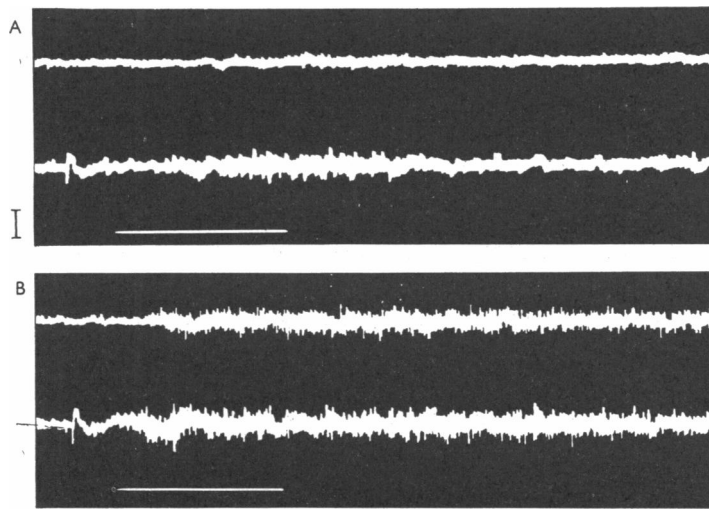

Fig. 4. Responses in hypogastric nerves on injection of acetylcholine into the arteries supplying the inferior mesenteric ganglion. Fourteen days after axotomy. Injection marked by signal (2·2 sec duration): A, 32 μg in 0·25 ml. of 0·9% NaCl; B, 500 μg in 0·25 ml. In each case, upper record is from previously cut side; lower record, control side. Vertical calibration: 20 μV.

and control sides (lower records) when acetylcholine was injected intra-arterially. Since the spikes are not synchronized, high amplification must be used, and the signal-to-noise ratio is small. The following doses were injected successively at 2- to 3-min intervals in 0·25 ml.: 7, 30, 125, and 500 μg. On the control side, a response was evident with the second dose, greater with the third dose, and equally great with the fourth dose. Occasionally the response to the fourth dose was smaller than that to the third; in this case, if the interval between doses was lengthened, the two responses were of the same amplitude. In seven experiments done between 5 and 15 days after axotomy, the previously cut side showed progressively diminishing sensitivity to the stimulating action of acetylcholine; but with higher doses, the responses were

as great as those of the control side, and there was no evidence of block even when block occurred on the control side. It should be emphasized that in these experiments the response to preganglionic volleys was much reduced on the cut side; for example, in the experiment (done 14 days after axotomy) illustrated in Fig. 4, no S_2 could be obtained on supramaximal preganglionic stimulation. In experiments in which acetylcholine was injected 18, 21 and 25 days after axotomy, the decreased sensitivity of the cut side was still evident, but now the largest responses which could be obtained were smaller than those of the control side. In experiments performed 33, 35 and 48 days after axotomy, sensitivity was close to normal but the amplitude of the largest responses remained less than that on the control side. The 'very much smaller' responses from axotomized ganglia reported by Brown & Pascoe (1954) doubtless correspond to our diminished responses 18 or more days after axotomy. Downman *et al.* (1953) found a situation in spinal motoneurones parallel to that described above, in that neurones which could not respond to the direct connexions from the afferent trunk could still respond to polysynaptic stimulation.

Axonal conduction. In two experiments during the 3rd week after axotomy (when little or no transganglionic response is obtained), the impulses recorded near the ganglia in the preganglionic trunks of the cut side were similar to those of the control side. In nineteen experiments the action potentials in the central stumps of the previously cut and control hypogastric nerves were compared on supramaximal postganglionic stimulation at different intervals after axotomy. In the first 15 days after axotomy, the amplitude of the C-fibre spikes of the two sides did not differ. These results confirm those of Brown & Pascoe (1954). At no time did we find the axons of the cut side to show fatigue when stimulated at 10 c/s. In seven of the eight experiments in which these studies were done 18 or more days after axotomy, the amplitude of the spike on the cut side was about half of that on the control side (curve *A* of Fig. 3).

This decrease of spike amplitude on the previously cut side could be accounted for by one of several hypotheses. (1) It may be an artifact resulting from the retraction and oedema of the nerve trunk. Since oedema and retraction were as apparent in the week before the 15th day as in the succeeding week, however, this explanation does not account for the difference noted in these periods. (2) The decreased amplitude may result from a smaller spike in each of the previously cut axons. This explanation is not excluded by the data available. It implies, however, that axotomy produces a change in the response of each fibre which lasts unchanged for at least 180 days, while the other results of axotomy disappear from almost all the fibres in less than 100 days. (3) The decreased spike amplitude on the previously cut side may result from the degeneration of some of the previously cut postganglionic

axons. In this case, if spike magnitude per conducting axon remains constant, a permanent decline in the amplitude of the action potential would be expected. Our results are consistent with this hypothesis and suggest that about half of the axotomized axons degenerate in the 3rd week (curve *A* of Fig. 3).

These findings suggest the possibility that some of the axotomized cells may die. The progressive failure of the transganglionic response in the first 2 weeks after section of the nerve could in this case result partly from the death of cells. Although the postganglionic trunk does not undergo the change which suggests axonal degeneration until the 2-week period is past, the cell bodies might have died some days earlier. This would block the transmission of the preganglionic volley to the corresponding axons during their period of survival. This hypothesis was tested in a series of experiments described in the next section.

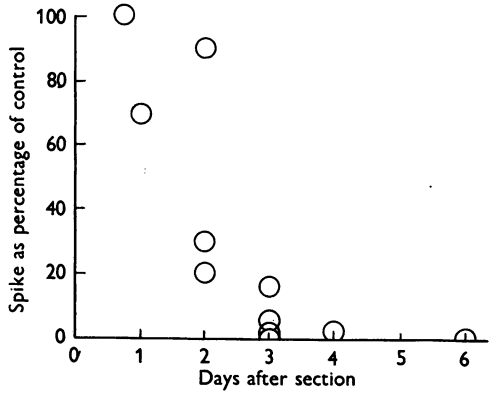

Fig. 5. Temporal course of changes in spike height of directly stimulated C-fibres in peripheral stump of hypogastric nerve after section near inferior mesenteric ganglion. Abscissae: days after section. Ordinates: spike height of previously cut side as percentage of that of control side.

Temporal course of degeneration of the distal stump after axotomy. In the preliminary operation the right hypogastric nerve was cut close to the inferior mesenteric ganglion. On a later day the peripheral stump of this nerve was dissected for at least 2 cm distal to the cut, excised, and laid in a chamber with its proximal end on stimulating electrodes and its distal end on recording electrodes. The more distal stimulating electrode was at least 3 mm from the cut end, and the conduction distance was usually 6 mm. The action potentials in C-fibres elicited by supramaximal stimuli were compared with those of a length of hypogastric nerve from the control side. In Fig. 5, the amplitude of the former, expressed as percentage of that of the latter, is plotted against the time after section. The results indicate that some of the C-fibres fail to conduct 24 hr after their section and that few if any function 4 days after section.

Langley & Anderson (1895) noted the absence of the usual responses to stimulation of the distal end of the hypogastric nerve in the cat 5 or more days after the nerve had been cut. Tuckett (1896) found that the responses of the iris to stimulation of the postganglionic branches of the superior cervical ganglion of the rabbit required progressively stronger shocks and finally disappeared when tested at intervals between 19 and 40 hr after section of the branches at their emergence from the ganglion. He also noted that the non-myelinated fibres of these branches progressively lost their ability to take the colour of methylene blue in the same period. Ranson (1912) found the degeneration of non-myelinated axons in the peripheral stump of the cut sciatic of the dog to occur about twice as rapidly as that of the myelinated fibres. The disappearance of function in the latter was reviewed by Rosenblueth (1950).

If the effects of death of the cell body in the ganglion on the survival of its axon are the same as those of surgical section of the axon, these data suggest that the decrease of the spike of the directly stimulated central stump of the postganglionic trunk occurring 15–18 days after axotomy (curve *A* of Fig. 3) represents the degeneration of axons whose cell bodies had died, on the average, between 2 and 3 days earlier. Hence little if any of the decline of transganglionic response (curve *B* of Fig. 3) can be attributed to death of cell bodies.

DISCUSSION

The main purpose of the experiments reported has been to work out the natural history of the physiological effects of axotomy as an aid to their correlation with the concurrent biochemical and anatomical changes. Accordingly, we will first discuss the phenomena we have studied and then consider their relation to parallel findings in other sites.

In the inferior mesenteric ganglion the physiological syndrome initiated by axotomy extends over a period of more than 2 months. Beginning 2 days after the section, transmission of impulses across the ganglion becomes subject to fatigue at progressively lower frequencies of stimulation. Within the next 3 days, even the rested ganglion becomes unable to transmit a volley of normal size to its postganglionic axons, and as the remainder of the first 2 weeks proceeds, transmission deteriorates and finally is almost abolished. During this period, tetanic stimulation induces a subsequent enhancement of transmission which is relatively greater than normal; yet even the enhanced volley is smaller than normal. Inhibition of cholinesterase with eserine does not increase the transmission. At the same time, the ganglion becomes progressively more sensitive to ganglion-blocking agents and less sensitive to the stimulating action of acetylcholine. Nevertheless, even at the end of this period the axons proximal to the section conduct impulses normally when they are stimulated

directly, and acetylcholine, injected intra-arterially in suitable doses, is still able to stimulate the ganglion cells which cannot transmit the preganglionic volley.

Concerning the mechanism of the disappearance of postganglionic responses on preganglionic stimulation after axotomy, little can be added to the discussion presented by Brown & Pascoe (1954). It is clear that the fatigue and block occur in the ganglion rather than in the pre- or postganglionic axons. The increased sensitivity to ganglion-blocking agents reported above probably represents the mirror image of the decreased sensitivity to injected acetylcholine and speaks, as Brown & Pascoe's data do, against the hypothesis that the failure of transmission results from the disappearance of the ability of the ganglion to destroy acetylcholine. Since, despite the diminished sensitivity to acetylcholine, something like the usual amount of stimulation of ganglion cells may be obtained with high enough doses, even when transmission is abolished, the most likely explanation of the ganglionic block is a relative interference with the excitatory process initiated in the postganglionic cell body by acetylcholine.

As the climax of the syndrome is reached, in the third week after axotomy, a new change comes on. Direct stimulation of the postganglionic trunk produces smaller responses. The asynchronous discharge provoked in the ganglion cells by acetylcholine also becomes smaller at this time. We have suggested that the diminution of response results from the death of about half of the axotomized ganglion cells and the consequent degeneration of their axons.

The recovery of function in the surviving neurones is a slow and steady process still evident 72 days after axotomy (Fig. 3). In the experiments conducted 100 and 180 days after axotomy, the transmitted response was about half that of the control side, and the spike of the directly stimulated postganglionic trunk was also about half that of the control; sensitivity to tetraethylammonium had also returned to normal. We conclude that recovery is complete at these intervals, as judged by the functions we have studied.

On the assumption that changes in the magnitude of S_2 correspond to changes in the number of neurones responding to the preganglionic volley, curve *B* of Fig. 3 indicates that, from the 3rd week, when practically none of the surviving neurones respond, until the 10th to 14th week, when recovery is complete, neurones are recovering one by one. According to this interpretation, some neurones recover the ability to respond to the preganglionic volley as early as 21 days after axotomy, whereas others do not recover this ability until 72–100 days after axotomy. Two findings suggest that cells which regain the ability to respond to the preganglionic volley require further time before recovery is complete: (1) the persistent increase of post-tetanic enhancement seen after the 20th day (curves *C* of Fig. 3), suggesting that a relatively large fraction of the surviving cells are subliminally excited in this period, and

(2) persistence of low sensitivity to acetylcholine until 25 days after axotomy and return to normal by 33 days.

At the present time no single portion of the temporal course of the effects of axotomy in the inferior mesenteric ganglion can be regarded as typical of the syndrome as a whole. Those who study the neurones mainly 3 weeks after section of their axons are sampling the early part of a slow process of recovery. At this time a small fraction of the cells are recovering or have recovered their ability to transmit the preganglionic volley, while most of them cannot do this and will remain unresponsive to preganglionic volleys for several weeks. Perhaps these cells may, for the purposes of morphological or biochemical studies, be considered to be in a relatively steady state during the 4th week. It would seem profitable to make further studies of the syndrome in its first 2 weeks, when the most active change is in progress.

In a wide variety of neurones, axotomy has long been known to produce an anatomical syndrome called 'the axonal reaction'. The earliest changes are in some instances visible one day after the section. During a 2-week period the Nissl bodies break into smaller and smaller bits and diminish in quantity, the nucleus is displaced toward the periphery of the cell, and swelling of the cell body occurs. The climax of anatomical change comes in the 3rd week, and then alterations previously observed revert to normal over a period of 50–100 days (Bodian & Mellors, 1945). The changes in the function of the inferior mesenteric ganglion described above parallel this orderly sequence of anatomical events. The parallel is more striking than could be observed in the study of the phrenic nerve (Acheson *et al.* 1942), since there the indicator was the periodic, asynchronous discharge from the respiratory centre, whereas with the ganglion synchronized volleys of impulses could be delivered at will via the preganglionic fibres. In studying the responses of axotomized spinal motoneurones to afferent volleys, Campbell *et al.* (1949) and Downman *et al.* (1953) have described changes in the monosynaptic spike which have a similar temporal course: progressive diminution (5–13 days), absence (13–30 days), and recovery (35–56 days). The inferior mesenteric ganglion differs in that transmission begins to show recovery earlier (about 20 days after axotomy; Fig. 3*B*). A difference with respect to the time of complete recovery may also exist (motoneurones, 56 days; ganglion, 72–100 days), but the small number of experiments performed at these intervals makes this interpretation less convincing.

A more striking difference between the spinal motoneurones and the sympathetic ganglion cells is the proposed death of about half of the latter about $2\frac{1}{2}$ weeks after axotomy. The hypothesis that the ganglion cells die is based upon good physiological evidence but needs anatomical confirmation. Few if any of the axotomized motoneurones of the monkey's spinal cord die (Howe & Mellors, 1945), and the same would appear to be true of most of the

sites in which the axonal reaction has been studied in neurones having rather heavily myelinated axons. Yet Van Gehuchten (1897) found that many of the neurones of the nodose ganglion disappeared when the corresponding vagus was cut 2 cm below the ganglion. Moreover, on cutting the nerve trunk just distal to the C_2 dorsal-root ganglion in the rat, Ranson (1909) observed that about half of the cells of the ganglion disappeared, the ones which disappeared being almost exclusively those which gave rise to non-myelinated axons. When he cut the sciatic nerve in the dog, at a distance of several centimetres from the dorsal-root ganglion, however, few of the cells died, but again the cells having non-myelinated axons gave evidence of severe axonal reaction (Ranson, 1912). Since physiological differences exist between dorsal-root C-fibres and sympathetic C-fibres (Gasser, 1950), it is safer for the question at hand to rely upon evidence in sympathetic ganglia. Unfortunately, anatomical studies of the axonal reaction in this tissue have been scanty. After cutting (necessarily very close to the ganglion) all the branches of the superior cervical ganglion except the cervical sympathetic trunk, Levinsohn (1903) found that most of the cells of that ganglion died. De Castro (1932) noted that the reaction of autonomic ganglion cells to injury of their axons is very marked.

The discovery of physiological effects of axotomy has led to renewed study of the axonal reaction in spinal motoneurones (Barr & Hamilton, 1948) and to the discovery of parallel changes in certain enzymic activities and other biological phenomena in them (Howe & Mellors, 1945; Bodian & Mellors, 1945). Chromatolysis is known to occur in autonomic ganglia on postganglionic axotomy (De Castro, 1932), but systematic studies of its temporal course or of the biochemical changes which may accompany it in this tissue do not appear to have been reported.

SUMMARY

1. The right hypogastric nerve was cut 3 or more cm below the inferior mesenteric ganglion in the cat. At different intervals after the section of the nerve, its action potentials were compared with those of the (left) control.

2. Two days after axotomy, fatigue of the transganglionic response occurs. Thereafter progressive failure of transmission occurs, and at the end of 2 weeks almost no transganglionic response can be obtained.

3. During this period, post-tetanic enhancement increases when it is expressed as percentage of the non-tetanized spike on the cut side, but the absolute size of the enhanced spike is less than that of the control side.

4. Eserine decreased the failing transganglionic response on the 8th and 9th day after axotomy and did not increase the barely recognizable response in the 3rd week.

5. The axotomized ganglion is blocked by progressively smaller doses of tetraethylammonium or atropine as the 1st week after axotomy progresses.

6. From the 5th to the 15th day after axotomy, the ganglion requires, for stimulation, increasing doses of acetylcholine, injected intra-arterially. Even when no transganglionic response can be detected on preganglionic stimulation, sufficient doses of acetylcholine elicit responses from the axotomized side which are comparable to those elicited from the control side.

7. In the 3rd week, direct electrical stimulation of the postganglionic trunk elicits smaller responses, suggesting a disappearance of about half of the neurones at this time. At the same time, the asynchronous discharge of impulses produced by suitable doses of intra-arterial acetylcholine also diminishes.

8. In additional studies, the loss of conduction in the peripheral stump of the cut hypogastric nerve was shown to occur within 4 days after the section.

9. Recovery of function of the ganglion begins in the 3rd week and seems complete between 72 and 100 days after axotomy. During this period, the individual neurones are presumed to be recovering, one by one, their ability to transmit the preganglionic volley.

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