**Title**
Functional blockade of impulse trains caused by acute nerve compression



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**Publication Date**
1980

Peer reviewed

# 20

# Functional blockade of impulse trains caused by acute nerve compression

**Don L. Jewett**

Function in an injured nerve is completely lost if axonal conduction cannot occur. Such is the case in nerve injuries of the second degree or higher in Sunderland's classification (see also Chapter 2).[13] With a first degree injury axonal conduction can occur despite local demyelination (see also Chapters 4 and 18). The purpose of this chapter is to indicate the possibility of even milder forms of injury that can affect nerve function without a histological change—possibly the basis for a "zero degree" form of injury. The effects on axonal function to be described here could occur as the result of relatively mild injury, or they could be the consequence of inadequate healing (see "Discussion" at the end of this chapter).

It is important to realize that rapid, repetitive action potentials place greater physiological demands on axons than does the conduction of a single action potential. The corollary of this principle is that mildly impaired axonal function is reflected in the inability of the axon to transmit action potentials closely spaced in time: the greater the impairment, the less the ability to conduct impulses at high frequencies. In experimental animals it is easiest to apply repetitive trains of impulses (with differing intratrain frequencies) as a test of an impairment of axonal conduction.

The inability of impaired axons to transmit trains of impulses has been clearly documented in the case of impairment caused by localized cooling.[5,10] These experiments can form a model of the impaired axon under carefully controlled conditions. The analogy to nerve injury is reasonable since at sufficiently low temperatures complete blockage of axonal conduction occurs in both myelinated[10] and unmyelinated[5] fibers. Fig. 20-1 shows the type of data that can be obtained when a localized area of nerve is gradually cooled. This figure, taken from Franz and Iggo,[5] shows action potentials recorded from a single unmyelinated fiber. As a localized area between the stimulating and recording electrodes is cooled, the ability of the axon to conduct trains of impulses is impaired. The figure has been rearranged to show the single unit responses with increasing intratrain frequency from left to right and with decreasing temperature from top to bottom. As can be seen in Fig. 20-1, at normal temperature the axon is able to conduct all impulses in the trains at all frequencies up to the highest shown, 180 Hz. As the nerve is cooled, the axon loses its ability to transmit at higher frequencies first, while lower frequency trains are unaffected. However, as axonal conduction is further impaired by the cold, even the lower train frequencies are affected.

These results, as so far described, are readily intuited. What is surprising is the manner in which the trains of impulses are affected. It is to be noted that at the extreme, before complete axonal block, only the first impulse of the train traverses the cold region, while the rest of the impulses in the train are blocked. At lesser degrees of impairment the first action potential is always conducted;

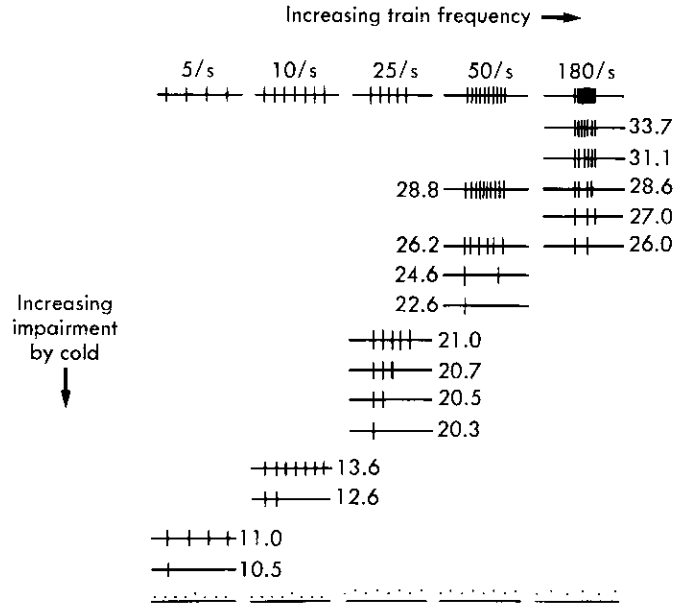


**Fig. 20-1.** Blocking pattern within trains of impulses in nonmyelinated axon (conduction velocity 0.9 m/sec) stimulated at different frequencies, which are indicated above each column. Control records with nerve at 37° C are shown in top row; nerve temperatures for other records are indicated at start of each trace. Repetitious traces have been omitted. Major time marks: 100 ms. (Adapted from Franz, D. N., and Iggo, A.: J. Physiol. (Lond.) 99:319, 1968.)

then there can be varying amounts of block of the remaining portion of the train (Fig. 20-1). Paintal[10] has offered an explanation for this interesting behavior. Blockade of high frequencies usually would be thought to be due to an increased refractory period. However, since this can only block every other impulse or every third impulse (the so-called alternating block), it could not explain how only the first action potential in a train traverses a region (which will be called "trains block"). The most probable explanation[10] is that the most impaired node in the cool region fires an action potential with a significantly lower height when the action potentials are sufficiently close together. At this decreased height there is insufficient current to activate the next node, yet the impaired node continues to follow the high frequency with similar, small, abortive spikes. Thus, according to this explanation, it is paradoxical that there must be a firing, impaired node in order to block conduction of the latter part of the train of impulses.

Whatever the explanation, it is certainly clear that a blockage of nerve impulse trains (that is, "trains" block) can occur. Such behavior would have an extreme effect on the functioning of either sensory or motor axons and can account for some of the phenomena seen with first degree injuries.

The purpose of this chapter is to show that a blockade of nerve impulse trains can also occur as a result of impaired conduction from acute compression of the nerve. The clinical implications of this result will be described.

## METHODS

Cats were anesthetized with intraperitoneal pentobarbital. A multilevel lumbar laminectomy provided intradural access to the lumbar dorsal rootlets. In the leg on either the posterior tibial or peroneal nerve, two sets of stimulating electrodes and a compression device were placed with the spacings shown in Fig. 20-2. All were kept under the surface of a mineral oil pool held by skin flaps.

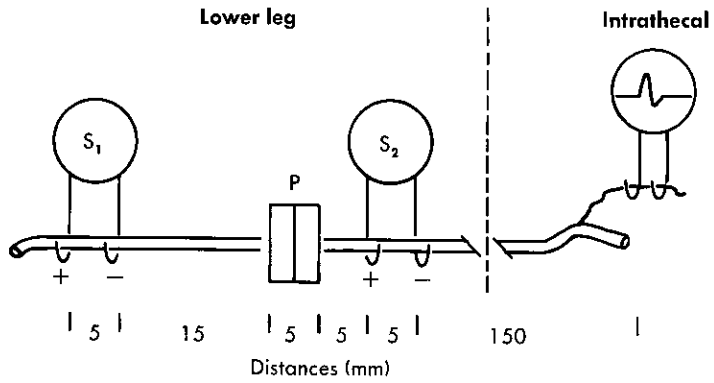


**Fig. 20-2.** Diagram of experimental arrangement, showing relationship of stimulating and recording electrodes. *P*, Balloon compression device, 5 mm long. $S_1$, Distal stimulating electrodes. Action potentials from here must conduct through compressed region. $S_2$, Proximal (control) stimulating electrodes.

Single units in the region of the lumbar laminectomy were hand-dissected under a binocular microscope beneath a mineral oil pool. All electrodes were Ag-AgCl. All single units were identified by their sharp threshold to stimulation (usually less than 0.1 volt) and their uniform spike height (not varying more than the baseline noise). The compression device was a plastic adapter fitted over the balloon of a urinary catheter. The amount of pressure was not measured but could be inferred physiologically (see "Results").

The arrangement of electrodes (Fig. 20-2) permitted stimulation of the axon of the single unit both proximal and distal to the region of compression, so that control recordings from the proximal electrodes could be obtained. Recordings were taken only from large myelinated fibers conducting between 30 and 50 m/sec. The temperature in the oil baths was not controlled, so slowing of conduction velocity owing to lowered temperature undoubtedly occurred.

## RESULTS

After each single unit was identified by a sharp threshold to increasing stimulus strength, the stimulus was set to at least $1^1/_2$ times the threshold value. Stimulation at the proximal electrode determined the maximum frequency that could be transmitted along the axon up to and including any damaged region at the recording electrode. After application of pressure, effects on trains of impulses from the distal electrode were not immediately apparent but were detected within 10 to 30 minutes. In no case did full conduction block occur, despite periods of compression up to 2 hours; thus the pressures applied to the nerve were presumably less than the 50 to 300 mm Hg pressure range over which conduction block has been found to occur in mammalian nerves.[2-4]

The effect of compression was to decrease the ability of the axon to conduct high-frequency impulse trains. For example, in Fig. 20-3 there is a conducted action potential for each distal stimulus at rates up to 135 Hz. At a frequency of 165 Hz, some impulses after the fourth are missing from the train. At 295 Hz only the first and third impulses in the train traverse the compressed region, and at 360 Hz only the first impulse in the train is conducted. However, at that time the first 12 impulses at 360 Hz were conducted over the nerve proximal to the compression. The difference between the proximal and distal stimulations indicates the degree of conduction impairment caused by compression between the pairs of stimulating electrodes. The inability to transmit all the proximal stimuli is

probably related to mechanical injury near the recording electrodes owing to the nerve splitting necessary to record the single unit.

Fig. 20-3 also demonstrates that there can be a mixture of both trains block and alternating block at some train frequencies, as shown in the second, third, and fourth tracings from the top.

The development of the impulse blockade during continuous application of pressure is shown in Fig. 20-4. After only 3 minutes of pressure, the stimulation at the distal electrodes could transmit at least nine consecutive impulses at 340 Hz. After 22 minutes of pressure only four impulses were transmitted before alternating block occurred (spike height is down as a result of changed conditions at the recording electrodes). However, at nearly the same time (third tracing) the compressed axon was still capable of transmitting each impulse at 260 Hz. However, after another 16 minutes the axon could not transmit all impulses at 260 Hz and after yet another 3 minutes shows complete trains block (except for the first impulse of the train) at 340 Hz (bottom tracing). Thus acute compression gradually impairs the ability of the axon to conduct trains of impulses: the longer the compression, the lower the frequency of impulses that still can be transmitted through the region without dropout.

After prolonged compression, recovery was either slow or not observed during the time the single units were recorded. Fig. 20-3 shows the results 1 hour after cessation of $1^1/_2$ hours of compression. With shorter durations of pressure, recovery of function could be observed (Fig. 20-5). In Fig. 20-5 the small spikes are those of a stimulated axon, while the large spikes are those of a

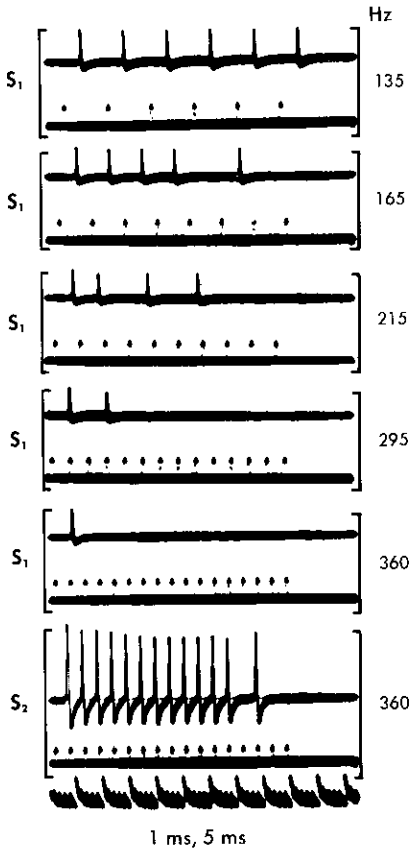


**Fig. 20-3.** Single unit recordings taken 1.5 hours after 1 hour of compression at differing train stimulus rates as indicated on right of each tracing. In each recording lower trace shows pattern and rate of stimulus presentation, while upper trace shows single unit response. Note that as train rate is increased, fewer impulses are transmitted through compressed region from $S_1$ stimulating electrodes; both trains block and alternate block occur; first action potential is always transmitted at this level of compression. Control stimulation at $S_2$ (bottom tracing) shows ability to follow 360 Hz much in excess of that which can traverse compressed region from $S_1$ (second tracing from bottom).

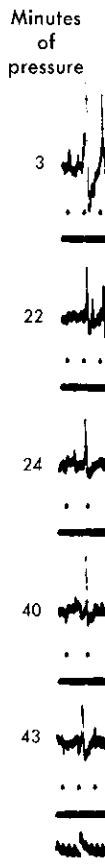


**Fig. 20-5.**
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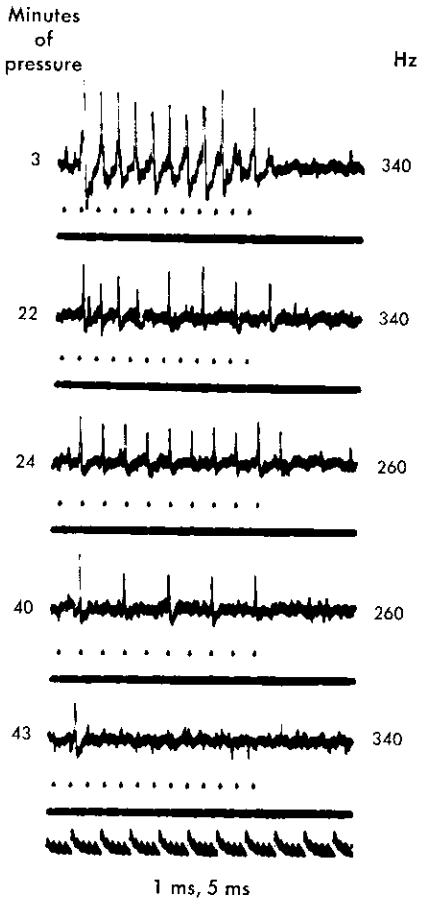


**Fig. 20-4.** Development of blockade during application of continuous compression, as shown by times to left of tracings. Note that top and bottom traces show stimulation at same frequency, differing only by amount of time nerve is compressed; some decrease in action potential heights occurs during sequence as a result of changes at recording electrodes, but control recording from $S_2$ taken after last tracing showed following at greater than 300 Hz.

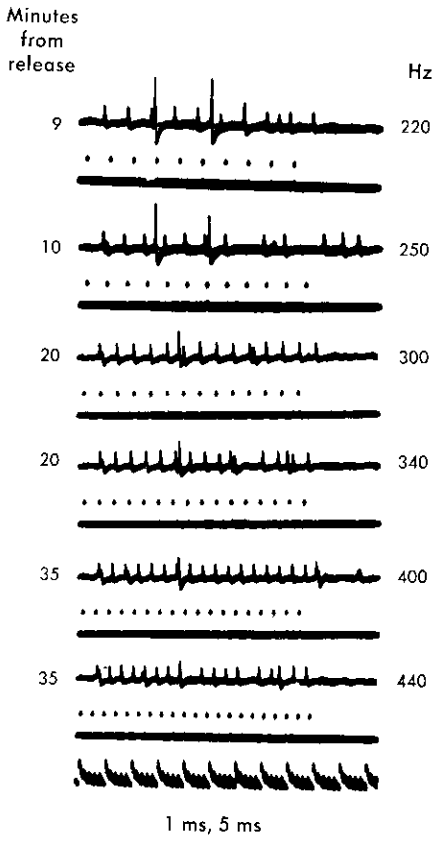


**Fig. 20-5.** Recovery of blockade after short (11 min) compression. Time after release of compression is shown on left, train frequency on right. Note that large single unit was firing spontaneously, and stimulated unit has smaller spike. At each time highest frequency at which all impulses conduct through compressed region is shown, together with higher frequency at which blockade occurs in latter part of impulse train.

spontaneously firing, unstimulated unit in the same nerve twig. It can be seen in Fig. 20-5 that about 10 minutes after release of 11 minutes of pressure the unit could transmit at about 220 Hz but had some interference with trains of impulses at rates above 250 Hz. Twenty minutes after release the axon could transmit at 300 Hz but not at 340 Hz. At 35 minutes it could transmit at 400 Hz but not at 440 Hz.

When there was interference with trains of impulses, the pattern of those impulses of the train that were conducted was not constant. As shown in Fig. 20-6, the pattern of the single impaired train is not consistent when multiple sweeps are overlaid. Thus, for similar sensory inputs, there may be different patterns transmitted to the central nervous system. Furthermore, if computer averaging techniques are used when detecting skin surface potentials, the dropouts may occur dispersed throughout the train.

Fast oscilloscope sweeps (not shown) were analyzed for comparison between the latency of the action potentials before and after compression. There was a reduction in conduction velocity from about 35 to 50 m/sec to less than 10 m/sec in the compressed region if one ascribes all slowing to the 5 mm length of the compression device. This implies that compound action potentials may have increased temporal dispersion, and hence lowered heights, even when no impulses are blocked. To correct for this it would be necessary to record the area under the monophasic action potential (see Chapter 15).

## DISCUSSION

The mechanism of conduction impairment caused by acute compression in these experiments is unknown. Hemostasis undoubtedly occurred, but by the indirect evidence noted in the results, arterial blockage is less likely to have occurred. Intussusception may have occurred, but in those cases where compression was for a short time and recovery occurred, one would have to postulate a reversible intussusception (see Chapter 4). Certainly there was not enough time for demyelination to occur, although prolonged compression might ultimately give such a histological picture (assuming that recovery does not occur within a few hours). The 10- to 30-minute period needed to affect conduction in the compressed region would be compatible with physical changes in axonal size in the compressed region owing to slow movement of the viscous axoplasm to noncompressed regions of the axon. Such diameter change might account for the blockades seen since

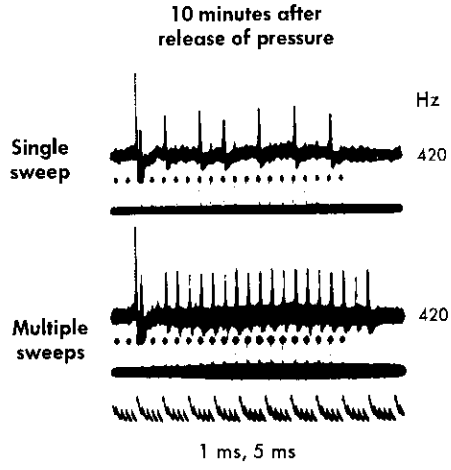


**Fig. 20-6.** Comparison of blockade pattern of single train with overlapped multiple stimulations. Note that except for period just after first impulse pattern of activity is variable but still time-locked to stimuli from $S_1$.

smaller diameter fibers are less able to transmit high frequencies of nerve impulses than larger fibers.[5,8-10] If this were the mechanism, then when an axon tapers distal to a nerve repair or has multiple branches that are smaller than the main axon, centrifugal conduction would be affected, with possible trains block at the region of axonal narrowing (see Chapter 9). Irrespective of the mechanism of trains block that results from acute compression, it seems reasonable to assume that impaired axonal conduction from a variety of different mechanisms can lead to the same functional result of dropout or complete block of trains of nerve impulses.

There are a number of clinical implications of these findings. The possible effects on tapered nerve fibers arising from repaired nerves has already been mentioned. In the anterior compartment syndrome increased pressure may lead to progressive loss of motor power in the following sequence: (1) muscle weakness, (2) a flick of contraction at the start of each voluntary effort, and finally (3) paralysis of the involved muscle. One can hypothesize that if the loss is due to a pressure block on the axon, then the weakness corresponds to a time when action potentials are dropping out of the continuous barrage of impulses being generated by the CNS; the flick of contraction may represent blockade of impulse trains with only the first few impulses in a train able to traverse the compressed region; and the paralysis indicates a complete conduction block.

Many of the characteristics of first degree lesions (also termed "neurapraxia"[11]) are consistent with the idea of blockade of impulse trains. Momentary compression can be one of the causes of neurapraxia.[11] The period of functional loss can be variable. It is much shorter than in more severe forms of nerve injury. There may be no significant demyelination, just as we have postulated for the acute compressions reported here. If an injured nerve has impaired conduction that would lead to either trains block or alternating block, then we would expect that the axons normally having the fastest firing rates might be those that are most affected, namely, motor nerves, proprioceptive fibers, and those serving transient touch. These are the modalities most often involved in neurapraxia. Slower firing, smaller fibers, such as autonomic axons, would be less affected, as is also the case in neurapraxia. (This explanation presumes that there is a differential effect on larger fibers, although this effect has not been experimentally verified.) It should be noted that in the clinical evaluation of touch one often uses a pin to detect sensation. This could stimulate only a few action potentials, the first of which could be transmitted through a region that would block a train of impulses. On the other hand, rapid impulse trains, such as those that occur when attempting maximal muscle contractions, would be blocked; hence there would be a more severe functional loss in a motor fiber than in a sensory fiber of similar diameter. Thus this might be the explanation for the clinical observation that motor function is affected more than sensory function. Another possibility is that trains block may occur where there was a continuous barrage of activity associated with muscle stretch receptors; this in turn might change spinal cord excitability at an unconscious level and thus affect the motor power in this manner.

With chronic compression, such as might occur with localized inflammatory response around an injury, it is possible that large fibers may be selectively affected mechanically, as compared with smaller fibers.[12]

Compound action potentials to trains of stimuli have been recorded in normal human median nerves[1] and ulnar nerves.[7,14] In recordings in the carpal tunnel syndrome, trains of impulses have been shown to be a more sensitive objective measure than the EMG or sensory conduction studies.[6] Compound action potential recordings such as these demonstrate the usefulness of trains of impulses in the analysis of human nerve function but must be interpreted with care, since changes in the height of the compound action potential can be due to a number of different causes as follows: (1) a change in the height of the individual action potentials in the later part of the train (see bottom trace of Fig.

20-3), (2) a temporal dispersion of the action potentials either by decreased conduction in the impaired region or by differential effects on conduction related to differing axonal size,[12] or (3) the change in the number of axons contributing action potentials to the compound potential. Thus small changes in the height of the compound action potential may be due to either of the first two mechanisms. However, the changes observed in the reference literature just cited are sufficiently great to indicate that some dropout of action potentials must be occurring under the conditions observed.

Many variables remain to be investigated, such as the interaction between the amount and duration of compression, the effect of the length of axon compressed, and the potentiating effects of factors like inflammation, anoxia, and drugs. However, it seems reasonably safe to prognosticate that trains of impulses are likely to be a better measure of impaired conduction than complete axonal block in milder forms of nerve injury. Similarly, trains of impulses may be important in evaluating the time course of functional recovery as regrowing axons mature and enlarge. Permanent impairment of train conduction may still result after nerve repair if the distal axons do not recover their full diameters.

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# DISCUSSION

**W. Newmar (San Francisco):** In the carpal tunnel syndrome, we see sensory dropout before motor dropout. How do we explain this?

**Jewett:** First of all clinical tests of both sensation and motor power are relatively coarse, so that there may be physiological impairment of maximum performance before clinical manifestations are apparent. The degree of impairment will relate to the diameters of the axons as well as the firing frequencies, so it is conceivable that either motor dropout or sensory dropout could be affected first. Finally, there is no single unit data on chronic compression comparable to what I showed with respect to acute compression. All the chronic data are based on compound potentials. Perhaps the relationship of affected firing frequency and diameter may be different in the chronic case, although there is no question that in chronic compression there is decreased function.

**Newmar:** With a compartment syndrome, isn't it a good possibility that it is the muscle that is affected before the nerve?

**Jewett:** I have no data on muscle action potentials. It would be of considerable interest to see if muscle were affected as well. In the compartment syndrome the muscle would be under uniform pressure throughout its length. The experiments in which nerves were placed in hyperbaric chambers indicate that high pressure can be tolerated if the pressure is uniformly distributed. As Dr. Waxman has indicated in this volume, it is the transition areas in nerve where conduction failure is likely. Therefore in compartment syndromes one would suspect the region of nerve as it entered the high-pressure region as being the most susceptible. This is theoretical, of course, and needs experimental verification.

**Roger Crumly (San Francisco):** In Bell's palsy, it has been shown that patients that have lower function of the involved submaxillary gland and lacrimal gland tend to have poorer results in regard to regeneration. Yet we have been shown by Dr. Sunderland that the facial nerve is a monofunicular nerve throughout the temporal bone, so that if this is a compressive lesion, why are these smaller nerves prognostic indicators? Dr. Jewett's data suggest that the large motor fibers going to the facial muscles should be the most sensitive to compression. Are the poorer results evidence that there is an increased pressure in those patients that have secretomotor nerve involvement?

**Jewett:** The presence of a palsy implies complete conduction block, a first degree lesion. I agree that smaller fiber involvement may well indicate the severity of the compressive lesion. This is reasonable since large fibers are compressed proportionally more than small fibers.

**Sunderland:** The facial nerve in Bell's palsy is actually analogous to the median nerve in the carpal tunnel syndrome, hence we must consider it a conduction block injury. Clearly we are beginning to broaden our classification and understanding of conduction block lesions. There are many factors that we do not yet understand about them. I wish to emphasize the importance of an adequate blood supply. The nodes must be oxygen sensitive, and impairment of blood supply must clearly have significant effects on conduction properties.

**Ochoa:** On the use of the term "neurapraxia," I quite agree with Sir Sidney that we had better drop it because it is confusing. Neurapraxia has been used interchangeably to express two totally different concepts. One is the immediately reversible block that is ischemic, and the other one is

a prolonged demyelinating block. Now what are we going to do with the term? We must drop it because it is confusing, but we have to replace it with something else, and I would suggest that we expand the nerve injury classification in order to accomodate the main concept of neurapraxia, which is primarily a myelin and a Schwann cell lesion. I would suggest that we incorporate, in agreement with Dr. Jewett, a "zero degree" classification to bring in the demyelinating block. We probably even need a "zero-zero degree" to avoid the confusion of the demyelinating block with the purely ischemic block.

**Sunderland:** I think that is most helpful and certainly in conduction block, we now need subgrades of a first degree lesion.

**Editor:** Readers may also find the following reference of interest. Smith, D. O., and Hatt, H.: Axon conduction block in a region of dense connective tissue in crayfish, J. Neurophysiol. 39:794, 1976.

# NERVE REPAIR AND REGENERATION

## its clinical and experimental basis

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