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ABSTRACT: This article reviews the epidemiology and classification of traumatic peripheral nerve injuries, the effects of these injuries on nerve and muscle, and how electrodiagnosis is used to help classify the injury. Mechanisms of recovery are also reviewed. Motor and sensory nerve conduction studies, needle electromyography, and other electrophysiological methods are particularly useful for localizing peripheral nerve injuries, detecting and quantifying the degree of axon loss, and contributing toward treatment decisions as well as prognostication.

TRAUMATIC INJURY TO PERIPHERAL NERVES

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EPIDEMIOLOGY OF PERIPHERAL NERVE TRAUMA

Traumatic injury to peripheral nerves results in considerable disability across the world. In peacetime, peripheral nerve injuries commonly result from trauma due to motor vehicle accidents and less commonly from penetrating trauma, falls, and industrial accidents. Of all patients admitted to Level I trauma centers, it is estimated that roughly 2 to 3% have peripheral nerve injuries.[30,36] If plexus and root injuries are also included, the incidence is about 5%.[30]

In the upper limb, the nerve most commonly reported injured is the radial nerve, followed by ulnar and median nerves.[30,36] Lower limb peripheral nerve injuries are less common, with the sciatic most frequently injured, followed by peroneal and rarely tibial or femoral nerves. Fractures of nearby bones are commonly associated, such as humeral fractures with radial neuropathy.

In wartime, peripheral nerve trauma is much more common, and much of the knowledge about peripheral nerve injury, repair, and recovery comes from experience derived in the American Civil War, World Wars I and II, and subsequent wars.[20,35,40]

Peripheral nerve injuries may be seen as an isolated nervous system injury but may also often accompany central nervous system trauma, not only compounding the disability, but making recognition of the peripheral nerve lesion problematic. Of patients with peripheral nerve injuries, about 60% have a traumatic brain injury.[30] Conversely, of those with traumatic brain injury admitted to rehabilitation units, 10 to 34% have associated peripheral nerve injuries.[7,14,39] It is often easy to miss peripheral nerve injuries in the setting of central nervous system trauma. Because the neurological history and examination is limited, early hints to a superimposed peripheral nerve lesion might be only flaccidity, areflexia, and reduced movement of a limb.

Peripheral nerve injuries are of significant import as they impede recovery of function and return to work and carry risk of secondary disabilities from falls, fractures, or other secondary injuries. An understanding of the classification, pathophysiology, and electrodiagnosis of these lesions is critical to the appropriate diagnosis, localization, and management of peripheral nerve trauma.

CLASSIFICATION OF NERVE INJURIES

For the purposes of this article, trauma is defined as injury resulting from kinetic energy applied to the nerve or limb. This includes, for example, the kinetic energy of the patient moving at high speed into a car or wall, a bullet moving through tissue with a high velocity, or a sudden stretch of a limb. Kinetic energy (KE) is proportional to the mass of the object (m) and the square of the velocity (v):

$$KE = \tfrac{1}{2}\, mv^2.$$

Thus, a doubling of the velocity (e.g., bullet velocity or motor vehicle speed) results in a fourfold increase in kinetic energy applied to the body or body part. Knife or other sharp wounds are also included in this review, though the amount of kinetic energy necessary for a significant peripheral nerve injury is probably lower. Although burns and electrical injuries also derive from high amounts of energy (thermal or electrical) applied to tissue, these injuries will not be considered here because the pathophysiology of the injury is significantly different from those wounds resulting from kinetic energy.

There are two predominant schemes that have been proposed for classification of peripheral nerve traumatic injuries: that of Seddon[35] and that of Sunderland[40] (Table 1). The former is more commonly used in the literature. Seddon has used the terms "neurapraxia," "axonotmesis," and "neurotmesis" to describe peripheral nerve injuries.[35] Neurapraxia is a comparatively mild injury with motor and sensory loss but no evidence of Wallerian degeneration. The nerve distally conducts normally. Focal demyelination and/or ischemia are thought to be the etiologies of the conduction block. Recovery may occur within hours, days, weeks, or up to a few months. Axonotmesis is commonly seen in crush injuries, nerve stretch injuries (such as from motor vehicle accidents and falls), or percussion injuries (such as from gunshot wounds). The axons and their myelin sheaths are broken, yet the surrounding stroma (i.e., the Schwann tubes, endoneurium, and perineu-

rium) remains partially or fully intact. Wallerian degeneration occurs, but subsequent axonal regrowth may proceed along the intact endoneurial tubes. Recovery ultimately depends upon the degree of internal disorganization in the nerve as well as the distance to the end organ. Sunderland's classification (see below) further divides this category. Neurotmesis describes a nerve that has been either completely severed or is so markedly disorganized by scar tissue that axonal regrowth is impossible. Examples are sharp injury, some traction injuries, and percussion injuries, or injection of noxious drugs. Prognosis for spontaneous recovery is extremely poor without surgical intervention.

Sunderland[40] uses a more subdivided scheme to describe peripheral nerve injuries, with five groups instead of three. First-degree injury represents conduction block with completely intact stroma and corresponds to Seddon's classification of neurapraxia. Prognosis is good. Second-degree injury involves transection of the axon but with completely intact endoneurium and stroma. Recovery can occur by axonal regrowth along endoneurial tubes. Third-degree injury represents transection of the axon and endoneurial tubes, but the surrounding perineurium is intact. Recovery depends upon how well the axons can cross the site of the lesion and find endoneurial tubes. Fourth degree injury involves loss of continuity of axons, endoneurial tubes, and perineurium. Individual nerve fascicles are transected, and the continuity of the nerve trunk is maintained only

Table 1. Classification systems for nerve injury.*

Seddon classification	Sunderland classification	Pathology	Prognosis
Neurapraxia	First degree	Myelin injury or ischemia	Excellent recovery in weeks to months
Axonotmesis		Axon loss Variable stromal disruption	Good to poor, depending upon integrity of supporting structures and distance to muscle
	Second degree	Axon loss Endoneurial tubes intact Perineurium intact Epineurium intact	Good, depending upon distance to muscle
	Third degree	Axon loss Endoneurial tubes disrupted Perineurium intact Epineurium intact	Poor Axonal misdirection Surgery may be required
	Fourth degree	Axon loss Endoneurial tubes disrupted Perineurium disrupted Epineurium intact	Poor Axonal misdirection Surgery usually required
Neurotmesis	Fifth degree	Axon loss Endoneurial tubes severed Perineurium severed Epineurium severed	No spontaneous recovery Surgery required Prognosis after surgery guarded

*Adapted from Dillingham.[8]

by the surrounding epineurium. Traction injuries commonly produce these types of lesions. Prognosis is usually poor without surgical intervention because of the marked internal disorganization of guiding connective tissue elements and associated scarring. Fifth-degree injury describes transection of the entire nerve trunk and is similar to Seddon's neurotmesis.

Some authors have described another degree of injury, known as sixth-degree injury.[25] This is a mixed lesion with both axon loss and conduction block occurring in some fibers. This type of lesion is probably quite common and requires skillful electrodiagnostic data collection and analysis to separate it from pure axon-loss lesions.

EFFECTS OF NEURAPRAXIA ON NERVE AND MUSCLE

As noted above, neurapraxic injuries to peripheral nerves may be due to ischemia or focal demyelination. When ischemia for a brief period (i.e., up to 6 h) is the underlying cause, there are usually no structural changes in the nerve,[15] though there may be edema in other nearby tissues.

On the other hand, in neurapraxic lesions due to focal demyelination, there are anatomical changes predominantly affecting the myelin sheath but sparing the axon. Tourniquet paralysis has been used to produce an animal model of a neurapraxic lesion,[31] though it is recognized that acute crush injuries may be different in mechanism than prolonged application of a tourniquet. In this model, anatomical changes along the nerve are most marked at the edge of the tourniquet, where a significant pressure gradient exists between the tourniquet and nontourniquet areas. The pressure gradient essentially "squeezes" out the myelin, with resulting invagination of one paranodal region into the next. As a result, there is an area of focal demyelination at the edge of the tourniquet.[31] Larger fibers are more affected than are smaller fibers.

In this area of focal demyelination, impulse conduction from one node of Ranvier to the next is slowed as current leakage occurs and the time for impulses to reach threshold at successive nodes of Ranvier is prolonged. Slowing of conduction velocity along the nerve ensues. More severe demyelination results in complete conduction block. This has been reported to occur when internodal conduction times exceed 500 to 600 μs.[33] Because there are very few sodium channels in internodal segments of myelinated nerves, conduction in demyelinated nerves cannot simply proceed slowly, as it would for normally unmyelinated nerves. Thus, sufficient demyelination

results in block of conduction rather than simply severe slowing.

There are relatively few changes in muscle as a result of neurapraxic lesions. Disuse atrophy can occur when neurapraxia is more than transient. There remains debate as to whether muscle fibrillates after a purely neurapraxic lesion (see below).

EFFECTS OF AXONOTMESIS ON NERVE AND MUSCLE

Soon after an axonal lesion, the process of Wallerian degeneration starts to occur in nerve fibers. This process is well described elsewhere[10,27] and will be only briefly reviewed here. There are changes in both the axon and the nerve cell body. In the axon, a number of changes occur in the first 2 days, including leakage of intra-axonal fluid from the severed nerve, swelling of the distal nerve segment, and subsequently disappearance of neurofibrils in the distal segment. By day 3, there is fragmentation of both axon and myelin with start of digestion of myelin components. By day 8, the axon has been digested and Schwann cells are attempting to bridge the gap between the two nerve segments. Nerve fibers may also degenerate for a variable distance proximally; depending upon the severity of the lesion, this retrograde degeneration may extend for several centimeters.

There are also a number of changes at the nerve cell body level occurring after distal nerve trauma. Initially, within the first 48 h, the Nissl bodies (the cell's endoplasmic reticulum) break apart into fine particles. By 2 to 3 weeks after injury, the cell's nucleus becomes displaced eccentrically and the nucleolus is also eccentrically placed within the nucleus. These changes may reverse as recovery occurs.

ELECTRODIAGNOSIS: TIMING OF CHANGES AND DETERMINING DEGREE OF INJURY

Optimal timing of electrodiagnostic studies will vary according to clinical circumstances. For circumstances in which it is important to define a lesion very early, initial studies at 7 to 10 days may be useful at localization and separating conduction block from axonotmesis. On the other hand, when clinical circumstances permit waiting, studies at 3 to 4 weeks postinjury will provide much more diagnostic information, because fibrillations will be apparent on needle electromyography (EMG). Finally, in cases where a nerve lesion is surgically confirmed and needle EMG is used only to document recovery, initial studies at a few months postinjury may be most useful.

Changes may be seen in the compound muscle action potential (CMAP), late responses (F and H waves), sensory nerve action potential (SNAP), and needle EMG. Each of these studies has a somewhat different time course, which should be understood in order to evaluate peripheral nerve injury; they will also vary according to the severity of nerve injury.

COMPOUND MUSCLE ACTION POTENTIAL

Neurapraxia. In purely neurapraxic lesions, the CMAP will change immediately after injury, assuming one can stimulate both above and below the site of the lesion (Fig. 1). When recording from distal muscles and stimulating distal to the site of the lesion, the CMAP should always be normal because no axonal loss and no Wallerian degeneration has occurred. Moving the site of stimulation proximal to the lesion will produce a smaller or absent CMAP, as conduction in some or all fibers is blocked. It should be remembered that amplitudes normally fall with increasing distance between stimulation and recording; hence, there is some debate about how much of a drop in amplitude is sufficient to demonstrate conduction block. Amplitude drops exceeding 20% over a 25-cm distance or less are clearly abnormal; smaller

FIGURE 1. Response of CMAP to stimulation below (left panel) and above (right panel) a nerve lesion of different types immediately (day 1) and 10 days after injury.

changes over smaller distances are likely also suggestive of an abnormality. In addition to conduction block, partial lesions also often demonstrate concomitant slowing across the lesion. This slowing may be due to either loss of faster-conducting fibers or demyelination of surviving fibers. All these changes in the CMAP will generally persist until recovery takes place, typically by no more than a few months postinjury. Most importantly, the distal CMAP will never drop in amplitude in purely neurapraxic injuries, because no axon loss or Wallerian degeneration occurs and the distal nerve segment remains excitable.

Axonotmesis and Neurotmesis. Electrodiagnostically, complete axonotmesis (equivalent to Sunderland grades 2, 3, and 4) and complete neurotmesis look the same, because the difference between these types of lesions is in the integrity of the supporting structures, which have no electrophysiological function. Thus, these lesions can be grouped together as axonotmesis for the purpose of this discussion.

Immediately after axonotmesis and for a "few days" thereafter, the CMAP and motor conduction studies look the same as those seen in a neurapraxic lesion. Nerve segments distal to the lesion remain excitable and demonstrate normal conduction, whereas proximal stimulation results in an absent or small response from distal muscles. Early on, this picture looks the same as conduction block and can be confused with neurapraxia. Hence, neurapraxia and axonotmesis cannot be distinguished until sufficient time for Wallerian degeneration in all motor fibers has occurred, typically about 9 days postinjury.[6]

After enough time has passed for Wallerian degeneration to occur, the amplitude of the CMAP elicited with distal stimulation will fall. This starts at about day 3 and is complete by about day 9.[6] The time course is, however, influenced by the length of the distal nerve segment between the lesion and the muscle, i.e., shorter segments will be associated with more rapid degeneration. Neuromuscular junction transmission fails before nerve excitability.[16,17] Thus, in complete axonotmesis at day 9, one has a very different picture from neurapraxia. There are absent responses both above and below the lesion. Partial axon-loss lesions will produce small-amplitude motor responses, with the amplitude of the CMAP roughly proportional to the number of surviving axons. One can compare side-to-side CMAP amplitudes to estimate the degree of axon loss, though inherent side-to-side variability of up to 30 to 50% limits the accuracy of the estimate. Using the CMAP
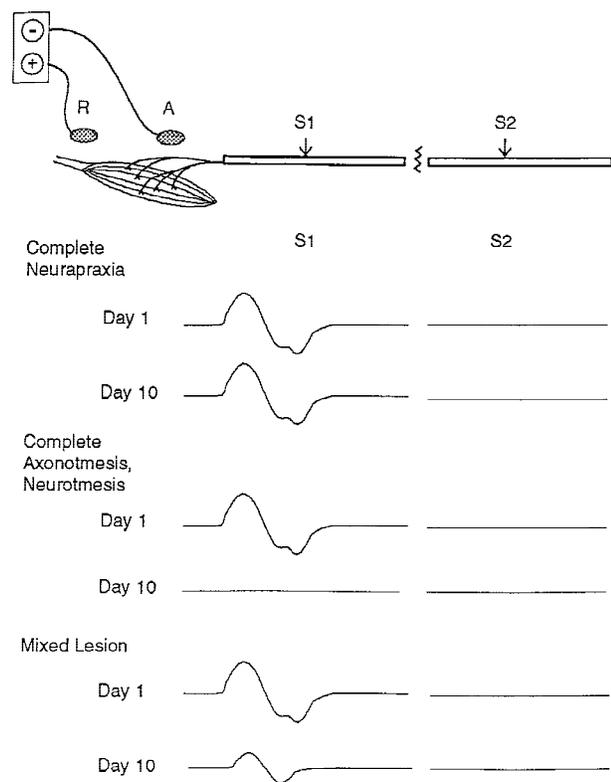
amplitude to estimate the degree of surviving axons is also most reliable only early after injury, before axonal sprouting has occurred. Use of this technique later after injury will tend to underestimate the degree of axon loss.

Mixed Lesions.   Lesions that have a mixture of axon loss and conduction block provide a unique challenge. These can usually be clarified by carefully examining amplitudes of the CMAP elicited from stimulation both above and below the lesion and by comparing the amplitude with distal stimulation with that obtained from the other side. The percentage of axon loss is best estimated by comparing the CMAP amplitude from distal stimulation with that obtained contralaterally. Of the remaining axons, the percentage with conduction block are best estimated by comparing amplitudes or areas obtained with stimulation distal and proximal to the lesion. Thus, if a 1-mV response is obtained with proximal stimulation, a 2-mV response is obtained distally, and a 10-mV response is obtained with distal stimulation contralaterally, one can deduce that probably about 80% of the axons are lost, and of the remaining 20%, half are blocked (neurapraxic) at the lesion site. As mentioned above, this analysis is most useful only in the acute phase, before reinnervation by axonal sprouting occurs.

F WAVES

F waves may change immediately after the onset of a neurapraxic lesion. In complete block, responses will be absent. However, in partial lesions, changes can be more subtle, because F waves are dependent upon only 3 to 5% of the axon population to elicit a response.[12] Thus, partial lesions may have normal minimal F-wave latencies and mean latencies, with reduced or possibly normal penetrance. Although F waves are conceptually appealing for detecting proximal lesions (e.g., brachial plexopathies), only in a few instances do they truly provide useful additional or unique information. They are sometimes useful in very early proximal lesions when conventional studies are normal because stimulation does not occur proximal to the lesion.

COMPOUND OR SENSORY NERVE ACTION POTENTIALS

Neurapraxia.   The SNAP and compound nerve action potential will show changes similar to the CMAP after focal nerve injury. In the setting of neurapraxia, there is a focal conduction block at the site of the lesion, with preserved distal amplitude. However, the criteria for establishing conduction block in sensory nerve fibers are substantially different than that

for the CMAP. When recording nerve action potentials, there is normally a greater drop in amplitude over increasing distance between stimulating and recording electrodes, due to temporal dispersion and phase cancellation.[22] Amplitude drops of 50 to 70% over a 25-cm distance are not unexpected, and it is less clear just what change in amplitude is abnormal. A large focal change over a small distance is probably significant. Slowing may also accompany partial conduction blocks, as for the CMAP. Responses elicited with stimulation and recording distal to the lesion are normal in pure neurapraxic injuries.

Axonotmesis and Neurotmesis.   Immediately after axonotmesis and for a few days thereafter, the SNAP looks the same as seen in a neurapraxic lesion. Nerve segments distal to the lesion remain excitable and demonstrate normal conduction, whereas proximal stimulation results in an absent or small response. Hence, neurapraxia and axonotmesis cannot be distinguished until sufficient time for Wallerian degeneration in all sensory fibers has occurred, typically about 11 days postinjury.[6] It takes slightly longer for sensory nerve studies to demonstrate loss of amplitude than for motor studies, i.e., 11 days versus 9 days, due to the earlier failure of neuromuscular junction transmission compared with nerve conduction.

NEEDLE ELECTROMYOGRAPHY

Neurapraxia.   The needle EMG examination in purely neurapraxic lesions will show changes in recruitment with debatable abnormalities in spontaneous activity. As mentioned earlier, there is debate as to whether fibrillation potentials are recorded after a purely neurapraxic lesion. One study of peripheral nerve lesions in baboons has failed to demonstrate fibrillations in purely neurapraxic lesions.[18] However, study of purely neurapraxic lesions in rats[5] has suggested fibrillations occur in blocked, but not denervated, muscle fibers. There are limited reports of fibrillations in humans with apparently predominantly neurapraxic nerve lesions,[43,48] but it is difficult to know whether any axon loss had occurred in these patients, because nerve conduction studies (NCSs) are not particularly sensitive for detecting minimal axon loss. Needle EMG is more sensitive for detecting motor axon loss than are NCSs, and, hence, it is easy to imagine situations in which NCSs are completely normal, but needle EMG detects minimal or mild axon loss.

Independent of whether or not the needle EMG demonstrates fibrillation potentials in neurapraxia,

the most apparent change on needle EMG will be changes in recruitment. These occur immediately after injury. In complete lesions (i.e., complete conduction block), there will be no motor unit action potentials (MUAPs). In incomplete neurapraxic lesions, there will be reduced numbers of MUAPs firing more rapidly than normal (i.e., reduced or discrete recruitment). Because no axon loss occurs in neurapraxic injuries, there will be no axonal sprouting and no changes in MUAP morphology (e.g., duration, amplitude, or phasicity) at any time after injury.

Axonotmesis and Neurotmesis. With an axon-loss lesion, needle EMG will demonstrate fibrillation potentials and positive sharp waves a number of days after injury. The time between injury and onset of fibrillation potentials will be dependent in part upon the length of the distal nerve stump. When the distal stump is short, it takes only 10 to 14 days for fibrillations to develop. With a longer distal stump (e.g., ulnar-innervated hand muscles in a brachial plexopathy), 21 to 30 days is required for full development of fibrillation potentials and positive sharp waves.[42] Thus, the electrodiagnostic medicine consultant needs to be acutely aware of the time since injury so that severity is not underestimated when a study is performed early after injury and so that development of increased fibrillation potentials over time is not misinterpreted as a worsening of the injury.

Density of fibrillation potentials and positive sharp waves is usually graded on a four-point scale. This is an ordinal scale, meaning that as numbers increase, the findings are worse. However, it is not an interval or ratio scale, i.e., 4+ is not twice as bad as 2+ or four times as bad as 1+. Moreover, 4+ fibrillation potential does not indicate complete axon loss and in fact may represent only a minority of axons lost.[3,9] Evaluation of recruitment and particularly of distally elicited CMAP amplitude is necessary before one can decide whether complete axon loss has occurred.

Fibrillation potential size will decrease over time since injury. Kraft[24] has demonstrated that fibrillations initially are several hundred microvolts in the first few months after injury. However, when lesions are more than 1 year old, they are unlikely to be more than 100 μV in size. Fibrillations will also decrease in number as reinnervation occurs, but this finding is not usually clinically useful for two reasons. First, because a qualitative or ordinal scale of fibrillation density is typically used and an accurate quantitative measurement of fibrillation density is not available, comparison of fibrillation numbers from one examination to the other is not reliable.[9] Sec-

ond, even in complete lesions, fibrillation density will eventually reduce because the muscle becomes fibrotic and the number of viable muscle fibers falls; in this case, reduction in fibrillation numbers does not predict recovery but rather muscle fibrosis.

Fibrillations may also occur after direct muscle injury as well as nerve injury. Partanen and Danner[32] have demonstrated that patients after muscle biopsy have persistent fibrillation potentials starting after 6 to 7 days and extending for up to 11 months. In patients who have undergone multiple trauma, coexisting direct muscle injury is common and can be potentially misleading when trying to localize a lesion.

When there are surviving axons after an incomplete axonal injury, remaining MUAPs are initially normal in morphology but demonstrate reduced or discrete recruitment. Axonal sprouting will be manifested by changes in morphology of existing motor units. Amplitude will increase, duration will become prolonged, and the percentage of polyphasic MUAPs will increase as motor unit territory increases.[9,11] This process occurs soon after injury. Microscopic studies demonstrate outgrowth of these nerve sprouts starting at 4 days after partial denervation.[21,27] Electrophysiological studies utilizing single-fiber EMG demonstrate increase in fiber density starting at 3 weeks postinjury.[26]

In complete lesions, the only possible mechanism of recovery is axonal regrowth. The earliest needle EMG finding in this case is the presence of small, polyphasic, often unstable MUAPs previously referred to as "nascent potentials." (This term is now discouraged because it implies an etiology; it is preferred to simply describe the size, duration, and phasicity of the MUAP.) Observation of these potentials is dependent upon establishing axon regrowth as well as new neuromuscular junctions, and this observation represents the earliest evidence of reinnervation, usually preceding the onset of clinically evident voluntary movement.[9] These potentials represent the earliest definitive evidence of axonal reinnervation in complete lesions. When performing the examination looking for new MUAPs, one must be sure to accept only "crisp," nearby MUAPs with a short rise time, because distant potentials recorded from other muscles can be deceptive.

Mixed Lesions. When there is a lesion with both axon loss and conduction block, needle EMG examination can be potentially misleading if interpreted in isolation. If, for example, a lesion results in destruction of 50% of the original axons and conduction block of the other 50%, then needle EMG will dem-

onstrate abundant (e.g., 4+) fibrillation potentials and no voluntary MUAPs. The electrodiagnostic medicine consultant should not then conclude that there is a complete axonal lesion but should instead carefully evaluate the motor NCSs to determine how much of the lesion is neurapraxic and how much axonotmetic. The important point here is to not take the presence of abundant fibrillations and absent MUAPs as evidence of complete denervation.

LOCALIZATION OF TRAUMATIC NERVE INJURIES

The localization of peripheral nerve injuries is sometimes straightforward but may be complicated by a variety of possible pitfalls. Localization is usually performed by two methods: (1) detecting focal slowing or conduction block on NCSs, or (2) assessing the pattern of denervation on needle EMG.

Localizing peripheral nerve lesions by NCSs usually requires that there be a focal slowing or conduction block as one stimulates above and below the lesion. To see such a change, there must be either focal demyelination or ischemia or the lesion should be so acute that degeneration of the distal stump has not yet occurred. Thus, lesions with partial or complete neurapraxia (due to either demyelination or ischemia) can be well localized with motor NCSs, as can very acute axonal injuries.

In pure axonotmetic or neurotmetic lesions, it is more difficult, if not impossible, to localize the lesion using NCSs. In such a case, there will be mild and diffuse slowing in the entire nerve due to loss of the fastest fibers or there will be no response at all. Conduction across the lesion site will be no slower than across other segments. In addition, provided enough time for Wallerian degeneration has elapsed (i.e., at least 9 days for motor fibers or 11 days for sensory fibers), there will be no change in amplitude as one traverses the site of the lesion. Thus, pure axon-loss lesions are not well localized along a nerve by NCSs.

There are some cases in which indirect inferences can be made about the location of purely axonal lesions. For instance, if the ulnar motor response is very small or absent and the median motor response is normal, this implies an ulnar neuropathy rather than a lower brachial plexus lesion. However, in such an instance, the site of pathology along the ulnar nerve may not be well defined. Another indirect inference that can be made based upon sensory NCSs is placement of the lesion at a preganglionic versus postganglionic location. Lesions that are proximal to the dorsal root ganglion, i.e., at the preganglionic level (proximal root, cauda equina, spinal cord) tend to have normal SNAP amplitudes, even in the setting of reduced or absent sensation.[1,41] This is a particularly poor prognostic sign when seen in the setting of possible root avulsion. On the other hand, lesions occurring distal to the dorsal root ganglion have small or absent SNAPs (when these are recorded in the appropriate distribution). Thus, SNAPs may be useful to differentiate root versus plexus or other preganglionic versus postganglionic locations. A limitation, particularly in partial lesions, is the wide variability in SNAP amplitudes seen in normal individuals. Mixed preganglionic and postganglionic lesions are also potentially difficult to interpret.

The other major electrodiagnostic method of determining the site of nerve injury is by needle EMG. Conceptually, if one knows the branching order to various muscles under study, one can determine that the nerve injury is between the branches to the most distal normal muscle and the most proximal abnormal muscle. There are, however, a number of potential problems with this approach. First, the branching and innervation for muscles is not necessarily consistent from one person to another. Sunderland[40] demonstrated a great deal of variability in branching order to muscles in the limbs, variability in the number of branches going to each muscle, and variability in which nerve or nerves supply each muscle. Thus, the typical branching scheme may not apply to the patient being studied, and, consequently, the lesion site can be misconstrued.

Second, the problem of muscle trauma and associated needle EMG findings can be misleading. As mentioned earlier, direct muscle trauma can result in positive sharp waves and fibrillations for months or longer after injury.[32] Practically speaking, this can result in erroneously proximal lesion sites or error in diagnosing more than one lesion. For example, in the setting of humeral fracture with radial neuropathy, the triceps not infrequently demonstrates fibrillation potentials, due to direct muscle trauma. However, one could be misled to localize the lesion to the axilla or higher rather than spiral groove, if the triceps findings are not recognized to come from direct muscle rather than nerve injury.

Third, the problem of partial lesions can make for misdiagnosis to more distal sites. In partial ulnar nerve lesions at the elbow, for example, the forearm ulnar innervated muscles are often spared.[4] This is thought to be at least partially due to sparing of the fascicles in the nerve that are preparing to branch to the flexor digitorum profundus and the flexor carpi ulnaris, i.e., they are in a relatively protected position. This finding could lead one to inadvertently localize the lesion to the distal forearm or wrist. Simi-

larly, a lesion involving the median nerve in the arm (above the elbow) has been reported to cause findings only in the anterior interosseous distribution.[46] Intraneural topography needs to be considered when making a diagnosis based on branching.[45]

Localization of brachial plexus lesions deserves special consideration. In such cases, it is important to differentiate injury to the root (e.g., avulsion) from plexus injuries and from multiple peripheral nerve injuries. Differentiation between root and plexus lesions is primarily accomplished by examination of the paraspinal muscles and SNAP amplitudes. Both these methods are subject to the limitations mentioned above for needle EMG and sensory NCSs. Distinguishing between plexus lesions and peripheral nerve is sometimes more complex. An intimate knowledge of brachial plexus anatomy is required to allow distinction between a peripheral nerve distribution of abnormalities and a plexus distribution. Sampling of muscles from the cord and trunk levels of the plexus (e.g., latissimus dorsi, pectoralis major, and infraspinatus) is also often helpful. Even with this knowledge, however, multiple peripheral nerve lesions (e.g., axillary and radial) can be erroneously ascribed to a single plexus insult (e.g., posterior cord).

MECHANISMS OF RECOVERY

There are several possible mechanisms of recovery after traumatic nerve injury; knowledge of these mechanisms, along with the type of nerve injury, allows estimation of the probable course of recovery.

For motor fibers, resolution of conduction block (in neurapraxic lesions), muscle fiber hypertrophy (in partial lesions), distal axonal sprouting of spared axons, and axonal regeneration from the site of injury may contribute to recovery of strength (Fig. 2).

Resolution of conduction block, whether based upon ischemia or demyelination, is probably the first mechanism to promote recovery of strength after nerve injury. Improvement after a solely ischemic lesion is relatively quick. Demyelinating injuries take longer, as remyelination over an injured segment may take up to several months,[13] depending upon the severity of demyelination and the length of the demyelinated segment.

In normal adults performing strengthening exercises, there are generally two mechanisms of increasing force production: initial neural mechanisms followed by later muscle fiber hypertrophy. The initial neural mechanisms are thought to involve improved synchronization of motor unit firing,[28,29] and they result in increased efficiency (defined as muscle force per unit of electrical activity) in the absence of
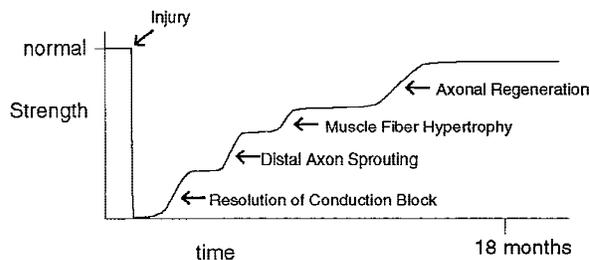

FIGURE 2. Conceptual model of strength increases after a mixed lesion.

muscle fiber changes. After several weeks, there is muscle fiber hypertrophy, which results in further increases in strength. In patients with partial nerve lesions, it is unclear how much neural changes alone (i.e., increased efficiency of firing) can contribute to increased strength because there is loss of nerve fibers. However, it is likely that working the existing muscle fibers to fatigue in the setting of partial nerve injuries produces enlargement of muscle fibers and consequent increases in force production.

Partial axonotmesis of motor nerves also produces distal sprouting of motor fibers from intact axons. It has been observed that within 4 days after nerve injury, sprouts are starting to form from intact axons, typically from distal nodes of Ranvier (nodal sprouts) or from nerve terminals (terminal sprouts) near denervated muscle fibers.[21] Partial recovery in twitch tension has been reported as early as 7 to 10 days postinjury,[2] although electrophysiological correlates (e.g., polyphasic long-duration motor units) usually take longer. Sometimes, when axonal regeneration occurs, those muscle fibers reinnervated by distal sprouting become dually innervated, i.e., by both the sprout and the newly regenerated fiber.[19,21] It is not well understood how multiple synapses are reduced.

Axonal regeneration contributes to recovery in both partial and complete axonotmesis and, with surgical approximation, neurotmesis. In complete axon-loss lesions, this is the only mechanism for muscle recovery. It is noted that in the 24 to 36 h after injury, the proximal nerve stump has started to sprout regenerating axons and these have started to penetrate the area of injury. The recovery that results from this process depends upon the degree of injury, presence of scar formation, approximation of the two nerve ends, and age of the patient.

In relatively more minor axonotmetic lesions, in which the endoneurial tubes are preserved (i.e., Sunderland second-degree injuries), the axons can traverse the segment of injury in 8 to 15 days and then regenerate along the distal nerve segment at a rate of

1 to 5 mm/day,[40] slightly faster for crush injuries than for sharp laceration.

In more severe axonotmetic lesions in which there is distortion of endoneurial tubes with or without perineurial disruption (Sunderland third and fourth degrees), prognosis for spontaneous regrowth is worse. Extensive scarring reduces the speed at which regenerating axons can traverse the lesion and, more importantly, reduces the likelihood that they will ever reach their end organs. When regrowth occurs, it may also be misdirected to the wrong end organ, such as in arm diaphragm synkinesis (also known as "the breathing shoulder"). In some of these cases, particularly when a large neuroma is present, surgical intervention is required.

In complete neurotmesis (Sunderland fifth degree), axonal regrowth will usually not occur unless the nerve ends are freed from scar tissue and surgically reapproximated. After surgical intervention, using either direct approximation or cable grafting, nerve growth will often occur along the endoneurial tubes of the distal segments. Use of cable grafts (e.g., sural nerve graft) does not provide axons directly, because these die after harvesting; the graft simply provides a pathway for axonal regrowth to occur.[34,47]

In complete lesions, recovery of motor function will also depend upon integrity of the muscle when the axon reaches it. Muscles remain viable for reinnervation for 18 to 24 months postinjury. However, past this time, due to fibrosis and atrophy, motor axon regrowth is useless, because muscle fibers are no longer viable. For example, in complete lower trunk brachial plexus lesions, recovery of hand function is usually not expected no matter how good the surgical grafting might be; it simply takes too long for axons to reach the muscle.

Recovery of sensory function is dependent upon different mechanisms than motor recovery (Fig. 3). There may be redistribution of sensory distribution after an axonal injury, such that intact fibers provide cutaneous sensation to a larger area than previously.[38,44] The mechanisms of axonal regeneration are similar to those mentioned above for motor axons. An important difference, however, is that the end organs do not degenerate after 18 to 24 months as muscle does; hence, sensory recovery may continue for a longer period of time than motor recovery does.

ELECTRODIAGNOSTIC EVALUATION OF PROGNOSIS

Determining the pathophysiology of a peripheral nerve traumatic injury can help with estimating prognosis. Those injuries that are completely or largely neurapraxic have a good prognosis for recovery within a few months (usually up to 3 months postinjury). Resolution of ischemia and remyelination should be complete by this time.

Mixed injuries typically have two or more phases of recovery (Fig. 2). The neurapraxic component resolves quickly (as above) and muscle fiber hypertrophy can provide additional recovery, but the axonal component is slower, because it depends upon distal axonal sprouting and upon axonal regeneration from the site of the lesion. Thus, patients usually experience a relatively rapid but incomplete recovery followed by a slower further recovery. Sensory recovery may proceed for a longer time than motor (Fig. 3).

Partial axon-loss lesions usually represent axonotmesis, though a partial neurotmesis (e.g., a laceration through part of the nerve) cannot always be excluded in such cases. In axonotmesis, recovery will depend upon axonal sprouting and regeneration. Hence, there will be some early recovery followed possibly by a later recovery if or when regenerating axons reach their end organs. The amplitude of the CMAP provides some guide to prognosis. In facial nerve lesions, it has been demonstrated that patients with CMAP amplitudes 30% or more of the other side have an excellent outcome, those with 10 to 30% have good but not always complete recovery, and those with <10% have a poor outcome.[37]

Complete axonotmesis and neurotmesis have the worst prognosis. Recovery depends solely upon axonal regeneration, which may or may not occur, depending upon the degree of injury to the nerve. In many cases of complete axon loss, it is not possible to know the degree of nerve injury except by surgical exploration with or without intraoperative recording or looking for evidence of early reinnervation after the lesion.

As a consequence, it is often recommended to wait 2 to 4 months and look for evidence of reinnervation in previously completely denervated muscles near the site of the lesion.[23,47] Those lesions that have some spontaneous recovery are usually treated
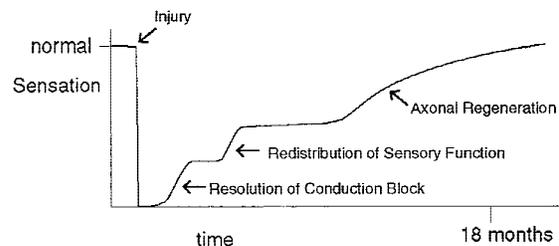

FIGURE 3. Conceptual model of sensory improvement after a mixed lesion.

conservatively, because operative repair is unlikely to improve upon natural recovery. Those with no evidence of axonal regrowth usually have operative exploration with possible grafting.

ELECTRODIAGNOSTIC EVALUATION AND SURGICAL INTERVENTION

Timing of surgical nerve reconstruction can be divided into immediate, early (1 month), delayed (3 to 6 months), and late (1 to 2 years or more). Electrodiagnostic evaluation can influence the decision to intervene at each of these time points.

Immediate reconstruction is usually indicated in patients with sharp nerve lacerations (e.g., from knife or glass wounds) and in whom the nerve ends are likely otherwise uninjured. Usually only complete injuries are considered for repair. Patients with blunt injury or extensive associated soft tissue injury are not typically operated upon immediately, because healing may be delayed. Electrodiagnostic evaluation at this time may be useful to demonstrate that the lesion is complete, but clinical examination and knowing the mechanism of injury are usually sufficient for decision making.

Early reconstruction is typically recommended for patients who have had blunt trauma or avulsion and are almost certain to have complete nerve disruption requiring surgical intervention. Patients with sharp nerve laceration who were not candidates for immediate reconstruction may also be operated upon at this time. Nerve grafting is usually indicated, because nerve ends have usually contracted and/or scars need to be resected. Electrodiagnostic evaluation in these patients is useful to demonstrate the precise site of injury as well as the extent of injury. Those patients with incomplete lesions are less likely to be operated on, because spontaneous recovery may occur, which is often better than that produced by surgical intervention.

Delayed nerve reconstruction is primarily indicated for patients in whom it is not clear whether there is any continuity of the nerve, such as with traction injuries. If continuity is in fact present, then natural recovery will likely be better than nerve grafting and surgical intervention is contraindicated. On the other hand, if there is no nerve continuity, grafting is required by 6 months so that the nerve can reinnervate the muscle before muscle degeneration occurs; grafting beyond 6 months is associated with a poorer surgical outcome. In these patients, electrodiagnostic evaluation is critical to decision making. If reinnervation has occurred in muscles just distal to the lesion, then careful observation is the more prudent course. Conversely, when there is no evidence of reinnervation in the muscles expected to first show recovery, then surgical grafting is more likely necessary.

Late nerve reconstruction, past 6 months, is usually not very helpful for motor recovery. Typically, this is more useful for pain control, such as neuroma resection. Electrodiagnostic evaluation can provide information about which nerves are in continuity but is not as critical as for those patients undergoing delayed reconstruction. When painful neuromas are present, sensory NCSs are often normal, because many axons may be intact; hence, sensory neuromas cannot be ruled out with NCSs.

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