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. Out of all patients admitted to Level I trauma centers, it is estimated that roughly 2–3% have peripheral nerve injuries. If plexus and root injuries are also included, the incidence is about 5%.

In the upper limb, the nerve most commonly reported injured is the radial nerve, followed by ulnar and median nerves. 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 our knowledge about peripheral nerve injury, repair and recovery comes from experience derived in World War I and II, and subsequent wars.

Peripheral nerve injuries may be seen as an isolated nervous system injury, but may also often accompany CNS 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. Conversely, of those with traumatic brain injury admitted to rehabilitation units, 10–34% have associated peripheral nerve injuries. It is often easy to miss peripheral nerve injuries in the setting of CNS trauma. Since the neurologic 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

There are two predominant schemes that have been proposed for classification of peripheral nerve traumatic injuries; that of Seddon

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and that of Sunderland\textsuperscript{40} (Table 1). The former is more commonly used in the literature. Seddon has used the terms \textit{neurapraxia}, \textit{axonotmesis}, and \textit{neurotmesis} to describe peripheral nerve injuries.\textsuperscript{40} \textit{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. \textit{Axonotmesis} is commonly seen in crush injuries. The axons and their myelin sheaths are broken, yet the surrounding stroma (i.e. the endoneurium, perineurium, and epineurium) 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 (below) further divides this category. \textit{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 or injection of noxious drugs. Prognosis for spontaneous recovery is extremely poor without surgical intervention. Sunderland\textsuperscript{40} uses a more subdivided scheme to describe peripheral nerve injuries, with five groups instead of three.

### Table 1 Classification systems for nerve injury

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<thead>
<tr>
<th>Seddon Classification</th>
<th>Sunderland Classification</th>
<th>Pathology</th>
<th>Prognosis</th>
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<tr>
<td>Neurapraxia</td>
<td>First Degree</td>
<td>Myelin Injury or Ischemia</td>
<td>Excellent recovery in weeks to months</td>
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<tr>
<td>Axonotmesis</td>
<td></td>
<td>Axons Disrupted Variable Stromal Disruption</td>
<td>Good to poor, depending upon integrity of supporting structures and distance to muscle</td>
</tr>
<tr>
<td>Second Degree</td>
<td>Axons Disrupted</td>
<td>Endoneurial Tubes Intact Perineurium Intact</td>
<td>Good, depending upon distance to muscle</td>
</tr>
<tr>
<td>Third Degree</td>
<td>Axons Disrupted</td>
<td>Endoneurial Tubes Intact Perineurium Intact</td>
<td>Poor</td>
</tr>
<tr>
<td>Fourth Degree</td>
<td>Axons Disrupted</td>
<td>Axonal misdirection</td>
<td>Surgery may be required</td>
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<tr>
<td>Neurotmesis</td>
<td>Fifth Degree</td>
<td>Axon Disrupted</td>
<td>Poor</td>
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<tr>
<td></td>
<td>Endoneurial Tubes Disrupted</td>
<td>Axonal misdirection</td>
<td>Surgery usually required</td>
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<td></td>
<td>Perineurium Disrupted</td>
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<td>Epineurium Intact</td>
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<td></td>
<td>Epineurium Disrupted</td>
<td>No spontaneous recovery</td>
<td>Surgery required</td>
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<td>Prognosis after surgery guarded</td>
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Adapted from Dillingham.\textsuperscript{40}

Electrodiagnosis: Timing of Changes and Determining Degree of Injury

1. The Compound Motor Action Potential

**Neurapraxia:** In purely neurapraxic lesions, the compound muscle action potential (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 since no axonal loss and no Wallerian degeneration has occurred. Moving 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 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 post injury. Most importantly, the distal CMAP will never drop in amplitude in purely neurapraxic injuries, since no axon loss or Wallerian degeneration occurs and the distal nerve segment remains normally excitable.

**Axonotmesis and Neurotmesis:** Electrodagnostically, complete axonotmesis (equivalent to Sunderland grades 2, 3 and 4) and complete neurotmesis look the same, since the difference between these types of lesions is in the integrity of the supporting structures, which have no electrophysiologic 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 neurapraxia lesion. Nerve segments distal to the lesion remain excitable and demonstrate normal conduction while 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 can not be distinguished until sufficient time for Wallerian degeneration in all motor fibers has occurred, typically about 9 days post injury. 4

As Wallerian degeneration occurs, the amplitude of the CMAP elicited with distal stimulation will fall. This starts at about day 3 and is complete by about day 9. 4 Neuromuscular junction transmission fails before nerve excitability. 5,16 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 30–50% limits the accuracy of the estimate. Using the CMAP amplitude to estimate the

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**Fig. 1** Diagrammatic representation of changes in the compound muscle action potential (CMAP) after neurapraxia.

**Fig. 2** Diagrammatic representation of changes in the compound muscle action potential (CMAP) after axonotmesis and neurotmesis.
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 which have a mixture of axon loss and conduction block provide a unique challenge. These can usually be sorted out by carefully examining amplitudes of the CMAP elicited from stimulation both above and below the lesion and by comparing the amplitude with distal stimulation to 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 (Fig. 3).

2. **Compound or Sensory Nerve Action Potentials**

**Neurapraxia:** The sensory nerve action potential (SNAP) and compound nerve action potential (CNAP) 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. Amplitude drops of 50-70% 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, the SNAP looks the same as seen in a neurapraxic lesion. Nerve segments distal to the lesion remain excitable and demonstrate normal conduction while proximal stimulation results in an absent or small response. Hence neurapraxia and axontomesis cannot be distinguished until sufficient time for Wallerian degeneration in all sensory fibers has occurred, typically about 11 days post injury.

It takes slightly longer for sensory nerve studies to demonstrate loss of amplitude than for motor studies, i.e. 11 days vs. 9 days, due to the earlier failure of neuromuscular junction transmission compared to nerve conduction.

3. **Needle Electromyography**

**Neurapraxia:** The needle EMG examination in purely neurapraxic lesions will show neurogenic 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 neuapraxic lesion. One study of peripheral nerve lesions in baboons has failed to demonstrate fibrillations in purely neuapraxic lesions\(^{17}\). On the other hand, study of purely neuapraxic lesions in rats,\(^ {39} \) has suggested fibrillations occur in blocked, but not denervated, muscle fibers. There are limited reports of fibrillations in humans with apparently predominantly neuapraxic nerve lesions,\(^ {33,40} \) but it is difficult to know whether or not any axon loss had occurred in these patients, since nerve conduction studies are not sensitive for detecting minimal axon loss. Needle EMG is more sensitive for detecting motor axon loss than nerve conduction studies, and hence it is easy to imagine situations in which nerve conduction studies are within normal limits, 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. In incomplete neurapraxic lesions, there will be reduced numbers of motor unit action potentials firing more rapidly than normal (i.e. reduced or discrete recruitment). Recruitment changes alone are not specific for neurapraxia or axon loss.

Since 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) anytime after injury.

**Axonotmesis and Neurotmesis:** A number of days after an axon loss lesion, needle EMG will demonstrate fibrillation potentials and positive sharp waves. The time between injury and onset of fibrillation potentials will be dependent in part upon the length of distal nerve stump.

When the lesion is distal and the distal stump is short, it takes only 10–14 days for fibrillations to develop. With a proximal lesion and a longer distal stump (e.g. ulnar innervated hand muscles in a brachial plexopathy), 21–30 days are required for full development of fibrillation potentials and positive sharp waves.\(^ {43} \) Thus, the electromyographer 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 also so that development of increased fibrillation potentials over time is not misinterpreted as a worsening of the injury.

Fibrillation and positive sharp wave density are usually graded on a 1–4 scale. This is an ordinal scale, meaning that as numbers increase findings are worse. However it is not an interval or ratio scale, i.e. 4+ is not twice as bad as 2+ or 4 times as bad as 1+. Moreover, 4+ fibrillation potentials does not reflect complete axon loss, and in fact may represent only a minority of axons lost.\(^ {39,49} \) Evaluation of recruitment and particularly of distally elicited CMAP amplitude are necessary before one can decide on whether or not 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 over 100 μV in size. Fibrillations will also decrease in number as reinnervation occurs, however this finding is not usually clinically useful for two reasons. First, since 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.\(^ {9} \) Second, even in complete lesions, fibrillation density will eventually reduce since the muscle becomes fibrotic and the number of viable muscle fibers falls; in this case, reduc-
tion 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\(^{12}\) have demonstrated that patients after muscle biopsy have persistent fibrillation potentials starting after 6–7 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.\(^{2,12,17}\) Electrophysiologic studies utilizing single fiber EMG demonstrates increase in fiber density starting at 3 weeks post injury.\(^{26}\)

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 motor unit potentials previously referred to as "nascent potentials." 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 motor unit potentials, one must be sure to accept only "crisp", nearby motor unit potentials with a short risetime, since distant potentials recorded from other muscles can be deceptive and could erroneously suggest intact innervation.

**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 demonstrate abundant (e. g. 4+) fibrillation potentials and no voluntary MUAPs. The electromyographer should not then conclude that there is a complete axonal lesion, but should instead carefully evaluate the motor nerve conduction studies to figure out how much of the lesion is neuapraxic and how much axonotmetic. The important point here is to not take the presence of abundant fibrillations and absent voluntary MUAPs as evidence of complete denervation.

**Localization of Traumatic Nerve Injuries**

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

Localizing peripheral nerve lesions by nerve conduction studies 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 either be 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 neuapraxia (due to either demyelination or ischemia) can be well localized with motor nerve conduction studies, as can very acute axonal injuries.

In pure axonotmetic or neurotmetic lesions, it is more difficult if not impossible to localize the
lesion using nerve conduction studies. 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 nerve conduction studies.

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 nerve conduction studies is placement of the lesion at a pre vs. post ganglionic location. Lesions that are proximal to the dorsal root ganglion, i.e. at the pre-ganglionic level (proximal root, cauda equina, spinal cord) tend to have normal sensory nerve action potential amplitudes, even in the setting of reduced or absent sensation. This is a particularly bad 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 vs. plexus or other pre-vs. post-ganglionic locations. A limitation, particularly in partial lesions, is the wide variability in SNAP amplitudes seen in normal individuals. Mixed pre-and post-ganglionic 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 has 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. 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 mislead 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. This is thought 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 distally to the distal forearm or wrist. Similarly, a lesion involving the
median nerve in the arm (above the elbow) has been reported to cause findings only in the anterior interosseous distribution.\textsuperscript{40} Intraneuronal topography needs to be considered when making a diagnosis based on branching.\textsuperscript{43}

**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 three months post injury). Resolution of ischemia and remyelination should be complete by this time.

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

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. Thus 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 10–30% have good but not always complete recovery, and those with < 10% have a poor outcome.\textsuperscript{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 2–4 months and look for evidence of reinnervation in previously completely denervated muscles near the site of the lesion.\textsuperscript{23,47} Those lesions that have some spontaneous recovery are usually treated conservatively since operative repair is unlikely to improve upon natural recovery. Those with no evidence of axonal regrowth usually have operative exploration with possible grafting.

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**References**

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29) Moritani T, de Vries HK: Neural factors versus hypertrophy in the time course of muscle strength gain. Am J Phys Med 1979; 58: 115–130
30) Noble J, Munro, CA, Prasad VSSV, Midha R: Analysis of upper and lower extremity peripheral nerve injuries in a population of patients with multiple injuries. J Trauma 1998; 45: 116-122
42) Thesleff S: Physiological effects of denervation of muscle. Ann NY Acad Sci 1974; 228: 89–103