1 Approach to Nerve Conduction Studies and Electromyography

Electrodiagnostic (EDX) studies play a key role in the evaluation of patients with neuromuscular disorders. Among these studies are included nerve conduction studies (NCSs), repetitive nerve stimulation, late responses, blink reflexes, and needle electromyography (EMG), in addition to a variety of other specialized examinations. *NCSs and needle EMG form the core of the EDX study*. They are performed first, and usually yield the greatest diagnostic information. NCSs and needle EMG are complementary, and therefore are always performed together and during the same setting. Performed and interpreted correctly, EDX studies yield critical information about the underlying neuromuscular disorder and allow use of other laboratory tests in an appropriate and efficient manner. Likewise, the information gained from EDX studies often leads to specific medical or surgical therapy. For example, a patient with a peripheral neuropathy clinically, who is subsequently found to have an acquired demyelinating neuropathy with conduction blocks on EDX studies, most often has a potentially treatable condition.

In practice, EDX studies serve as an extension of the clinical examination and should always be considered as such. Accordingly, a directed neurologic examination should always be performed before EDX studies in order to identify key clinical abnormalities and establish a differential diagnosis. With numerous nerves and literally hundreds of muscles available, it is neither desirable for the patient nor practical for the electromyographer to study them all. *In each case, the study must be individualized, based on the neurologic examination and differential diagnosis, and modified in real time as the study progresses and further information is gained.*

NCSs and EMG are most often used to diagnose disorders of the peripheral nervous system (Figure 1–1, Box 1–1). These include disorders affecting the primary motor neurons (anterior horn cells), primary sensory neurons (dorsal root ganglia), nerve roots, brachial and lumbosacral plexuses, peripheral nerves, neuromuscular junctions, and muscles. In addition, these studies may provide useful diagnostic information when the disorder arises in the central nervous system (e.g., tremor or upper motor neuron weakness). Occasionally, information from the EDX study is so specific that it suggests a precise etiology. In most cases, however, the exact etiology cannot be defined based on EDX studies alone.

LOCALIZATION OF THE DISORDER IS THE MAJOR AIM OF THE ELECTRODIAGNOSTIC STUDY

The principal goal of every EDX study is to localize the disorder. The differential diagnosis is often dramatically narrowed once the disorder has been localized. Broadly speaking, the first order of localization is whether the disorder is neuropathic, myopathic, a disorder of neuromuscular transmission, or a disorder of the central nervous system (CNS). For example, in patients with pure weakness, EDX studies can be used to localize whether the disorder is caused by dysfunction of the motor neurons/

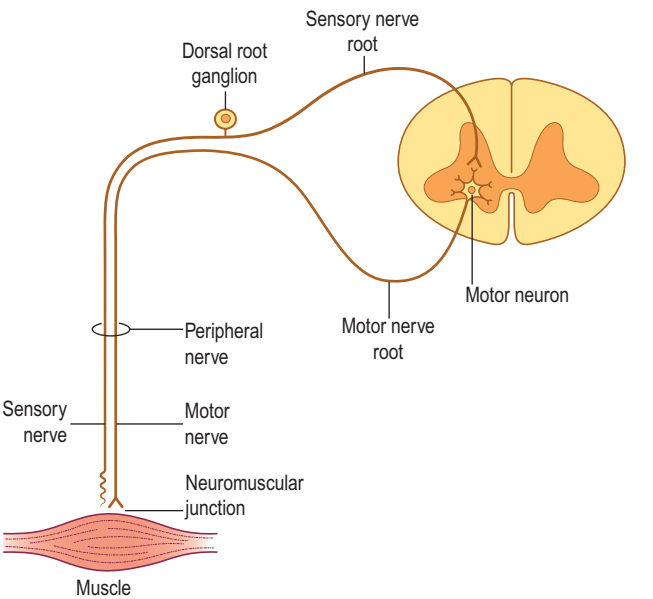

FIGURE 1–1 Elements of the peripheral nervous system. Note that the primary motor neuron resides within the spinal cord, whereas the primary sensory neuron, the dorsal root ganglion, lies outside the spinal cord. The dorsal root ganglion is a bipolar cell. Its proximal process forms the sensory nerve root; the distal process becomes the peripheral sensory nerve.

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axons, neuromuscular junctions, muscles, or has a central etiology. The pattern of nerve conduction and especially EMG abnormalities usually can differentiate among these possibilities and guide subsequent laboratory investigations. For example, a patient with proximal muscle weakness may have spinal muscular atrophy (i.e., a motor neuron disorder), myasthenic syndrome (i.e., a neuromuscular junction disorder), or polymyositis (i.e., a muscle disorder), among other disorders, including those with central etiologies (e.g., a parasagittal frontal lesion). EDX studies can easily differentiate among these conditions, providing key information to guide subsequent evaluation and treatment, which differ markedly among these diseases.

Box 1–1. Disorders of the Peripheral Nervous System

- Motor neuronopathy
  - Amyotrophic lateral sclerosis
  - Spinal muscular atrophy
  - Infectious (poliomyelitis, West Nile virus)
  - Monomelic amyotrophy
- Sensory neuronopathy
  - Paraneoplastic
  - Autoimmune
  - Toxic
  - Infectious
- Radiculopathy
  - Disk herniation
  - Spondylosis
  - Neoplastic
  - Infarction
  - Infectious
  - Inflammatory
- Plexopathy
  - Radiation induced
  - Neoplastic
  - Entrapment
  - Diabetic
  - Hemorrhagic
  - Inflammatory
- Neuropathy
  - Entrapment
  - Polyneuropathy
    - Demyelinating
    - Axonal
  - Mononeuritis multiplex
- Neuromuscular junction disorders
  - Myasthenia gravis
  - Lambert–Eaton myasthenic syndrome
  - Botulism
  - Toxic
  - Congenital
- Myopathy
  - Inherited
    - Muscular dystrophy
    - Congenital
    - Metabolic
  - Acquired
    - Inflammatory
    - Toxic
    - Endocrine
    - Infectious

Once the localization is determined to be neuropathic, myopathic, a disorder of the NMJ or of the CNS, EDX studies can usually add other important pieces of information to localize the problem further (Figure 1–2). For instance, the differential diagnosis of a patient with weakness of the hand and numbness of the fourth and fifth fingers includes lesions affecting the ulnar nerve, lower brachial plexus, or C8-T1 nerve roots. If EDX studies demonstrate an ulnar neuropathy at the elbow, the differential diagnosis is limited to a few conditions, and further diagnostic studies can be directed in a more intelligent manner. In this situation, for instance, there is no need to obtain a magnetic resonance imaging scan of the cervical spine to assess a possible cervical radiculopathy because the EDX studies demonstrated an ulnar neuropathy at the elbow as the source of the patient's symptoms.

In a patient with a CNS disorder who is mistaken as having a peripheral disorder, the EDX study often correctly suggests that the localization is central. For example, transverse myelitis may mimic Guillain–Barré syndrome, or a small acute cortical stroke may mimic the pattern of a brachial plexopathy. In settings such as these, the EDX study is often the first test to suggest that the correct localization is central rather than peripheral.

Neuropathic Localization

Neuropathic is probably the most common localization made on EDX studies. Neuropathic literally means a disorder of the peripheral nerves. However, in common usage, it includes the primary sensory and motor neurons as well. EDX studies are particularly helpful in neuropathic conditions. First, in conjunction with the history and examination, they can usually further localize the disorder to the neurons, roots, plexus, or peripheral nerve. In the case of peripheral nerve, further localization is usually possible to a single nerve (mononeuropathy), multiple individual

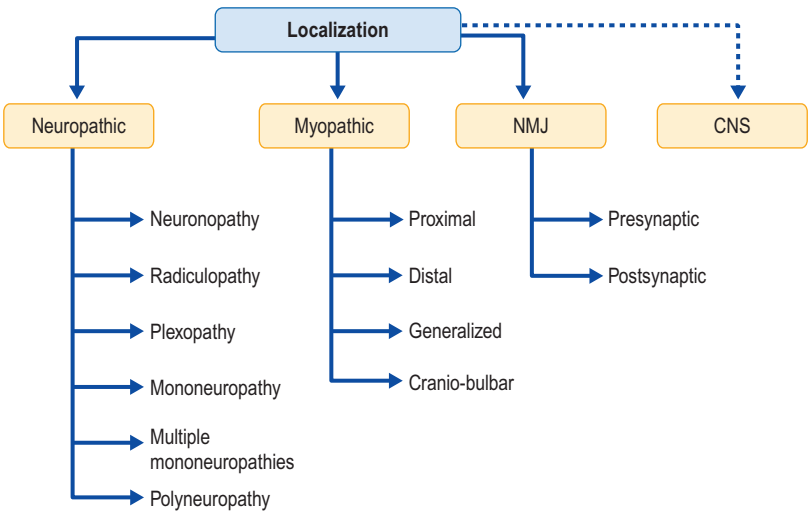

FIGURE 1–2 Possible localizations determined from the electrodiagnostic study.

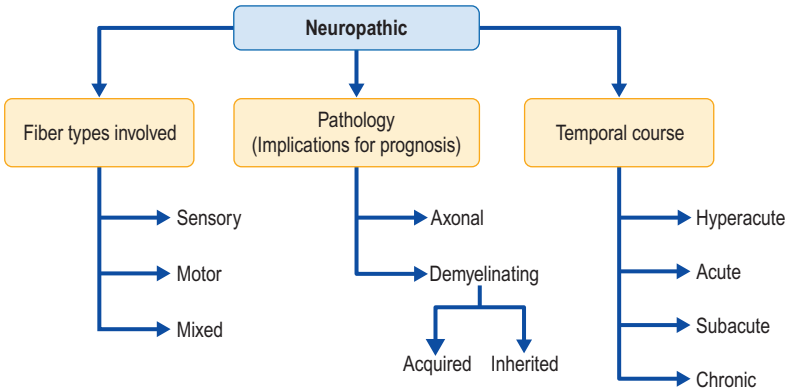

FIGURE 1–3 Key EDX findings in a neuropathic localization.

nerves (mononeuropathy multiplex) or all nerves (polyneuropathy). In the case of a single nerve, the exact segment of nerve responsible for the problem may be localized in some cases.

In the case of neuropathic lesions, EDX studies often yield further key information, including the fiber types involved, the underlying pathophysiology, and the temporal course of the disorder (Figure 1–3).

Information About the Fiber Types Involved and the Underlying Nerve Pathophysiology can be Gained, which then Further Narrows the Differential Diagnosis

In the case of neuropathic disorders, the involved fiber types and the underlying pathology can usually be determined. First, EDX studies are more sensitive than the clinical examination in determining which fiber types are involved: motor, sensory, or a combination of the two. Sensorimotor polyneuropathies are common and suggest a fairly large differential diagnosis. On the other hand, predominantly motor or predominantly sensory neuropathies are rare and suggest a much more limited set of disorders. For instance, a patient with numbness in the hands and feet and diminished reflexes may be diagnosed with a peripheral neuropathy. However, if EDX studies demonstrate abnormal sensory nerve conductions with completely normal motor nerve conductions and needle EMG, then the differential diagnosis changes from a peripheral neuropathy to a pure sensory neuropathy or neuronopathy, which has a much more limited differential diagnosis.

Second, EDX studies often can define whether the underlying pathophysiology is demyelination or axonal loss. Although most demyelinating neuropathies have some secondary axonal loss and many axonal loss neuropathies have some secondary demyelination, EDX studies usually can differentiate between a primary demyelinating and a primary axonal neuropathy. Because EDX studies usually can make this differentiation quickly and non-invasively, nerve biopsy is essentially never required to make this determination. Furthermore, the differentiation between primary axonal and primary demyelinating pathology is of considerable diagnostic and prognostic importance, especially in the case of polyneuropathies. The vast majority of polyneuropathies are associated with primary axonal degeneration, which has an extensive differential diagnosis. In contrast, the number of true electrophysiologic primary demyelinating neuropathies is extremely small. They are generally subdivided into those that are inherited and those that are acquired. EDX studies can typically make that determination as well. The finding of an unequivocal primary demyelinating polyneuropathy on EDX studies often leads quickly to the correct diagnosis and, in the case of an acquired demyelinating polyneuropathy, often suggests a potentially treatable disorder.

Assessing the Degree of Axonal Loss versus Demyelination has Implications for Severity and Prognosis

A nerve that has sustained a demyelinating injury often can remyelinate in a very short time, usually weeks. However, if there has been substantial axonal loss, whether primary or secondary, the prognosis is much more guarded. The rate of axonal regrowth is limited by the rate of slow axonal transport, approximately 1 mm per day. Clinically, axonal loss lesions can rarely be differentiated from demyelinating ones, especially in the acute setting. For example, in a patient who awakens with a complete wrist and finger drop, the etiology usually is compression of the radial nerve against the spiral groove of the humerus. However, the paralysis could result from either conduction block (i.e., demyelination) or axonal loss, depending on the severity and duration of the compression. Clinically, both conditions appear the same. Nevertheless, if the injury is due to axonal loss, it has a much worse prognosis and a longer rehabilitation time to recovery than a similarly placed lesion that is predominantly demyelinating in nature. EDX studies can readily differentiate axonal from demyelinating lesions.

Assessment of the Temporal Course can Often be Made

For neuropathic conditions, there is an orderly, temporal progression of abnormalities that occurs in NCSs and needle EMG. A combination of findings often allows differentiation among hyperacute (less than one week), acute (up to a few weeks), subacute (weeks to a few months), and chronic (more than a few months) lesions. The time course suggested by the EDX findings may alter the

impression and differential diagnosis. For example, it is not uncommon for a patient to report an acute time course to his or her symptoms, whereas the EDX studies clearly indicate that the process has been present for a longer period of time than the patient has been aware of.

Conversely, the temporal course described by the patient may impact the interpretation of the EDX findings. For instance, the finding of a normal ulnar sensory nerve action potential recording the little finger, in a patient with numbness of the little finger, has very different implications depending on the time course of the symptoms. If the symptoms are truly less than one week in duration, the normal ulnar sensory response could indicate an ulnar neuropathy (with incomplete wallerian degeneration), a proximal demyelinating lesion, or a lesion at the level of the nerve root or above. On the other hand, if the symptoms have been present for several weeks or longer, the same finding would indicate either a proximal demyelinating lesion or a lesion at the level of the nerve root or above. *These temporal changes underscore the electromyographer's need to know the clinical time course of symptoms and signs in order to ensure an accurate interpretation of any electrophysiologic abnormalities.*

Myopathic Localization

In the case of myopathic (i.e., muscle) disease, EDX studies can also add key information to further define the condition (Figure 1–4). First, the distribution of the abnormalities may suggest a particular diagnosis: are they proximal, distal or generalized? Most myopathies preferentially affect proximal muscles. Few myopathies, such as myotonic dystrophy type I, affect distal muscles. Some very severe myopathies (e.g., critical illness myopathy) can be generalized. In rare myopathies, there is prominent bulbar weakness; accordingly, EDX abnormalities may be most prominent in the bulbar muscles. Most myopathies are fairly symmetric; the finding of asymmetry either clinically and/or on EDX studies can be very helpful in narrowing the differential diagnosis. For example, inclusion body myositis may present asymmetrically, whereas polymyositis and dermatomyositis do not.

Second, the presence of spontaneous activity on needle EMG is helpful in limiting the differential diagnosis and suggesting certain underlying pathologies. Most myopathies are bland with little or no spontaneous activity. However, myopathies which are inflammatory, necrotic and some which are toxic may be associated with active denervation. In addition, other myopathies may have prominent myotonic discharges at rest. The presence of myotonic discharges in a myopathy markedly narrows the differential diagnosis to only a few possible disorders.

Lastly is the issue of the temporal course. Although this determination is more challenging than with neuropathic lesions, in some myopathies, a determination can be made if the myopathy is acute, subacute, or chronic, a finding which again narrows the differential diagnosis.

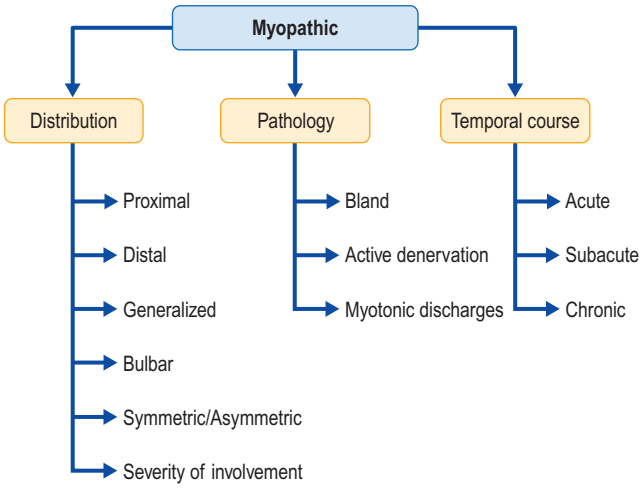

FIGURE 1–4 Key EDX findings in a myopathic localization.

Neuromuscular Junction Localization

Disorders of the neuromuscular junction (NMJ) are distinctly uncommon. However, when they occur, EDX studies not only help in identifying them, but can add other key pieces of information (Figure 1–5). First is the distribution of the abnormalities on EDX testing: are they proximal, bulbar or generalized? For instance, myasthenia gravis preferentially affects oculobulbar muscles and then proximal muscles on EDX studies, whereas myasthenic syndrome is a generalized disorder on EDX studies, although clinically it has a predilection for proximal muscles.

Broadly speaking, the underlying pathology can be divided into pre-synaptic and post-synaptic disorders. EDX studies are usually very good at making this determination. Myasthenia gravis is the prototypic post-synaptic disorder, whereas myasthenic syndrome and botulism target the presynaptic junction.

Lastly is the issue of the etiology of the NMJ disorder, whether it is acquired or inherited. Almost all NMJ disorders are acquired. However, there are rare inherited NMJ disorders. In some of these, there may be unique findings on EDX testing that suggest one of these rare disorders.

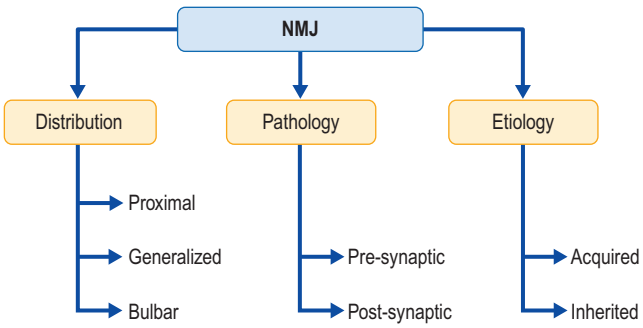

FIGURE 1–5 Key EDX findings in a neuromuscular junction localization.

Box 1–2. Patient Encounter

1. Take a brief history and perform a directed physical examination
2. Formulate a differential diagnosis
3. Formulate a study based on the differential diagnosis
4. Explain the test to the patient
5. Perform the nerve conduction studies and modify which nerve conduction studies to add based on the findings as the test proceeds
6. Perform the needle electromyography study and modify which additional muscles to sample, based on the findings as the test proceeds

PATIENT ENCOUNTER

Every EDX study begins with a *brief* history and *directed* physical examination (Box 1–2). *This point cannot be overemphasized*. Some may (incorrectly) argue that the history and clinical exam are not part of the EDX exam, and that the EDX needs to stand on its own. Nothing could be further from the truth. One is not expected to perform the same detailed history and physical examination that is done in the office consultation setting. *However*, before starting every study, the EDX physician must know some basic facts:

- What are the patient's symptoms?
- How long have they being going on?
- Is there any important past medical history (e.g., diabetes, history of chemotherapy, etc.)?
- Is there muscle atrophy?
- What is the muscle tone (normal, decreased or increased)?
- Is there weakness and, if so, where is it and how severe is it?
- What do the reflexes show (normal, decreased or increased)?
- Is there any loss of sensation and, if so, what is the distribution; what modalities are disturbed (e.g., temperature, pain, vibration, etc.)?

The duration, type, and distribution of symptoms, along with the physical examination, help determine the differential diagnosis, which in turn is used to plan the EDX studies. The EDX study is planned only after the differential diagnosis is determined. For instance, the EDX evaluation of a patient with slowly progressive proximal weakness is very different from that of a patient with numbness and tingling of the fourth and fifth fingers. In the former case, the differential diagnosis includes disorders of the anterior horn cell, motor nerve, neuromuscular junction, or muscle. In the latter case, the differential diagnosis includes an ulnar neuropathy at its various entrapment sites, a lower trunk brachial plexus lesion, or cervical radiculopathy. The EDX plan includes which nerves and muscles to study and whether specialized tests, such as repetitive nerve stimulation, may be helpful. The study can always be amended as the testing proceeds. Before beginning, however, one should first explain to the patient in simple terms what the test involves. Many patients are very anxious about the examination and may have slept poorly or not at all the night before the EDX study. A simple explanation, both before the test begins and while it is ongoing, can greatly reduce a patient's anxiety.

After the test is explained to the patient, the NCSs are performed first, followed by the needle EMG. A proper balance must be maintained among obtaining a thorough study, collecting the necessary information to answer the clinical question, and minimizing patient discomfort. If performed correctly, nearly all NCSs and needle EMG can be completed within 1.0 to 1.5 hours. Rarely, a longer study is needed if specialized tests such as repetitive nerve stimulation are performed in addition to the standard studies. There clearly is a limit to what most patients can tolerate. The electromyographer should always remember the Willy Sutton rule concerning robbing banks: "Go where the money is." If there is any question as to whether a patient will tolerate the entire examination, the study should begin with the area of interest. For instance, in the patient with numbness and tingling of the fourth and fifth fingers, the ulnar motor and sensory studies should be done first. Likewise, needle EMG examination of the ulnar-innervated muscles, as well as the C8-T1 non-ulnar-innervated muscles, are of most interest in such a patient. Plan ahead and consider which nerve conduction studies and needle examination of which muscles should be performed first, in case the patient can tolerate only one or two nerve conductions or examination of only a few muscles by EMG.

CARDINAL RULES OF NERVE CONDUCTION STUDIES AND ELECTROMYOGRAPHY

EDX studies rely on the physician's ability to pay meticulous attention to technical details during the study while keeping in mind the bigger picture of why the study is being performed. As more data are obtained, the study must be analyzed in real time and the test altered as needed. Analysis of online results gives the electromyographer the opportunity to modify the strategy as the testing proceeds, an opportunity that is lost once the patient has left the laboratory. The following cardinal rules of EDX studies should always be kept in mind while an EDX study is being performed (Figure 1–6):

1. *NCSs and EMG are an extension of the clinical examination.* NCSs and EMG cannot be performed without a good clinical examination. Every examination must be individualized based on the patient's symptoms and signs and the resulting differential diagnosis. If marked abnormalities are found on electrophysiologic testing in the same distribution where the clinical examination is normal, either the clinical examination or the electrophysiologic testing must be called into question. One usually finds that

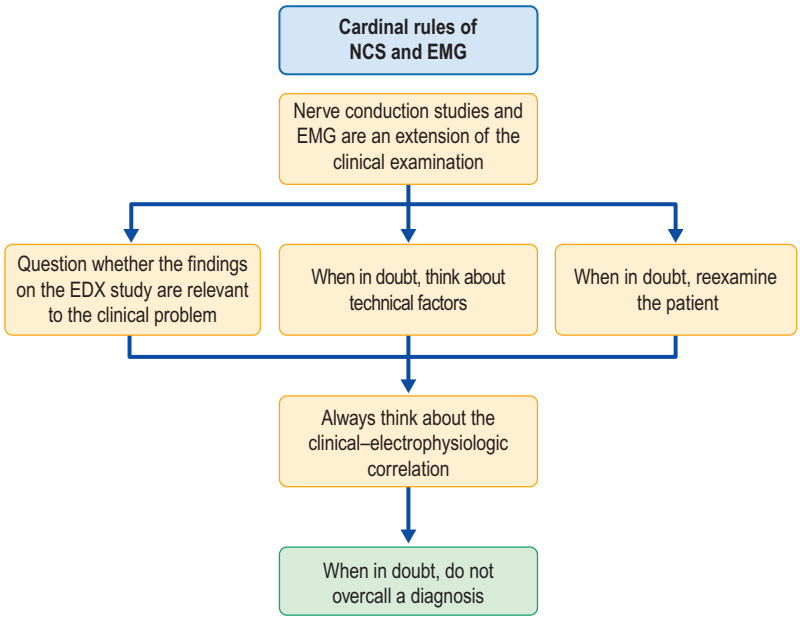

FIGURE 1–6 Cardinal rules of nerve conduction studies and electromyography.

the better the clinical examination, the better the differential diagnosis, and thus the more clearly directed the EDX studies will be.

2. When in doubt, always think about technical factors. EDX studies rely upon collecting and amplifying very small bioelectric signals in the millivolt and microvolt range. Accomplishing this is technically demanding; a large number of physiologic and non-physiologic factors can significantly interfere with the accuracy of the data. Accurate NCSs and EMG depend on intact equipment (e.g., EMG machine, electrodes, and stimulator), as well as correct performance of the study by the electromyographer. Technical problems can easily lead to absent or abnormal findings. Failure to recognize technical factors that influence the EDX study can result in type I errors (i.e., diagnosing an abnormality when none is present), and type II errors (i.e., failing to recognize an abnormality when one is present). Although both are important, type I errors are potentially more serious (e.g., the patient is labeled with an abnormal EDX study result, such as neuropathy, when the "abnormality" on the EDX testing is simply due to unrecognized technical errors). Such faulty diagnoses can lead to further inappropriate testing and treatment. If there is an unexpected abnormal EDX finding that does not fit the clinical examination, the lack of a clinical–electrophysiologic correlation should suggest a technical problem. For instance, if a routine sural nerve sensory conduction study shows an absent potential but the patient has a normal sensory examination of the lateral foot (i.e., sural territory), one should suspect a technical problem (e.g., improper electrode placement or too low stimulus intensity). If the data are not technically accurate, then correct data interpretation can never occur, either at the time of the study or later by the treating physician.
3. *When in doubt, reexamine the patient.* This is essentially an extension of cardinal rule number 1. In the example given with rule number 2, if the sural sensory response is absent after all possible technical factors have been corrected, the clinician should reexamine the patient. If the patient has clear loss of vibration at the ankles, there is less concern about an absent sural sensory response. If the patient's sensory examination is normal on reexamination, the absent sensory response does not fit the clinical findings, and technical factors should be investigated further.
4. *EDX findings should be reported in the context of the clinical symptoms and the referring diagnosis.* In every study, electrophysiologic abnormalities must be correlated with the clinical deficit. Because electrophysiologic studies are quite sensitive, it is not uncommon for the electromyographer to discover mild, subclinical deficits of which the patient may not be aware. For example, a diabetic patient referred to the EMG laboratory for polyneuropathy may show electrophysiologic evidence of a superimposed ulnar neuropathy but have no symptoms of such. Accordingly, the electromyographer should always report any electrophysiologic abnormality in the context of its clinical relevance so that it can be properly interpreted.
5. *When in doubt, do not overcall a diagnosis.* Because electrophysiologic tests are very sensitive, mild, subclinical, and sometimes clinically insignificant findings often appear on EDX testing. This occurs partly because of the wide range of normal values,

which vary with the nerve and muscle being tested. In addition, there are a variety of physiologic and non-physiologic factors that may alter the results of both NCSs and EMG, despite attempts to control for them. These factors, often when combined, may create minor abnormalities. Such minor abnormalities should not be deemed relevant unless they correlate with other electrophysiologic findings and, most importantly, with the clinical history and examination. It is a mistake to overcall an electrophysiologic diagnosis based on minor abnormalities or on findings that do not fit together well. Sometimes, the clinical or electrophysiologic diagnosis is not clear-cut and a definite diagnosis cannot be reached.

Occasionally, NCSs and EMG are clearly and definitely abnormal but a precise diagnosis still cannot be determined. For example, consider the patient whose clinical history and examination suggest an ulnar neuropathy at the elbow. The EDX study often demonstrates abnormalities of the ulnar nerve in the absence of any localizing findings, such as conduction block or slowing across the elbow. Although the referring surgeon usually wants to know whether the ulnar neuropathy is at the elbow, often the only accurate impression the electromyographer can give is one of a non-localizable ulnar neuropathy that is at, or proximal to, the most proximal abnormal ulnar-innervated muscle found on EMG.

6. *Always think about the clinical–electrophysiologic correlation.* This rule combines all of the earlier rules. One usually can be certain of a diagnosis when the clinical findings, NCSs, and EMG abnormalities all correlate well. Consider again the example of the patient with weakness of the hand and tingling and numbness of the fourth and fifth fingers. If NCSs demonstrate abnormal ulnar motor and sensory potentials associated with slowing across the elbow, and the needle EMG shows denervation and reduced numbers of motor unit potentials in all ulnar-innervated muscles and a normal EMG of all non-ulnar-innervated muscles, there is a high degree of certainty that the patient truly has an ulnar neuropathy at the elbow, and the electrophysiologic abnormalities are indeed relevant.

If all three results fit together, the diagnosis is secure. However, if the NCSs and EMG findings do not fit together and, more importantly, they do not correlate with the clinical findings, the significance of any electrical abnormalities should be seriously questioned. Consider a patient with pain in the arm who has an otherwise normal history and examination. If the NCSs are normal except for a low ulnar sensory potential and the EMG demonstrates only mild reinnervation of the biceps, one should be reluctant to interpret the study as showing a combination of an ulnar neuropathy and a C5 radiculopathy. These mild abnormalities, which are not substantiated by other electrophysiologic findings and do not have clear clinical correlates, may have little to do with the patient's pain. In such a case, the patient should be reexamined. If no clinical correlate is found, the studies should be rechecked. If the abnormalities persist, they may be noted as part of the impression but interpreted as being of uncertain clinical significance.

When performed properly, NCSs and EMG can be very helpful to the referring physician. However, the limitations of EDX studies must be appreciated, technical factors well controlled, and a good differential diagnosis established before each study. Otherwise, the study may actually do a disservice to the patient and to the referring physician by leading them astray by way of minor, irrelevant, or technically induced "abnormalities." If the cardinal rules of NCSs and EMG are kept in mind, EDX studies are far more likely to be of help to the referring clinician and the patient with a neuromuscular disorder.

2 Anatomy and Neurophysiology

The electromyographer need not have detailed knowledge of all the electrical and chemical events that occur at a molecular level in order to perform an electrodiagnostic (EDX) study. However, every electromyographer must have a basic understanding of anatomy and physiology in order to plan, perform, and properly interpret an EDX study. In the everyday evaluation of patients with neuromuscular disorders, nerve conduction studies (NCSs) and electromyography (EMG) serve primarily as extensions of the clinical examination. Knowledge of gross nerve and muscle anatomy is required to be able to perform these studies. For NCSs, one needs to know the location of the various peripheral nerves and muscles so that the stimulating and recording electrodes are properly positioned. For the needle EMG study, knowledge of gross muscle anatomy is crucial for inserting the needle electrode correctly into the muscle being sampled. On the microscopic level, knowledge of nerve and muscle anatomy and basic neurophysiology are required to appreciate and interpret the EDX findings both in normal individuals and in patients with various neuromuscular disorders. Lastly, knowledge of anatomy and physiology are crucial to understanding the technical aspects of the EDX study and appreciating its limitations and potential pitfalls.

ANATOMY

The strict definition of the peripheral nervous system includes that part of the nervous system in which the Schwann cell is the major supporting cell, as opposed to the central nervous system in which the glial cells are the major support cells. The peripheral nervous system includes the nerve roots, peripheral nerves, primary sensory neurons, neuromuscular junctions (NMJs), and muscles (Figure 2–1). Although not technically part of the peripheral nervous system, the primary motor neurons (i.e., anterior horn cells), which are located in the spinal cord, are often included as part of the peripheral nervous system as well. In addition, cranial nerves III through XII are also considered to be part of the peripheral nervous system, being essentially the same as peripheral nerves, except that their primary motor neurons are located in the brainstem rather than the spinal cord.

The primary motor neurons, the *anterior horn cells*, are located in the ventral gray matter of the spinal cord. The axons of these cells ultimately become the motor fibers in peripheral nerves. Their projections first run through the white matter of the anterior spinal cord before exiting ventrally as the *motor roots*. In contrast to the anterior horn

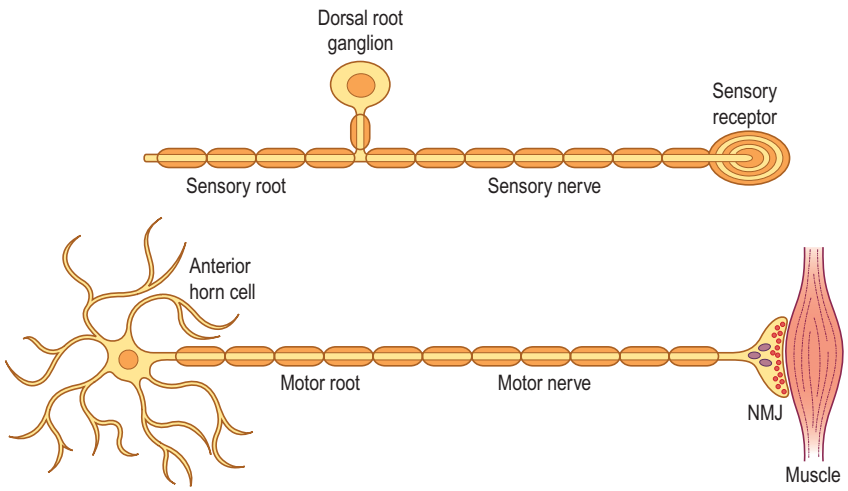

FIGURE 2–1 Elements of the peripheral nervous system. The peripheral nervous system includes the peripheral motor and sensory nerves; their primary neurons, the anterior horn cells, and dorsal root ganglia; the neuromuscular junctions (NMJs); and muscle. The dorsal root ganglion, a bipolar cell located distal to the sensory root, is anatomically different from the anterior horn cell. Consequently, lesions of the nerve roots result in abnormalities of motor nerve conduction studies but do not affect the sensory conduction studies, as the dorsal root ganglion and its peripheral nerve remain intact.

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cell, the primary sensory neuron, also known as the *dorsal root ganglion* (DRG), is not found within the substance of the spinal cord itself but rather lies outside the spinal cord, near the intervertebral foramen. The dorsal root ganglia are bipolar cells with two separate axonal projections. Their central projections form the *sensory nerve roots*. The sensory roots enter the spinal cord on the dorsal side to either ascend in the posterior columns or synapse with sensory neurons in the dorsal horn. The peripheral projections of the DRGs ultimately become the sensory fibers in peripheral nerves. Because the DRGs lie outside the spinal cord, this results in a different pattern of sensory nerve conduction abnormalities, depending on whether the lesion is in the peripheral nerve or proximal to the DRG, at the root level (see Chapter 3).

Motor and sensory roots at each spinal level unite distal to the DRG to become a mixed *spinal nerve*. There are 31 pairs of spinal nerves (8 cervical, 12 thoracic, 5 lumbar, 5 sacral, 1 coccygeal; Figure 2–2). Each spinal nerve divides into a *dorsal* and *ventral ramus* (Figure 2–3). Unlike the dorsal and ventral nerve roots, the dorsal and ventral rami both contain motor and sensory fibers. The dorsal ramus runs posteriorly to supply sensory innervation to the skin over the spine and muscular innervation to the paraspinal muscles at that segment. The ventral ramus differs, depending on the segment within the body. In the thoracic region, each ventral ramus continues as an *intercostal nerve*. In the lower cervical to upper thoracic (C5–T1) region, the ventral rami unite to form the *brachial plexus* (Figure 2–4). In the mid-lumbar to sacral regions, the ventral rami intermix to form the *lumbosacral plexus* (Figure 2–5).

Within each plexus, motor and sensory fibers from different nerve roots intermix to ultimately form individual *peripheral nerves*. Each peripheral nerve generally supplies muscular innervation to several muscles and cutaneous sensation to a specific area of skin, as well as sensory innervation to underlying deep structures. Because of this arrangement, motor fibers from the same nerve root supply muscles innervated by different peripheral nerves, and sensory fibers from the same nerve root supply cutaneous sensation in the distribution of different peripheral nerves. For instance, the C5 motor root supplies the biceps (musculocutaneous nerve), deltoid (axillary nerve), and brachioradialis (radial nerve), among other muscles (Figure 2–6). Similarly, C5 sensory fibers innervate the lateral arm (axillary nerve) and forearm (lateral antebrachial cutaneous sensory nerve), in addition to other nerves.

All muscles supplied by one spinal segment (i.e., one nerve root) are known as a *myotome*, whereas all cutaneous areas supplied by a single spinal segment are known as a *dermatome* (Figure 2–7). For both myotomes and dermatomes, there is considerable overlap between adjacent segments. Because of the high degree of overlap between spinal segments, a single root lesion seldom results in significant sensory loss and never in anesthesia. Likewise, on the motor side, even a severe single nerve root lesion usually results in only mild or moderate weakness and never in paralysis. For instance, a severe lesion of the C6 motor root causes weakness of the biceps; however, paralysis would not occur because C5 motor fibers also innervate the biceps. In contrast, a severe peripheral nerve lesion usually results in marked sensory and motor deficits because contributions from several myotomes and dermatomes are affected.

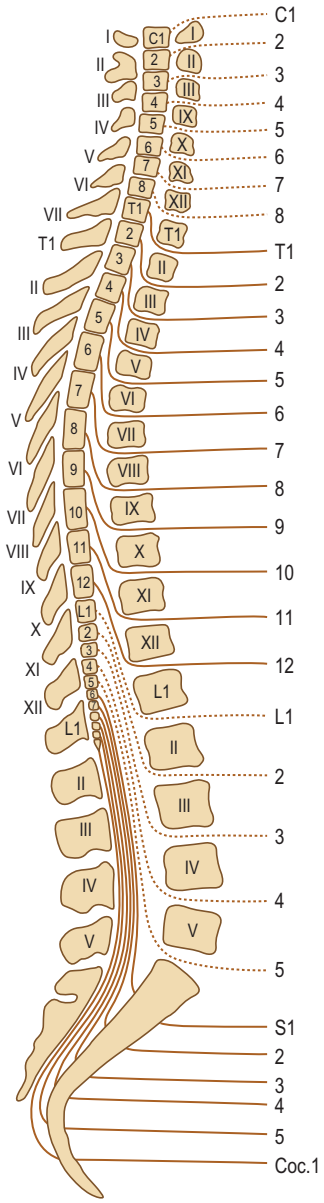


FIGURE 2–2 Spinal cord and nerve roots. The spinal cord is divided into 31 segments (8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal). At each segment, motor and sensory fibers leave the spinal cord as nerve roots before exiting the bony spinal column. In the adult, the spinal cord usually ends at the level of the L1 vertebra. Consequently, below this level, only the lumbosacral nerve roots, known as the cauda equina, are present within the spinal column. (From Haymaker, W., Woodhall, B., 1953. Peripheral nerve injuries. WB Saunders, Philadelphia, with permission.)

At the microscopic level, nerve fibers are protected by three different layers of connective tissue: the epineurium,

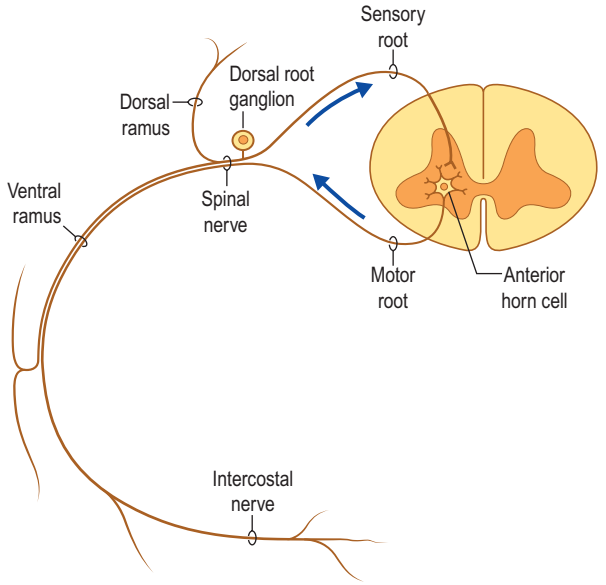


FIGURE 2–3 Nerve roots and rami. The motor root, originating from anterior horn cells, leaves the cord ventrally, whereas the sensory root enters the cord on the dorsal side. Immediately distal to the dorsal root ganglion, the motor and sensory roots come together to form the spinal nerve. Each spinal nerve quickly divides into a dorsal and ventral ramus. Each ramus contains both motor and sensory fibers. The dorsal rami supply sensation to the skin over the spine and muscular innervation to the paraspinal muscles. The ventral rami continue as intercostal nerves in the thoracic region. In the lower cervical region, the ventral rami fuse to form the brachial plexus. In the mid-lumbar through sacral segments, the ventral rami intermix to form the lumbosacral plexus.

perineurium, and endoneurium (Figure 2–8). The thick *epineurium* surrounds the entire nerve and is in continuity with the dura mater at the spinal cord level. Within the epineurium, axons are grouped into fascicles, surrounded by *perineurium*. A final layer of connective tissue, the *endoneurium*, is present between individual axons. Effectively, a *blood–nerve barrier* is formed by the combination of vascular endothelium supplying the nerve and the connective tissue of the perineurium. Together, the three layers of connective tissue give peripheral nerve considerable tensile strength, usually in the range of 20 to 30 kg. However, the weakest point of a nerve occurs where the nerve roots meet the spinal cord, where the nerve can sustain only 2 to 3 kg of force. For this reason, nerve root avulsion may occur after a significant trauma and especially after a stretch injury.

PHYSIOLOGY

The primary role of nerve is to transmit information reliably from the anterior horn cells to muscles for the motor system and from the sensory receptors to the spinal cord for the sensory system. Although functionally nerves may seem similar to electrical wires, there are vast differences between the two. At the molecular level, a complex set of chemical and electrical events allows nerve to propagate an electrical signal.

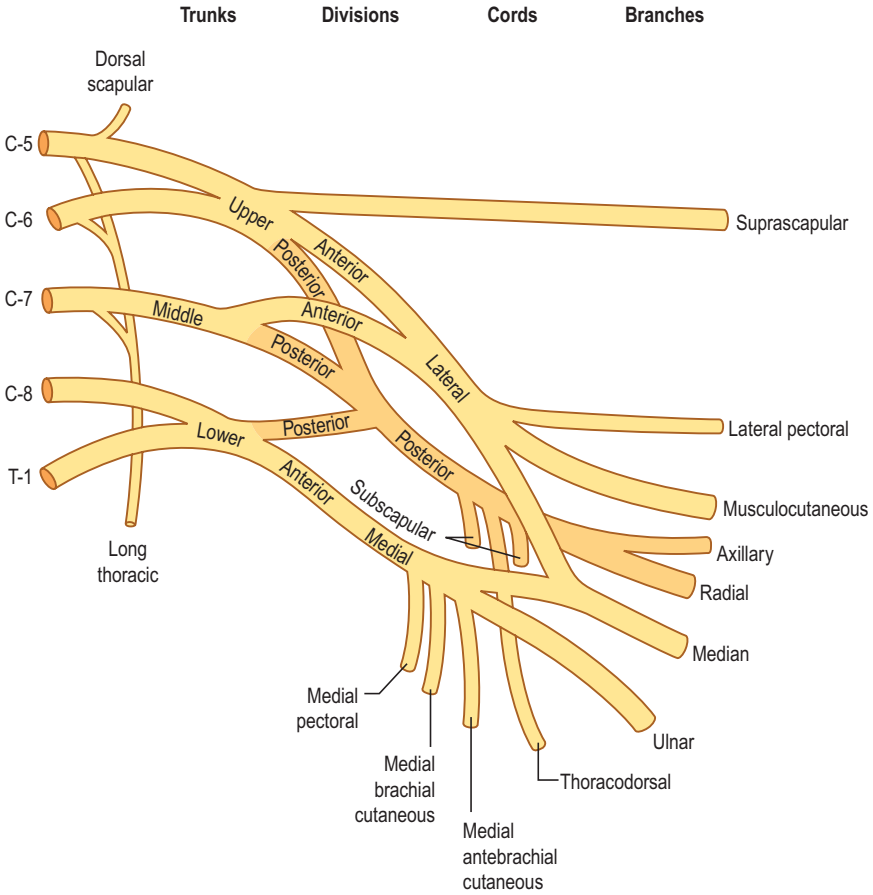


FIGURE 2–4 Brachial plexus. The ventral rami of the C5–T1 nerve roots intermix to form the brachial plexus between the neck and shoulder. From the brachial plexus, the major upper extremity peripheral nerves are derived.

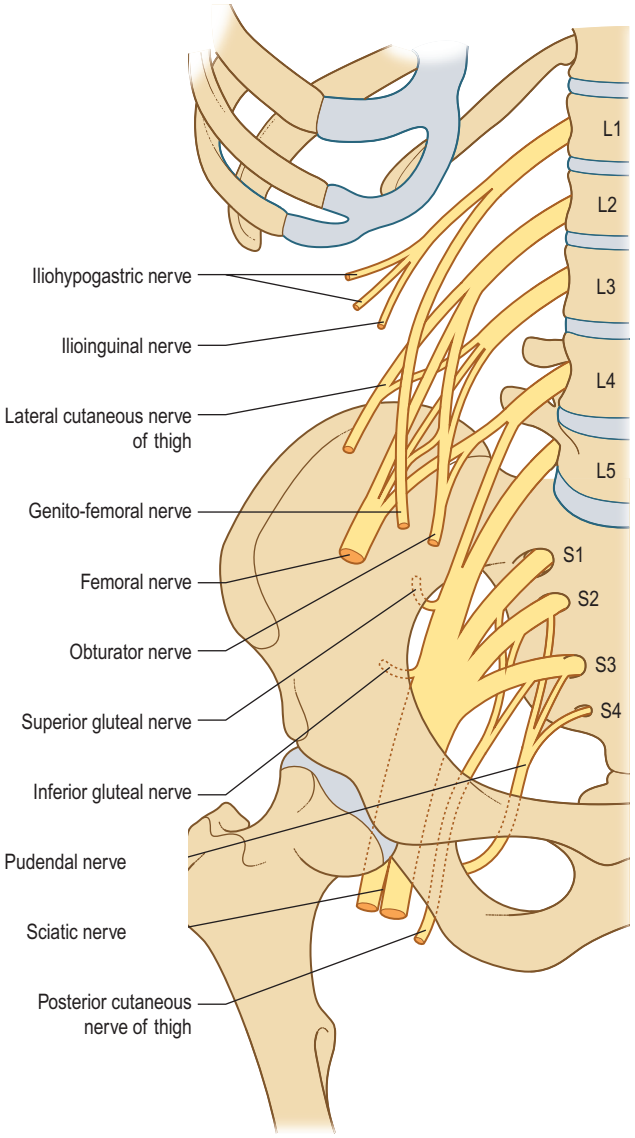


FIGURE 2–5 Lumbosacral plexus. The L1–S4 nerve roots intermix in the pelvis to form the lumbosacral plexus. From this plexus, the individual major peripheral nerves of the lower extremity are derived. (From Mayo Clinic and Mayo Foundation. 1956. Clinical examinations in neurology. WB Saunders, Philadelphia, with permission.)

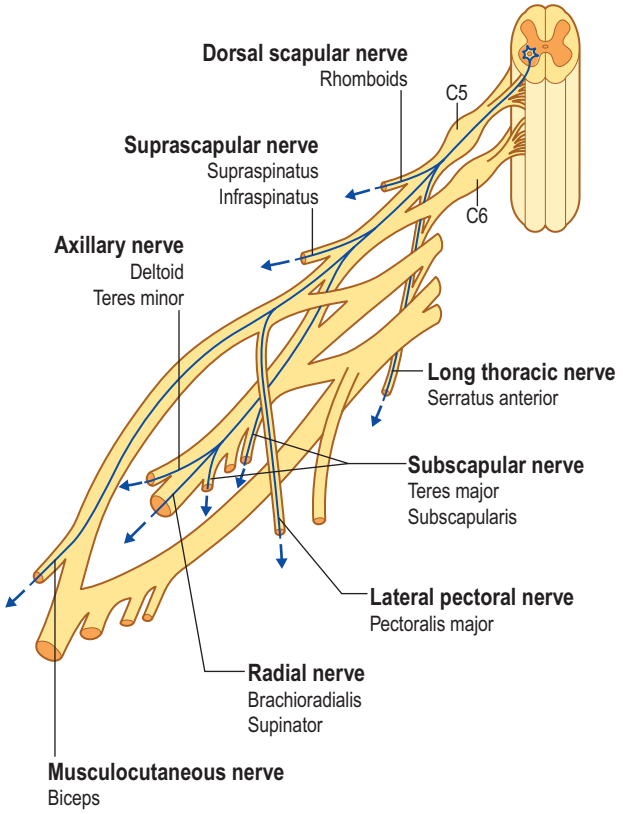


FIGURE 2–6 Myotomal and peripheral nerve innervation. Motor fibers from one nerve root, a myotome, supply muscles innervated by different peripheral nerves. For example, the C5 motor root supplies the biceps (musculocutaneous nerve), deltoid (axillary nerve), and brachioradialis (radial nerve), among other muscles. (Adapted from Haymaker, W., Woodhall, B., 1953. Peripheral nerve injuries. WB Saunders, Philadelphia, with permission.)

The axonal membrane of every nerve is electrically active. This property results from a combination of a specialized membrane and the sodium/potassium (Na^+/K^+) pump (Figure 2–9). The specialized axonal membrane is semipermeable to electrically charged molecules (anions and cations). The membrane is always impermeable to large negatively charged anions, and it is relatively impermeable to sodium in the resting state. This semipermeable membrane, in conjunction with an active Na^+/K^+ pump that moves sodium outside in exchange for potassium, leads to concentration gradients across the membrane. The concentration of sodium is larger outside the membrane, whereas the concentration of potassium and larger anions is greater inside. The combination of these electrical and chemical gradients results in forces that create a resting equilibrium potential. At the nerve cell soma, this resting membrane potential is approximately 70 mV negative inside compared with the outside; distally in the axon it is approximately 90 mV negative.

The membrane of the axon is lined with *voltage-gated sodium channels* (Figure 2–10). These structures are essentially molecular pores with gates that open and close. For many ion channels, gates open in response to molecules that bind to the channel. In the case of the voltage-gated sodium channel, the gate is controlled by a voltage sensor that responds to the level of the membrane potential. If current is injected into the axon, depolarization occurs (i.e., the axon becomes more positive internally). Voltage sensors within the sodium channel respond to the depolarization by opening the gate to the channel and allowing sodium to rush into the axon, driven both by concentration and by electrical gradients. Every time a depolarization of 10 to 30 mV occurs above the resting membrane potential (i.e., *threshold*), it creates an *action potential* and a cycle of positive feedback; further depolarization occurs and more sodium channels open (Figure 2–11). Action potentials are always all-or-none responses, which then propagate away from the initial site of depolarization. The axon does not remain depolarized for long, however, because the opening

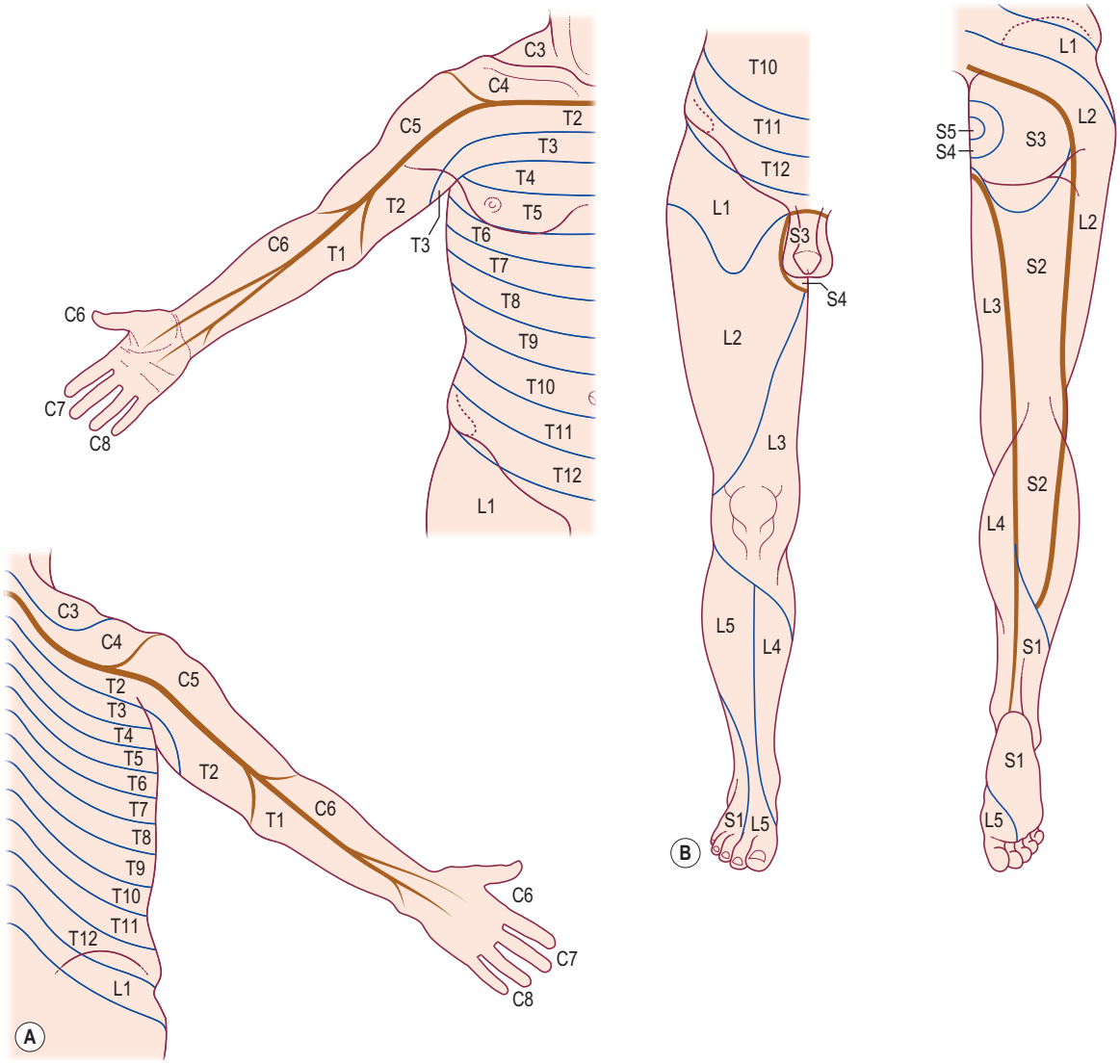
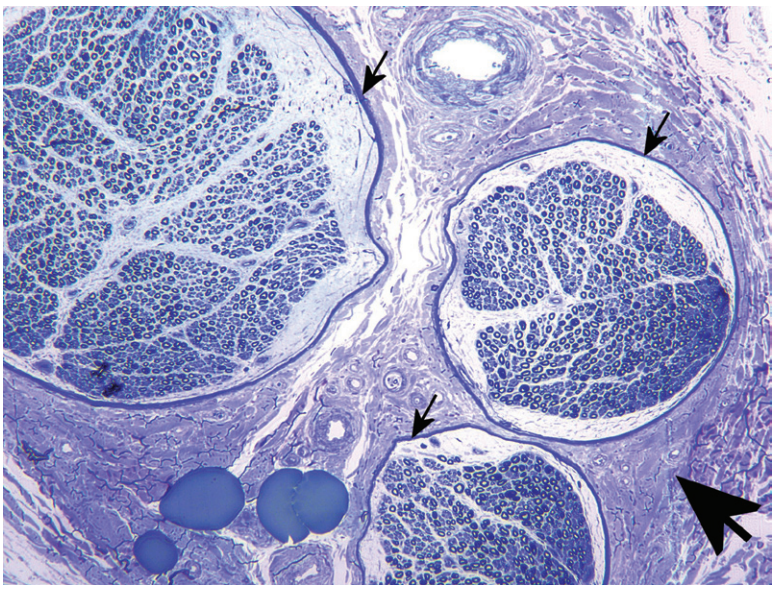


FIGURE 2–7 Dermatomes. The cutaneous area supplied from one spinal segment (i.e., one sensory nerve root) is known as a dermatome. Despite the apparent simplicity of dermatomal charts, in actuality, there is a wide overlap of adjacent dermatomes. Consequently, a nerve root lesion, even if severe, never results in anesthesia but rather altered or decreased sensation.
(From O'Brien M.D., 1986. Aids to the examination of the peripheral nervous system. Baillière Tindall, London.)

FIGURE 2–8 Internal peripheral nerve anatomy. Myelinated fibers are recognized as small dark rings (myelin) with a central clearing (axon) in this one micron thick, semi-thin section of plastic embedded nerve tissue. The endoneurium is present between axons. Axons are grouped into fascicles, surrounded by perineurium (small arrows). Surrounding the entire nerve is the last layer of connective tissue, the epineurium (large arrow).



of the sodium channels is time limited. Sodium channels have a second gate, known as the *inactivation gate*. Inactivation of the sodium channel occurs within 1 to 2 ms. During this time, the membrane is not excitable and cannot be opened (i.e., *refractory period*). The inactivation gate of the sodium channel has been modeled as a "hinged lid." From a practical point of view, the refractory period limits the frequency that nerves can conduct impulses. It also ensures that the action potential continues to propagate in the same direction (i.e., the area of nerve behind the depolarization is refractory when the area ahead is not, so that the impulse will continue forward and will not return backwards).

In addition to sodium channel inactivation, depolarization also results in the opening of potassium channels, which also then drives the membrane voltage more negative. These factors, along with the Na^+/K^+ pump, then reestablish the resting membrane potential.

The conduction velocity of the action potential depends on the diameter of the axon: the larger the axon, the less resistance and the faster the conduction velocity. For typical unmyelinated axons the conduction velocity of an action potential is very slow, typically in the range of 0.2 to 1.5 m/s. Conduction velocity can be greatly increased with the addition of myelin. *Myelin* insulation is present on all fast-conducting fibers and is derived from Schwann cells, the major supporting cells in the peripheral nervous system. Myelin is composed of concentric spirals of Schwann cell membrane (Figure 2–12). For every myelinated fiber, successive segments are myelinated by *single* Schwann cells. Each segment of the axon covered by myelin is termed the "internode." At small gaps between successive internodes, the axon is exposed; these areas are known as the nodes of Ranvier. They are very small, in the range of 1–2 µm in length.

Most of the nerve is effectively insulated with myelin, and depolarization occurs by way of *saltatory conduction*, whereby depolarization occurs only at the nodes of Ranvier. After one node depolarizes, the current jumps to the next adjacent node, and the cycle continues (Figure 2–13). The physiology of normal saltatory conduction was first shown in a series of elegant experiments on normal animal myelinated nerve fibers, recording along the motor root in very small increments, and measuring the current as a function of distance and latency (Figure 2–14). From an electrical point of view, myelin insulates the internode and reduces the capacitance. A lower capacitance results in less current lost as the action potential jumps from node to node. Although more current is needed for saltatory conduction than for continuous conduction, much less nerve membrane has to be depolarized. For unmyelinated fibers, depolarization has to occur over the entire length of the nerve (i.e., continuous conduction), which takes more time than in myelinated fibers. In myelinated fibers, the axonal membrane only needs to depolarize at the nodes of Ranvier; the internodes do not depolarize, but rather the action potential jumps over them. As the internode is approximately 1 mm in length and the node of Ranvier is only 1–2 µm in length, markedly less axonal membrane needs to depolarize in order to propagate an action potential. The lower the total depolarization time, the faster the conduction velocity. In myelinated axons, the density of sodium channels is highest in nodal areas, the areas undergoing depolarization. Myelinated human peripheral nerve fibers typically conduct in the range of 35 to 75 m/s, far faster than could ever be achieved by increasing the diameter of unmyelinated fibers.

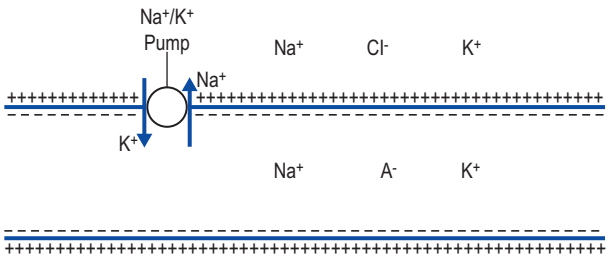


FIGURE 2–9 Resting membrane potential. At rest, the axonal membrane is negatively polarized, inside compared to outside. This resting potential results from the combination of a membrane that is semipermeable to charged particles and an active Na^+/K^+ pump. At rest, the concentration of Na^+ and Cl^- is higher in the extracellular space, with the concentration of K^+ and large anions (A^-) greater inside the axon.

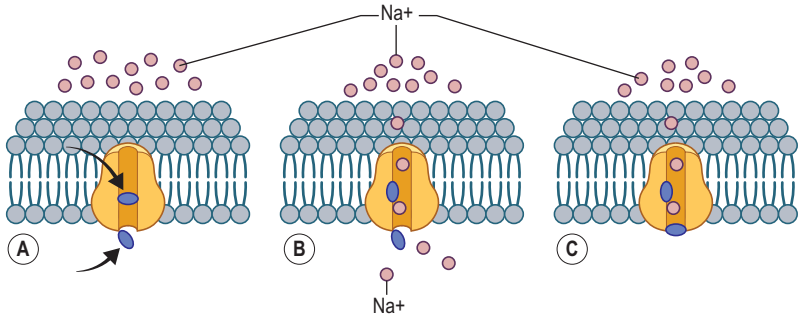


FIGURE 2–10 Voltage-gated sodium channel. The axonal membrane is lined with voltage-gated sodium channels. These channels are molecular pores with gates that open and close; when open, gates are selective for sodium **A**. There are two gates: an activation gate (large arrow) and an inactivation gate (small arrow). If current is injected into the axon, depolarization occurs, and the voltage-gated activation gate opens, allowing the influx of sodium into the axon **B**, driven both by concentration and electrical gradients. However, the opening of the sodium channels is time limited. Inactivation of the sodium channel occurs within 1 to 2 ms **C**. The inactivation gate of the sodium channel has been modeled as a "hinged lid," which closes the end of the channel within 1 to 2 ms of depolarization, preventing further depolarization.

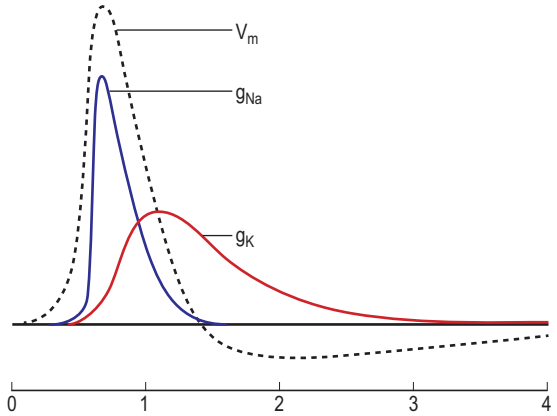


FIGURE 2–11 Action potential. When the resting membrane voltage (V_m) is depolarized to threshold, voltage-gated sodium channels are opened, increasing Na^+ conductance (g_{Na}), resulting in an influx of sodium and further depolarization. The action potential, however, is short lived, due to the inactivation of the sodium channels within 1 to 2 ms and an increase in K^+ conductance (g_K). These changes, along with the Na^+/K^+ pump, allow the axon to reestablish the resting membrane potential.

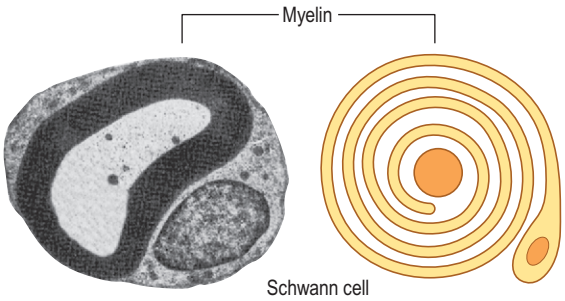


FIGURE 2–12 Schwann cell and the myelin sheath. **Left:** Electron micrograph of a single Schwann cell and myelinated axon. **Right:** Schematic of the same. Myelin insulation is derived from Schwann cells and is present on all fast-conducting fibers, both motor and sensory. Myelin is composed of concentric spirals of Schwann cell membrane, with each Schwann cell supporting a single myelinated axon.

Not all human peripheral nerve fibers are myelinated. Unmyelinated fibers, which conduct very slowly (typically 0.2–1.5 m/s), primarily mediate pain, temperature, and autonomic functions. Schwann cells also support these unmyelinated fibers; however, one Schwann cell typically surrounds several unmyelinated fibers, but without the formation of concentric spirals of myelin.

When an individual axon is depolarized, an action potential propagates down the nerve. Distally, the axon divides into many twigs, each of which goes to an individual muscle fiber. An axon, along with its anterior horn cell and all muscle fibers with which it is connected, is known as a motor unit (Figure 2–15). Depolarization of all the muscle fibers in a motor unit creates an electrical potential known as the *motor unit action potential* (MUAP). Analysis of MUAPs is an important part of every needle EMG examination. When an action potential is generated, all muscle fibers in the motor unit are normally activated, again an all-or-none response. However, before a muscle fiber can

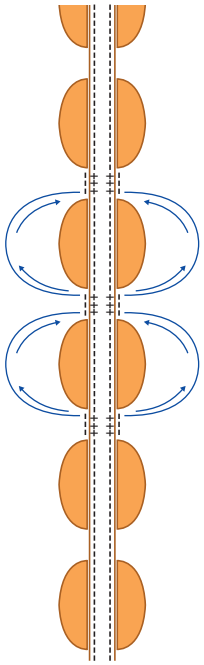


FIGURE 2–13 Saltatory conduction. Myelinated fibers propagate action potentials by way of saltatory conduction. Depolarization only occurs at the small uninsulated areas of membrane between internodes, with the action potential jumping from node to node. Thus, less membrane needs to be depolarized, less time is required, and, consequently, conduction velocity dramatically increases. Most human peripheral myelinated fibers conduct in the range of 35 to 75 m/s.

be activated, the nerve action potential must be carried across the NMJ. The NMJ is essentially an electrical–chemical–electrical link from nerve to muscle. It is formed from two specialized membranes, one on nerve and one on muscle, separated by a thin synaptic cleft (Figure 2–16). As a nerve action potential travels to the presynaptic side of the NMJ, voltage-gated calcium (Ca^+) channels are activated, allowing an influx of Ca^+. Increasing Ca^+ concentration results in the release of acetylcholine, the neurotransmitter at the NMJ. Acetylcholine diffuses across the synaptic cleft to bind to specialized acetylcholine receptors on the muscle membrane. These receptors, when activated, allow an influx of sodium and depolarization of the muscle fiber. As is the case with nerve, once threshold is reached, a muscle fiber action potential is created that spreads throughout the muscle fiber. Following the muscle fiber action potential, a complex set of molecular interactions occurs within the muscle fiber, resulting in increasing overlap of the major muscle fiber filaments: actin and myosin, with the final result of muscle shortening, contraction, and generation of force (Figure 2–17).

CLASSIFICATION

Multiple peripheral nerve classification schemes exist (Table 2–1). Peripheral nerves can be classified based on the following attributes: (1) myelinated or unmyelinated,

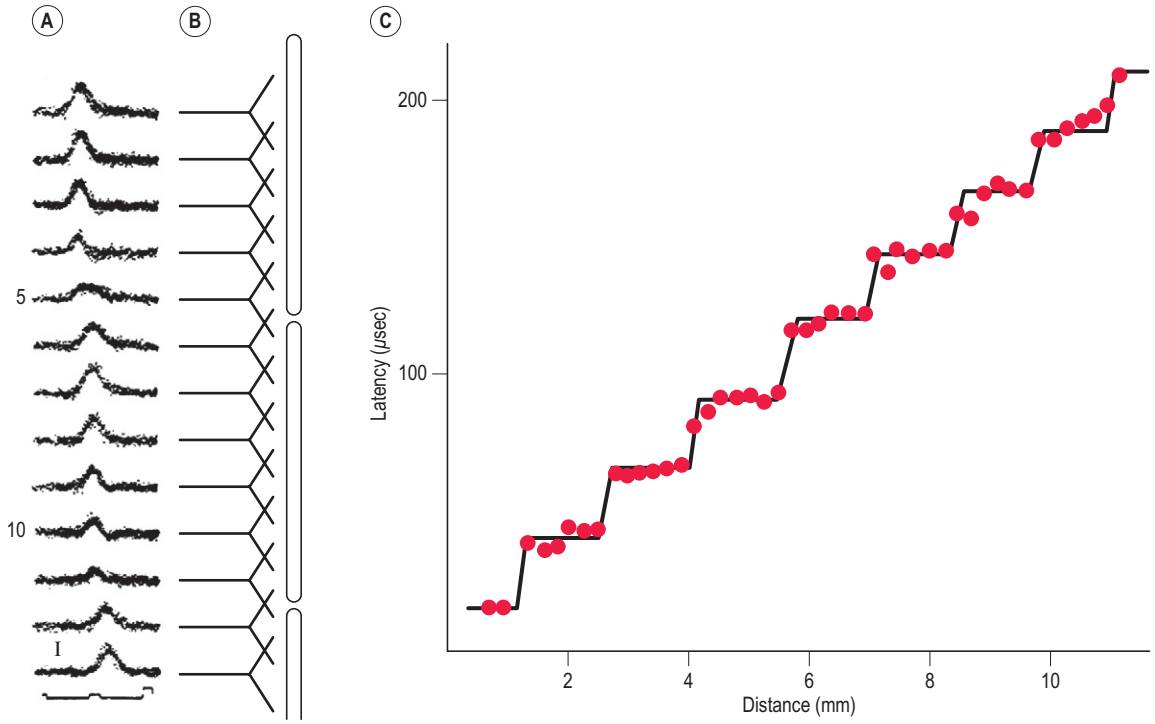


FIGURE 2–14 Demonstration of saltatory conduction. Recording of a normal single fiber from an intact ventral root in a rat: **A:** successive records of external longitudinal current recorded from a single fiber as electrodes were moved along a ventral root in steps of 0–2 mm. **B:** Lines from each record indicate positions of electrodes with respect to underlying nodes and internodes. **C:** Latency to peak of external longitudinal current as a function of distance. Note how the distance/latency graph is a "staircase" configuration. As current proceeds down a normal myelinated axon, the latency (i.e., the conduction time) abruptly increases approximately every 1.0–1.5 mm. This is the depolarization time at the nodes of Ranvier. Conversely, note the flat part of the staircase graph; here the latency stays almost exactly the same despite a change in distance. This is the saltatory conduction jumping from node to node.
(From Rasminsky, M., Sears, T.A., 1972. Internodal conduction in undissected demyelinated nerve fibres. J Physiol 227, 323–350, with permission.)

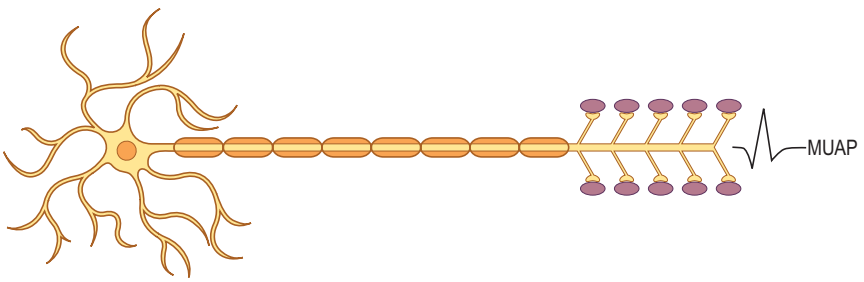


FIGURE 2–15 Motor unit. The motor unit is defined as one axon, its anterior horn cell, and all connected muscle fibers and neuromuscular junctions. A nerve fiber action potential normally always results in depolarization of all the muscle fibers of the motor unit creating an electrical potential known as the motor unit action potential (MUAP). Analysis of motor unit action potentials is a large part of the needle electromyographic examination.

(2) somatic or autonomic, (3) motor or sensory, and (4) diameter.

There are several important points to glean from Table 2–1, some of which are directly relevant to clinical electrodiagnostic testing. First is the direct relationship between fiber diameter and conduction velocity: the larger the diameter, the faster the conduction velocity. The large myelinated fibers are the fibers that are measured in clinical NCSs. Indeed, all routine motor and sensory conduction velocity and latency measurements are from the largest and fastest fibers of the particular peripheral nerve that is being studied. Large-diameter fibers have the most myelin and the least electrical resistance, both of which result in faster conduction velocities. The small myelinated (Aδ, B) and unmyelinated (C) fibers carry autonomic information (afferent and efferent) and somatic pain and temperature sensations. *These fibers are not recorded with standard nerve conduction techniques*. Thus, neuropathies that preferentially affect only small fibers may not reveal any abnormalities on NCSs.

Second, routine sensory conduction studies typically record cutaneous nerves innervating skin. The largest and fastest cutaneous fibers are the Aβ fibers from hair and skin follicles. Note that the size and conduction velocities of

these fibers are similar to those of the muscle efferent fibers from the anterior horn cells that are recorded during routine motor studies. These myelinated fibers have velocities in the range of 35 to 75 m/s.

Third, the largest and fastest fibers in the peripheral nervous system are not recorded during either routine motor or sensory NCSs. These are the muscle afferents, the Aα fibers (also known as Ia fibers), which originate from muscle spindles and mediate the afferent arc of the muscle stretch reflex. *These fibers are recorded only during mixed nerve studies, in which the entire mixed nerve is stimulated and recorded*. Therefore, mixed nerve conduction velocities usually are faster than either routine motor or cutaneous sensory conduction velocities because they contain these Ia fibers. Because the Ia fibers have the largest diameter and accordingly the greatest amount of myelin, they often are affected early by demyelinating lesions such as those found in entrapment neuropathies. For example, in the EDX evaluation of carpal tunnel syndrome, the mixed nerve study from the palm to the wrist often is more sensitive in detecting abnormalities than either the routine motor or sensory conduction study.

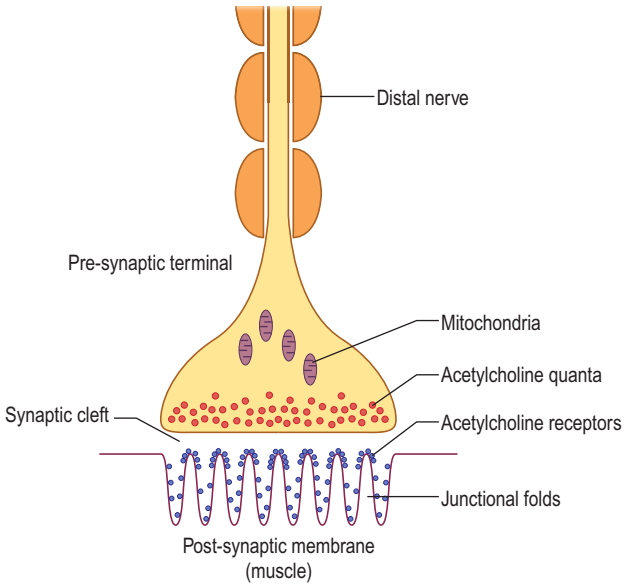


FIGURE 2–16 Neuromuscular junction. The neuromuscular junction is a specialized junction between the terminal axon and muscle fiber. When the nerve action potential invades the presynaptic terminal, acetylcholine is released and diffuses across the synaptic cleft to bind to acetylcholine receptors on the muscle membrane. This binding results in a muscle endplate potential, which, once threshold is reached, causes the generation of a muscle fiber action potential.

RECORDING

All potentials obtained during NCSs and needle EMG result from the extracellular recording of intracellular events, from either nerve or muscle. NCSs usually are performed by recording with surface electrodes over the skin, and EMG potentials by recording with a needle electrode placed within the muscle. In both procedures, intracellular electrical potentials are transmitted through tissue to the recording electrodes. The process of an intracellular electrical potential being transmitted through extracellular fluid and tissue is known as *volume conduction*. Although the theory of volume conduction is complex and beyond the scope of this text, volume-conducted potentials can be modeled as either near-field or far-field potentials. *Near-field potentials* can be recorded only close to their source, and the characteristics of the potential depend on the distance between the recording electrodes and the electrical source (i.e., the *action potential*). With near-field potentials, a response generally is not seen until the source is close to the recording electrodes. The closer the recording electrodes are to the current source, the higher the amplitude. Compound muscle action potentials, sensory nerve action potentials, and MUAPs recorded during routine motor conduction, sensory conduction, and needle EMG studies, respectively, are essentially all volume-conducted near-field potentials.

Volume-conducted, near-field potentials produce a characteristic triphasic waveform as an advancing action potential approaches and then passes beneath and away from a recording electrode (Figure 2–18, top). In practice, most sensory and mixed nerve studies display this triphasic waveform morphology, as do fibrillation potentials and most MUAPs. The electrical correlate of an action potential traveling toward, under, and then away from the recording electrode is an initial positive phase, followed by a negative

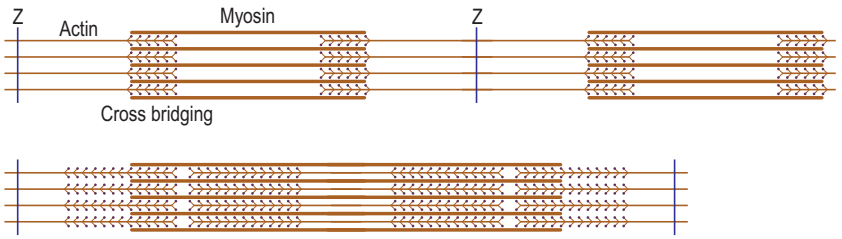


FIGURE 2–17 Actin and myosin. Following a muscle fiber action potential, muscle contraction results from a complex set of molecular interactions, ultimately ending with the overlapping of two interlacing muscle proteins, actin and myosin. This overlap, which occurs along with the formation of energy-dependent cross-bridges, effectively results in shortening of the muscle and the generation of force. Actin filaments are connected by Z lines. The sarcomere, a unit of muscle, is defined from one Z line to the next. The overlapping pattern of actin and myosin filaments gives muscle its striated appearance.

Table 2–1. Peripheral Nerve Classification Schemes

Fiber Type(s)	Name	Subtype	Diameter (mm)	Conduction Velocity (m/s)	Alternative Classification	
Myelinated Somatic Afferent/Efferent						
Cutaneous afferent	A	β δ	6–12 1–5	35–75 5–30	α	
Muscle afferent	A	α β δ	12–21 6–12 1–5	80–120 35–75 5–30	I II III	Ia, Ib
Muscle efferent Anterior horn cells (α and γ motor neurons)	A		6–12	35–75		
Myelinated Autonomic Efferent						
Preganglionic efferent	B		3	3–15		
Unmyelinated Somatic/Autonomic Afferent/Efferent						
Postganglionic efferent	C		0.2–1.5	1–2		
Afferent to dorsal root ganglion (pain)	C		0.2–1.5	1–2	IV	
Sensory Receptor	**Fiber Type**					
Hair follicle	Aβ					
Skin follicle	Aβ					
Muscle spindle	Aa					
Joint receptor	Aβ					
Pain, temperature	Aδ, C					

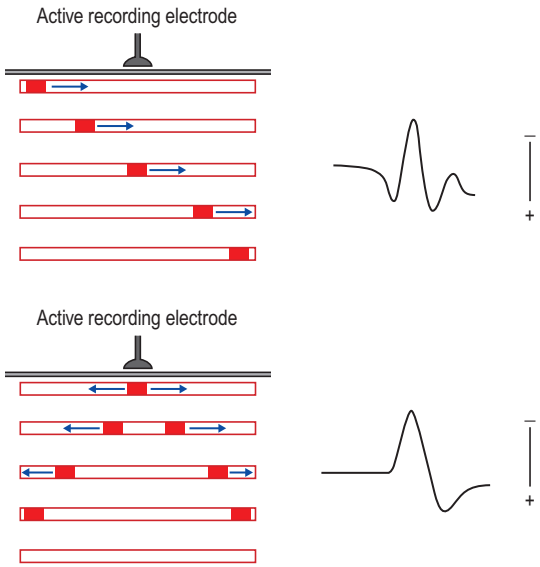


FIGURE 2–18 Volume conduction and waveform morphology. **Top:** An advancing action potential recorded by volume conduction will result in a triphasic potential that initially is positive, then is negative, and finally is positive again. **Bottom:** If the depolarization occurs directly beneath the recording electrode, the initial positive phase will be absent, and a biphasic, initially negative potential will be seen. Note that, by convention, negative is up and positive is down in all nerve conduction and electromyographic traces.

phase and then a trailing positive phase, respectively. The first positive peak represents the time that the action potential is beneath the active electrode; this is the point at which the onset latency should be measured for nerve action potentials. The initial positive peak may be very small or absent with some sensory responses. In that case, the initial negative deflection best marks the true onset of the potential.

If a volume-conducted, near-field action potential begins directly under the recording electrode, the initial deflection will be negative (Figure 2–18, bottom). During routine motor NCSs, this is the expected compound muscle action potential morphology if the active electrode is correctly placed over the motor point (i.e., *endplate*) of the muscle. There is no advancing action potential, as muscle fiber depolarization begins at the endplate; hence, the waveform has no initial positive deflection. This results in a characteristic biphasic potential with an initial negative deflection (Figure 2–19, top). If the electrode is inadvertently placed off the motor point, a triphasic potential with an initial positive deflection will be seen (Figure 2–19, middle). If the depolarization occurs at a distance but never passes under the recording electrode, characteristically only a positive deflection will occur (Figure 2–19, bottom). For example, this pattern is seen when stimulating the median nerve and recording a hypothenar muscle, as might be done during routine motor studies looking for an anomalous

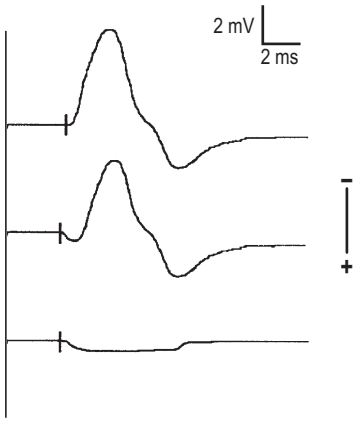


FIGURE 2–19 Volume conduction and motor potentials. With the active recording electrode (G1) over the motor point, depolarization first occurs at that site, with the depolarization subsequently spreading away. The corresponding waveform has an initial negative deflection without any initial positivity (top trace). If the active recording electrode is off the motor point, depolarization begins distally and then travels under and past the active electrode, resulting in an initial positive deflection (middle trace). If the depolarization occurs at a distance and never travels under the recording electrode, only a small positive potential will be seen (bottom trace). Note that, by convention, negative is up and positive is down in all nerve conduction and electromyographic traces.

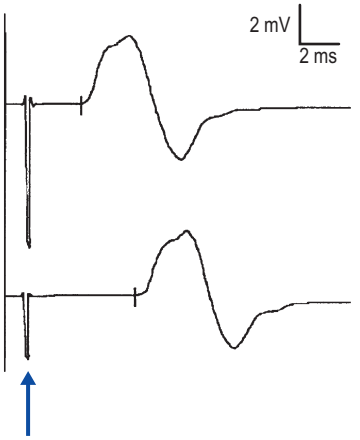


FIGURE 2–20 Near-field and far-field potentials. Median motor study, recording the abductor pollicis brevis muscle, stimulating at the wrist (top trace) and antecubital fossa (bottom trace). At each site, a compound muscle action potential is present, representing a near-field recording of the underlying muscle fiber action potentials. The compound muscle action potential latencies occur at different times, reflecting their different arrival times at the recording electrode. At the start of each trace is the stimulus artifact. The stimulus artifact is an example of a far-field potential, being transmitted instantaneously and seen at the same time, despite the difference in distances between the two stimulation sites.

innervation. The muscle action potential of the median-innervated thenar muscles occurs at a distance but never travels under the recording electrodes located over the hypothenar muscles. The result is a small positive deflection, volume-conducted potential.

The other type of volume-conducted potential is the *far-field potential*. Far-field potentials are electrical potentials that are distributed widely and instantly. Two recording electrodes, one closer and the other farther from the source, essentially see the source at the same time. Although far-field potentials are more often of concern in evoked potential studies, they occasionally are important in NCSs. The stimulus artifact seen at the onset of all NCSs is a good example of a far-field potential (Figure 2–20). The shock artifact is instantly transmitted and is seen at the same time at distal and proximal recording sites. Those potentials whose latencies do not vary with distance from the stimulation site usually are all far-field potentials.

Suggested Readings

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Basic Nerve Conduction Studies 3

After the history is taken and a directed physical examination is performed, every study begins with the nerve conduction studies (NCSs). The needle electromyography (EMG) examination is performed after the NCSs are completed, because the findings on the NCSs are used in the planning and interpretation of the needle examination which follows.

Peripheral nerves usually can be easily stimulated and brought to action potential with a brief electrical pulse applied to the overlying skin. Techniques have been described for studying most peripheral nerves. In the upper extremity, the median, ulnar, and radial nerves are the most easily studied; in the lower extremity, the peroneal, tibial, and sural nerves are the most easily studied (see Chapters 10 and 11). Of course, the nerves selected for study depend on the patient's symptoms and signs and the differential diagnosis. Motor, sensory, or mixed nerve studies can be performed by stimulating the nerve and placing the recording electrodes over a distal muscle, a cutaneous sensory nerve, or the entire mixed nerve, respectively. The findings from motor, sensory, and mixed nerve studies often complement one another, and yield different types of information based on distinct patterns of abnormalities, depending on the underlying pathology.

MOTOR CONDUCTION STUDIES

Motor conduction studies are technically less demanding than sensory and mixed nerve studies; thus; they usually are performed first. Performing the motor studies first also has other major advantages. It is not uncommon for the sensory responses to be very low in amplitude or absent in many neuropathies. Performing the motor studies first allows one to know where the nerve runs, where it should be stimulated, and how much current is needed, and also gives some information about whether the nerve is normal or abnormal. On the other hand, if the sensory study is done before the motor study, one might spend a lot of unnecessary time stimulating and trying to record a sensory response which is not present. For example, imagine a patient with a moderately severe median neuropathy at the wrist who is sent for an EDX evaluation. If the median motor study is performed first, the correct stimulation site can be confirmed, the amount of current needed to stimulate the median nerve will be known, and one will also know that the median nerve is abnormal, before doing the median sensory study. Then, when performing the median sensory study, one is confident of where to stimulate the nerve and how much current is needed. In this case, if no sensory response is present, one can have a high degree of certainty that the response is truly absent, and move along to the next nerve to be studied. However, if the sensory conduction study is done first, and is absent, it will not be as obvious if the absent response is due to a technical problem, or is truly absent. One can waste a lot of time unnecessarily trying to figure this out. Do the motor conduction study first; your study will be more efficient, and the patient will tolerate the study much better.

Motor responses typically are in the range of several millivolts (mV), as opposed to sensory and mixed nerve responses, which are in the microvolt (μV) range. Thus, motor responses are less affected by electrical noise and other technical factors. For motor conduction studies, the gain usually is set at 2 to 5 mV per division. Recording electrodes are placed over the muscle of interest. In general, the *belly–tendon montage* is used. The active recording electrode (also known as G1) is placed on the center of the muscle belly (over the motor endplate), and the reference electrode (also known as G2) is placed distally, over the tendon to the muscle (Figure 3–1). The designations G1 and G2 remain in the EMG vernacular, referring to a time when electrodes were attached to grids (hence the G) of an oscilloscope. The stimulator then is placed over the nerve that supplies the muscle, with the cathode placed closest to the recording electrode. It is helpful to remember "black to black," indicating that the black electrode of the stimulator (the cathode) should be facing the black recording electrode (the active recording electrode). For motor studies, the duration of the electrical pulse usually is set to 200 ms. Most normal nerves require a current in the range of 20 to 50 mA to achieve supramaximal stimulation. As current is slowly increased from a baseline 0 mA, usually by 5 to 10 mA increments, more of the underlying nerve fibers are brought to action potential, and subsequently more muscle fiber action potentials are generated. The recorded potential, known as the *compound muscle action potential* (CMAP), represents the summation of all underlying individual muscle fiber action potentials. When the current is increased to the point that the CMAP no longer

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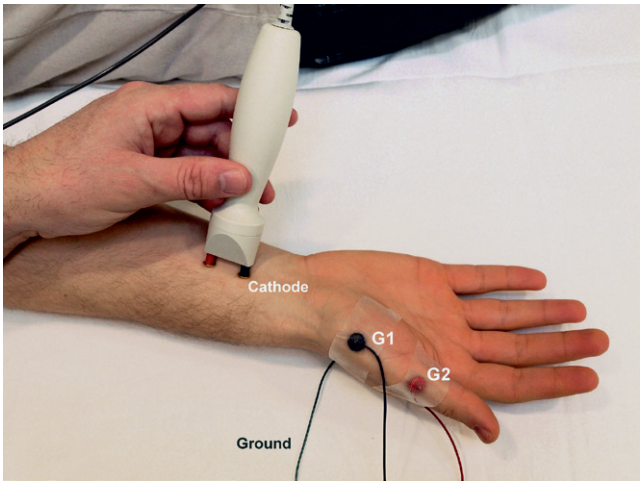

FIGURE 3–1 Motor conduction study setup. Median motor study, recording the abductor pollicis brevis muscle, stimulating the median nerve at the wrist. In motor studies, the "belly–tendon" method is used for recording. The active recording electrode (G1) is placed on the center of the muscle, with the reference electrode (G2) placed distally over the tendon.

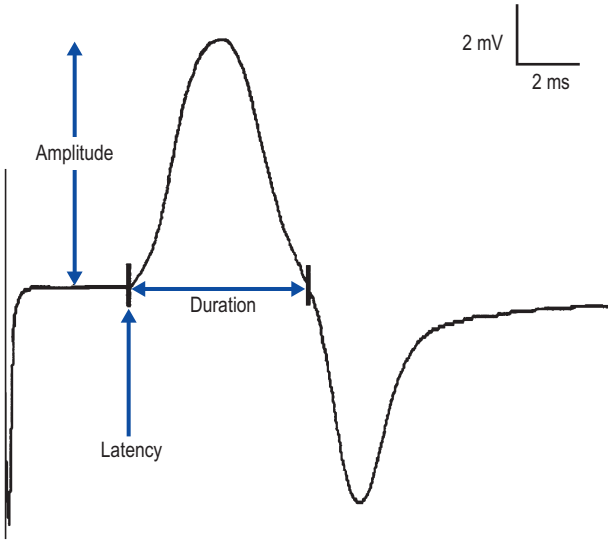

FIGURE 3–2 Compound muscle action potential (CMAP). The CMAP represents the summation of all the underlying muscle fiber action potentials. With recording electrodes properly placed, the CMAP is a biphasic potential with an initial negative deflection. Latency is the time from the stimulus to the initial negative deflection from baseline. Amplitude is most commonly measured from baseline to negative peak but also can be measured from peak to peak. Duration is measured from the initial deflection from baseline to the first baseline crossing (i.e., negative peak duration). In addition, negative CMAP area (i.e., the area above the baseline) is calculated by most modern computerized electromyographic machines. Latency reflects only the fastest conducting motor fibers. All fibers contribute to amplitude and area. Duration is primarily a measure of synchrony.

increases in size, one presumes that all nerve fibers have been excited and that supramaximal stimulation has been achieved. The current is then increased by another 20% to ensure supramaximal stimulation.

The CMAP is a biphasic potential with an initial negativity, or upward deflection from the baseline, if the recording electrodes have been properly placed with G1 over the motor endplate. For each stimulation site, the latency, amplitude, duration, and area of the CMAP are measured (Figure 3–2). A motor conduction velocity can be calculated after two sites, one distal and one proximal, have been stimulated.

Latency

The latency is the time from the stimulus to the initial CMAP deflection from baseline. Latency represents three separate processes: (1) the nerve conduction time from the stimulus site to the neuromuscular junction (NMJ), (2) the time delay across the NMJ, and (3) the depolarization time across the muscle. Latency measurements usually are made in milliseconds (ms), and reflect only the fastest conducting motor fibers.

Amplitude

CMAP amplitude is most commonly measured from baseline to the negative peak and less commonly from the first negative peak to the next positive peak. CMAP amplitude reflects the number of muscle fibers that depolarize. Although low CMAP amplitudes most often result from loss of axons (as in a typical axonal neuropathy), other causes of a low CMAP amplitude include conduction block from demyelination located between the stimulation site and the recorded muscle, as well as some NMJ disorders and myopathies.

Area

CMAP area also is conventionally measured as the area above the baseline to the negative peak. Although the area cannot be determined manually, the calculation is readily performed by most modern computerized EMG machines. Negative peak CMAP area is another measure reflecting the number of muscle fibers that depolarize. Differences in CMAP area between distal and proximal stimulation sites take on special significance in the determination of conduction block from a demyelinating lesion (see section on Conduction Block).

Duration

CMAP duration usually is measured from the initial deflection from baseline to the first baseline crossing (i.e., negative peak duration), but it also can be measured from the initial to the terminal deflection back to baseline. The former is preferred as a measure of CMAP duration because when CMAP duration is measured from the initial to terminal deflection back to baseline, the terminal CMAP returns to baseline very slowly and can be difficult to mark precisely. Duration is primarily a measure of synchrony (i.e., the extent to which each of the individual muscle fibers fire at the same time). Duration characteristically increases in conditions that result in slowing of some motor fibers but not others (e.g., in a demyelinating lesion).

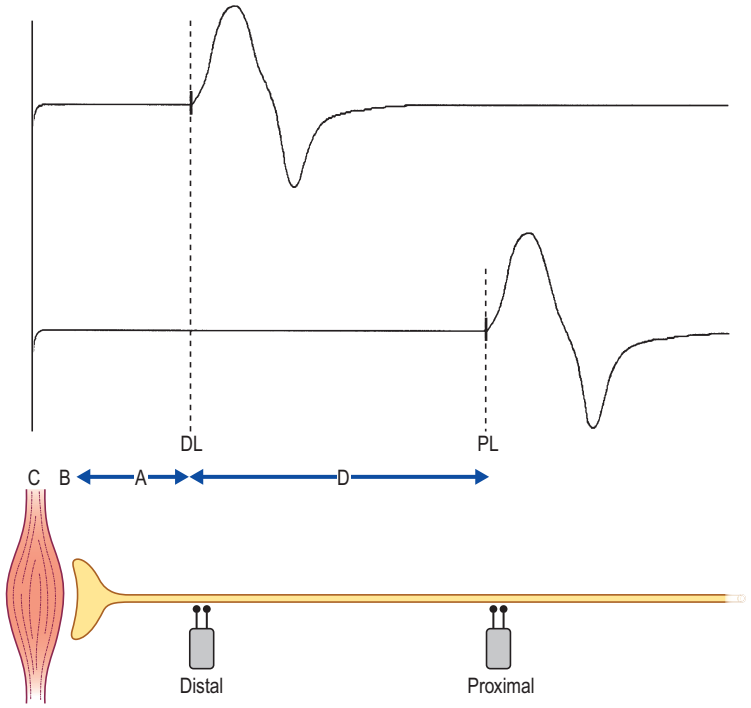

FIGURE 3–3 Motor conduction velocity (CV) calculation. **Top:** Median motor study, recording abductor pollicis brevis, stimulating wrist and elbow. DL, distal motor latency; PL, proximal motor latency. The only difference between distal and proximal stimulations is the latency, with PL being longer than DL. **Bottom:** DL represents three separate times: the nerve conduction time from the distal stimulation site to the neuromuscular junction (NMJ) (A), the NMJ transmission time (B), and the muscle depolarization time (C). Accordingly, DL cannot be used alone to calculate a motor conduction velocity. Two stimulations are necessary. PL includes the nerve conduction time from the distal stimulation site to the neuromuscular junction (A), the NMJ transmission time (B), and the muscle depolarization time (C), as well as the nerve conduction time between the proximal and distal stimulation sites (D). If DL (A+B+C) is subtracted from PL (A+B+C+D), only the nerve conduction time between the distal and proximal stimulation sites (D) remains. The distance between those two sites can be measured, and a conduction velocity can be calculated (distance/time). Conduction velocity reflects only the fastest conducting fibers in the nerve being studied.

Conduction Velocity

Motor conduction velocity is a measure of the speed of the fastest conducting motor axons in the nerve being studied, which is calculated by dividing the distance traveled by the nerve conduction time. However, motor conduction velocity cannot be calculated by performing a single stimulation. The distal motor latency is more than simply a conduction time along the motor axon; it includes not only (A) the conduction time along the distal motor axon to the NMJ, but also (B) the NMJ transmission time and (C) the muscle depolarization time. Therefore, to calculate a true motor conduction velocity, without including NMJ transmission and muscle depolarization times, two stimulation sites must be used, one distal and one proximal.

When the nerve is stimulated proximally, the resulting CMAP area, amplitude, and duration are, in general, similar to those of the distal stimulation waveform. The only major difference between CMAPs produced by proximal and distal stimulations is the latency. The proximal latency is longer than the distal latency, reflecting the longer time and distance needed for the action potential to travel. The proximal motor latency reflects four separate times, as opposed to the three components reflected in the distal motor latency measurement. In addition to (A) the nerve conduction time between the distal site and the NMJ, (B) the NMJ transmission time, and (C) the muscle depolarization time, the proximal motor latency also includes (D) the nerve conduction time between the proximal and distal stimulation sites (Figure 3–3). Therefore, if the distal motor latency (containing components A+B+C) is subtracted from the proximal motor latency (containing components A+B+C+D), the first three components will cancel out. This leaves only component D, the nerve conduction time between the proximal and distal stimulation sites, without the distal nerve conduction, NMJ transmission, and muscle depolarization times. The distance between these two sites can be approximated by measuring the surface distance with a tape measure. A conduction velocity then can be calculated along this segment: (distance between the proximal and distal stimulation sites) divided by (proximal latency−distal latency). Conduction velocities usually are measured in meters per second (m/s).

It is essential to note that both latency and conduction velocity reflect only the fastest conducting fibers in the nerve being studied. By definition, conduction along these fibers arrives first and thus it is these fibers that are the ones measured. The many other slower conducting fibers participate in the CMAP area and amplitude but are not

reflected in either the latency or conduction velocity measurements.

SENSORY CONDUCTION STUDIES

In contrast to motor conduction studies, in which the CMAP reflects conduction along motor nerve, NMJ, and muscle fibers, in sensory conduction studies only nerve fibers are assessed. Because most sensory responses are very small (usually in the range of 1 to 50 μV), technical factors and electrical noise assume more importance. For sensory conduction studies, the gain usually is set at 10 to 20 μV per division. A pair of recording electrodes (G1 and G2) are placed in line over the nerve being studied, at an interelectrode distance of 2.5 to 4 cm, with the active electrode (G1) placed closest to the stimulator. Recording ring electrodes are conventionally used to test the sensory nerves in the fingers (Figure 3–4). For sensory studies, an electrical pulse of either 100 or 200 ms in duration is used, and most normal sensory nerves require a current in the range of 5 to 30 mA to achieve supramaximal stimulation. This is less current than what is usually required for motor conduction studies. Thus, sensory fibers usually have a lower threshold to stimulation than do motor fibers. This can easily be demonstrated on yourself; when slowly increasing the stimulus intensity, you will feel the paresthesias (sensory) before you feel or see the muscle start to twitch (motor). As in motor studies, the current is slowly increased from a baseline of 0 mA, usually in 3 to 5 mA increments, until the recorded sensory potential is maximized. This potential, the *sensory nerve action potential* (SNAP), is a compound potential that represents the summation of all the individual sensory fiber action potentials. SNAPs usually are biphasic or triphasic potentials. For each stimulation site, the onset latency, peak latency, duration, and amplitude are measured (Figure 3–5). Unlike motor studies, a sensory conduction velocity can be calculated with one stimulation site alone, by taking the measured distance between the stimulator and active recording electrode and dividing by the onset latency. No NMJ or muscle time needs to be subtracted out by using two stimulation sites.

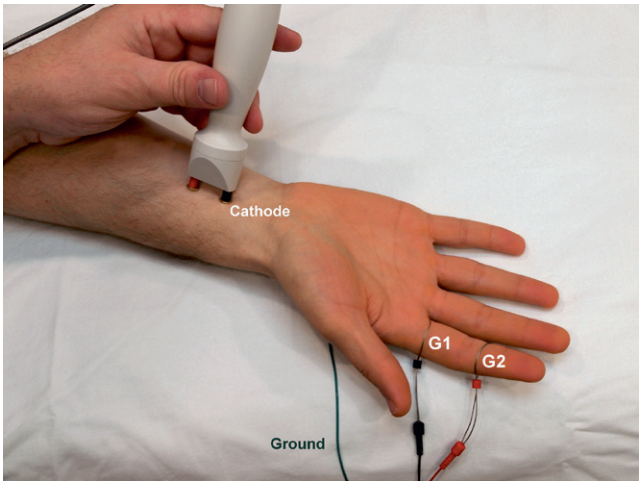

FIGURE 3–4 Sensory conduction study setup. Median sensory study, antidromic technique. Ring electrodes are placed over the index finger, 3 to 4 cm apart. The active recording electrode (G1) is placed more proximally, closest to the stimulator. Although the entire median nerve is stimulated at the wrist, only the cutaneous sensory fibers are recorded over the finger.

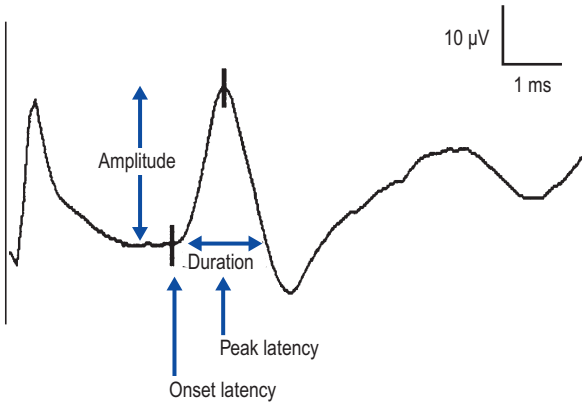

FIGURE 3–5 Sensory nerve action potential (SNAP). The SNAP represents the summation of all the underlying sensory fiber action potentials. The SNAP usually is biphasic or triphasic in configuration. Onset latency is measured from the stimulus to the initial negative deflection for biphasic SNAPs (as in the waveform here) or to the initial positive peak for triphasic SNAPs. Onset latency represents nerve conduction time from the stimulus site to the recording electrodes for the largest cutaneous sensory fibers in the nerve being studied. Peak latency is measured at the midpoint of the first negative peak. Amplitude most commonly is measured from baseline to negative peak but also can be measured from peak to peak. Duration is measured from the initial deflection from baseline to the first baseline crossing (i.e., negative peak duration). Only one stimulation site is required to calculate a sensory conduction velocity, as sensory onset latency represents only nerve conduction time.

Onset Latency

The onset latency is the time from the stimulus to the initial negative deflection from baseline for biphasic SNAPs or to the initial positive peak for triphasic SNAPs. Sensory onset latency represents nerve conduction time from the stimulus site to the recording electrodes for the largest cutaneous sensory fibers in the nerve being studied.

Peak Latency

The peak latency is measured at the midpoint of the first negative peak. Although the population of sensory fibers represented by the peak latency is not known (in contrast to the onset latency, which represents the fastest conducting fibers in the nerve being studied), measurement of peak latency has several advantages. The peak latency can be ascertained in a straightforward manner; there is practically no interindividual variation in its determination. In contrast, the onset latency can be obscured by noise or by the stimulus artifact, making it difficult to determine precisely. In addition, for some potentials, especially small ones, it may be difficult to determine the precise point of deflection from baseline (Figure 3–6). These problems do not occur in marking the peak latency. Normal values exist for

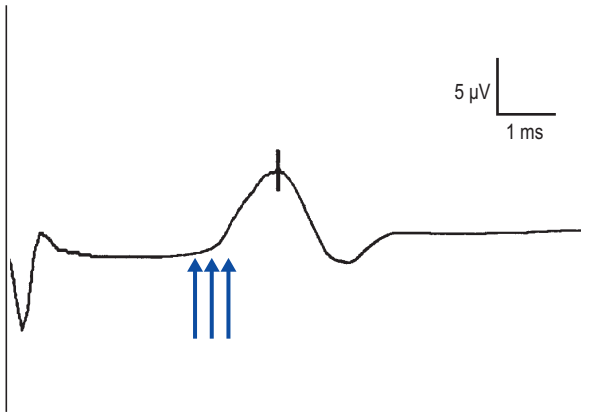

FIGURE 3–6 Sensory nerve action potential (SNAP) onset and peak latencies. Onset and peak latency measurements each have their own advantages and disadvantages. Onset latency represents the fastest conducting fibers and can be used to calculate a conduction velocity. However, for many potentials, especially small ones, it is difficult to precisely place the latency marker on the initial deflection from baseline (blue arrows: possible onset latencies). Marking the peak latency is straightforward, with nearly no inter-examiner variation. However, the population of fibers represented by peak latency is unknown; it cannot be used to calculate a conduction velocity.

peak latencies for the most commonly performed sensory studies stimulated at a standard distance. Note that the peak latency cannot be used to calculate a conduction velocity.

Amplitude

The SNAP amplitude is most commonly measured from baseline to negative peak, but it can also be measured from the first negative peak to the next positive peak. The SNAP amplitude reflects the sum of all the individual sensory fibers that depolarize. Low SNAP amplitudes indicate a definite disorder of peripheral nerve.

Duration

Similar to the CMAP duration, SNAP duration is usually measured from the onset of the potential to the first baseline crossing (i.e., negative peak duration), but it also can be measured from the initial to the terminal deflection back to baseline. The former is preferred given that the SNAP duration measured from the initial to terminal deflection back to baseline is difficult to mark precisely, because the terminal SNAP returns to baseline very slowly. The SNAP duration typically is much shorter than the CMAP duration (typically 1.5 vs. 5–6 ms, respectively). Thus, duration is often a useful parameter to help identify a potential as a true nerve potential rather than a muscle potential (Figure 3–7).

Conduction Velocity

Unlike the calculation of a motor conduction velocity, which requires two stimulation sites, sensory conduction velocity can be determined with one stimulation, simply by

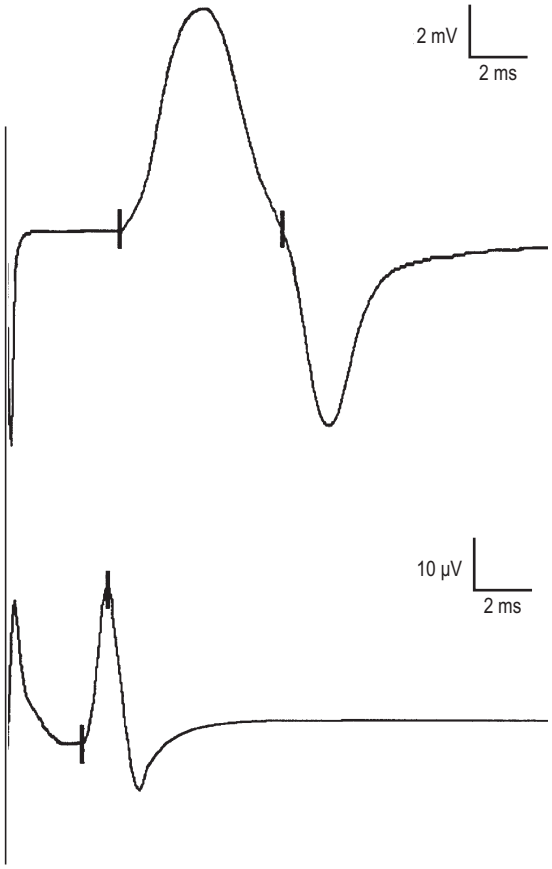

FIGURE 3–7 Compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) comparison. CMAPs **(top)** and SNAPs **(bottom)** both are compound potentials but are quite different in terms of size and duration. CMAP amplitude usually is measured in millivolts, whereas SNAPs are small potentials measured in the microvolt range (note different gains between the traces). CMAP negative peak duration usually is 5 to 6 ms, whereas SNAP negative peak duration is much shorter, typically 1 to 2 ms. When both sensory and motor fibers are stimulated (such as when performing antidromic sensory or mixed studies), these differences (especially duration) usually allow an unknown potential to be recognized as either a nerve or muscle potential.

dividing the distance traveled by the onset latency. Essentially, distal conduction velocity and onset latency are the same measurement; they differ only by a multiplication factor (i.e., the distance). Sensory conduction velocity represents the speed of the fastest, myelinated cutaneous sensory fibers in the nerve being studied.

Sensory conduction velocity along proximal segments of nerve can be determined by performing proximal stimulation and calculating the conduction velocity between proximal and distal sites, in a manner similar to the calculation for motor conduction velocity: (distance between the proximal and distal stimulation sites) divided by (proximal latency − distal latency). However, proximal sensory studies result in smaller amplitude potentials and often are more difficult to perform, even in normal subjects, because of the normal processes of phase cancellation and temporal dispersion (see later). Note that one can also determine the sensory conduction velocity from the proximal site to the

recording electrode by simply dividing the total distance traveled by the proximal onset latency.

Special Considerations in Sensory Conduction Studies: Antidromic versus Orthodromic Recording

When a nerve is depolarized, conduction occurs equally well in both directions away from the stimulation site. Consequently, sensory conduction studies may be performed using either antidromic (stimulating toward the sensory receptor) or orthodromic (stimulating away from the sensory receptor) techniques. For instance, when studying median sensory fibers to the index finger, one can stimulate the median nerve at the wrist and record the potential with ring electrodes over the index finger (antidromic study). Conversely, the same ring electrodes can be used for stimulation, and the potential recorded over the median nerve at the wrist (orthodromic study). Latencies and conduction velocities should be identical with either method (Figure 3–8), although the amplitude generally is higher in antidromically conducted potentials.

In general, the antidromic technique is superior for several reasons, but each method has its advantages and disadvantages. Most important, the amplitude is higher with antidromic than with orthodromic recordings, which makes it easier to identify the potential. The SNAP amplitude is directly proportional to the proximity of the recording electrode to the underlying nerve. For most antidromically conducted potentials, the recording electrodes are closer to the nerve. For example, in the antidromically conducted median sensory response, the recording ring electrodes are placed on the finger, very close to the underlying digital nerves just beneath the skin from which the potential is recorded. When the montage is reversed for orthodromic recording, there is more tissue (e.g., the transverse carpal ligament and other connective tissues) at the wrist separating the nerve from the recording electrodes. This results in attenuation of the recorded sensory response, resulting in a much lower amplitude. The higher SNAP amplitude obtained with antidromic recordings is the major advantage of using this method. The antidromic technique is especially helpful when recording very small potentials, which often occur in pathologic conditions. Furthermore, because the antidromic potential generally is larger than the orthodromic potential, it is less subject to noise or other artifacts.

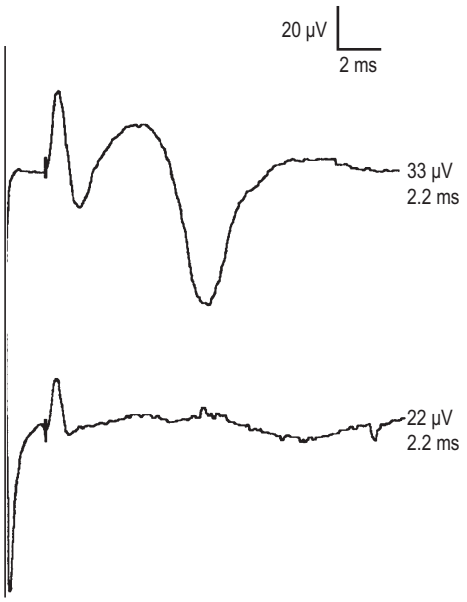

FIGURE 3–8 Antidromic and orthodromic sensory studies. Median sensory nerve action potential (SNAPs). **Top trace:** Antidromic study, stimulating wrist, recording index finger. **Bottom trace:** Orthodromic study, stimulating index finger, recording wrist. Latencies and conduction velocities are identical for both. The antidromic method has the advantage of a higher-amplitude SNAP but is followed by a large volume-conducted motor potential. If the SNAP is absent in an antidromic study, care must be taken not to confuse the volume-conducted motor potential as the sensory potential. Note the difference in duration between SNAP and CMAP, which helps discriminate between the SNAP and the volume-conducted motor potential that follows.

However, the antidromic method has some disadvantages (Figure 3–9). Since the entire nerve is often stimulated, including the motor fibers, this frequently results in the SNAP being followed by a volume-conducted motor potential. It usually is not difficult to differentiate between the two, because the SNAP latency typically occurs earlier than the volume-conducted motor potential. However, problems occur if the two potentials have a similar latency or, more importantly, if the sensory potential is absent. When the latter occurs, one can mistake the first component of the volume conducted motor potential for the SNAP, where none truly exists. It is in this situation that measuring the duration of the potential can be helpful in distinguishing a sensory from a motor potential. If one is still not sure, performing an orthodromic study will settle the issue, as no volume conducted motor response will occur with an orthodromic study. In this case, the antidromic and orthodromic potentials should have the same onset latency.

Lesions Proximal to the Dorsal Root Ganglion Result in Normal Sensory Nerve Action Potentials

Peripheral sensory fibers are all derived from the dorsal root ganglia cells, the primary sensory neurons. These cells have a unique anatomic arrangement: they are bipolar cells located outside the spinal cord, near the intervertebral foramina. Their central processes form the sensory nerve roots, whereas their peripheral projections ultimately become peripheral sensory nerves. Any lesion of the nerve root, even if severe, leaves the dorsal root ganglion and its peripheral axon intact, although essentially disconnected from its central projection. *Accordingly, SNAPs remain normal in lesions proximal to the dorsal root ganglia, including lesions of the nerve roots, spinal cord, and brain* (Figure 3–10). It is not uncommon, in the EMG lab, for a patient to have sensory symptoms or sensory loss but to have normal SNAPs in that distribution. This combination of clinical and electrical findings should always suggest the

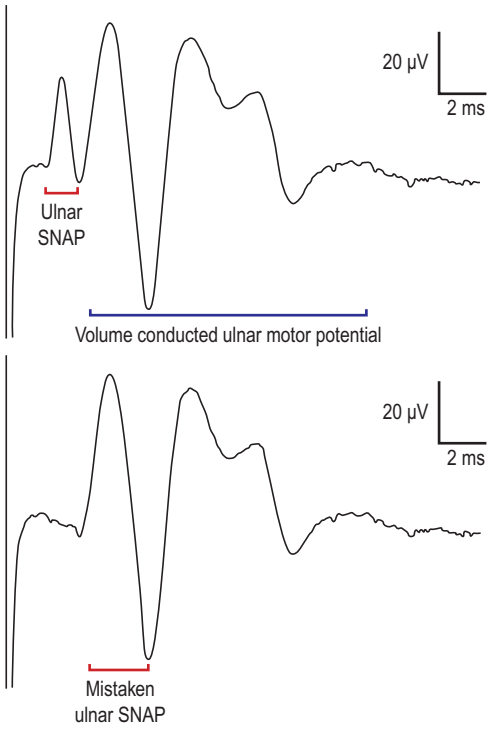

FIGURE 3–9 Misinterpretation error with antidromic sensory studies. In an antidromic study, the entire nerve is stimulated, including both sensory and motor fibers, which frequently results in the SNAP being followed by a volume-conducted motor potential. **Top:** Normal antidromic ulnar sensory response, stimulating the wrist and recording the fifth digit. Notice the ulnar SNAP, which is followed by the large, volume-conducted motor response. One can recognize the SNAP by its characteristic shape, and especially by its brief negative peak duration of approximately 1.5 ms. Also, notice that the SNAP usually occurs earlier than the volume-conducted motor response. **Bottom:** If the sensory response is absent, and an antidromic study is performed, one might mistake the first component of the volume-conducted motor response for the SNAP. The key to not making this mistake is to note the longer duration of the motor potential, which often has a higher amplitude and slowed latency/conduction velocity. In this case, the negative peak duration of this mistaken potential is approximately 2.5 ms. In some cases, one still may not be certain. In those situations, performing the study orthodromically will settle the issue as no volume-conducted motor potential will occur with an orthodromic study. The onset latencies of the orthodromic and antidromic potentials should be the same. The problem with an orthodromic study is that the amplitude is often much lower than with the antidromic method. (Note: Sensory responses are normally very low, in the microvolt range.)

possibility of a lesion proximal to the dorsal root ganglia, although rarely other conditions can produce the same situation.

The situation is quite different for motor fibers. The primary motor neurons, the anterior horn cells, are located in the ventral gray matter of the spinal cord. Axons from the motor neurons form the motor roots and, ultimately, the motor fibers in the peripheral nerves. Lesions of the motor roots effectively disconnect the peripheral motor fibers from their primary neurons, resulting in degeneration of motor fibers throughout the peripheral nerve. Consequently, a nerve root lesion often results in abnormalities on motor NCSs and especially needle EMG.

Proximal Stimulation: Normal Temporal Dispersion and Phase Cancellation

During routine motor conduction studies, the CMAPs recorded by proximal and distal stimulations are nearly identical in configuration. If measured carefully, the proximal CMAP duration may increase slightly, and both the area and amplitude may fall slightly. If the same proximal and distal stimulation sites are used for sensory studies, however, the proximal SNAP varies greatly from the distal one in terms of duration, area, and amplitude. The duration of the proximal potential is markedly increased, and the amplitude and area are greatly reduced compared to the distal potential (Figure 3–11). These changes are normal findings that result from a combination of temporal dispersion and phase cancellation.

For both sensory and motor studies, the recorded potential (SNAP, CMAP) is a *compound* potential. In the case of sensory studies, many individual sensory fibers depolarize and summate to create the SNAP. Within any sensory nerve, there are large, medium, and smaller myelinated fibers, which depolarize and conduct at slightly different velocities. In general, the larger fibers depolarize before the smaller ones. Likewise, there is a normal variation in the size of individual sensory fiber action potentials, with larger fibers generally having larger amplitudes. Temporal dispersion occurs as these individual nerve fibers fire at slightly different times (i.e., larger, faster fibers depolarize before smaller, slower ones). Temporal dispersion normally is more prominent at proximal stimulation sites because the slower fibers progressively lag behind the faster fibers (Figure 3–12). This is analogous to a marathon race in which one runner runs a 5-minute mile and the other a 6-minute mile. At the beginning of the race, both runners are very close to each other (less dispersion), but by the end of the race they are far apart (greater dispersion).

With proximal stimulation, there is a greater lag time between the faster and slower conducting fibers, leading to increased duration and temporal dispersion of the waveform. If temporal dispersion alone were at work, the amplitude would decrease as the potential was spread out, but the area would be preserved. This would indeed be the case if each sensory fiber action potential were monophasic in configuration. However, single sensory fiber action potentials usually have either a biphasic or triphasic configuration. A single, large sensory myelinated fiber has a negative duration of about 0.5 ms, approximately half the normal duration of the distal SNAP (typical duration is 1.3 ms). This implies that after the first 0.5 ms, the trailing positive phase of the fastest potential overlaps with the leading negative phases of the slower fibers. When overlap occurs between the positive phase of one sensory fiber action potential and the negative phase of another, phase cancellation occurs, resulting in a smaller summated potential. This results in a drop of area, as well as a further drop in amplitude.

Although temporal dispersion and phase cancellation usually are thought of as occurring at proximal stimulation

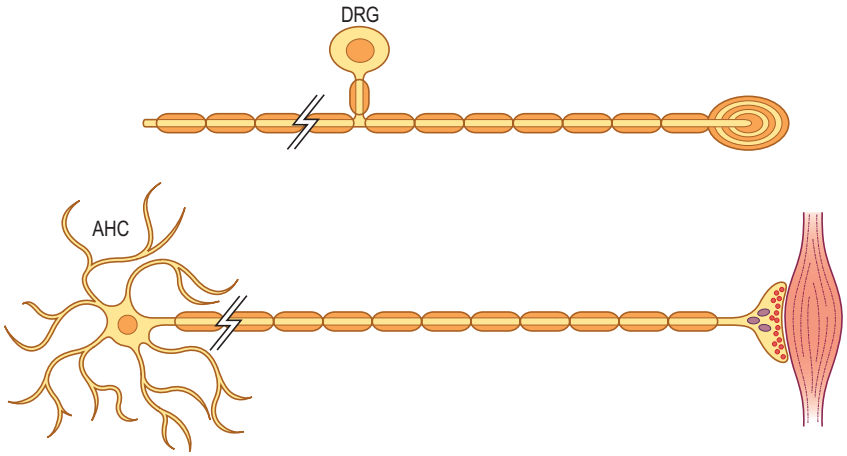

FIGURE 3–10 Nerve root lesions and nerve conduction studies. Anatomic differences between sensory and motor nerve fibers result in different patterns of nerve conduction abnormalities in nerve root lesions. The sensory nerve **(top)** is derived from the dorsal root ganglia (DRG). The DRG are bipolar cells whose central processes form the sensory roots and distal processes continue as the peripheral sensory nerve fibers. The motor nerve **(bottom)** is derived from the anterior horn cell (AHC), which resides in the ventral gray matter of the spinal cord. Lesions of the nerve roots separate the peripheral motor nerve from its neuron, the AHC, but leave the DRG and its distal processes intact. Thus, nerve root lesions may result in degeneration of the motor fibers distally and, accordingly, abnormalities on motor nerve conduction studies and/or needle electromyogram. However, the distal sensory nerve remains intact in lesions of the nerve roots, as the lesion is proximal to the DRG. Thus, results of sensory conduction studies remain normal.

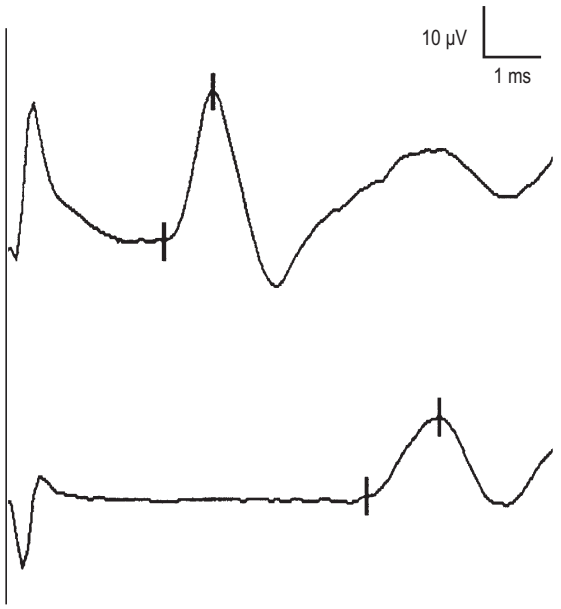

FIGURE 3–11 Proximal sensory studies. Normal median sensory study, recording index finger, stimulating wrist **(top trace)** and elbow **(bottom trace)**. Note that in normal subjects, proximal stimulation results in sensory nerve action potentials (SNAPs) that are longer in duration and lower in amplitude and area. This occurs as a result of normal temporal dispersion and phase cancellation. If the SNAP is small at the distal stimulation site, it may be difficult or impossible to obtain a potential with proximal stimulation.

sites, the effect is present to some degree even with distal stimulation. For example, the median SNAP is higher in amplitude and shorter in duration when stimulating in the palm and recording the index finger than when stimulating at the usual distal site in the wrist. This is because some normal temporal dispersion and phase cancellation occur even at the usual distal stimulation sites. The effects of temporal dispersion are not as apparent with distal stimulation, however, because the slower fibers do not have as much time to lag behind, and phase cancellation is less prominent. This results in a distal potential with a larger amplitude and area than the more proximal potential. At proximal stimulation sites, phase cancellation results in a potential with a smaller amplitude and area and a longer duration.

Temporal dispersion and phase cancellation also occur in motor studies but are much less marked (Figure 3–12). The CMAP is the summation of many individual motor unit action potentials (MUAPs). An individual MUAP has a negative peak duration of 5 to 6 ms, very similar to the CMAP duration. With such similar durations, most MUAPs are in phase with each other. In addition, the range of normal conduction velocities is smaller for motor than for sensory fibers. Because the slowest motor fibers do not lag as far behind the fastest fibers with proximal stimulation, the effects of temporal dispersion and phase cancellation are not as marked for motor as they are for sensory fibers.

MIXED CONDUCTION STUDIES

In many respects, mixed NCSs are comparable to sensory studies. Both studies measure compound nerve action potentials, which are stimulated and recorded in a similar manner. However, for mixed nerve studies, the potential reflects both motor and sensory fiber action potentials generated along the nerve. Although theoretically any mixed nerve can be studied, in practice, the median, ulnar, and distal tibial nerves are most often selected for examination. These mixed nerve studies are used most often in the electrodiagnosis of median neuropathy at the wrist, ulnar neuropathy at the elbow, and tibial neuropathy across the tarsal tunnel, respectively.

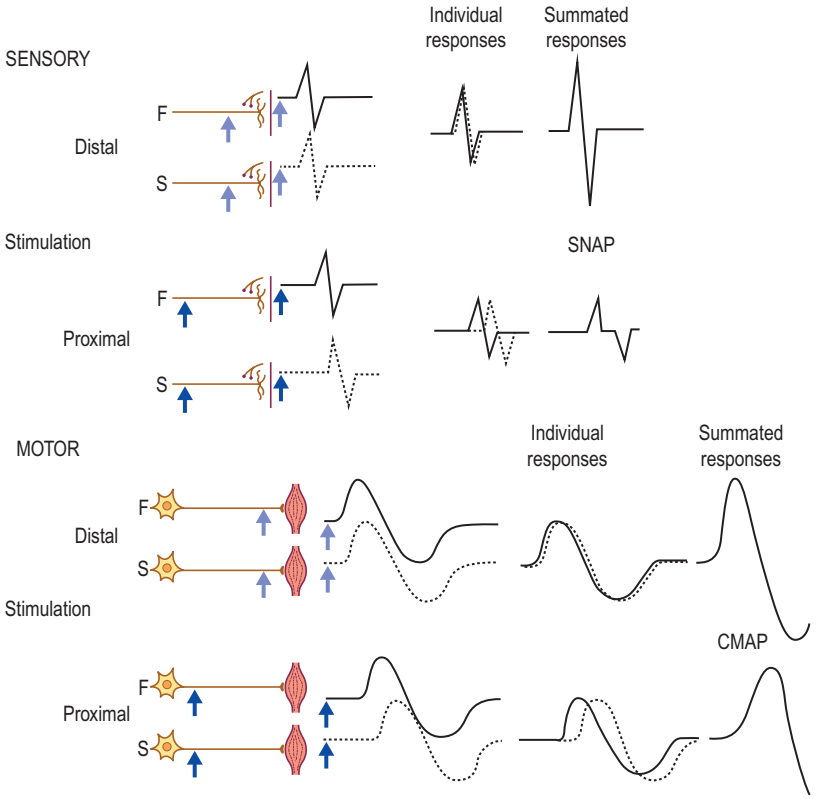

FIGURE 3–12 Temporal dispersion and phase cancellation in nerve conduction studies. Sensory nerve action potentials (SNAPs) and compound muscle action potentials (CMAPs) both are compound potentials, representing the summation of individual sensory and muscle fiber action potentials, respectively. In each case, there are fibers that conduct faster (F) and those that conduct more slowly (S). With distal stimulation, fast and slow fiber potentials arrive at the recording site at approximately the same time. However, with proximal stimulation, the slower fibers lag behind the faster fibers. For sensory fibers **(top traces),** the amount of temporal dispersion at proximal stimulation sites results in the negative phase of the slower fibers overlapping with the positive trailing phase of fastest fibers. These superimposed positive and negative phases cancel each other out, resulting in a decrease in area and amplitude, beyond the decrease in amplitude and increase in duration from the effects of temporal dispersion alone. The effects of temporal dispersion and phase cancellation are less prominent for motor fibers **(bottom traces).** The duration of individual motor fiber potentials is much longer than that of single sensory fibers. Thus, for the same amount of temporal dispersion, there is much less overlap between negative and positive phases of motor fiber action potentials.
(From Kimura, J., Machida, M., Ishida, T., et al., 1986. Relationship between size of compound sensory or muscle action potentials, and length of nerve segment. Neurology 36, 647, with permission of Little, Brown and Company.)

At first glance, one might presume that mixed nerve studies, which record motor and sensory fibers in combination, offer little advantage over routine motor and sensory studies performed independently. During routine motor or sensory NCSs, however, the largest and fastest fibers in the body are not recorded. These fibers are the sensory muscle afferents, the Ia fibers, which supply the muscle spindles. *These largest fibers are recorded only during mixed nerve studies, wherein the entire mixed nerve is stimulated and also recorded*. Mixed nerve conduction velocities usually are faster than either routine motor or cutaneous sensory conduction velocities because they include these Ia fibers. Furthermore, because the Ia fibers have the largest diameter, and accordingly the greatest amount of myelin, they often are the fibers earliest affected by demyelinating lesions, such as occur in entrapment neuropathies.

For a mixed NCS, the settings are similar to those used for sensory conduction studies. The gain usually is set at 10 to 20 μV per division because the responses are quite small (usually in the range of 5 to 100 μV). A pair of recording electrodes (G1 and G2) is placed in line over the mixed nerve, at an interelectrode distance of 2.5 to 4 cm, with the active electrode (G1) closest to the stimulator (Figure 3–13). The recorded potential, the mixed nerve action potential (MNAP), is a compound potential that represents the summation of all the individual sensory and motor fiber action potentials. MNAPs usually are biphasic or triphasic potentials. Onset latency, peak latency, duration, amplitude, and conduction velocity are measured using methods similar to those used in sensory conduction studies.

PRINCIPLES OF STIMULATION

Use Supramaximal Stimulation

In order to obtain correct and reproducible data during NCSs, it is essential that all fibers within a nerve are stimulated at all locations. If the current is too low, not all fibers will be depolarized (submaximal stimulation).

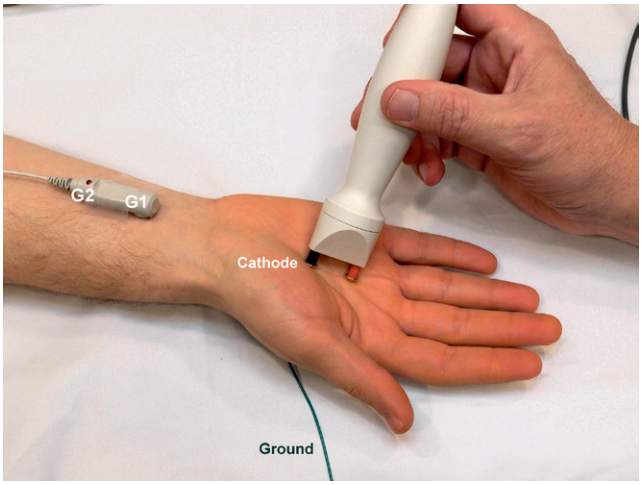

FIGURE 3–13 Mixed nerve study setup. Median mixed study, stimulating median nerve in the palm, recording median nerve at the wrist. The active recording electrode (G1) faces the cathode of the stimulator. Mixed studies stimulate and record all motor and sensory fibers, including the muscle afferents, the Ia fibers, which are not recorded in either routine sensory or motor conduction studies.

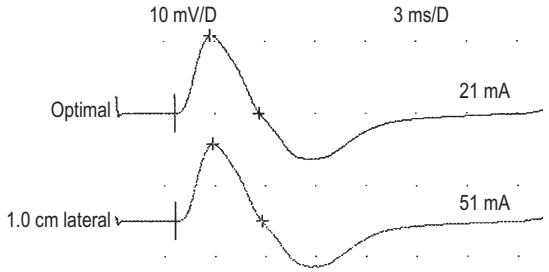

FIGURE 3–14 Optimal stimulator position and supramaximal stimulation. In this example, the median nerve is stimulated at the wrist while recording the abductor pollicis brevis muscle. In the top trace, the stimulator has been placed in the optimal location directly over the nerve. In the lower trace, the stimulator has been moved 1 cm lateral to that position. Supramaximal stimulation is then achieved. Note that in both examples, the resultant compound muscle action potential is identical. However, the current needed to obtain supramaximal stimulation, when stimulating laterally, is more than twice that needed at the optimal position.

Conversely, if it is too high, current may spread and depolarize nearby nerves (co-stimulation). Different degrees of current intensity are required in different individuals and in different anatomic locations in order to depolarize all nerve fibers. For instance, some nerves lie just under the skin (e.g., ulnar nerve at the elbow), whereas others are much deeper (e.g., tibial nerve at the popliteal fossa). At each stimulation site, it is essential that supramaximal stimulation be used to ensure that all axons within a given nerve are depolarized. To achieve supramaximal stimulation, the current intensity is slowly increased until the amplitude of the recorded potential reaches a plateau. The current intensity then is increased an additional 20 to 25% to ensure that the potential no longer increases. It is only at this point that supramaximal stimulation is achieved. This procedure needs to be used at all locations. *One of the most common mistakes in performing NCSs is to stop increasing the current once the potential is within the normal range. In this case, the potential may be "normal" but not supramaximal.*

Optimize the Stimulation Site

One may be tempted to routinely use higher stimulation intensities in order to assure supramaximal stimulation. However, this practice can lead to technical errors due to the spread of the stimulus to nearby adjacent nerves, in addition to causing pain to the patient (see Chapter 8). One of the most useful techniques to master is placement of the stimulator at the optimal location directly over the nerve, which yields the highest CMAP amplitude with the least stimulus intensity (Figure 3–14). This technique is easily learned. The stimulator is placed over a site where the nerve is expected to run, based on anatomic landmarks. The stimulus intensity is slowly increased until the first small submaximal potential is recorded. At this point, the stimulus current is held constant, and the stimulator is moved parallel to the initial stimulation site, both slightly laterally and then slightly medially (Figure 3–15). The position that yields the highest response is the position closest to the nerve. Because the stimulus intensity is low, this procedure is not painful for the patient. Once the optimal position is determined, the current is increased to supramaximal. It often is surprising how little current is required to obtain supramaximal stimulation using this technique, leading to many fewer technical errors and better patient tolerance and cooperation.

IMPORTANT BASIC PATTERNS

Several basic patterns of nerve conduction abnormalities can be recognized, depending on the underlying pathology. For example, abnormalities noted in motor conduction studies may be seen with disorders of the anterior horn cell, nerve root, nerve, NMJ, or muscle. In contrast, sensory or mixed nerve conduction abnormalities always imply a primary disorder of the peripheral nerve.

Neuropathic Lesions

Neuropathic lesions can be divided into those that primarily affect either the axon or the myelin sheath. Axonal loss may be seen after physical disruption of the nerve or as a result of numerous toxic, metabolic, or genetic conditions that can damage the metabolic machinery of the axon. Demyelination resulting from loss or dysfunction of the myelin sheath is seen most often in entrapment or compressive neuropathies. Otherwise, demyelination occurs in only a limited number of conditions, some of which are genetic (e.g., Charcot–Marie–Tooth polyneuropathy), some toxic (e.g., diphtheria), and others the consequence of a presumed immunologic attack on the myelin (e.g.,

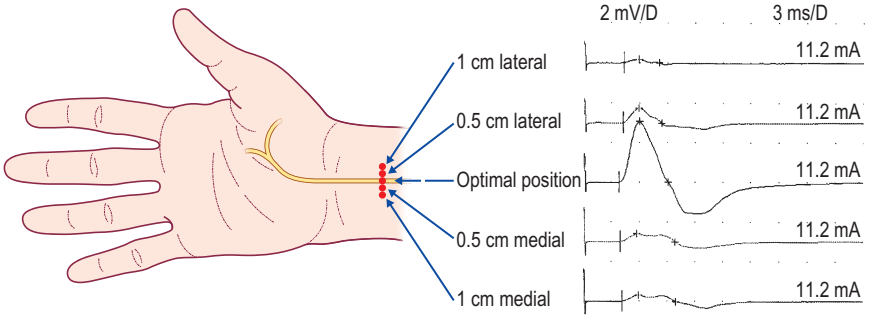

FIGURE 3–15 Optimizing the stimulator position over the nerve. The stimulator is placed over a site where the nerve is expected to run, based on anatomic landmarks. The stimulus intensity is slowly increased until the first small submaximal potential is recorded. At this point, the stimulus current is held constant, and the stimulator is moved parallel to the initial stimulation site, both slightly laterally and then slightly medially. Note in this example that moving the stimulator by very small increments (0.5 cm) markedly changes the amplitude of the compound muscle action potential. The optimal site is the one with the largest potential, which is directly over the nerve. Because the stimulus intensity is low (in this case, 11.2 mA), this procedure of optimizing the stimulator site is not painful for the patient. Once the optimal position is determined, the current is increased to supramaximal. Using this technique markedly reduces the amount of current necessary to achieve supramaximal stimulation, reduces a host of possible technical errors as well as patient discomfort, and increases efficiency.

Guillain–Barré syndrome). *In neuropathic lesions, one of the key pieces of diagnostic information obtained from NCSs is the differentiation of a primary axonal loss lesion from a primary demyelinating lesion.*

Axonal Loss

Axonal loss is the most common pattern seen on NCSs. *Reduced amplitude is the primary abnormality associated with axonal loss*. Amplitudes of the CMAP, SNAP, and MNAPs reflect the number of underlying motor, sensory, and mixed nerve axons, respectively. As axons are lost, the amplitudes of these potentials decrease. The best way to assess the amount of axonal loss is to compare the amplitude of a potential with a previous baseline value, a normal control value, or the contralateral (asymptomatic) side. *Note that although axonal loss lesions generally result in reduced amplitudes, the corollary is not necessarily true: reduced amplitudes do not necessarily imply an axonal loss lesion* (see the next two sections on Demyelination and Conduction Block).

In axonal loss lesions, conduction velocity and distal latency are normal, provided that the largest and fastest conducting axons remain intact. The typical pattern associated with axonal loss is one of reduced amplitudes with preserved latencies and conduction velocities (Figure 3–16B). Mild slowing of distal latency and conduction velocity may occur if the largest and fastest conducting axons are lost. Marked slowing, however, does not occur. To understand this concept and the possible range of slowing in axonal loss lesions, consider the examples shown in Figure 3–17. Every nerve contains a normal range of myelinated fibers with different axonal diameters and conduction velocities. In the median nerve, for instance, the largest-diameter (and accordingly the fastest) myelinated fibers conduct at a velocity of approximately 65 m/s. At the other end of the normal range, there are slower fibers that conduct as slowly as 35 m/s. The vast majority of fibers lie between these two extremes. However, whereas all fibers contribute to amplitude and area, only the fastest conducting fibers contribute to the conduction velocity and latency measured by routine NCSs.

In lesions associated with axonal loss, one can consider two possible extremes of conduction velocity abnormalities. At one extreme, there may be severe loss of axons with only a few of the fastest fibers remaining (Figure 3–17B). While amplitude markedly decreases, the conduction velocity and distal latency remain normal, due to the preservation of the fastest conducting fibers. At the other extreme, if all axons are lost except for a few of the normal most slowly conducting fibers (Figure 3–17C), the amplitude will also fall dramatically. In addition, conduction velocity will drop, but only as low as 35 m/s (approximately 75% of the lower limit of normal), reflecting the conduction velocity of the slowest conducting fibers. Greater slowing cannot occur in a pure axonal loss lesion because normal myelinated fibers do not conduct any more slowly than this. Latencies become prolonged in a similar fashion, but there is a limit to this prolongation, such that the latencies generally do not exceed 130% of the upper limit of normal. In general, axonal loss lesions result in a pattern somewhere between these two extremes. When there is random dropout of fibers, the amplitude falls, the conduction velocity slows slightly, and the distal latency mildly prolongs (Figure 3–18).

Thus, with axonal loss lesions, (1) amplitudes decrease, (2) conduction velocities are normal or slightly decreased but never below 75% of the lower limit of normal, and (3) distal latencies are normal or slightly prolonged but never greater than 130% of the upper limit of normal.

The only exception to these criteria for axonal loss lesions occurs in hyperacute axonal loss lesions, such as might occur following a nerve transection. In such a case, results of NCSs performed within 3 to 4 days of an acute axonal loss lesion remain normal, provided both stimulation and recording are done distal to the lesion. Between days 3 to 10, the process of wallerian degeneration occurs: the nerve

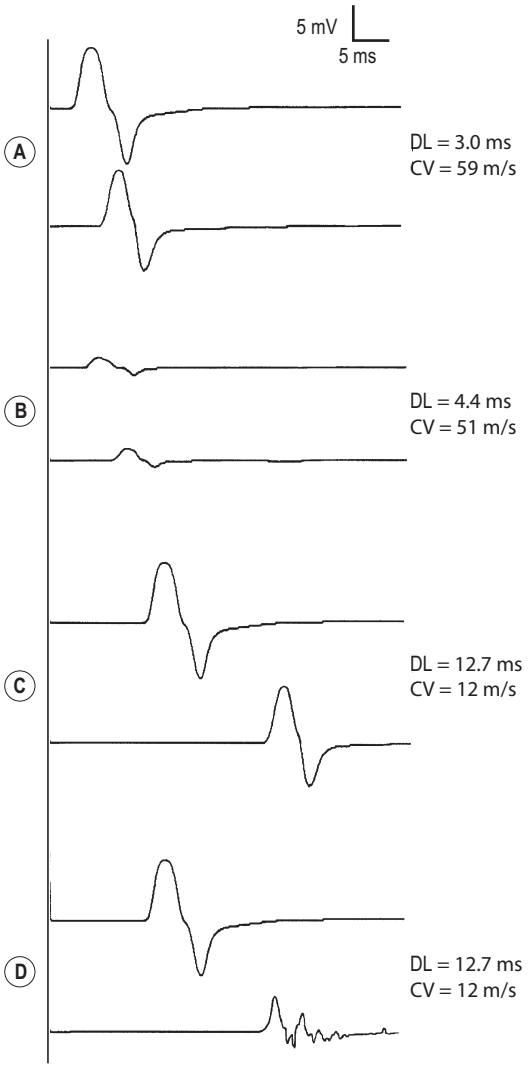

FIGURE 3–16 Patterns of nerve conduction abnormalities. Depending on whether the underlying nerve pathology is axonal loss or demyelination, different patterns of abnormalities are seen on nerve conduction studies. **A:** Normal study. Note the normal distal latency (DL) <4.4 ms, amplitude >4 mV, and conduction velocity (CV) >49 m/s. **B:** Axonal loss. In axonal loss lesions, amplitudes decrease; CV is normal or slightly slowed, but not <75% of the lower limit of normal; and DL is normal or slightly prolonged, but not >130% of the upper limit of normal. The morphology of the potential does not change between proximal and distal sites. **C:** Demyelination resulting in uniform slowing is most often associated with inherited conditions (e.g., Charcot–Marie–Tooth polyneuropathy). CV is markedly slowed (<75% lower limit of normal) and DL is markedly prolonged (>130% of the upper limit of normal). However, there usually is no change in configuration between proximal and distal stimulation sites. **D:** Demyelination with conduction block/temporal dispersion. Marked slowing of conduction velocity and distal latency, but also with change in potential morphology (conduction block/temporal dispersion) between distal and proximal stimulation sites, is most often associated with acquired causes of demyelination. This pattern may be seen in Guillain–Barré syndrome or other acquired demyelinating conditions.

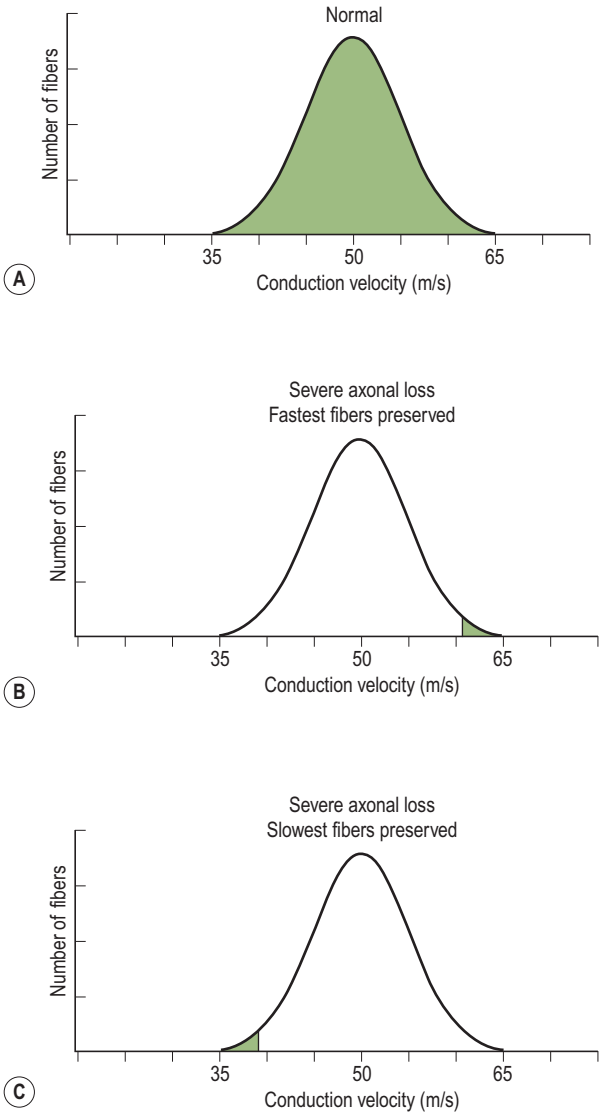

FIGURE 3–17 Conduction velocity slowing and axonal loss lesions. Every nerve contains a normal range of myelinated fibers with different axonal diameters and conduction velocities. For example, in the normal median nerve (**A**), the fastest myelinated fibers conduct at a velocity of approximately 65 m/s. At the other end of the normal range, there are slower fibers that conduct as slowly as 35 m/s. Whereas all fibers contribute to amplitude and area, only the fastest conducting fibers contribute to the conduction velocity and latency measured by routine nerve conduction studies. In lesions associated with axonal loss, there is a range of possible conduction velocity slowing. At one extreme (**B**), severe axonal loss may occur with sparing of only a few of the fastest fibers remaining (outlined in green). While amplitude markedly decreases, conduction velocity and distal latency remain normal, due to the preservation of the fastest conducting fibers. At the other extreme (**C**), if all axons are lost, except for a few of the slowest conducting fibers (outlined in green), the amplitude also falls dramatically. However, conduction velocity can only drop as low as 35 m/s (≈75% of the lower limit of normal). Greater slowing cannot occur in a pure axonal loss lesion because normal myelinated fibers do not conduct any slower than this. Latencies also prolong in a similar fashion, but there is a limit to this prolongation, generally no greater than 130% of the upper limit of normal. Thus, with axonal loss lesions, (1) amplitudes decrease, (2) conduction velocities are normal or slightly decreased, but never below 75% of the lower limit of normal, and (3) distal latencies are normal or slightly prolonged, but never greater than 130% of the upper limit of normal.

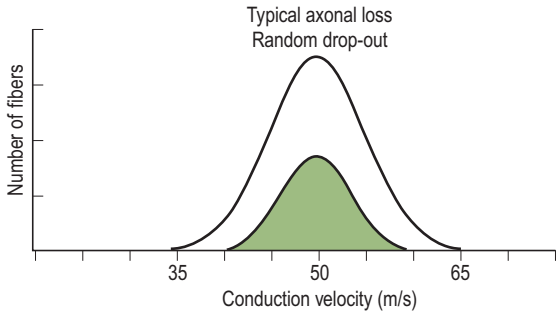

FIGURE 3–18 Typical axonal loss pattern. With random dropout of fibers from axonal loss (outlined in green), the normal distribution of nerve fibers and their associated conduction velocities changes to a smaller bell-shaped curve. In this case, the amplitude decreases while the conduction velocity and distal latency slightly slow. This is the more typical pattern of axonal loss than the extreme examples shown in Figure 3–17, where only a few of either the fastest or slowest normal fibers remain after severe axonal loss.

distal to the transection undergoes degeneration, resulting in a low amplitude potential both distally and proximally. The process of wallerian degeneration is earlier for motor fibers (typically between days 3–5) compared to sensory fibers (typically between days 6–10). Once wallerian degeneration is complete, the typical pattern of axonal loss will be seen on NCSs.

A unique situation occurs if stimulation is performed distal and proximal to an acute axonal loss lesion during the first 3 days after the nerve insult. In this case, the amplitude will be normal with distal stimulation, but reduced with proximal stimulation. This pattern simulates conduction block, a pattern typically associated with demyelination but, in fact, is best termed *pseudo-conduction block*. This type of acute axonal loss pattern is distinctly unusual, and in common practice, is seen only in two situations: (1) acute trauma/transection of a nerve, or (2) nerve infarction, as occurs most classically in vasculitic neuropathy. In such situations, the only way to differentiate an acute axonal loss lesion resulting in pseudo-conduction block from a true demyelinating conduction block is to repeat the study after an additional week, when wallerian degeneration is complete. In the case of an axonal loss lesion, the typical axonal pattern will be present after 1 week (low amplitudes, normal or slightly prolonged latencies, normal or slightly slow conduction velocity) whereas in a true demyelinating lesion, the conduction block pattern will persist.

Demyelination

Myelin is essential for saltatory conduction. Without myelin, nerve conduction velocity is either markedly slowed or blocked (Figure 3–16C and D). On NCSs, demyelination is associated with marked slowing of conduction velocity (slower than 75% of the lower limit of normal), marked prolongation of distal latency (longer than 130% of the upper limit of normal), or both. Conduction velocities and latencies slower than these cutoff values imply primary demyelination; such values are not seen with axonal loss lesions, even in severe lesions associated with loss of the fastest conducting fibers. This is because there are simply no normal myelinated axons that conduct this slowly (n.b., there are small myelinated Aδ pain fibers that conduct in this range, but these fibers are neither stimulated nor recorded with routine nerve conduction techniques). *Essentially, any motor, sensory, or mixed nerve conduction velocity that is slower than 35 m/s in the arms or 30 m/s in the legs signifies unequivocal demyelination*. Only in the rare case of regenerating nerve fibers after a complete axonal injury (e.g., nerve transection) can conduction velocities be this slow and not signify a primary demyelinating lesion.

Occasionally, the electromyographer will encounter conduction velocity slowing that approaches these cutoff values. When this occurs, interpretation of whether the slowing represents demyelination or axonal loss is aided by knowledge of the amplitude of the potential. A conduction velocity near the cutoff value where the amplitude is normal usually represents demyelination, whereas a borderline velocity with a markedly reduced amplitude most often implies severe axonal loss. Consider the following example:

Median motor study	Conduction velocity (m/s)	Distal motor amplitude (mV)
Case 1	35	7
Case 2	35	0.2

In this example, both cases have a conduction velocity of 35 m/s, which is right at the cutoff value for slowing of the median nerve in the demyelinating range (i.e., 75% of the lower limit of normal). In case 1 the amplitude is normal, and the conduction velocity likely represents demyelination. In case 2, however, the amplitude is very low at 0.2 mV and is accompanied by the same slowed conduction velocity. This markedly low amplitude implies that there has likely been severe axonal loss. In this situation, the severely slowed conduction velocity most likely represents severe axonal loss, with loss of the fastest and intermediate conducting fibers and preservation of the more slowly conducting fibers. Using more than one piece of information for interpretating EDX findings is a recurring theme in EDX studies: it is often not one piece of information that leads to a correct interpretation and diagnosis, but putting several pieces of data together.

Amplitude changes associated with demyelination are variable. At first glance, it might appear that reduced amplitudes are always a marker of axonal loss rather than demyelination. This is not completely true, however, and depends on two conditions:

- whether sensory or motor studies are performed
- whether or not *conduction block* is present, and if present, where the stimulation site is in relationship to the conduction block.

Sensory amplitudes often are low or absent in demyelinating lesions. Sensory amplitudes are reduced due to the normal processes of temporal dispersion and phase cancellation. These are exaggerated by demyelinative slowing,

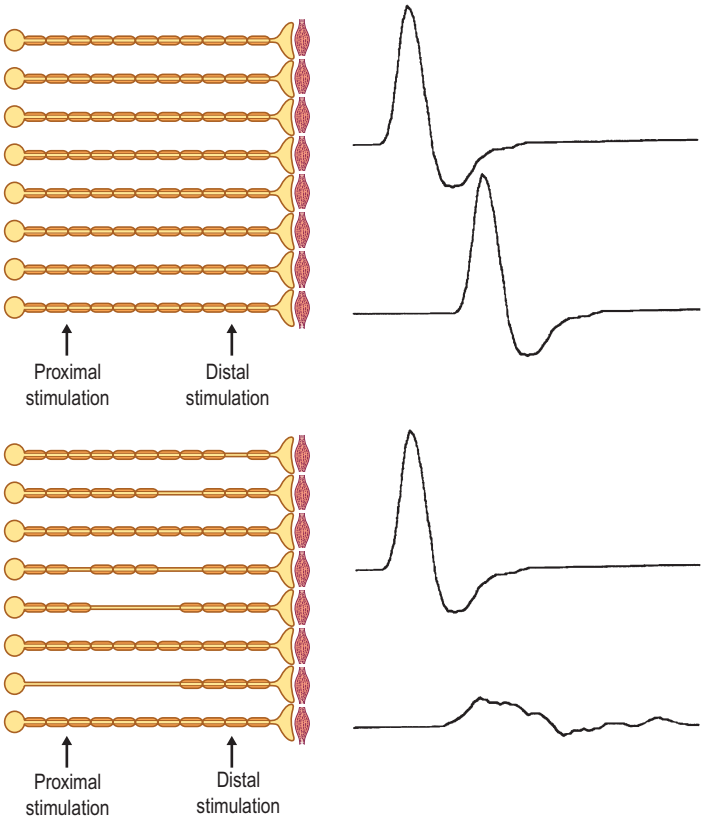

FIGURE 3–19 Model of conduction block. In acquired demyelinating lesions, demyelination is often a patchy, multifocal process. When the nerve is stimulated proximal to the conduction block, the compound muscle action potential (CMAP) drops in amplitude and area and becomes dispersed **(bottom).** In a normal nerve **(top),** the CMAP morphology usually is similar between distal and proximal stimulation sites.
(Adapted from Albers, J.W., 1987. Inflammatory demyelinating polyradiculoneuropathy. In: Brown, W.F., Bolton, C.F., (Eds.), Clinical electromyography. Butterworth-Heinemann, Stoneham, MA, with permission.)

which further lowers sensory amplitudes by changing the range of conduction velocities, thereby increasing the temporal dispersion and phase cancellation. Think again about the analogy of two marathon runners: one running at 13 miles per hour and another at 6.5 miles per hour. To complete the marathon of 26 miles, the first runner takes 2 hours, and the second takes 4 hours. Thus, they finish 2 hours apart. Consider this normal temporal dispersion. Now, imagine that both runners run half as fast as their normal speed, 6.5 miles per hour and 3.25 miles per hour. Consider this demyelination. It will take the first runner 4 hours to complete the marathon, and the second runner, 8 hours. Now, the two runners finish 4 hours apart. Thus, they are more temporally dispersed than normal. In the world of nerve conductions, more temporal dispersion results in more phase cancellation (i.e., negative phases of some fiber action potentials cancelling out positive phases of other fiber action potentials), and thus lower or absent sensory potentials.

Conduction Block

Reduced amplitudes in demyelinating lesions are seen when conduction block is present, as occurs in acquired demyelination (Figure 3–19). If a conduction block is present in a demyelinating lesion, then the site of stimulation and the location of the conduction block will determine the CMAP amplitude (Figure 3–20). The amplitude will be low if the nerve is stimulated proximal to the conduction block. If the conduction block is present between the normal distal stimulation site and the recording electrodes, both the distal and proximal CMAP amplitudes will be low and may simulate an axonal loss lesion (Figure 3–20, top). In this situation, it may be difficult to prove that a conduction block is present. If the conduction block is present between distal and proximal stimulation sites, which is the usual situation, the CMAP amplitude will be normal distally, below the block, but will be decreased at the proximal stimulation site, above the block (Figure 3–20, middle). Finally, if both the proximal and distal stimulation sites are distal to, or below the block, the CMAP amplitudes will remain normal both distally and proximally (Figure 3–20, bottom).

In demyelinating lesions, the crucial question that often must be addressed is how much of a drop in either amplitude or area is needed to properly identify a conduction block. From studies of normal subjects, CMAP amplitude and area generally do not decrease by more than 20%, and CMAP duration generally does not increase by more than 15%, when recorded from the typical distal and proximal stimulation sites (i.e., wrist to elbow, ankle to knee).*

*The only normal exception to these findings occurs during routine tibial motor studies. The tibial CMAP often is smaller in amplitude and area, and more dispersed, when stimulating at the popliteal fossa than when stimulating at the ankle. The reason for this finding is not completely clear, although, in some cases, supramaximal stimulation is difficult to achieve at the popliteal fossa. In practice, one should always be cautious calling a proximal drop in amplitude or area a conduction block during routine tibial motor studies. A drop in amplitude up to 50% may be seen in normal subjects when stimulating the tibial nerve at the popliteal fossa.

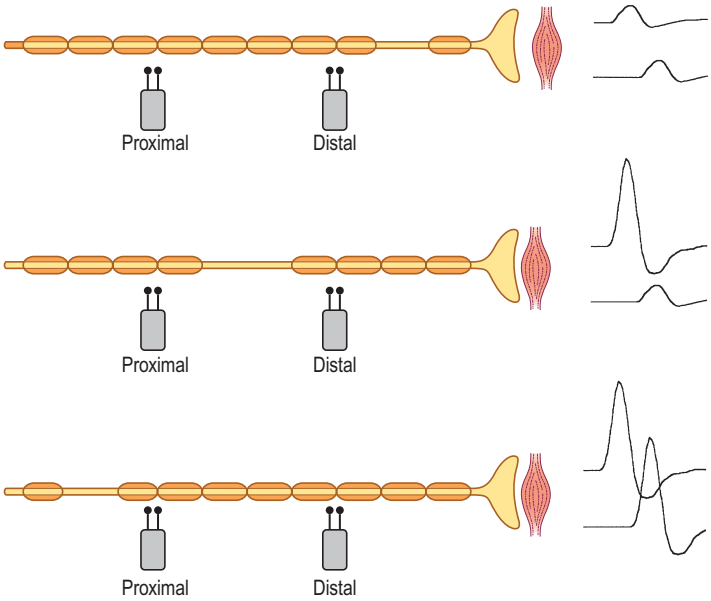

FIGURE 3–20 Compound muscle action potential (CMAP) amplitude and conduction block location. In demyelinating lesions, the site of stimulation and the presence and location of the conduction block will determine the CMAP amplitude. **Top:** If a conduction block is present between the usual distal stimulation site and the muscle, amplitudes will be low at both distal and proximal stimulation sites, the pattern usually associated with axonal loss lesions. **Middle:** If a conduction block is present between distal and proximal stimulation sites, a normal CMAP amplitude will be recorded with distal stimulation and a reduced CMAP amplitude will be recorded with proximal stimulation. **Bottom:** If a conduction block is proximal to the most proximal stimulation site, the nerve remains normal distally, although effectively disconnected from its proximal segment. This results in normal CMAP amplitudes both distally and proximally. Late responses may be abnormal (see Chapter 4).

These studies imply that any drop in either CMAP amplitude or area of more than 20% denotes conduction block, and any increase in CMAP duration of more than 15% signifies abnormal temporal dispersion. The effects of normal temporal dispersion, of course, depend on the distance. If more proximal stimulation is performed than in routine motor studies (e.g., axilla or Erb's point stimulation), these values must be modified. In general, for Erb's point stimulation, the cutoff values are doubled (i.e., area or amplitude drop of more than 40%, duration increase of more than 30%). In a similar vein, any abrupt drop in either CMAP area or amplitude over a short segment, even if <20%, and especially if associated with slowing, usually implies conduction block.

Although these guidelines regarding conduction block are useful, sophisticated studies using computer simulation techniques have questioned the proper electrophysiologic criteria for conduction block. Use of these techniques has shown that many of the amplitude and area criteria once considered diagnostic of motor conduction block in demyelinating lesions actually overlap with the amplitude and area drop that can be seen from a combination of temporal dispersion and phase cancellation alone, without conduction block.

In normal motor studies, temporal dispersion and phase cancellation generally do not lead to an appreciable drop in the proximal CMAP amplitude and area for the reasons discussed earlier. In demyelinating lesions, however, the conduction velocities may be very slow, and temporal dispersion and phase cancellation become more prominent for motor fibers. Using computer simulation models, CMAP *area* has been demonstrated to fall by 50%, and amplitude even farther, solely from the effects of temporal dispersion and phase cancellation in demyelinating lesions, without any conduction block (Figure 3–21). *Thus, the criteria of more than a 50% drop in area between proximal and distal stimulation sites should be used to define electrophysiologic conduction block. Of course, it is important to remember that both conduction block as well as abnormal temporal dispersion and phase cancellation signify acquired demyelination.*

In any patient with a peripheral nerve disorder, the presence of demyelination is a key finding for several reasons. In entrapment neuropathies, the exact localization of the lesion can be accomplished only by demonstrating focal

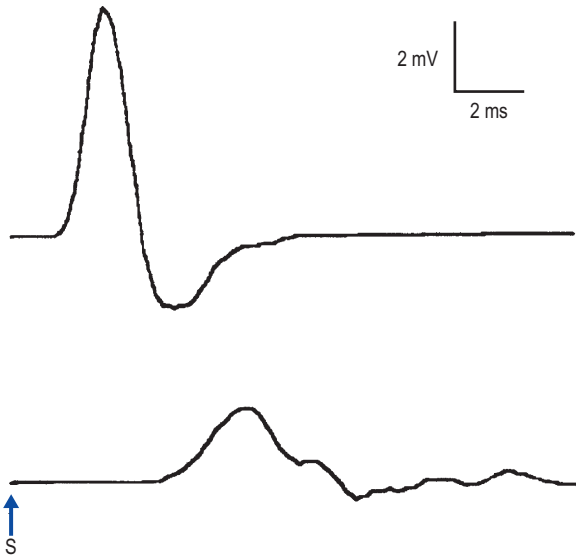

FIGURE 3–21 Temporal dispersion without conduction block. A marked drop in proximal compound muscle action potential (CMAP) amplitude usually means conduction block. In the figure above, there is no conduction block between distal and proximal stimulation sites. The drop in amplitude was entirely due to abnormal temporal dispersion from a demyelinating lesion. To differentiate conduction block from abnormal temporal dispersion requires a drop in area >50%, which is not seen here.
(From Rhee, E.K., England, J.D., Sumner, A.J., 1990. A computer simulation of conduction block: effects produced by actual block versus interphase cancellation. Ann Neurol 28, 146, with permission of Little, Brown and Company.)

Table 3–1. Radial Motor Studies Across the Spiral Groove

Patient No.	Radial CMAP (involved side)		Radial CMAP (contralateral side)	
	Below Spiral Groove (mV)	Above Spiral Grove (mV)	Below Spiral Groove (mV)	Above Spiral Grove (mV)
1	4	0.5	5	4.8
2	1	0.5	5	4.8

CMAP, compound muscle action potential.

demyelination, either by conduction velocity slowing or by conduction block across the lesion site. In addition, the relative degree of conduction block across a lesion site indicates how much weakness and sensory loss are due to demyelination rather than axonal loss. This factor has direct implications for prognosis and the time course of recovery. For example, contrast two patients (Table 3–1), each of whom has a severe wrist drop from a radial neuropathy across the spiral groove ("Saturday night palsy").

In both patients, there is a drop in amplitude across the spiral groove on the involved side. In patient 1, the distal CMAP amplitude (below the spiral groove) is slightly smaller than that on the contralateral, asymptomatic side. This comparison implies only a small amount of axonal loss (4 vs. 5 mV). However, there is a large drop in amplitude (4 vs. 0.5 mV) across the spiral groove, which implies that most of the patient's weakness is secondary to conduction block. Conduction block signifies demyelination; therefore, the prognosis is good. The patient will likely recover quickly over several weeks as remyelination occurs. Contrast this situation with that of patient 2, in whom there is a marked loss of CMAP amplitude below the spiral groove compared with the contralateral side (1 vs. 5 mV). This implies significant axonal loss. Although there is some conduction block across the spiral groove (1 vs. 0.5 mV), most of this patient's weakness is secondary to axonal loss, which implies a longer and possibly less complete recovery process.

Box 3–1. Demyelinating Neuropathies

Hereditary

- Charcot–Marie–Tooth, Type I (CMT1)†
- Charcot–Marie–Tooth, Type IV (CMT4)†
- Charcot–Marie–Tooth, X-linked (CMTX)†
- Dejerine–Sottas disease‡
- Refsum disease
- Hereditary neuropathy with liability to pressure palsy (HNPP)
- Metachromatic leukodystrophy
- Krabbe disease
- Adrenoleukodystrophy
- Cockayne syndrome
- Niemann–Pick disease
- Cerebrotendinous xanthomatosis
- Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE)

Acquired

- Acute inflammatory demyelinating polyradiculoneuropathy (AIDP, the most common variant of Guillain–Barré syndrome)
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
  - Idiopathic
  - Associated with human immunodeficiency virus (HIV) infection
  - Associated with MGUS (especially IgM)
  - Associated with anti-MAG antibodies
  - Associated with osteosclerotic myeloma
  - Associated with Waldenström macroglobulinemia
- Multifocal motor neuropathy with conduction block ($\pm GM_1$ antibodies)
- Diphtheria
- Toxic (i.e., amiodarone, perhexiline, arsenic, glue sniffing, buckthorn shrub poisoning)

Although the list of demyelinating neuropathies is short compared to the differential for axonal neuropathies, it usually can be quickly narrowed even further by clinical history, age of onset, and the presence or absence of systemic and central nervous system features. From a practical point of view, the differential diagnosis of a subacute/chronic demyelinating neuropathy in an adult is likely either an inherited neuropathy (CMT type I) or CIDP and one of its variants. MGUS, monoclonal gammopathy of undetermined significance; MAG, myelin associated glycoprotein.

†The nomenclature of demyelinating Charcot–Marie–Tooth inherited polyneuropathies is complex. Type 1 refers to autosomal dominant, Type 4 to autosomal recessive, and Type X to X-linked. Each type has several subtypes based on the specific genetic defect. Although the conduction velocities are in the demyelinating range, CMTX in males may have more intermediate conduction velocities (e.g., 25–38 m/s) than the more common CMT1 group. In female carriers of CMTX, conduction velocities are only slightly slow or in the normal range.

‡Dejerine–Sottas disease is a historical term used to denote a severe demyelinating neuropathy in children. Formerly considered a distinct entity with autosomal recessive inheritance, genetic analysis has demonstrated that Dejerine–Sottas is a syndrome caused by either recessive inheritance or *de novo* mutations with autosomal dominant inheritance. The recessive forms are now incorporated into the CMT4 group, but the de novo autosomal dominant mutations are on the same genes implicated for CMT1, but with the genetic defect resulting in a much more severe demyelinating neuropathy.

Finally, the presence of demyelination in a patient with polyneuropathy has special significance because very few polyneuropathies show primarily demyelinating features on NCSs (Box 3–1). In patients with demyelinating polyneuropathies, the presence of conduction block at non-entrapment sites often can be used to differentiate between acquired and inherited conditions. In patients with inherited demyelinating polyneuropathies (e.g., Charcot–Marie–Tooth polyneuropathy, Type I), there is uniform slowing of conduction velocity without the

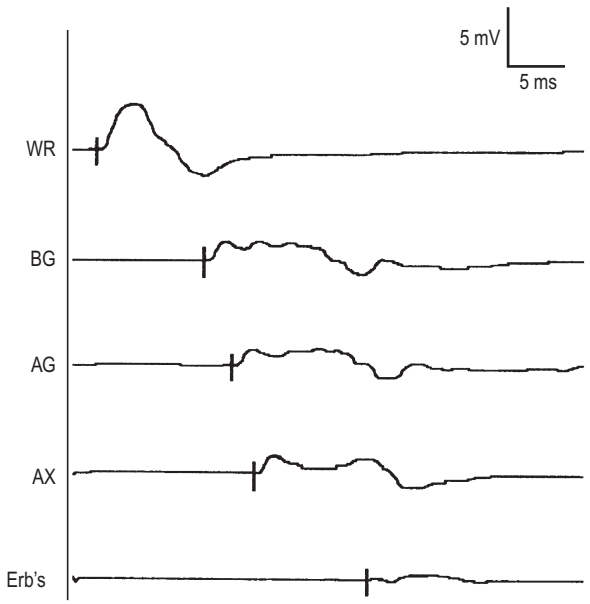

FIGURE 3–22 Conduction block and chronic inflammatory demyelinating polyneuropathy (CIDP). Ulnar motor study in a patient with CIDP, recording abductor digiti minimi, stimulating wrist (WR), below groove (BG), above groove (AG), axilla (AX), and Erb's point. Note the conduction block/temporal dispersion pattern between wrist and below elbow, and between axilla and Erb's point. Conduction block and abnormal temporal dispersion are markers of acquired demyelination. They do not occur in inherited demyelinating neuropathies, except in common areas of entrapment or compression.

presence of conduction blocks. This is in contrast to acquired demyelinating polyneuropathies (e.g., Guillain–Barré syndrome, chronic inflammatory demyelinating polyneuropathy), in which demyelination often is patchy and focal, resulting in conduction block on NCSs (Figure 3–22).

Myopathy

In myopathic disorders, sensory conduction studies are always normal unless there is a superimposed neuropathic condition. Because most myopathies primarily affect proximal muscles and most motor conduction studies record distal muscles, CMAP amplitudes and distal latencies are also generally normal. However, some rare myopathic disorders preferentially affect distal muscles, and in such situations CMAP amplitudes may be low. The same is true if the myopathy is severe and generalized (e.g., critical illness myopathy). Even in these situations, however, the distal latencies and conduction velocities will remain normal.

Neuromuscular Junction Disorders

As in myopathic disorders, sensory studies are normal in disorders of the NMJ. Abnormalities of the CMAP may be seen depending on whether the NMJ pathology is presynaptic or postsynaptic. In postsynaptic disorders (e.g., myasthenia gravis), the motor studies, including the CMAP amplitude, usually are completely normal. However, the situation is different in presynaptic disorders (e.g., Lambert–Eaton myasthenic syndrome, botulism). In these conditions, CMAP amplitudes usually are low at rest, with normal latencies and conduction velocities. To demonstrate a disorder of NMJ transmission, repetitive nerve stimulation, exercise testing, or both need to be performed (see Chapter 6).

Suggested Readings

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