

Weakness; Myopathy, Anterior horn cell disease, Neuropathies and Neuromuscular transmission defects

In the neurological evaluation of weakness, we distinguish between **upper motor neuron** weakness, and **lower motor neuron** weakness. The differences are tabulated below.

Lower motor neuron weakness (LMN)

Flaccid
Decreased tone
Decreased muscle stretch reflexes
Profound muscle atrophy
Fasciculations present
May have sensory disturbances

Upper motor neuron weakness (UMN)

Spasticity, including a Babinski response
Increased tone
Increased muscle stretch reflexes
Minimal muscle atrophy
Fasciculations absent
May have associated sensory disturbances

Fasciculations are irregular contractions of a group of muscle fibers innervated by one axon. Clinically this appears as a small muscle twitch.

It is also customary, and very helpful, to classify LMN weakness on the basis of the anatomical station affected.

These stations are:

- 1) The anterior (ventral) horn cell.
- 2) The peripheral nerve, (ventral and dorsal **nerve roots** i.e., radiculopathy or **nerve** i.e., neuropathy.)
- 3) The neuromuscular junction.
- 4) The muscle (i.e. myopathy).

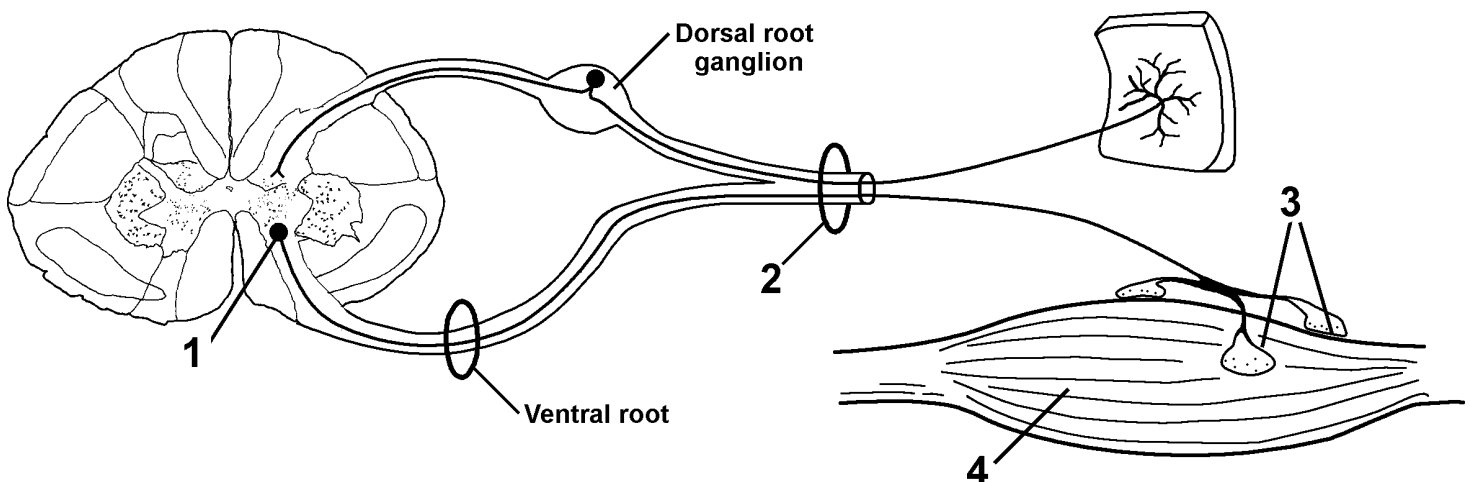


Figure 1. The 4 anatomic stations underlying lower motor neuron weakness

The axons in the **dorsal roots** have been classified based upon their conduction velocities and their sizes. This has led to some confusion in the literature (and for medical students!!). The classification scheme based upon fiber size uses **Roman numerals**. Thus, there are **I, II, III and IV fiber types**. You already have heard about the **Ia** fibers and that they are associated with muscle spindles and are large and fast conducting. You also have heard that the **Ib** fibers are associated with the Golgi tendon organs and are little smaller and slower conducting than the **Ias**. Also remember that **II** fibers are associated with muscle spindles but are slower conducting and smaller than the **Ias** and **Ibs**. **II** fibers are also associated with receptors carrying information from

encapsulated nerve endings used in two point discrimination, vibration and conscious proprioception. **III** fibers are smaller than **I**s and **II**s and are only lightly myelinated and relatively slow conducting. Such fibers are associated with cooling and first pain. Finally, **IV** fibers are unmyelinated and convey second pain and warming.

Now let's turn to the classification that uses **letters** versus Roman numerals. The largest and fastest conducting fibers are called **A** fibers. **A α** (alpha) fibers are comparable to the **I**s and **I**bs. **A β** (alpha-beta) fibers are equivalent to **II** fibers in size and conduction velocities. **A δ** (**deltas**) are equivalent to **III**s and associated with cooling and first pain. **B** fibers are smaller than **A** fibers, are lightly myelinated and are visceral afferents; they have no equivalent in the Roman numeral system. Finally, **C** fibers are **unmyelinated** and equivalent to **IV** fibers. In addition to carrying second pain and warming such fibers are postganglionic autonomics (but these do not travel in the dorsal roots).

What about **ventral root** fibers. The processes of lower motor neurons that innervate **extrafusal** muscle fibers are **A α s** (or just **alpha** motor neurons). The preganglionic autonomic axons in the ventral root are **B** fibers. Finally, there are axons in the ventral roots that innervate the intrafusal (**not** extrafusal) fibers of the muscle spindles. These are called **A γ** (gamma) motor neurons (no equivalent in Roman numerals).

Remember, A and B fibers are myelinated and Cs are not. In the Roman numeral system, just remember that only the IVs are not myelinated. This is important, since demyelinating diseases would affect the somatic and visceral afferents and efferent fibers in peripheral nerves, pain and temperature would not be affected.

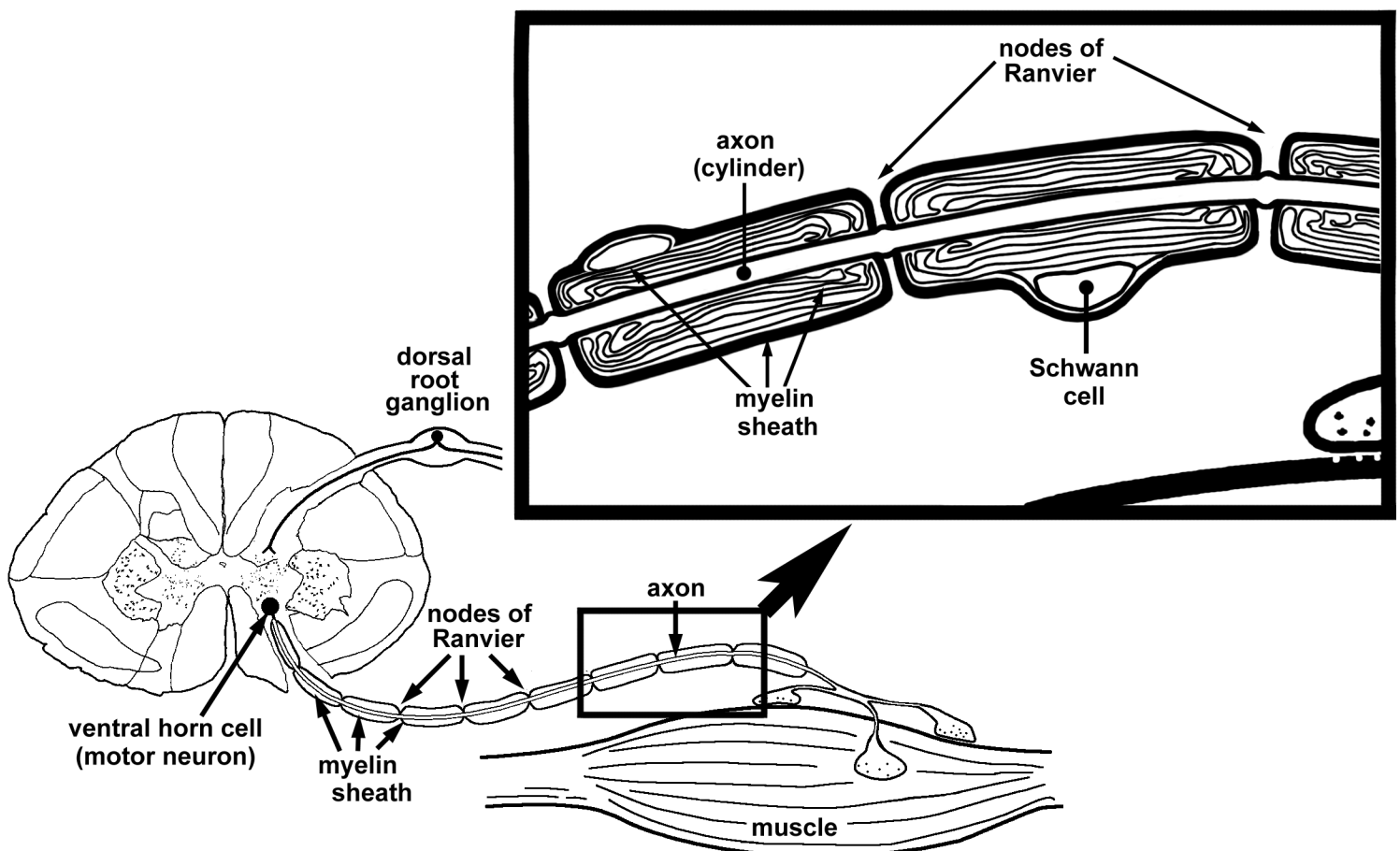


Figure 3. A myelinated nerve fiber.

Muscle

One anterior or ventral horn cell, and thus one axon, innervates a few hundred or even a few thousand muscle fibers. The muscle fibers innervated by a single anterior horn cell are collectively known as a **motor unit**. The “territory” of such a motor unit spans 10-15 mm in a muscle however it is rare that directly adjacent muscle fibers are innervated by the same anterior horn cell/axon. The figure below shows the seemingly random pattern of innervation of adjacent muscle fibers by individual anterior horn cells. The clear muscle fibers below are innervated by a single anterior horn cell and comprise a motor unit. The vertically oriented fibers are innervated by a different anterior horn cell constituting a second motor unit and the horizontally oriented represent yet another.

We also need to distinguish between type 1 (slow contracting) muscle fibers and type 2 (fast contracting) muscle fibers. The type of muscle fiber is dependent on the type of anterior horn cell that innervates it. Thus if a muscle fiber is innervated by a type 1 anterior horn cell, it will contract slowly. Certain histochemical reactions, amongst others myosin ATPase, distinguish between type 1 and type 2 fibers. Thus muscle reacted with myosin ATPase will normally exhibit a checkerboard pattern as it is likely that the adjacent muscle fibers are innervated by another anterior horn cell of a different fiber type (figure 4).

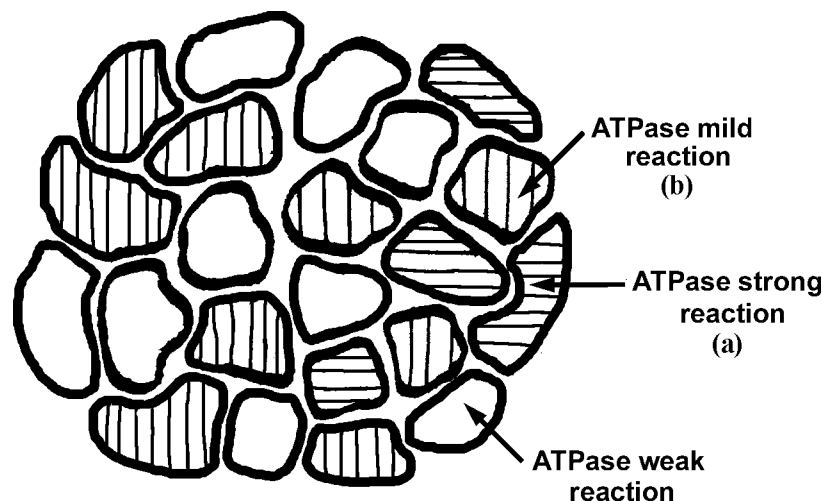


Figure 4. The clear fibers in the figure above are myosin ATPase free and are all innervated by one ventral horn cell. The striped fibers are the ATPase rich and would look similar under a microscope. However, we want to illustrate that the ATPase rich fibers are innervated by two different ventral horn cells (a and b; hence the different orientations of the stripes).

Neuromuscular junction

A muscle fiber is activated via a nerve impulse generated by an anterior horn cell. The impulse is conducted along the nerve fiber via saltatory conduction; that is an action potential is generated at one node of Ranvier and then jumps to the next node of Ranvier where another action potential is generated. Once the impulse reaches the neuromuscular junction, voltage sensitive Ca^{2+} channels are opened which allow for the influx of Ca^{2+} into the nerve terminal. Ca^{2+} entry into the nerve terminal initiates the fusion of acetylcholine containing vesicles with the presynaptic membrane and

the subsequent release of acetylcholine into the synaptic cleft. Acetylcholine binds to post-synaptic acetylcholine receptors on the muscle membrane. This induces an end plate potential which subsequently results in the generation of an action potential in the muscle fiber membrane (figure 5). The end result of this reaction is muscle fiber contraction.

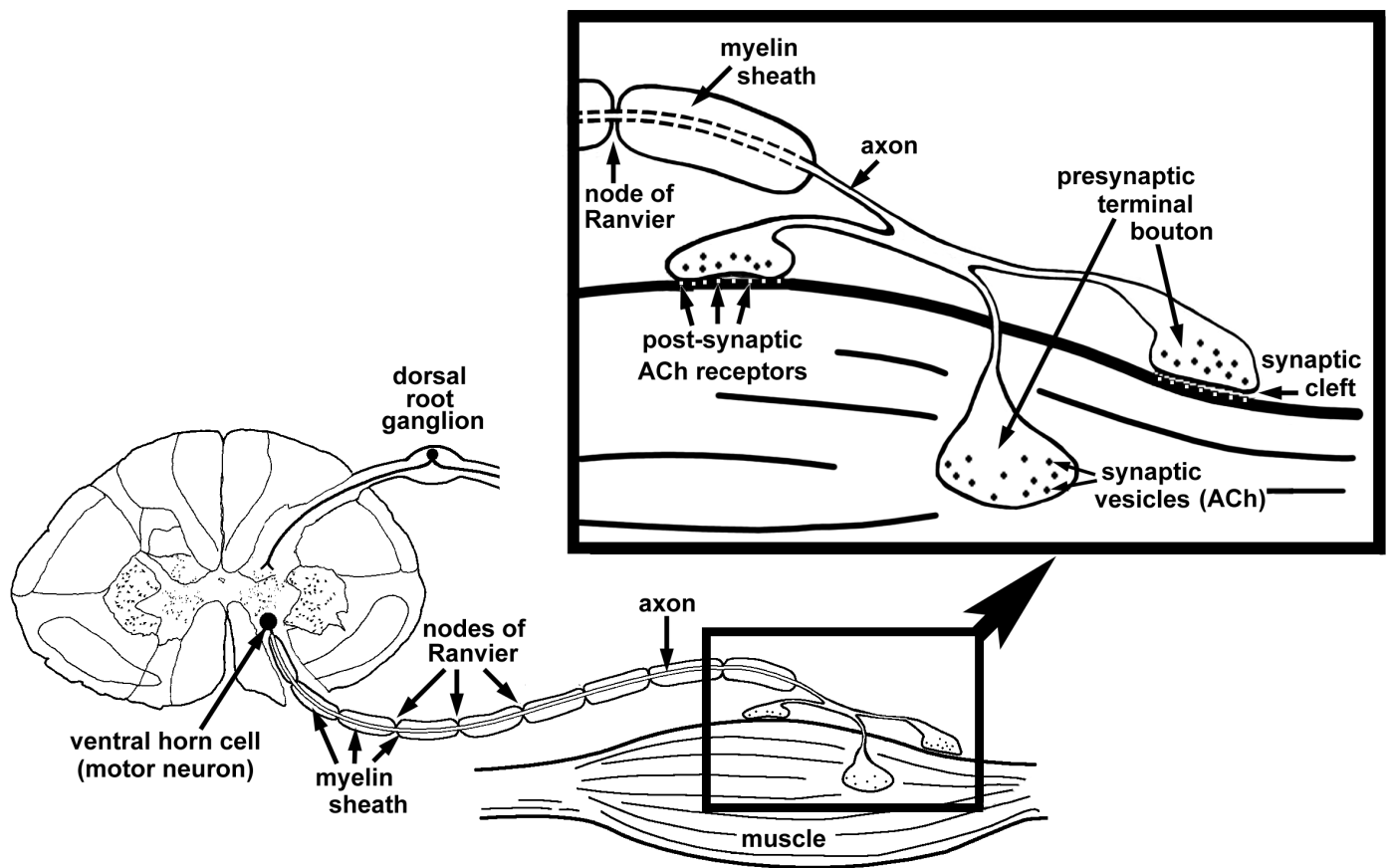


Figure 5. The neuromuscular junction.

III. Diagnosis of the different lower motor neuron subgroups

The diagnosis of a specific lower motor neuron syndrome starts with the localization of the disease to one of the 4 anatomic stations. This can be accomplished by a combination of the following investigations:

1) History and clinical examination

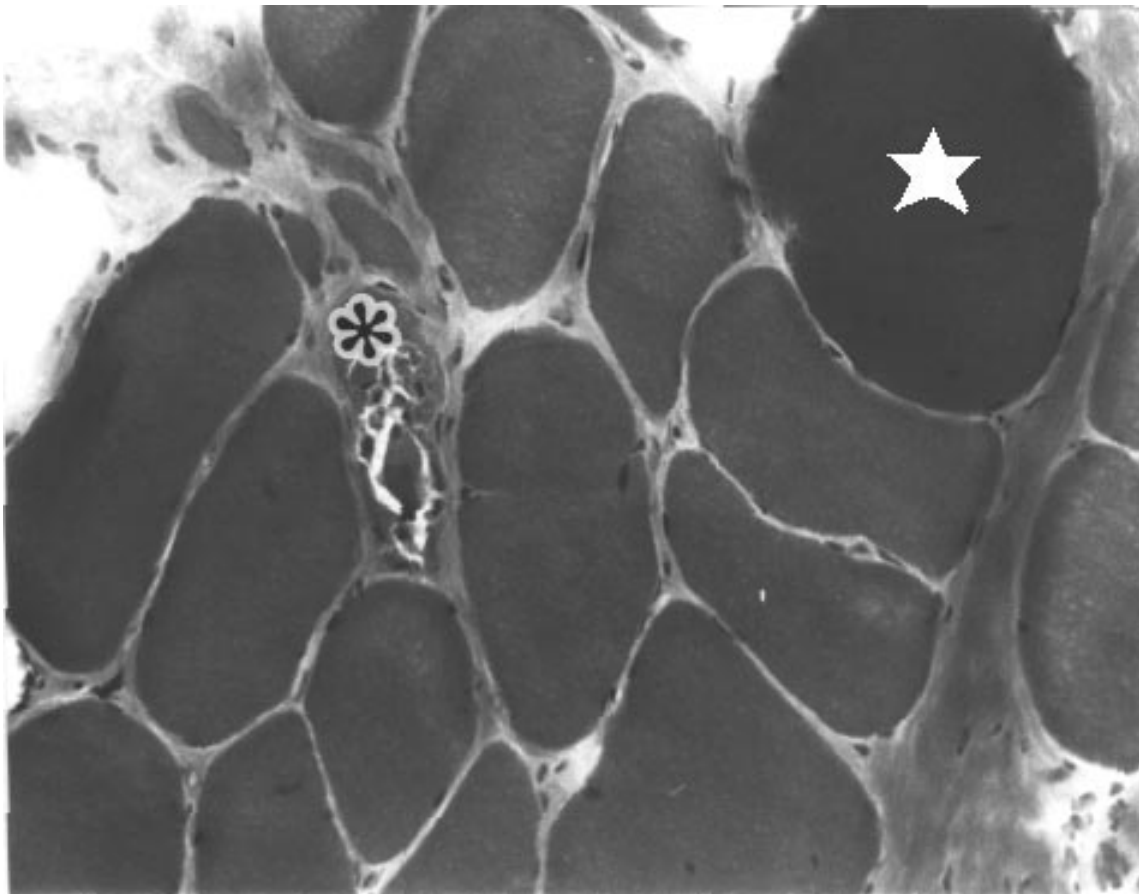
In recording the history it is of particular importance to document the following. The time of disease onset, the presence or absence of a family history of other similarly affected individuals, consanguinity (patients born from parent related by blood), the pattern and progression of muscle weakness, the presence or absence of sensory symptoms and the presence of fatigability. The clinical examination serves to corroborate the clinical history, and to document the patterns of weakness, sensory loss, fatigability and reflex changes.

2) Histological examination of muscle or nerve biopsy specimens

These will be dealt with in more detail during the neuropathology section of your Pathology course.

Muscle histology

Muscle is not too smart and can only react in a limited number of ways to insult. Thus most **primary muscle diseases** have non-specific features in common, such as muscle fiber necrosis, evidence for muscle fiber regeneration, structural abnormalities such as centrally located muscle fiber nuclei and an increase in muscle connective tissue (figure 6). Some primary muscle diseases do show diagnostic changes such as nemaline rod formations or central cores. **Inflammation** in muscle is



important as it may indicate a treatable disease.

Figure 6. Typical, non-specific pathological findings in a primary myopathy. A necrotic fiber (asterix), and a hypercontracted muscle fiber (star), are shown. The entire muscle is shortened and thus, the hypercontracted fiber is thicker. The connective tissue between the muscle fibers is increased.

Muscle denervation

Anterior horn cell disease or a peripheral neuropathy result in exactly the same histological findings in the muscle! The poor muscle can only interpret these events as “I am denervated.” The pathological hallmarks of denervation are **type grouping** and **group atrophy** (figure 7). Because one anterior horn cell/motor axon innervates a number of muscle fibers, it follows that disease of an anterior horn cell or axon results in denervation of a number of muscle fibers. These muscle fibers that have lost their innervation, may now be innervated by healthy axons that normally innervate adjacent muscle fibers. The end result is that now one axon innervates more muscle fibers than normal, (a giant motor unit) and also the normal checkerboard pattern of innervation is lost. That is, a whole group of type 1 or 2 fibers can now be seen adjacent to one another (type grouping). With progression of the disease, the axon that sprouted to innervate previously denervated muscle fibers may now also become diseased, resulting in an entire group of adjacent muscle fibers becoming atrophic (group atrophy).

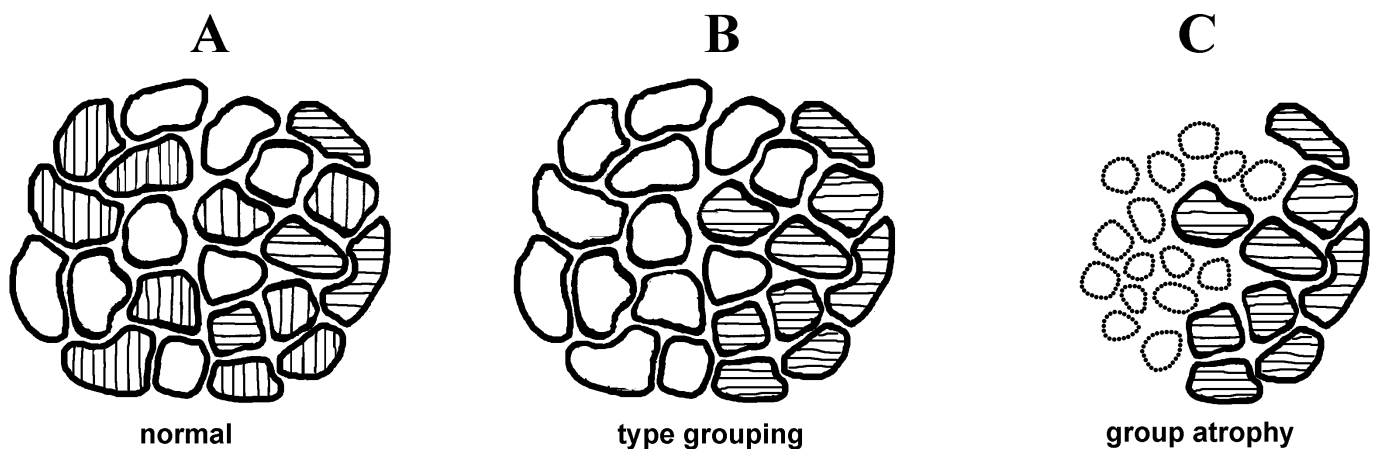








Figure 7. Imagine that the  fibers in A have lost their neuronal input. You can see how axons that innervated  fibers on the left side in A can sprout and innervate the denervated  fibers (B). On the right side (B) axons that innervated the  fibers sprout and take over the denervated  fibers. This is type grouping. Subsequently, the nerve to the  fibers dies and there is group atrophy (C).

Nerve histology

The nerve is equally unimaginative in its reaction to damage. In principle, only two pathological changes are seen. Firstly **axonal damage** results in Wallerian degeneration, a bead-like disruption of the peripheral nerve that involves both the axon cylinder and the surrounding myelin (Figure 8). This is seen in diseases affecting the axons in the peripheral nerve, or in anterior horn cell disease.



Figure 8. Wallerian degeneration seen in axonal damage.

Secondly **demyelination** results in peripheral nerves with shortened internodes or internodes with thinner myelin (figure 9). Remember the axon cylinder in demyelinating diseases is fine and healthy.



Figure 9. A nerve fiber with shortened internodes that are hypomyelinated; typical findings in demyelinating neuropathies.

3) Electromyographic (EMG) examination

This test consists of two parts:

a) Nerve conduction studies

Since there are few pure motor nerves to study, **motor nerve conduction** recording electrodes are placed over a distal **muscle** (i.e. thenar muscle group). The appropriate nerve (median) is then stimulated electrically and the **evoked responses** can be measured. These evoked responses recorded from the surface of the muscle are called a **compound muscle action potential (CMAP)**. The time it takes from stimulation to generation of the CMAP is the **conduction speed**.

The CMAP represents the action potentials of all muscle fibers activated by the nerve stimulation and the measured response can be compared to a known standard for such stimulation. Reduction in the strength of this response indicates a loss in overall muscle mass or the loss of motor fibers and must further be investigated as to its cause.

For **sensory nerve conduction studies**, the recording electrodes are placed over superficial **nerves** (e.g. the sural nerve is a pure sensory nerve). Stimulation of a sensory nerve leads to action potentials in all of the fibers of that nerve and an electrode on the surface of such a nerve records the **sensory nerve action potential (SNAP)**. Furthermore, by stimulating the same nerve over different segments the distances between stimulation sites can be measured and a conduction velocity for the nerve segment established.

**Median nerve stimulation at the elbow and wrist.
Recording is from the thenar muscle group.**

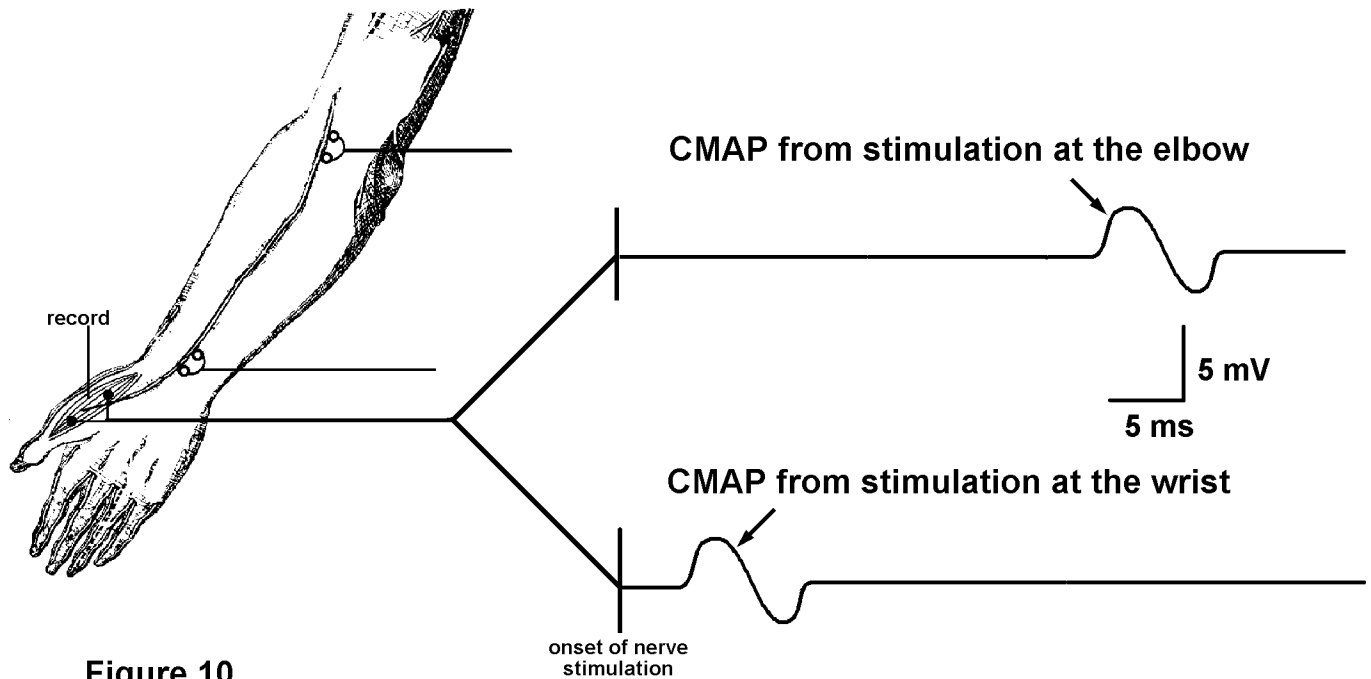


Figure 10

**Sural nerve stimulation at two points over the calf.
Recording over the nerve at the ankle.**

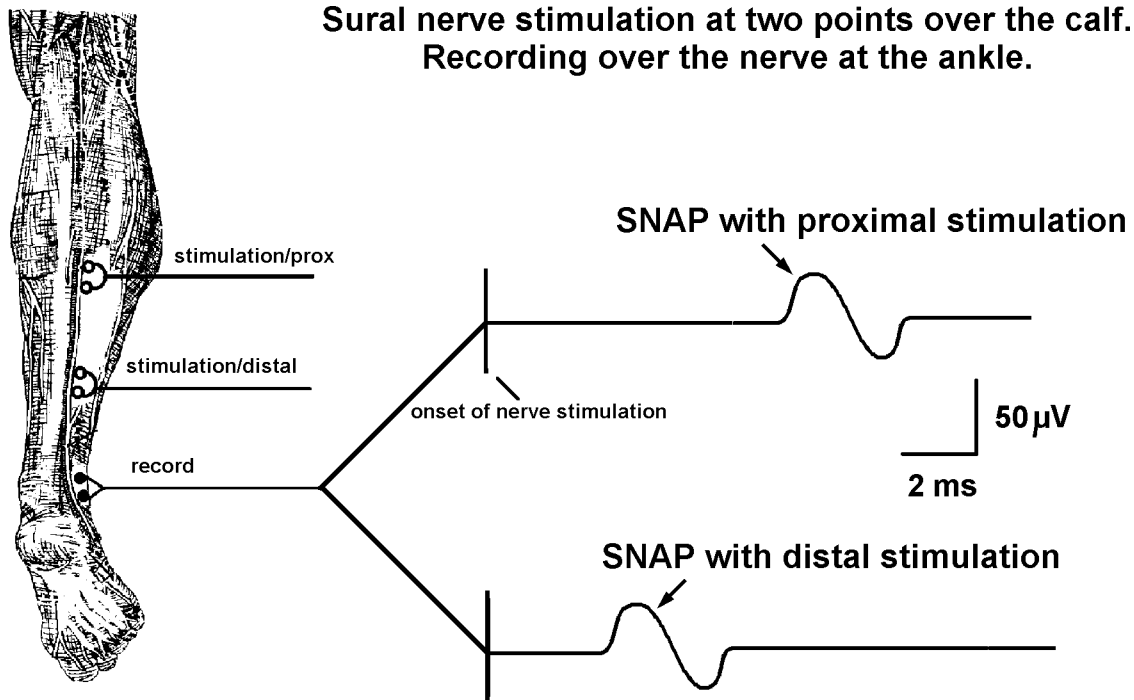


Figure 11

The conduction studies are followed by **repetitive nerve stimulation** studies. A routine motor nerve conduction study is performed but the nerve is stimulated supramaximally at 2-3 Hz and the amplitude of the first 4 CMAPs recorded. In **neuromuscular transmission defects** the CMAP amplitude **decreases** with successive stimuli as some muscle fibers are not depolarized due to the neuromuscular transmission defect (figure 12). This is called a **decremental response**. (The exact mechanism of the decremental response is complex and beyond the scope of this course!! Don't worry!)

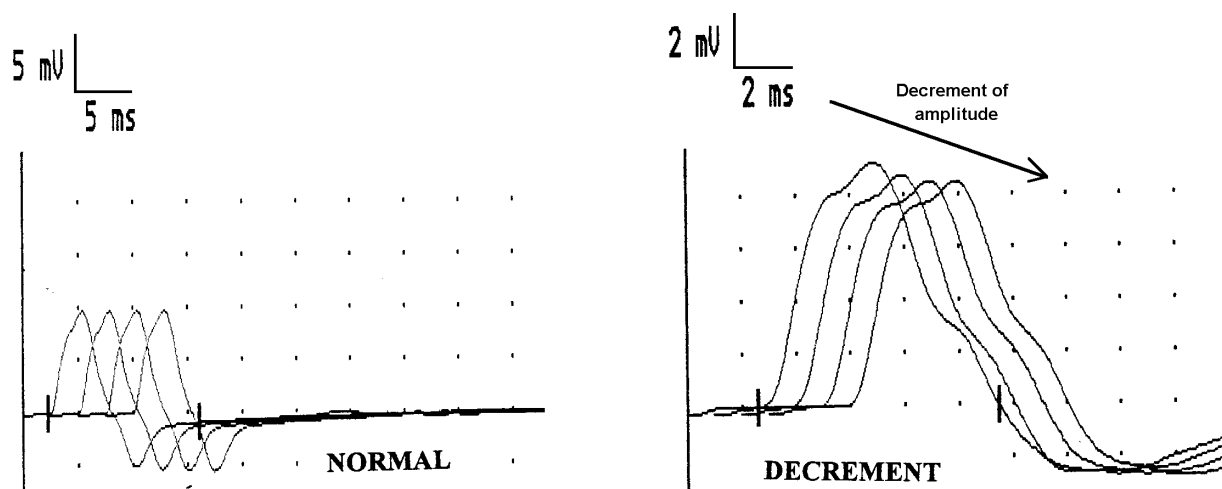


Figure 12. Repetitive nerve stimulation study. Four CMAPs are shown in each tracing. Note that the amplitudes of the responses are the same in a normal muscle, but that a decremental response is recorded in neuromuscular transmission defects.

Summary of nerve conduction findings in different disease groups

Station 1- Anterior (Ventral) Horn Cell disease: This results in low CMAP amplitudes in muscle innervated by the dying anterior horn cells whose axons travel in the nerve being stimulated. There are fewer (than normal) axons that are able to “drive” action potentials in the muscle, the end result being a smaller (than normal) CMAP. Since there is still a population of normal axons from other anterior horn cells (non diseased) nerve conduction velocity is normal, i.e. the nerve (for instance the median nerve) has normal axons that camouflage the dying ones. The sensory nerve conduction studies are normal because ventral horn cells give rise to only motor fibers. Cell bodies of sensory fibers lie in dorsal root or cranial nerve ganglia.

REMEMBER: axonal or anterior horn cell diseases do not slow nerve conduction velocities appreciably as the remaining axons conduct at normal speed. There are however too few normal axons and thus, the evoked potentials in the muscle (CMAPs) are small.

Station 2- Peripheral Nerve disease: The findings will depend on whether both the motor and sensory axons are affected. In most peripheral nerve diseases both become affected. If the changes result in damage only to the axis cylinders, the nerve conduction velocities are **normal** (healthy axons mask the defect), but both the **CMAP** and **SNAP** amplitudes will be reduced. If the peripheral nerve disease is predominantly demyelinating (i.e. **all** of the axons have demyelinated areas) the

findings are marked slowing in both the motor and sensory nerve conduction velocities and relatively normal CMAP and SNAP amplitudes (the axis cylinders are OK).

REMEMBER: demyelinating nerve diseases slow nerve conduction velocities, but the evoked potentials are of relatively normal amplitudes.

Station 3- Neuromuscular Junction disease: Nerve conduction studies (motor and sensory) are normal, but the hallmark of these diseases is a **decremental CMAP** response with repetitive nerve stimulation.

REMEMBER: neuromuscular transmission defects result in decremental CMAP responses with repetitive nerve stimulation.

Station 4- Muscle disease: Nerve conduction studies are normal, but the CMAP amplitudes will be low, as there is loss of muscle fibers.

REMEMBER: primary muscle diseases result in low CMAP amplitudes, similar to the findings in ventral horn and axis cylinder lesions.

In addition to nerve conduction studies, the EMG also involves:

b) The needle examination

An electrode is introduced into the muscle and recordings are made with mild to moderate activation of the muscle. This test is accompanied by some discomfort, but if performed appropriately should not be torture!

Depolarization of muscle fibers in close proximity to the needle electrode will be recorded as **motor unit potentials (MUPs; compare with CMAPs)**. A normal muscle and a normal MUP is shown in figure 13.

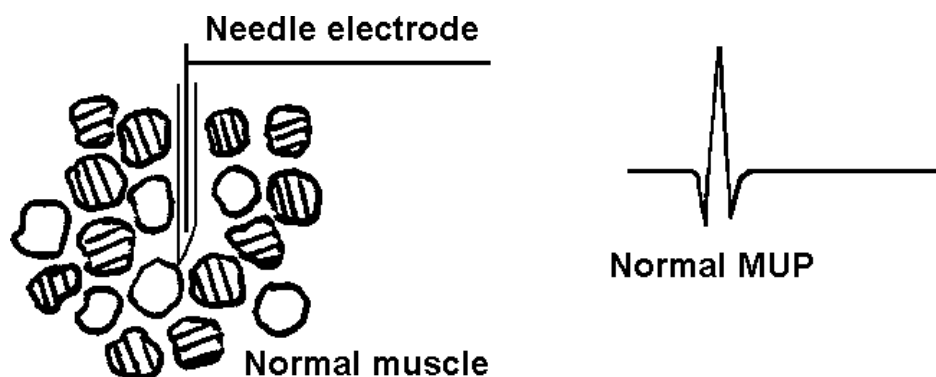
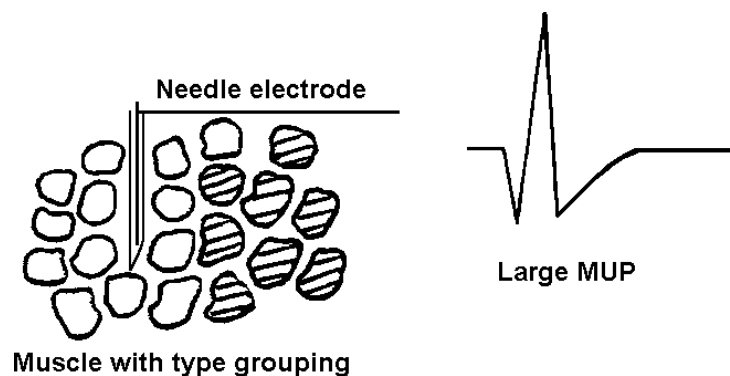


Figure 13. Normal muscle. The above muscle fibers are innervated by **three** different lower (alpha) motor neurons. Think of the MUP as representing the action potentials of the muscle fibers associated with **one** of these motor neurons (a motor unit). For example, a slight contraction of the muscle during a movement will fire all of the “clear fibers” above, but neither of the “striped fiber” groups.

By analyzing the size of the MUP (mostly the amplitude and duration), we can make a distinction between diseases that are primarily myopathic (disease of the muscle) versus those which result from denervation (neurogenic). As described in the section on the anatomy of muscle fibers, the muscle fibers innervated by one anterior horn cell/motor axon are spread over 10-15mm of the muscle. Furthermore, the territory innervated by adjacent anterior horn cells overlap so that adjacent muscle fibers are normally innervated by different anterior horn cells or motor axons. I know we have covered this before, but other peoples children never listen! **With damage to an anterior horn cell or a motor axon** the denervated muscle fibers usually become reinnervated by another motor axon with the result that more muscle fibers are innervated by the same anterior horn cell or motor axon in close proximity to the EMG needle. This is seen histologically as **type grouping** as shown in figure 7. In simplified terms this results in larger MUPs (**“neurogenic” MUPs**), figure 14. You might wonder why, if there is reinnervation (or “sprouting”) and larger MUPs, why are the CMAPs smaller? Well, that is because muscle fibers are also dying (remember group atrophy?)

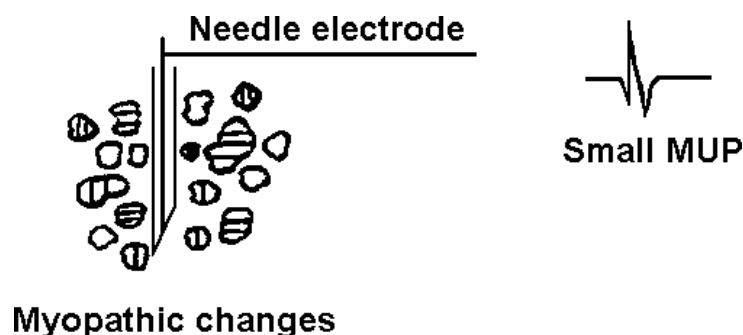
Figure 14. Neurogenic atrophy with type grouping. A large MUP is recorded. Think about the



single active motor neuron in Figure 13 as innervating more muscle fibers. When it fires there will be more muscle fiber action potentials and thus a larger MUP.

On the other hand in a **primary muscle disease**, there is loss of muscle fibers, or muscle fibers have a smaller mean diameter than normal, resulting in small MUPs (**“myopathic” MUPs**), figure 15.

Figure 15. Myopathic muscle. A small MUP is recorded.



Fasciculations are noted clinically as a contraction of a small group of muscle fibers. They result from the spontaneous discharge of an anterior horn cell or a motor axon with the subsequent contraction of all the muscle fibers innervated by that anterior horn cell or motor axon. Fasciculations can also be recorded with the needle electrode. Clinically, fasciculations are seen after reinnervation of muscle fibers and they are particularly common in amyotrophic lateral sclerosis (motor neuron disease).

Fibrillation potentials on the other hand are not visible through the skin. They are the small potentials generated by single muscle fibers once the muscle fibers become denervated. When a muscle fiber is denervated, several pathological changes take place. The acetylcholine receptors spread all across the muscle fiber instead of being grouped in a well-defined geographical area, the end-plate. This spread may play a role in attracting new innervation to the denervated muscle fiber from adjacent nerve sprouts. The muscle fiber becomes much more sensitive to free acetylcholine released spontaneously from adjacent nerve fibers and is depolarized and repolarized spontaneously as these molecules reach it. Each single depolarization is electrically detected as a single muscle fiber action potential. If the muscle fiber reinnervates successfully, these potentials disappear again. Thus they are seen in axonal neuropathies provided reinnervation does not keep up with denervation. In active myopathies, portions of the muscle fiber also become denervated from its endplate because of focal muscle fiber necrosis. Fibrillation potentials can therefore also be seen in active myopathies.

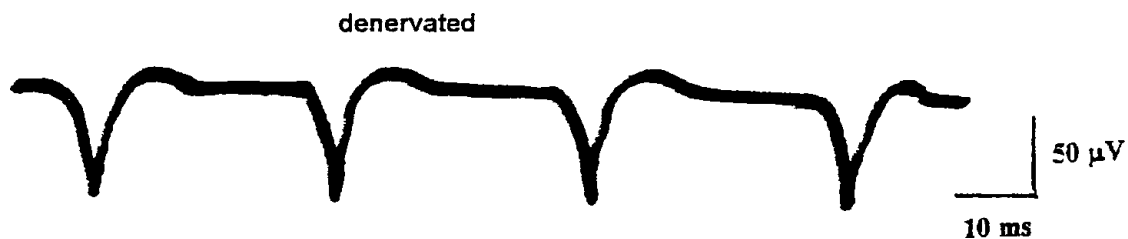


Figure 16. Fibrillation potentials. Each complex represents the spontaneous discharge of a single muscle fiber as recorded with a needle electrode in the muscle. Note that the discharge intervals are absolutely constant.

4) Biochemical studies

Numerous studies are available but only neuromuscular transmission defects and primary muscle diseases (myopathies) will be discussed.

Neuromuscular transmission defects. In myasthenia gravis, **acetylcholine receptor antibodies** destroy the post synaptic acetylcholine receptors and they are detectable in blood samples.

Primary muscle diseases - With muscle breakdown of any kind, **creatine phosphokinase (CK)** is released into the blood where it can be measured.

5) Genetic studies

The genetic defects of many neuromuscular diseases are now known and can be detected in peripheral blood or in muscle.

IV. Let us put this all together!

1. Anterior horn cell diseases

Common causes of anterior horn cell diseases are **poliomyelitis, motor neuron disease and spinal muscular atrophy**. Only **spinal muscular atrophy** will be discussed further. This is usually an autosomal recessively inherited disease with onset at any time from infancy to adulthood. The primary pathology is the progressive loss of anterior horn cells until the patients become so weak that they die usually from an associated lung infection. The reason for the progressive loss of anterior horn cells is not clear, but the disease is associated with an abnormality on chromosome 4.

EMG findings: Normal nerve conduction velocities, normal SNAP amplitudes, low CMAP amplitudes, large MUPs on needle examination, fasciculations.

Histology: Type grouping and group atrophy.

Biochemistry: Defect on chromosome 4.

2. Peripheral nerve diseases

This encompasses a vast number of diseases and only a cursory overview will be attempted.

Clinical features

Damage to the peripheral nervous system results in motor, sensory and autonomic dysfunction. A **neuropathy** is any disease of the nerves. There are a number of different classes of neuropathies, but we will consider only one of them here.

Distal polyneuropathy: All the nerves are affected distally in the extremities. Clinically the patients have sensory loss in a glove and stocking distribution, weakness and absent tendon reflexes in distal extremity muscles (e.g. ankle jerk). Longer nerves are affected more severely and thus the changes predominate in the legs. Most distal polyneuropathies are purely sensory or affect the sensory and motor nerves together. Pure motor distal neuropathies are rare. Depending on the etiology, the neuropathies can be axonal (axis cylinder), demyelinating, or show features of both. Diseases that cause distal polyneuropathies include diabetes, toxins, and vitamin deficiency/alcohol abuse. Many of these neuropathies are familial.

EMG findings

a) Predominantly axonal disease: Normal motor and sensory nerve conduction velocities with low or absent CMAP and SNAP amplitudes. Needle examination shows large MUPs that result from denervation and subsequent re-innervation. Fasciculations.

b) Predominantly demyelinating disease: Relatively normal CMAP and SNAP amplitudes with slowed nerve conduction velocities. Needle examination reveals normal MUPs as the axons are not damaged and the muscle fibers are not denervated. In practice pure demyelination is rare and some associated axonal damage is common.

Histology

Type grouping and group atrophy only if there is axonal (axis cylinder) damage.

3. Neuromuscular transmission defects

Only **myasthenia gravis** will be discussed further. This disease is characterized by abnormal fatigue with exercise. Myasthenia gravis commonly affects young woman and has a predilection for ocular, facial, masticator and proximal upper extremity muscles. Typically the patients recover to some degree after rest. Thus they feel much better in the morning, but become weaker as the day progresses. When the extraocular eye muscles are affected, diplopia (double vision) and ptosis (drooping of upper eyelid) are common and bothersome signs. This is an auto-immune disease with antibodies destroying the acetylcholine receptors (a postsynaptic defect).

Neuromuscular transmission defects

EMG findings:

Normal nerve conduction velocities, CMAP and SNAP amplitudes.

Decremental response on repetitive nerve stimulation.

Needle examination: Relatively normal MUPs.

Biochemistry:

Acetylcholine receptor antibodies are present in blood.

Histology:

Usually normal.

4. Primary muscle diseases (myopathies)

Muscle dystrophies (dystrophy = faulty development) are genetically determined diseases with onset at any time after birth. They are diagnosed on the pattern of muscle involvement. For example **Duchenne muscle dystrophy** is characterized by large calves, proximal muscle weakness and weakness of the latissimus dorsi muscles and pectoral muscles. **Myotonic dystrophy** patients show myotonia (an inability to relax a muscle after contraction) in addition to muscle weakness.

There also are **congenital myopathies**, **metabolic myopathies** and **inflammatory myopathies** that are beyond the scope of this course.

EMG findings:

Normal motor and sensory nerve conduction studies. The CMAPs are low because of loss in muscle bulk. Needle examination show small MUPs.

Biochemical findings:

All progressive myopathies have increased CK blood levels indicating the breakdown of muscle.

Histological findings:

Non-specific myopathic features such as large fibers, necrotic fibers, and increased connective tissue.

IN SUMMARY:

Anterior horn cell diseases. Clinically characterized by selective involvement of muscles. EMG findings are those of low CMAP amplitudes (fewer axons firing muscle fibers), normal SNAP amplitudes (ventral horn cell axons are not sensory), relatively normal nerve conduction velocities (normal axons camouflage dead ones), large “neurogenic” MUPs (normal axons take over muscle fibers of dead ones), muscle histology shows type grouping and group atrophy (normal axons take over muscle fibers of dead axons [type grouping] and then eventually die [group atrophy] and blood CK is normal (CK levels become elevated if a muscle fiber breaks down, or if the muscle membrane becomes porous. Both conditions allow CK to leak from the muscle fiber into the blood. In neurogenic atrophy (of anterior horn cell or peripheral [axonal] nerve origin) the muscle membranes remain intact and thus CK levels remain normal). Fasciculations (grossly) and fibrillations (only upon needle exam) are present.

Peripheral nerve diseases. Clinically characterized by the associated findings of sensory and autonomic abnormalities. EMG findings depend on whether it is primarily an axonal (axon cylinder) or demyelinating neuropathy. Axonal EMG findings are those of low CMAP amplitudes (fewer axon cylinders in a nerve means fewer muscle fiber firing), lower SNAP amplitudes if axons in a sensory nerve, relatively normal nerve conduction velocities (normal axons camouflage dead ones), large “neurogenic” MUPs (normal axons take over muscle fibers of dead ones), muscle histology shows type grouping and group atrophy (normal axons take over muscle fibers of dead axons [type grouping] and then eventually die [group atrophy] and blood CK is normal. Fasciculations and fibrillations are present.

	Conduction velocity	CMAP amplitude	SNAP amplitude	Rep Stim	MUPS	Blood CK	Histology	Fasciculations	Fibrillations
AHC	N	↓	N	N	Large	N	Type grouping group atrophy	yes	yes
PN_{axonal}	N	↓	↓	N	Large	N	Type grouping group atrophy	yes	yes
PN_{demyelin}	↓	N	N	N	N	N	Normal	no	no
Myast. gravis	N	N	N	Decremental CMAP amplitude	N	N	Normal	no	no
Muscle disease	N	↓	N	N	Small	↑	Necrosis; inflam; degeneration; fat; connective tissue	no	yes w/ active myopathy
UMN lesion	N	N	N	N	N	N	Normal	no	no

Demyelination The EMG findings are those of relatively normal CMAP amplitudes (axis cylinders are fine, so normal number of muscle fibers are activated), normal SNAP amplitudes (axis cylinders are OK), reduced nerve conduction velocities (myelin loss=slowing), normal MUPs (axis cylinders are OK), muscle histology is normal (axis cylinders are OK) and CK is normal (no muscle fibers are dead!). No fasciculations or fibrillations.

You might wonder why normal myelinated fibers don't camouflage the diseased fibers. In reality, demyelinating neuropathies affect multiple focal areas of every nerve and you have normal segments in between. Thus, you do not find "normal" and "abnormal fibers", all the fibers are affected to some degree. In axonal neuropathies some fibers are affected, others not. The normal fibers conduct normally and thus you do not see significant slowing of nerve conduction velocities, but you see drop in the SNAP and CMAP amplitudes.

Neuromuscular transmission defects. Clinically characterized by abnormal fatigability; EMG shows normal nerve conduction velocities, normal CMAP and SNAP amplitudes, decremental CMAP responses to repetitive nerve stimulation; muscle histology is relatively normal; blood CK is normal. No fasciculations or fibrillations.

Primary muscle diseases. Clinically specific patterns of muscle weakness may be noted; EMG shows normal nerve conduction velocities with low CMAP amplitudes (fewer muscle fibers per motor unit), normal SNAP amplitudes, smaller "myopathic" MUPs, muscle histology shows myopathic changes; blood CK is elevated. Fibrillations are seen.

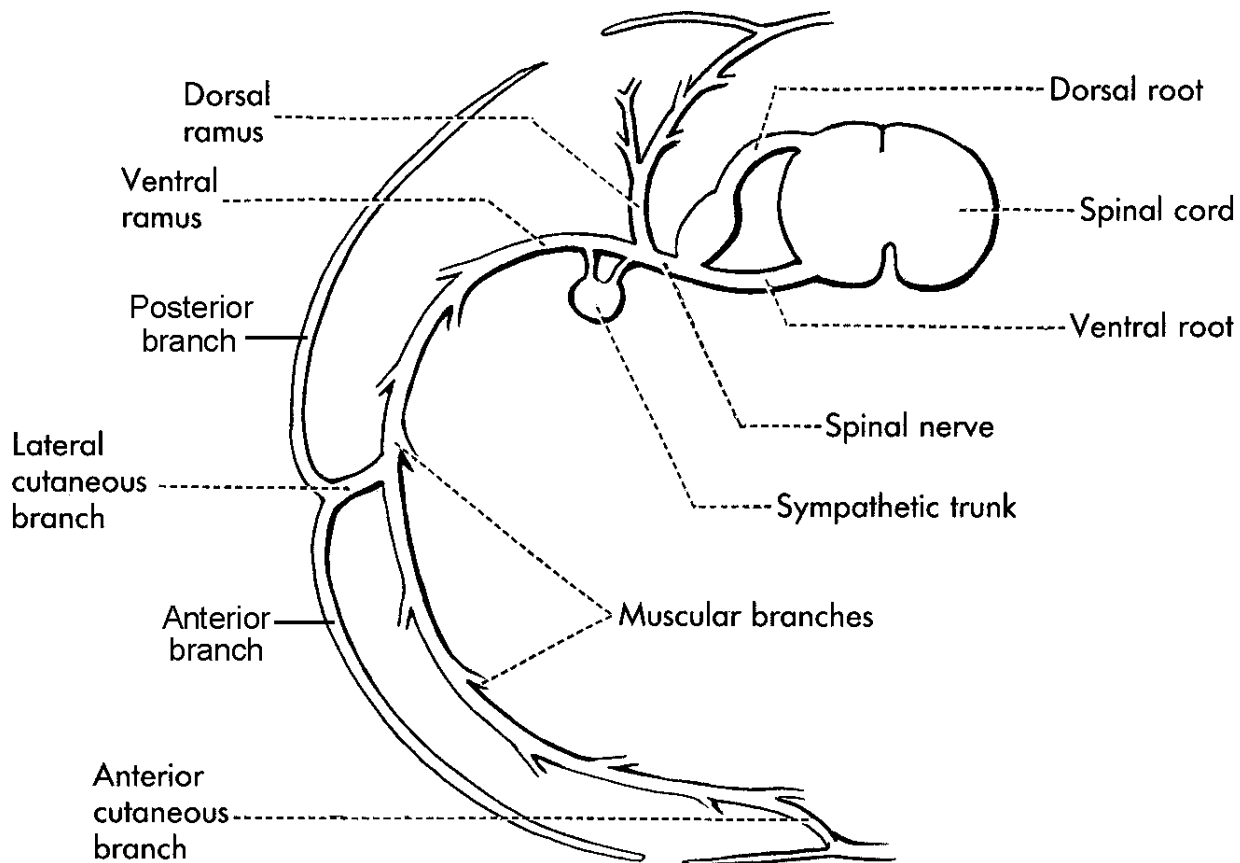
"SPEED PLAY"

Increased reflexes in a symptomatic limb suggest a central lesion, while reduced reflexes suggest a peripheral lesion.

Bilateral sensory and motor deficits throughout the body below a roughly horizontal level in the trunk, with normal function above that level, indicates a spinal cord lesion

RADICULOPATHIES

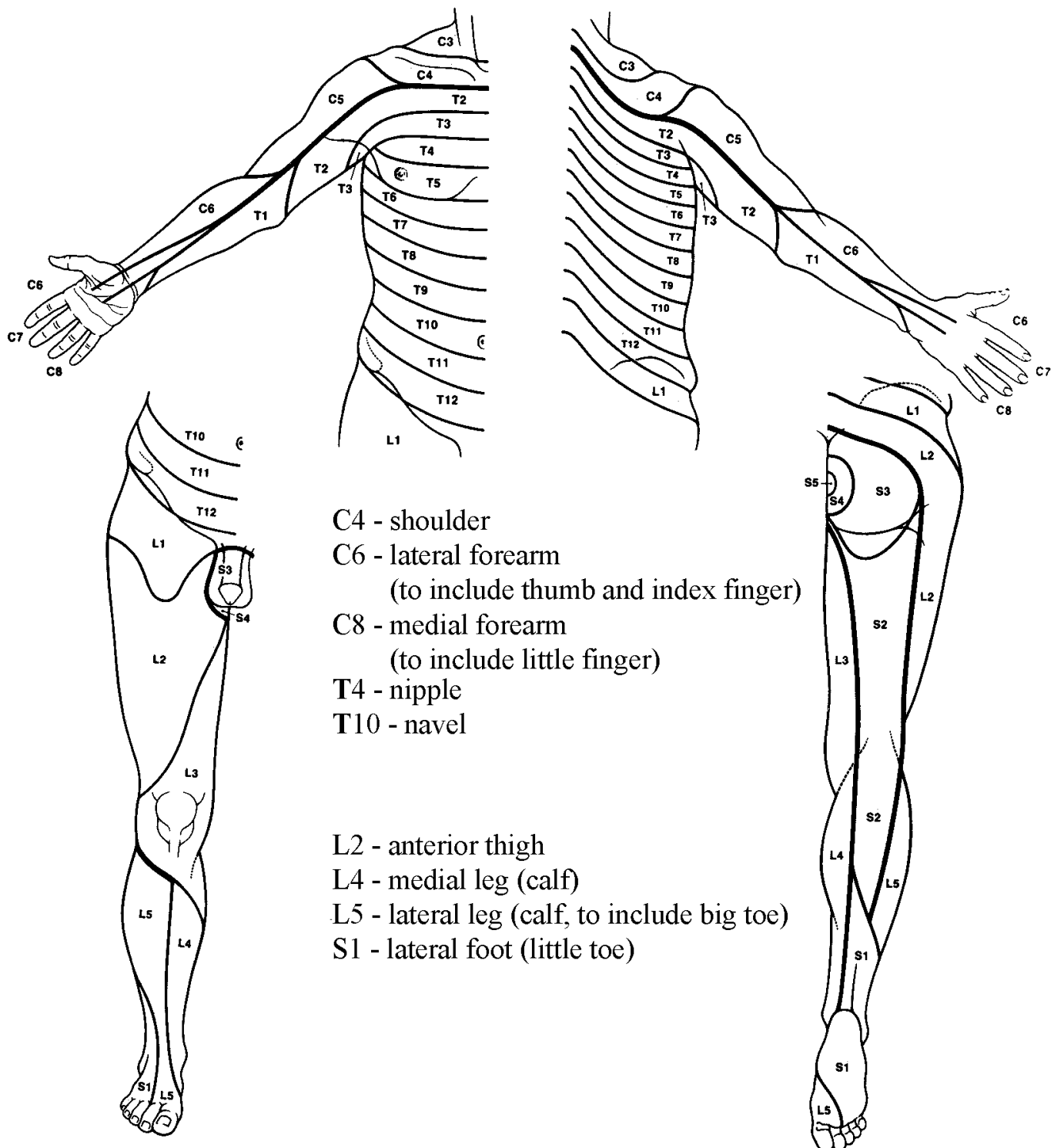
Radiculopathy (L. radicula = little root; pathos = disease) is an irritation of one or more of the many nerve roots that exit the spinal cord along its length. It usually presents as a combination of pain, weakness and numbness along the body region that the root supplies. Lateral spinal disc protrusion and bony spurs are common causes of radiculopathy. The motor, sensory and sundry other tracts, the spinal grey matter, and the spinal nerve roots should no longer be strangers to you. The terms and symptoms that will be discussed are used daily by clinical neurologists.



The peripheral nervous system begins at the nerve roots. Each segment of the spinal cord gives rise to a **ventral or anterior motor** and a **dorsal or posterior sensory** nerve root. The spinal nerve roots can be damaged as they traverse the spinal (vertebral) canal, but are especially vulnerable in the **intervertebral foramina**, where the ventral and dorsal spinal roots join to form the spinal nerves. Spinal nerves divide into dorsal and ventral rami. Dorsal rami supply the true back muscles and skin of the back, whereas ventral rami supply everything else except the head of course. Dorsal and ventral rami contain three types of fibers; sensory, somatomotor and visceromotor.

The distribution of sensory fibers in each spinal nerve is called a **dermatome**.

**You will need to understand the chart below
for the rest of your career!**



A group of muscles primarily innervated by the motor fibers in a single spinal nerve is called a **myotome**.

**You will need to understand the chart below
for the rest of your career !**

SEGMENTAL INNERVATION OF SOME MUSCLES OF THE UPPER LIMB		SEGMENTAL INNERVATION OF SOME MUSCLES OF THE LOWER LIMB	
Spinal Roots	Muscle Innervated	Spinal Roots	Muscle Innervated
C5/6	DELTOID BICEPS BRACHIORADIALIS INFRASPINATUS SUPRASPINATUS	L2/3	hip flexors ILIOPSOAS
C7	TRICEPS	L3/4	knee extensor Quadriceps
C7/8	Extensors and flexors of the wrist	L4/5	ankle dorsiflexion
C8/T1	Intrinsic muscles of the hand	S1	ankle plantar flexion

**You will need to understand the reflexes below
for the rest of your career !**

REFLEX	ROOT
BICEPS	C5
BRACHIORADIALIS	C6
TRICEPS	C7

REFLEX	ROOT
PATELLAR	L3/4
ACHILLES	S1/2

Root compression

The hallmark of acute or chronic nerve root compression is **PAIN**. Pain due to nerve root compression has certain characteristics:

- * it tends to follow a **dermatomal distribution**
- * it may be accompanied by **paresthesia** (para, abnormal + aisthesis, sensation, abnormal sensation such as pricking or tingling; heightened sensitivity) or sensory loss in a dermatomal distribution
- *dull pain is usually more proximal and difficult to localize
- *sharp pain usually localizes around the dermatomal borders

There is also a loss of power in the muscles innervated by the root.

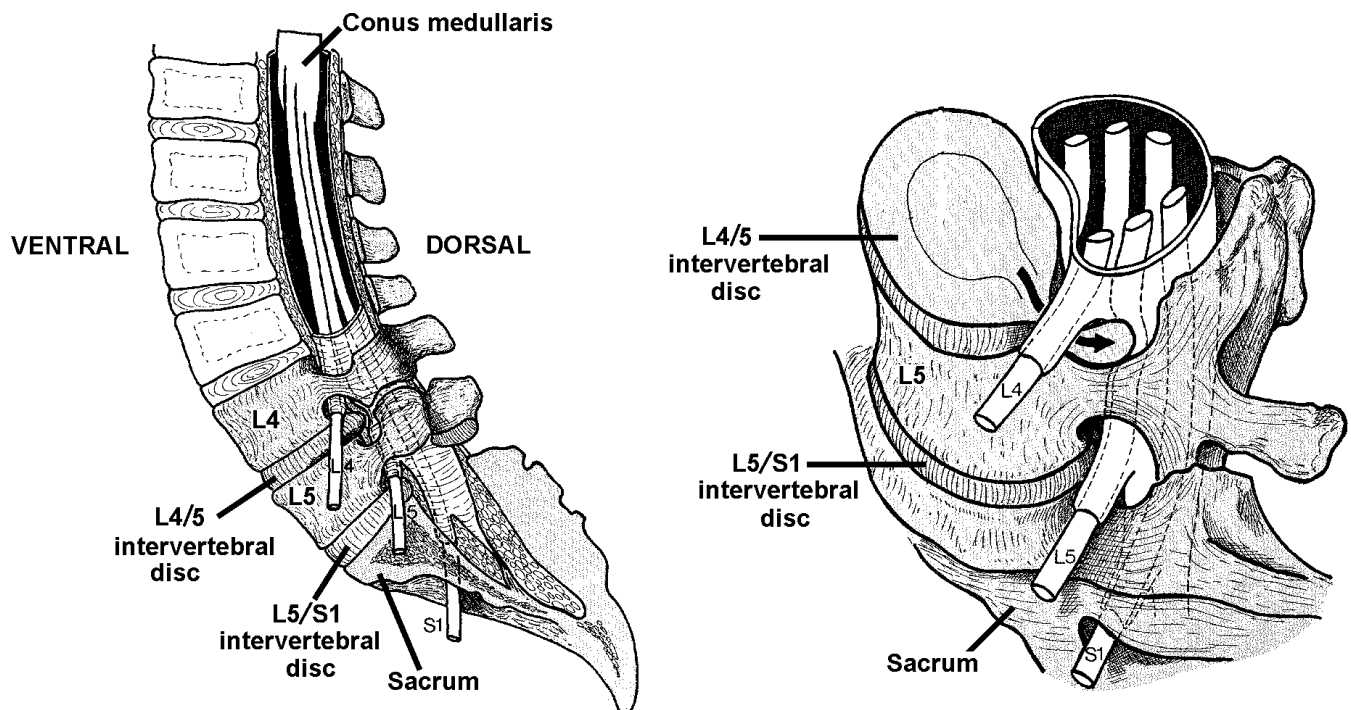
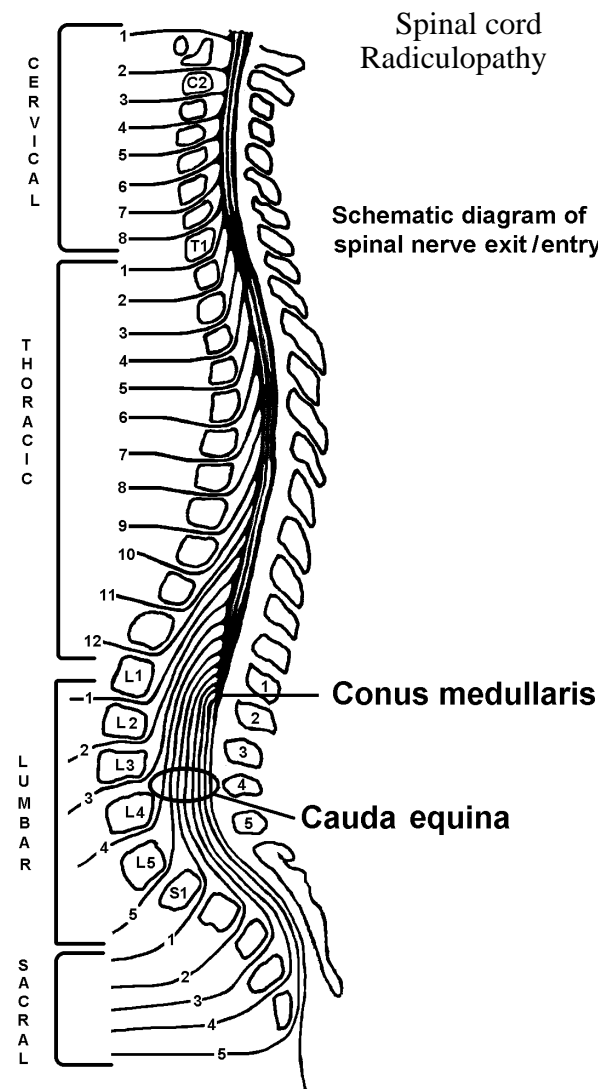
One of the primary causes of radiculopathy is intervertebral disc disease.

The lumbar roots emerge from **below** their respective vertebrae. These roots are vulnerable just above their exit foramina, as they are then the most ventral (anterior) and most lateral root in the vertebral canal and lie in the immediate path of a lateral disc herniation (L5 in the drawing on the right below). The intervertebral disc lying between vertebrae L4 and L5 is called the L4/5 disc. The disc between the L5 vertebrae and the sacrum is the L5/S1 disc. Since the L4 root emerges above the L4/5 disc, a lateral herniation of the L4/5 disc damages the L5 root. Moreover, a lateral herniation of the L5/S1 disc damages the S1 root. **KNOW THIS!!**

Intervertebral disc herniation and degeneration is the most common cause of compressive radiculopathy.

The natural history of most disc herniation is self-limited and does not require surgical therapy. One fifth of pain free people under the age of 60 have evidence of a herniated disc on MRI and 50% have evidence of a bulging disc. Hence a proper neurologic evaluation is required to define symptoms and deficits that can be linked to MRI findings. Current practice is to develop a rehabilitation program for back pain and to investigate structural causes and surgical therapies only when there is an objective neurologic deficit or pain that does not improve.

Lumbar intervertebral disc herniation occurs **most commonly at L4/5** (L5 root; 50%) and at L5/S1 (S1 root; 46.3%) interspace. Consequently, **compression of the 5th lumbar nerve root** is most common, with the first sacral nerve roots a close second.



A reason for the frequent compression of the L5 root may be the **tight fit** of the L5 root in its foramen since this root has the **largest diameter** and its intervertebral foramen is **narrower** than any other lumbar intervertebral foramen.

Syndromes associated with lumbosacral radiculopathies

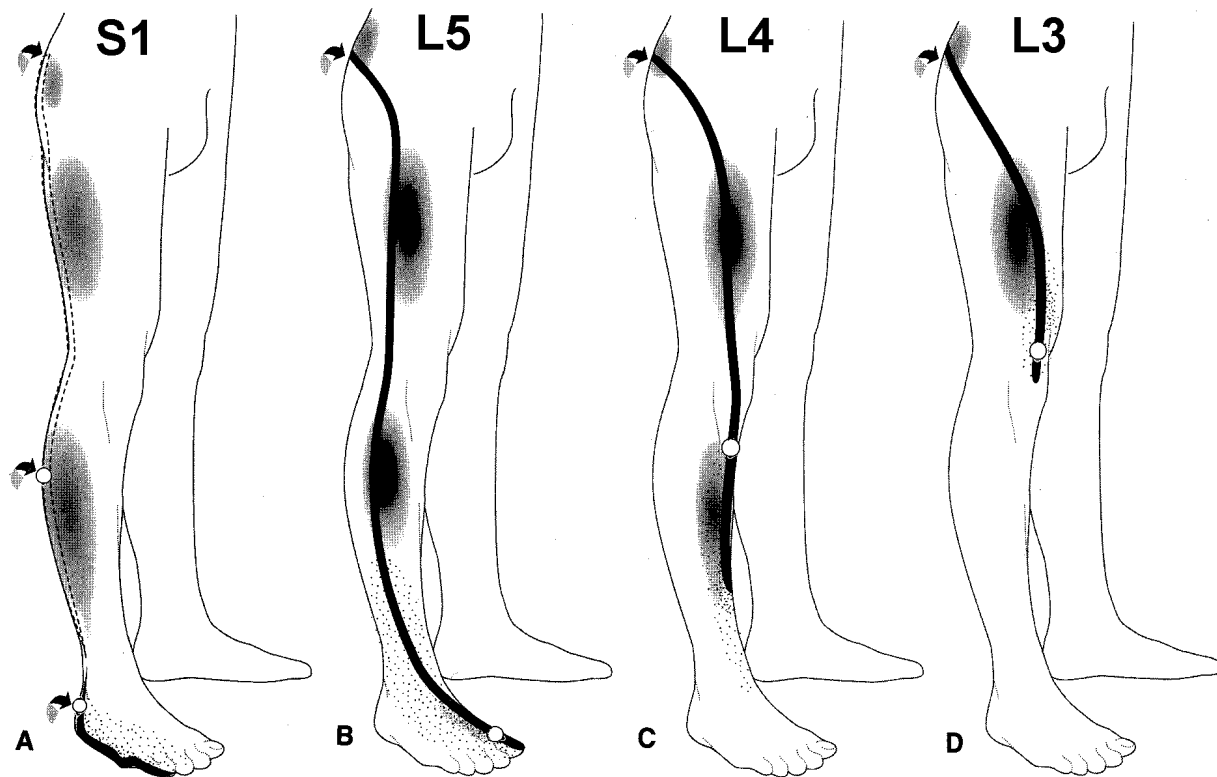
Posterior sciatica

- * pain which radiates along the posterior thigh and the posterolateral aspect of the leg is due to an **S1** or **L5** radiculopathy (nerve roots). When caused by **S1** irritation it may proceed to the **lateral aspect of the foot**; pain due to **L5** radiculopathy may radiate to the **dorsum of the foot** and to the **large toe**. **SO, L5 = DORSUM BIG TOE, S1 = LATERAL FOOT.**

Anterior sciatica

- * pain which radiates along the anterior aspect of the thigh into the anterior leg is due to **L4** or **L3** radiculopathy. **L2** pain is antero-medial in the thigh. Pain in the groin usually arises from an **L1** lesion.

The figure below illustrates the pain distribution in lumbar radiculopathies. You should note that areas associated with each root are larger than illustrated in the dermatome charts. The reason for these discrepancies are not known.

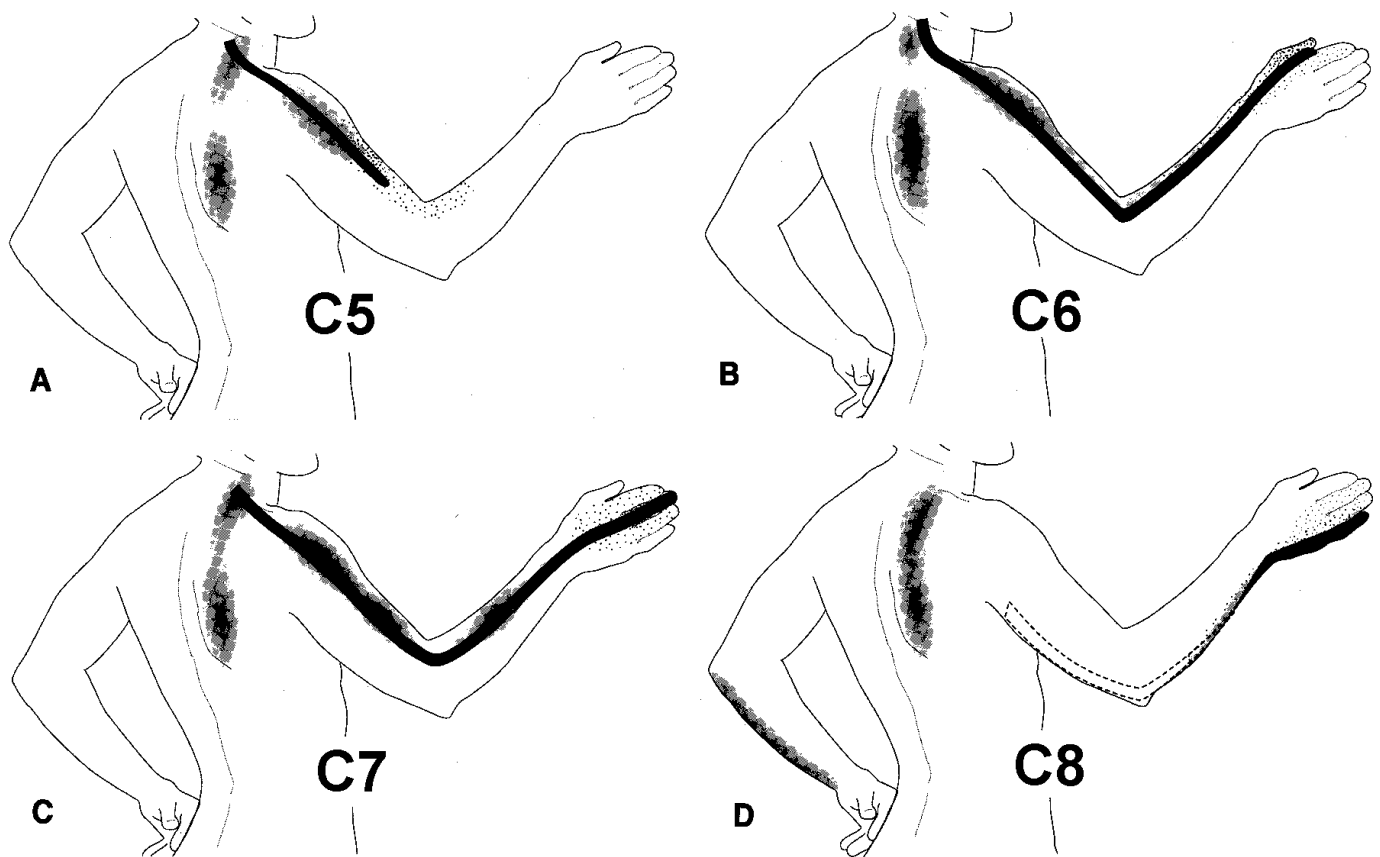


Anteroposterior view of the lower extremity. The black thick line represents the sharp, radiating pain, which often has a dermatomal distribution. The sharp radiating pain in S1 radiculopathy is indicated by interrupted lines. It tends to be in the center of the posterior thigh and calf. The diffuse gray areas represent the poorly localized dull ache. The circles indicate areas where pain may concentrate. The area covered by small dots indicates the location of paraesthesiae and sensory impairment. **A.** S1 radiculopathy. **B.** L5 radiculopathy. **C.** L4 radiculopathy. **D.** L3 radiculopathy.

Cervical radiculopathies (brachialgia = dull “achy” feeling in the arm and numbness and tingling in the hand)

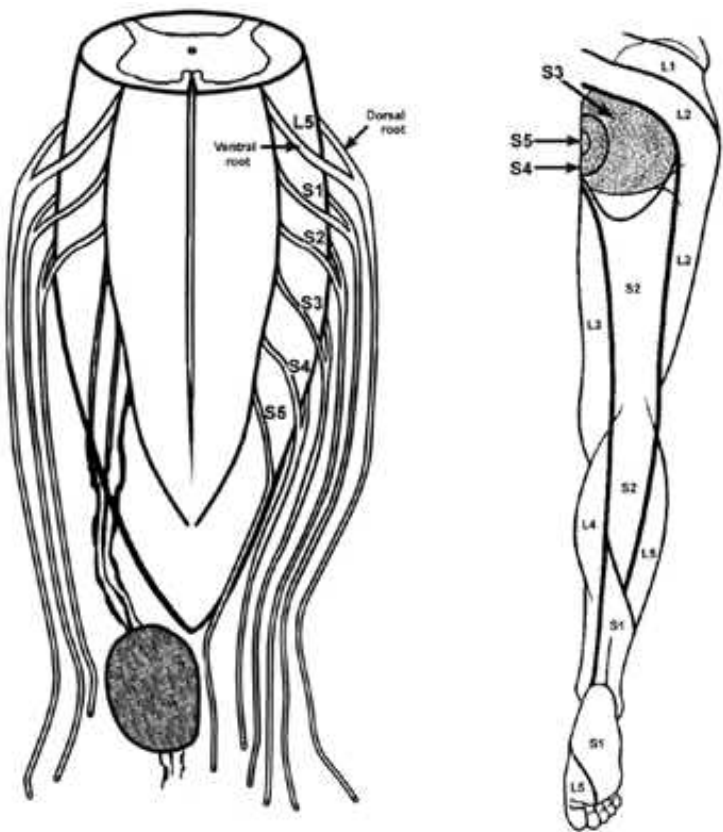
Because there are only 7 cervical vertebrae despite 8 cervical roots, the root number exiting between two vertebrae is always the number of the lower vertebra. For example, the C5 root exits between the C4-C5 vertebrae and would be effected by a C4/5 disc herniation; the C8 root exits between C7-T1 vertebrae and would be compressed by a C7/T1 disc.

Pain due to a **C6** and **C7** (the most common) radiculopathy radiates from the neck and from around the shoulder into outer aspect of the arm and forearm. **C6** radiculopathy may cause pain and numbness along the dorsal aspect of the **thumb and index finger**, **C7** pain and paresthesia may radiate into the **middle finger**.



Representation of the anterolateral aspect of the neck, shoulder, and upper limb. The thick black line represents the sharp, radiating pain, which often has a dermatomal distribution. Interrupted lines indicate sharp pain with a C8 radiculopathy, which is on the inner aspects of the arm and forearm. The diffuse gray areas represent the poorly localized dull ache. A dull ache medial to the shoulder blade is a common complaint in all cervical radiculopathies and is of no localizing value. The area covered by small dots indicates the location of paraesthesiae and sensory impairment. **A.** C5 radiculopathy. **B.** C6 radiculopathy. **C.** C7 radiculopathy. **D.** C8 radiculopathy.

The term cauda equina (horse’s tail) refers to the peripheral nerve roots which have left the spinal cord at approximately the level of the first lumbar vertebra. At that level, the structure of the spinal cord itself ends and the nerves going to the pelvis and the lower extremities continue through the spinal canal, leaving the spinal canal in pairs to the right and to the left as they pass to the pelvis and the lower extremities. Significant pressure obstructing the spinal canal at any level from L1 downward can cause cauda equina syndrome (CES).



Symptoms/sign	Cauda equina lesion
Spontaneous pain	May be most prominent symptom; severe; radicular type; in perineum, thighs and legs, and back
Sensory deficit	Saddle distribution; NO sensory dissociation; may be unilateral and assymetric
Motor loss	Asymmetric; more marked than following a conus lesion; atrophy may occur; fasciculations; hyporeflexia
Autonomic symptoms (including bladder and impotence)	Late; and less frequent in comparison to lesion of the conus medullaris (to be discussed under Autonomic dysfunction)
Reflexes	Ankle (S1-S2) and knee (L3-L4) jerk reflex may be absent
Onset	Gradual and unilateral

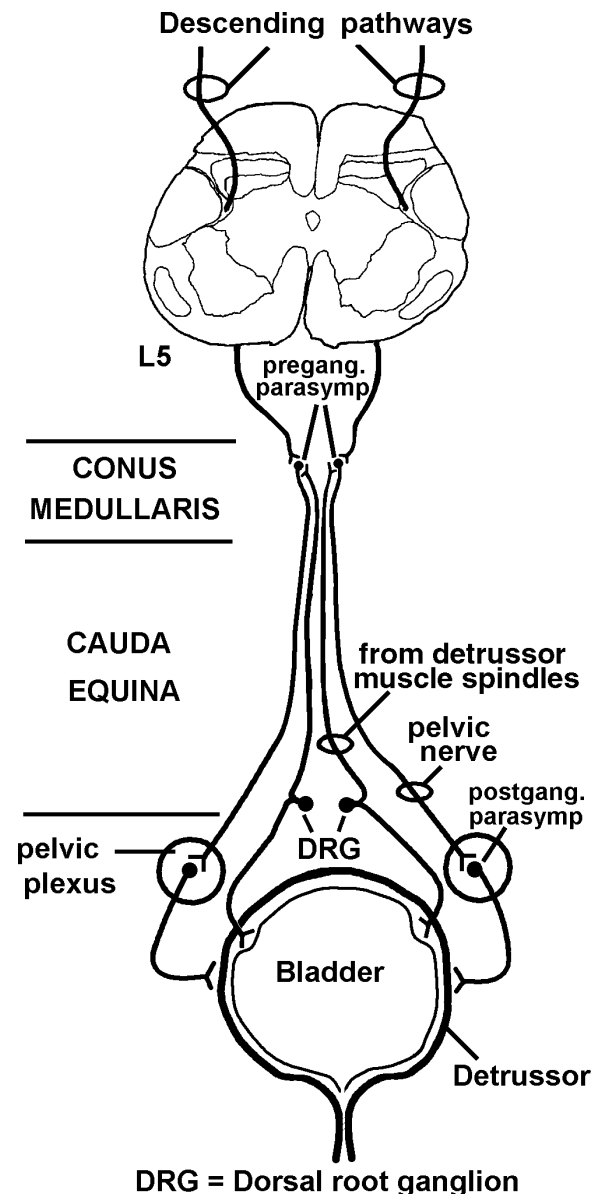
AUTONOMIC DYSFUNCTION IN SPINAL CORD DISEASES

MICTURITION

Normal bladder function depends on the coordinated activity of the bladder detrussor (smooth muscle) and the sphincter muscles (internal and external sphincters and muscles of pelvic floor). The actual act of voiding is under the control of higher cortical centers that develops as continence (contingere = to hold together) and is achieved in early childhood. Incontinence (lack of control of urinating) occurs when neuroanatomic pathways that innervate the bladder are interrupted or when there are physical problems with the pelvic floor and sphincter muscles. When dysfunction of the nervous system causes incontinence we use the term **neurogenic bladder**. Lesions of either upper or lower motor systems involved with micturition cause neurogenic bladders. Incontinence is an important symptom, and if it occurs in association with other neurological deficits that localize to the spinal cord, needs to be investigated aggressively.

The important points that you need to know in this course are that the bladder is controlled by areas of the brain that send axons down the spinal cord, traveling just medial to the LCST. These bilateral projections terminate on preganglionic parasympathetic neurons at S2, S3 and S4. The preganglionic parasympathetic neurons send their axons out the ventral roots of S2, S3 and S4 to synapse on postganglionic parasympathetic cells in ganglia near the bladder. These postganglionic parasympathetic cells in turn innervate the detrussor (smooth) muscle of the bladder for voiding.

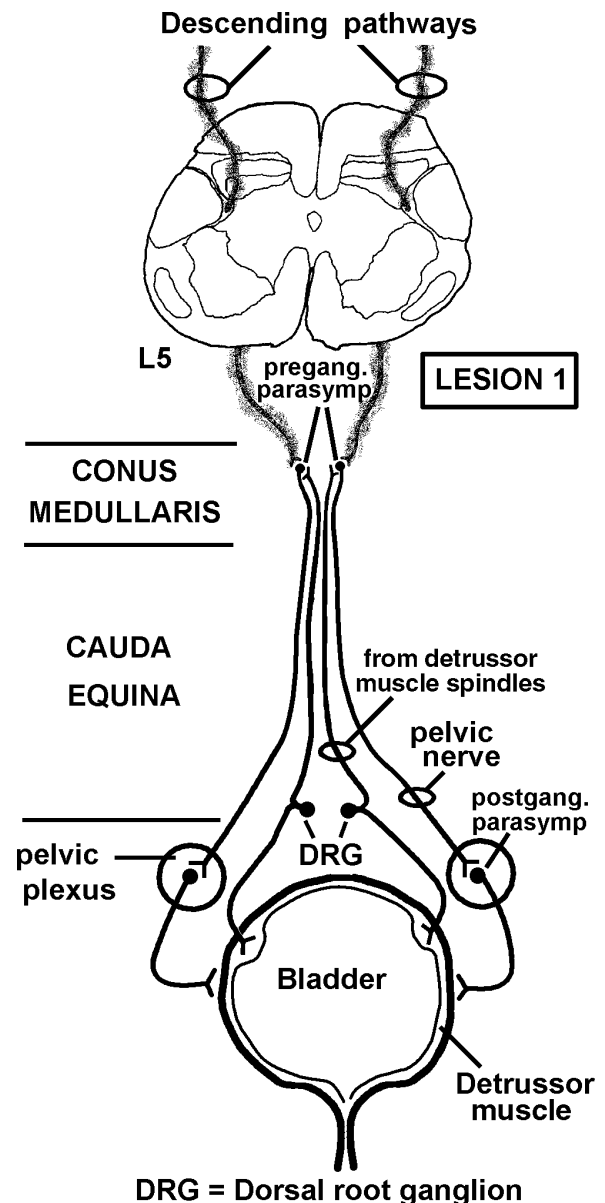
There are muscle spindles in the detrussor muscle whose cell bodies lie in dorsal root ganglia at S2, S3 and S4 (all are not shown in the diagram). When the bladder fills, the muscle spindles are stretched and increase their firing. This information enhances neuronal firing of the preganglionic parasympathetics at S2, S3 and S4 resulting in contraction of the bladder (voiding). This voiding reflex is normally controlled by the voluntary descending inputs from cortex.



You should be able to identify **upper** or **lower** motor dysfunction of the bladder. Both result in clinically divergent neurogenic bladders.

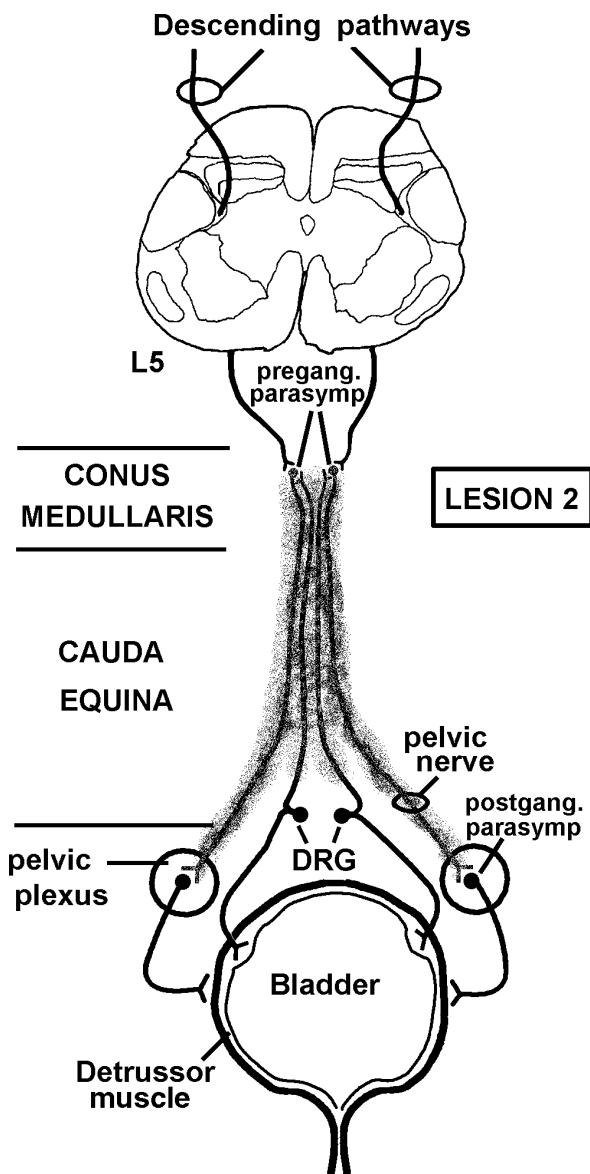
Lesion 1 - Upper Motor Neuron Lesion:

Think about what happens right after a lesion of the LCST. Spinal shock and flaccidity, right? This is similar to what happens when the descending pathways involved in bladder control are cut, only it has to be a bilateral lesion. For example, following a bilateral lesion of the entire spinal cord at C2 the detrusor initially becomes flaccid (like arm and leg muscles following a lesion of the LCST) and this results in urinary **retention**. The bag fills as there is no tone. There may be overflow incontinence when the bladder cannot physically hold any more urine. With time spasticity develops and the bladder contracts with small degrees of stretch (analogous to an increased muscle stretch reflex in the arm and leg following a lesion of the LCST). This causes urinary frequency and urgency (there are some sensory pathways intact); whenever the bladder fills a little, the increased stretch carried by afferents activate the parasympathetic motor neurons that control the detrusor and thus intermittent voiding. The bladder is **spastic** (also called UMN, autonomic or reflexive). Therefore, in acute lesions of the spinal cord rostral to the sacral cord (UMNL), two things occur. First there is a flaccid bladder (acute), then later there is a spastic bladder (chronic).



Lesion 2 - Lower Motor Neuron Lesion: (This is easier.)

When the parasympathetic lower motor neurons are injured or their axons compressed or disrupted, then the lesion results in weakness, atrophy, and hyporeflexia. The bladder does not contract and, if the sensory afferents are affected, no sensation of a full bladder will be perceived. If sensation is intact, but the motor efferents are affected, then there is an urge to void but good detrusor contraction is not possible. Lower motor neuron lesions can occur anywhere from the preganglionic parasympathetic neurons at S2, S3 and S4 (located in the conus medullaris), the sacral roots in the cauda equina, the pelvic nerve, the pelvic plexus, or the second order, postganglionic parasympathetic neurons that innervate the detrusor.



Remember, lesions of the spinal cord rostral to the sacral cord result first in a flaccid (atonic; acute) bladder, followed by a spastic (chronic, automatic) bladder. Lesions from S1 down, and involving all of the various nerves, result in **ONLY** a flaccid bladder (also called atonic, autonomous, or LMN).

We have already discussed deficits that result from lesions of the cauda equina. It is important to understand how these deficits differ from those following lesions of the conus medullaris.

In understanding the pathological basis of any disease involving the conus medullaris, keep in mind that this structure constitutes part of the spinal cord (the distal part of the cord) and is in proximity to the nerve roots. Thus, injuries to this area often yield a combination of upper motor neuron (UMN) and lower motor neuron (LMN) symptoms and signs in the dermatomes and myotomes of the affected segments. On the other hand, a cauda equina lesion is a LMN lesion because the nerve roots are part of the peripheral nervous system (PNS).

Let's compare these lesions

Symptoms/sign	Conus medullaris lesion	Cauda equina lesion
Spontaneous pain	Rare; bilateral and symmetric in perineum or thighs	May be most prominent symptom; severe; radicular type; in perineum, thighs and legs, and back
Sensory deficit	Numbness primarily in the perineum; bilateral; usually symmetric; sensory dissociation if lesion unilateral (pain & temp loss on one side, 2 point other)	Saddle distribution; NO sensory dissociation; may be unilateral and asymmetric
Motor loss	symmetric; can be hypo- and hyperreflexia fasciculations may be present	Asymmetric; more marked than following a conus lesion; atrophy may occur; fasciculations; hyporeflexia
Autonomic symptoms (including bladder and impotence)	Prominent early; overflow urinary incontinence and fecal incontinence	Late; and less frequent in comparison to lesion of the conus medullaris
Reflexes	Only ankle jerk (S1,S2) absent (preserved knee jerk [L3,L4])	Ankle (S1-S2) and knee (L3-L4) jerk reflex may be absent
Onset	Often sudden and bilateral	Often gradual and unilateral

RESPIRATION

There are respiratory centers in the medulla and pons that will be discussed during the Respiratory section of your Physiology course. What is important in this Neuroscience course is that some spinal cord lesions have effects on respiration. Respiratory centers in the medulla and pons control respiration via pathways to the spinal cord. These pathways influence the:

Diaphragm-the primary muscle for breathing. When this dome-shaped muscle contracts, it flattens, descending into the abdominal cavity, causing the lungs to inflate.

Intercostal muscles-They connect the ribs. When they contract, the chest wall is lifted up and outwards.

Accessory muscles-Are located in the neck and shoulders. When they contract, the first two ribs are elevated and the sternum is raised.

Abdominal muscles-Push the diaphragm up, causing the alveoli to be squeezed into a smaller space. These are muscles you use when you cough or sneeze.

The way your breathing is effected following spinal cord injury will depend on the level of your injury, whether the injury is complete or incomplete and how much improvement or recovery the patient may get. Everyone knows that there is voluntarily control of breathing. This voluntary control pathway for breathing travels via the corticospinal tract and is bilateral. In addition to the voluntary pathways for control of breathing there are involuntary pathways from the medulla and pons. The medullary and pontine pathways travel in the ventral funiculus and are also bilateral. Interestingly, Ondine's curse is a condition where the involuntary descending pathways are damaged (or their centers in the medulla and pons) while the voluntary pathway is OK. Thus, the patient can breath voluntarily but not involuntarily.

Keep in mind that the descending pathways from the medulla and pons are bilateral. Thus, unilateral lesions are not going to give signs of major respiratory failure.

Quadraplegia

If you have a very high injury in your neck (C1-3) all the LMNs of your breathing muscles are isolated from their UMN control centers. This causes paralysis of all the muscles that you need to breathe, including the diaphragm. This is rare but it may mean that you need a ventilator (respirator) to help you to breathe. If your injury is lower in the neck (C4 - C8), your diaphragm will be working and therefore you should be able to breathe on your own. However, your abdominal and intercostal muscles will all be paralysed and you will not be able to breathe as well as you did before your injury. You will need help to cough to clear your sputum and are more likely to have problems with chest infections from time to time. The higher the injury in your neck, the more difficulty you may find with your breathing. What would happen if the lesion was in the ventral horn of C3, 4 and 5?

Paraplegia

If you have a high paraplegia (above T6), some of the/intercostal muscles and all of the abdominal muscles will be paralysed and therefore breathing may still not be as good as before and you may need assistance to be able to cough well. The lower the level of your paraplegia (T6-T12) the more intercostal and abdominal muscles you will have working and the better your breathing will be. If your injury is below T12 all of the respiratory muscles will be working and your breathing should be close to as good as it was before your spinal cord injury.

Ondine's Curse (This is purely informational and is not meant to be sexist in any way)

There is a myth about the water nymph Ondine. Like all her sisters, she was magically beautiful. Free and independent, Ondine was very wary of men, since they are the only threat to a nymph's immortality. If a nymph ever falls in love with a mortal and bears his child, she loses her gift of everlasting life; she will start to age and will die after the span of a normal life. Despite all this, when Ondine saw the handsome young knight Sir Lawrence near her pond, she was impressed by him. When Lawrence saw her, he was, as they used to say, smitten by her beauty. He longed to know her better and came back many times to try to see her again. Ondine soon found herself looking forward to the knight's visits. In time they met, they spoke, and they fell in love. As happens in most fairy tales, these two attractive and special beings married. When they exchanged vows, Sir Lawrence said, "My every waking breath shall be my pledge of love and faithfulness to you." Ondine in turn promised, "As long as our love is true, my magic will serve as your shield and will never be turned against you." Unfortunately, however, this tale is not one in which the couple lives happily ever after.

A year after their marriage Ondine gave birth to Lawrence's son. From that moment on she began to age. Her body became susceptible to the weathering effects of sun, wind, and time, and her spectacular beauty began to slowly fade. Sir Lawrence, it turns out, seems to have been driven more by passion than by love. As Ondine's physical attractiveness diminished, he began to develop a wandering eye, with particular interest in some of the younger, prettier women living nearby.

One afternoon Ondine was walking near the stables when she heard the familiar and distinctive snoring of her husband. Amused by the fact that he had apparently fallen asleep in the middle of the day in this odd place, she decided to wake him up and take him home to finish his nap. When she entered the stable, however, she saw Sir Lawrence lying on a pile of hay in the arms of some woman. Items of clothing strewn around the stable told the story. Ondine's sacrifice of her immortality for this man, who had now betrayed her, demanded retribution. Still retaining enough magic to achieve her vengeance, Ondine kicked her husband awake, pointed her finger at him, and uttered her curse: "You swore faithfulness to me with every waking breath, and I accepted your oath. So be it. As long as you are awake, you shall have your breath, but should you ever fall asleep, then that breath will be taken from you and you will die!" The tale ends with the favorite line of many old story tellers: "And so it was."

Syndromes and Anatomic Localization

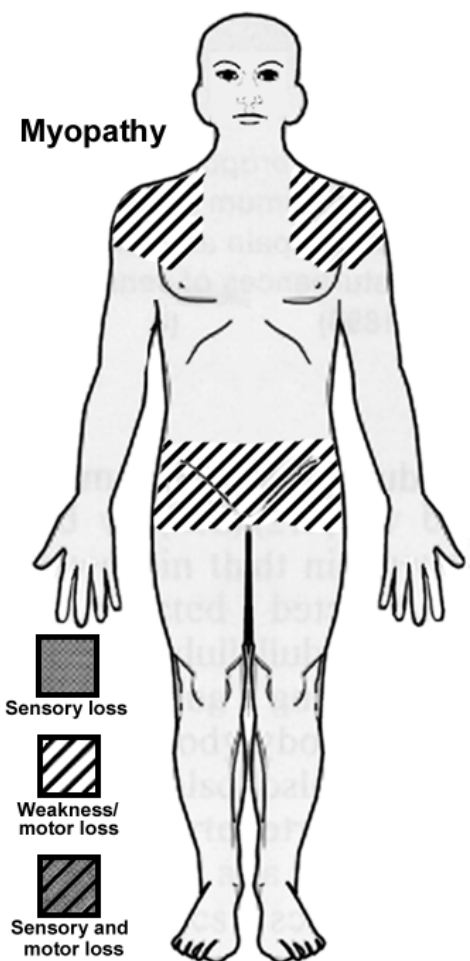
The basic principle of neurology is to define the anatomy of where the nervous system is affected and the etiology for what is going wrong. The anatomy is defined by symptoms, patterns of neurologic loss, and exam findings. Combinations and patterns of sensory and motor loss help define many anatomic sites. Without some concept of where the lesion is, appropriate evaluation with modern imaging techniques cannot be directed. MRI scans are amazing in revealing abnormalities, but cannot help if you do not know where to look. The etiology for lesions of the nervous system relate more to the onset or progression of deficit and often require confirmation using laboratory screening for specific conditions, e.g. B12 deficiency.

So far in this course you have been exposed to consequences of neurologic deficits located below the foramen magnum. You should be familiar with the following anatomic patterns of neurologic loss.

Myopathy

Affects specific muscles, usually proximal muscles giving weakness.
No sensory loss.

Myopathies may be inherited and then termed **dystrophies**. Other common causes of myopathy are inflammation (polymyositis), endocrine abnormalities or drugs/toxins.

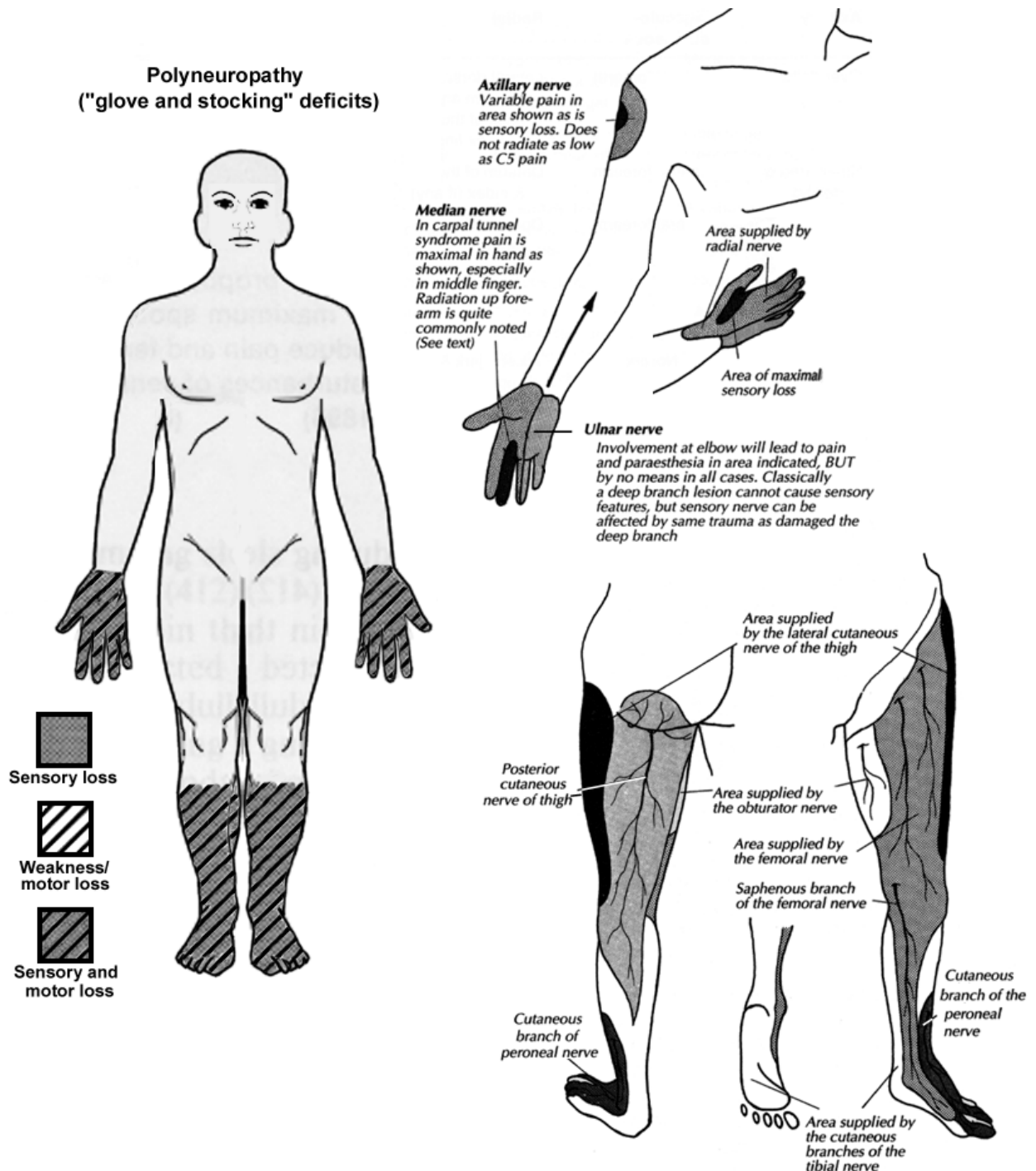


Neuromuscular Junction

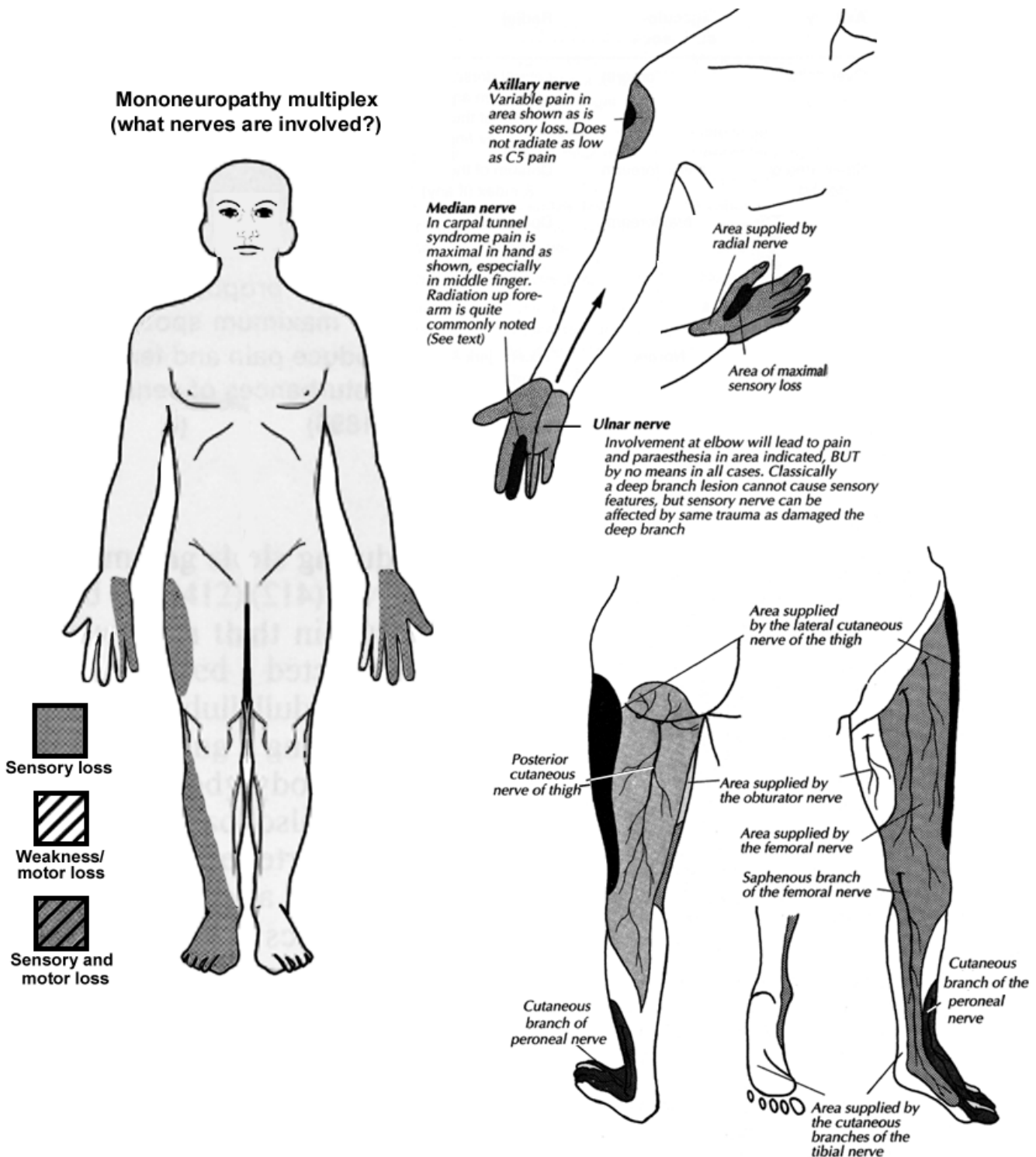
Weakness that is variable and affects some muscles preferentially especially extraocular muscles and oropharyngeal muscles. No sensory loss. Abnormal decremental response to repetitive stimulation.

Peripheral Nerve

You have already heard about distal polyneuropathies. Remember, a **neuropathy** is a disease of the nerve. In a **distal polyneuropathy** all of the nerves to the feet and hands (glove and stocking) may be affected. In the foot for example this could involve the common peroneal nerve (both superficial and deep branches) and the tibial nerve (medial and lateral plantar and calcaneal branches). The loss can be motor or sensory or both motor and sensory.

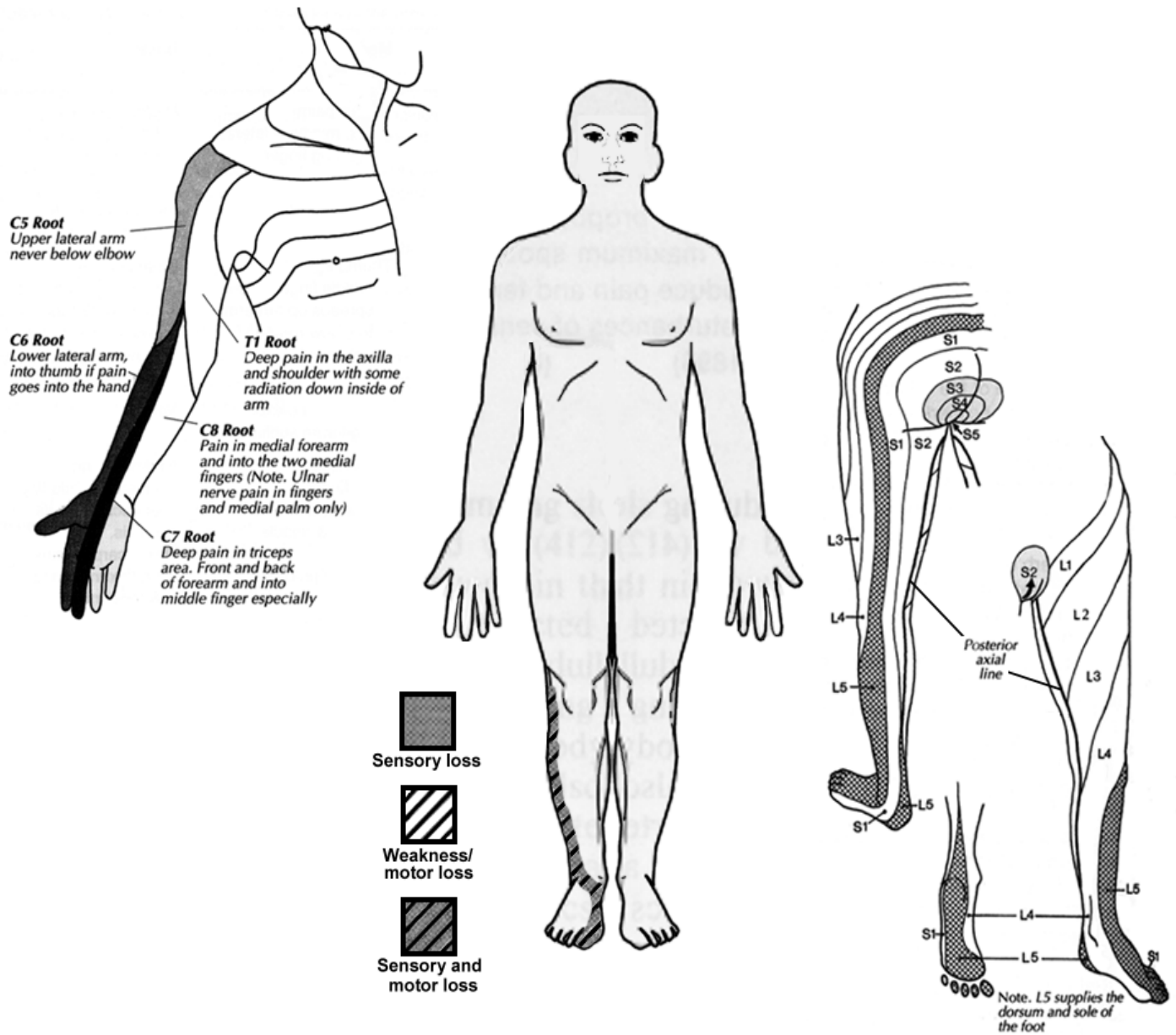


There are also diseases of specific nerves either from compression or vascular disease (usually vasculitis or small infarctions associated with diabetes). Common nerves to be compressed are the median at the wrist (carpal tunnel), ulnar at the elbow, peroneal at the fibular head, lateral cutaneous nerve of the thigh at the inguinal ligament. Diabetes often is associated with femoral nerve or cranial nerve lesions. When multiple nerves are affected the term mononeuropathy multiplex is used.



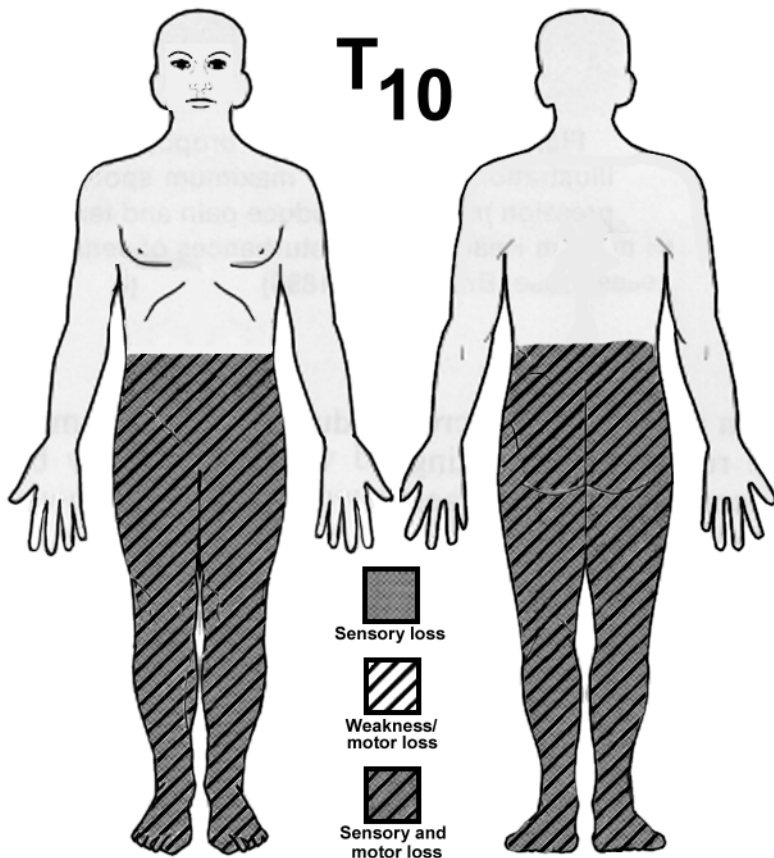
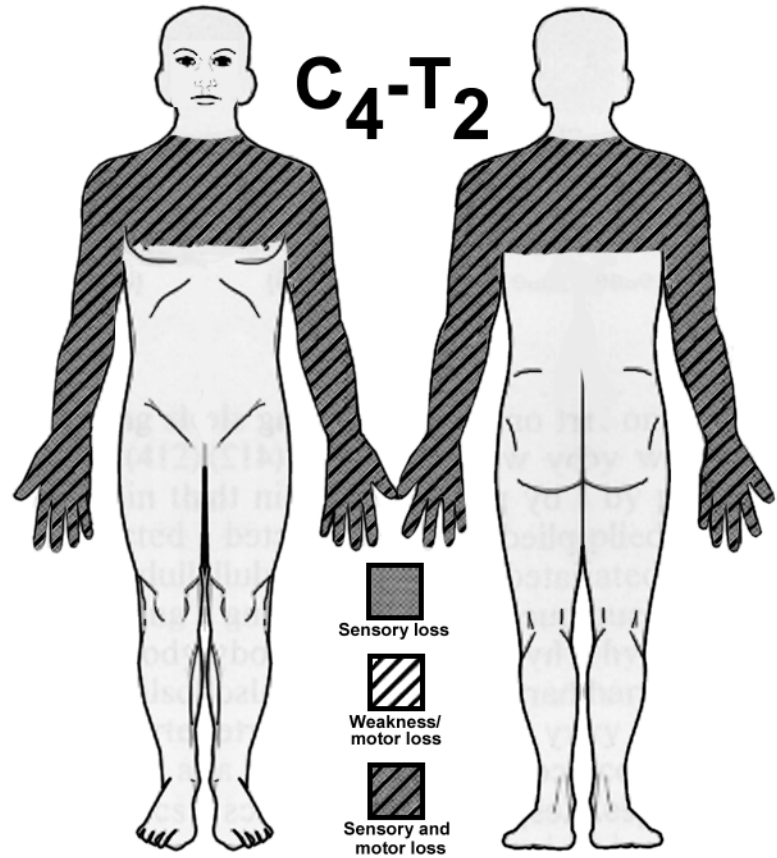
Radiculopathy

Pain, sensory, and motor loss. Referable to a dermatome and weakness in muscles innervated by the same root. Lower motor neuron.



Spinal Cord

Central cord e.g. syringomyelia: bilateral sensory with a cape distribution. Upper motor neuron. Lower motor neuron at the level of the lesion. Bowel bladder function may be involved.



Transverse lesion: bilateral sensory and motor loss with a level corresponding to the lesion. Bowel and bladder dysfunction.

CASE HISTORY I

CASE PRESENTATION

This 6 year old boy was brought to your office by his parents who were complaining that the boy had had progressive difficulty walking, climbing stairs and appeared “clumsy”. The child’s teacher also felt that the boy was always behind his peers in any physical activity. Academically he did well at school. The child was a product of normal pregnancy and normal delivery. His early developmental milestones were normal. He was able to walk independently at the age of 14 months.

The family history was noncontributory.

General physical examination was unremarkable except for slightly exaggerated lumbar lordosis (forward curvature).

Neurological examination showed normal mental status and cranial nerves. Motor examination showed marked enlargement of both calves. There was evidence of contractures in his Achilles tendons. He had prominent hyperlordosis of his lumbar spine. Muscle tone was slightly decreased. He had mild to moderate proximal weakness, especially in his legs but also to some extent in his arms. The boy had marked difficulty rising from the floor and did it by climbing up his thighs (positive Gowers’ sign). Sensation was normal. Tendon reflexes were decreased. Plantar reflexes were flexor. His gait was waddling.

QUESTIONS CASE HISTORY I

1) Where is the lesion/defect that might explain the findings on your clinical exam. Is the weakness caused by involvement of the corticospinal tract, anterior horn cells, roots, peripheral nerves, muscle, neuromuscular junction?

- 2) What could be the possible etiology?
- 3) What diagnostic tests would you order and why?

CASE HISTORY II

A 25 year old woman came to your office complaining of intermittent double vision for the last three weeks. She also has complained of fatigue. She has felt best during the early morning hours, but later, during the course of the day, she gradually develops double vision and diffuse weakness. Her boy-friend has observed that her right eyelid has been drooping frequently. She used to play competitive basketball while in college, but now she has been short of breath after climbing only 2 flights of stairs. Also, on a few occasions, she choked on food and her friends noted that her speech was slurred or thick.

On examination her mental status was normal. She had marked ptosis on the right side. Eye movement examination showed decreased movement in all directions in the right eye. There was also slightly decreased abduction in the left eye. On repetitive blinking she developed ptosis of the left eye lid and her right sided ptosis got much worse. Motor examination showed normal muscle bulk and tone. Muscle testing revealed that she was initially strong, but rapidly became “tired” or weak with repeated effort. She was unable to hold her arms abducted at 90 degrees for more than 30 seconds. All sensory modalities, reflexes, coordination and gait examination were normal. Plantar reflexes were flexor.

QUESTIONS CASE HISTORY II

1) Where is the lesion and why? Is it in the corticospinal tract, anterior horn cells, peripheral nerves, neuromuscular junction or muscle?

2) What is the possible etiology?

3) What diagnostic tests would you order and why? What results would you expect?

CASE HISTORY III

This 20 year old college student came to the emergency room complaining of tingling in her feet and fingers. She appeared anxious. Neurological examination showed no abnormality and she was discharged to home with a diagnosis of anxiety and hyperventilation. However, she returned to the emergency room the next day complaining of fatigue, weakness and shortness of breath. On specific questioning the patient admitted to having “flu like” illness 10 days before.

Her examination at this time showed mild diffuse weakness, decreased muscle tone and absent tendon reflexes. Plantar reflexes were flexor. Sensation to pain was slightly decreased in the feet. There was no sensory level. A sensory level is a region of the body below which a sensation(s) is lost and above which sensation is normal (for a lesion of the spinothalamic tract at T1, the level is T3). Her respiration rate was 26 (normal adult rate is 10-15). Mental status and cranial nerve examination was normal. She was admitted to the hospital for observation. Over the next two days her weakness dramatically increased and she developed respiratory failure and had to be intubated and placed on a ventilator.

During the first week of her illness she had frequent fluctuations of the heart rate and blood pressure.

QUESTIONS CASE HISTORY III

1) Where is the lesion and why? Is it in the brain, spinal cord, nerve roots, peripheral nerves, neuromuscular junction or muscle ?

2) What are the possible etiologies?

3) What diagnostic tests would you order and why? What results would you expect?

CASE HISTORY IV

A 45 year old delivery man comes to see you complaining of low back pain that has been intermittent for the past 6 months. The pain is in the middle of the lower back and usually radiates into the left buttock. The pain is made worse by sneezing, coughing, or when he hits a pot hole while driving. In some cases these maneuvers cause the pain to radiate down the back of his left leg into the bottom lateral aspect of his foot. Over the past 6 weeks, he has noted that it is difficult for him to stand on his tip toes and that this is primarily because of weakness in his left foot.

On exam he has a normal neurological exam except that his left ankle jerk is absent and he has weakness of his left gastrocnemius. There is abnormal sensation over the lateral aspect of the left foot. He cannot stand on his toes of his left foot. When you have him lying down, you cannot elevate his left leg above 35 degrees because of shooting pain into his left buttock and down the back of his left leg.

QUESTIONS CASE HISTORY IV

1) Where is the lesion?

2) What would an EMG/NCV study show?

3) What diagnostic testing would you order?

4) How should this patient be treated and what is his prognosis?

CASE HISTORY V

A 65 year old man presents with a six month history of progressive fatigue, weakness and leg cramps. On a few occasions he choked on food. His wife noted diffuse twitching of muscles on his chest and upper back. Two months ago he developed a foot drop in his left leg. He has not complained of any sensory symptoms. There has been no cognitive decline. He has no difficulty with bowel or bladder function. His family history is noncontributory.

Examination showed that the patient had normal mental status. Motor examination showed severe, bilateral diffuse muscle wasting in both upper and lower extremities. The most atrophied were the deltoid, triceps, biceps, hand muscles and quadriceps on either side and the left anterior tibialis. There were prominent fasciculations in all muscle groups. The muscle tone was increased, (spastic) in both upper and lower extremities. There was diffuse weakness in all 4 extremities with complete left foot drop. Neck extensors were profoundly weak so that the patient was barely able to keep his head up.

The tendon reflexes were hyperactive in all four extremities. The plantar reflexes were extensor (Babinski sign).

Sensory examination and coordination were normal.

His gait was characterized by decreased arm swing and limping of the left leg.

QUESTIONS CASE HISTORY V

1) Where is the lesion and why? Does it involve the corticospinal tracts, anterior horn cells, nerve roots, peripheral nerves, neuromuscular junction or muscle?

2) What are the possible etiologies and why?

3) What diagnostic tests would you order and why? What results would you expect?

CASE HISTORY VI

A healthy 25 year old woman is brought to the emergency room after being stabbed in the neck.

Examination shows:

- 1) left ptosis and meiosis (small pupil)
- 2) weakness of the left upper and lower extremities
- 3) absent left biceps stretch reflex
- 4) other left sided muscle stretch reflexes diminished
- 5) loss of left finger and toe joint position sense
- 6) loss of left finger and toe vibratory sensation
- 7) loss of pain and temperature sensation below C7 on **right**

- 1) Where is the location of the lesion?
- 2) Explain why each of the findings are present.

1.

2.

3.

4.

5.

6.

7.

3) Why might atrophy of the upper arm develop over time?