MEDICINE

432 Team

47 Peripheral Neuropathies

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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

Not Given! ☹

Extra sources are: Davidson, Kumar, Talley, UpToDate, MedScape, WebMD

Let's review some basics

- CNS vs PNS

Central nervous system (not our concerns in this lecture)	Brain and spinal cord (read more: source)
Peripheral nervous system	Everything else starting from the anterior horn cell, roots, cervical and lumbosacral plexi, peripheral nerves and their divisions. (explained more in page 4)

- Anatomy of a single nerve:

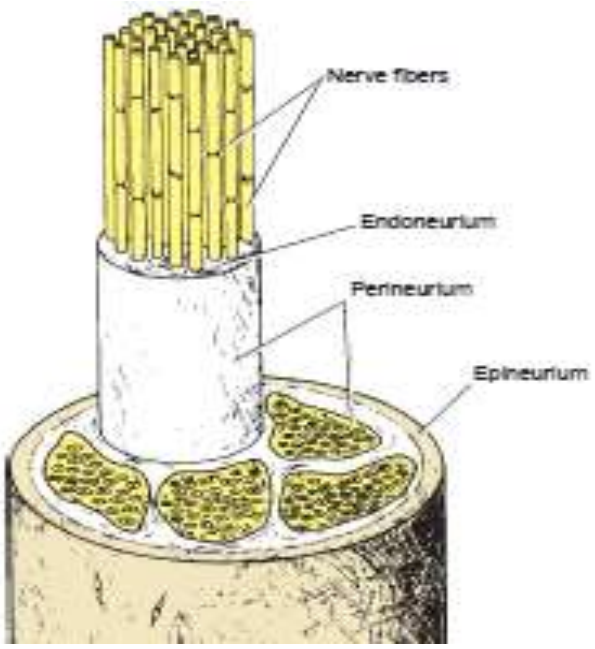
Each nerve contains many nerve fibers

Endoneurium[1]: the delicate connective tissue enveloping individual nerve fibers within a peripheral nerve, also called Henle's sheath.

Perineurium[2]: the sheath of connective tissue enclosing a bundle of nerve fibers.

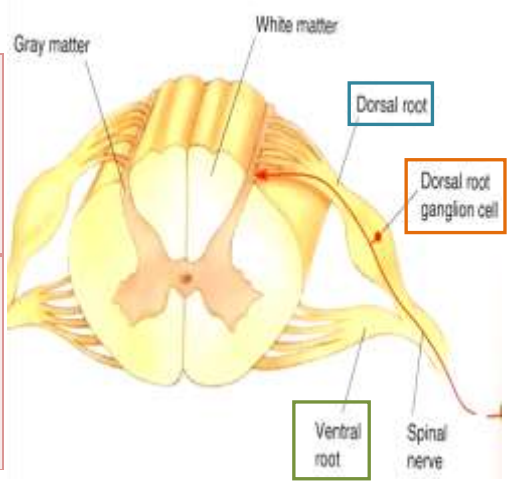
Epineurium[3]: the outmost layer of connective tissue of a peripheral nerve.

Sources: 1, 2, 3



- Motor vs Sensory: read more

Motor pathway	Starts as the axons of anterior horn cells (in the spinal cord) come out through the ventral root. It's divided into somatic and autonomic nervous system)
Sensory pathway	Starts from periphery where sensory cells receive stimuli and send it to the CNS. It enters the spinal cord through the dorsal root (passing through dorsal root ganglia)



- ***Conduction velocity*** *depends on the type of the fibers (each has different diameter, which suits the function) as you can see in the table:*

Fiber type		Conduction velocity	Fiber diameter	Functions	Myelin	Sensitivity to local anesthetics
A fibers	Alpha	70-120	12-20	Motor: skeletal muscles	Yes	Least
	Beta	40-70	5-12	Sensory (large fiber): touch, pressure, vibration	Yes	
	Gamma	10-50	3-6	Muscle spindle (reflexes)	Yes	
	Delta	6-30	2-5	Pain (sharp, localized) temperature, touch	Yes	
B fibers		3-15	<3	Sensory (small fibers) Preganglionic autonomic	Yes	
C fibers		0.5-2	0.4-1.2	Sensory (small fibers) Pain (deep) temperature, postganglionic autonomic	No	Most

From Slides

(you're NOT supposed to memorize it, but understanding this part will help you a lot through the lecture)

- ***Types of symptoms and defects:***

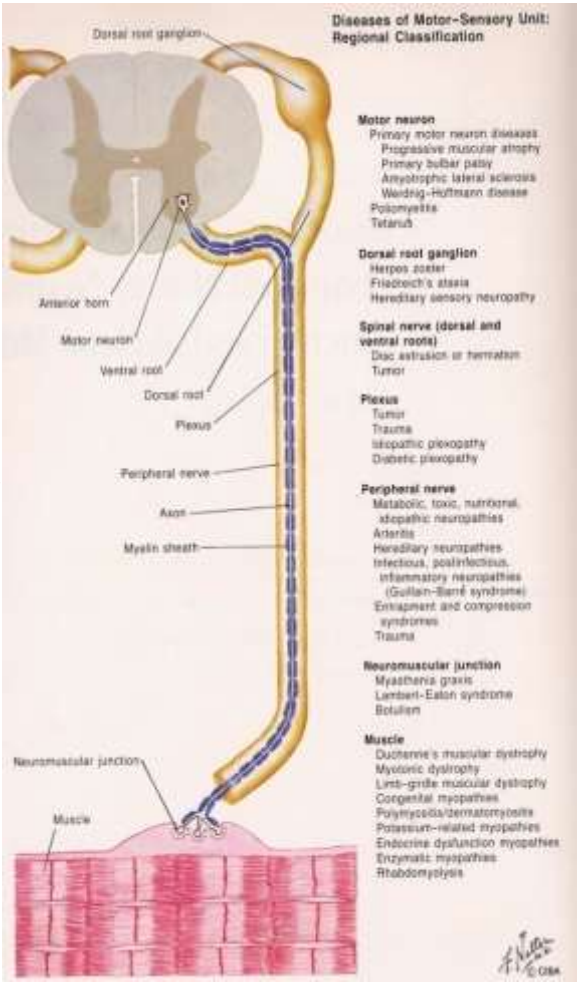
		LOSS OF FUNCTION (NEGATIVE SYMPTOMS)	ALTERED FUNCTIONS (POSITIVE SYMPTOMS)
MOTOR		**Wasting, hyopotonia, weakness, hyporeflexia and orthopedic deformity**	**Fasciculation and cramps**
SENSORY	Large fibers	**↓ Vibration, ↓ proprioception, hyporeflexia and sensory ataxia**	**Paresthesia**
	Small fibers	**↓ Pain and ↓ Temperature**	**Dysesthesias[1] and allodynia[2]**
AUTONOMIC		**↓ Sweating, hypotension, urinary retention, impotence and vascular color changes**	**↑ Sweating and hypertension**

Note: the term positive or negative has nothing to do with the presence or absence of the symptoms. It only describes the symptom.

1. It is defined as an unpleasant, abnormal sense of touch. It often presents as pain, but may also present as an inappropriate, but not discomforting, sensation.
2. Is a pain due to a stimulus which does not normally provoke pain (e.g. touch).

In the central nervous system we have Oligodendrocytes that produce myelin sheaths, while in the peripheral we have Schwann cells. So we have different disorders for each of them that can affect different antigens. Also, each person has different types of fibers that transfer his/her sensations (large and small fibers) so even sensations differs within the same person.

Peripheral Neuropathy:



1) PNS

a. Anterior horn cell (Motor neuron) (diseases affecting AHC are clinically separated from Peripheral neuropathies, they're called Motor Neuron Disorders)
b. Ventral root (pure motor)
c. Dorsal root ganglion
d. Dorsal root (pure sensory)
e. Plexus
f. Peripheral nerves
g. Neuromuscular junctions
h. Muscles
i. End organ receptor / small fiber neuropathy

Peripheral Neuropathy

2) Definition:

- **Peripheral neuropathy = any disorder of the peripheral nervous system** (from anterior horn cells to the muscle)
- Peripheral neuropathy describes damage to the peripheral nervous system. More than 100 types of peripheral neuropathy have been identified, each with its own characteristic set of symptoms, pattern of development, and prognosis.
- **Neuropathy**, can refer more generally to disorders of the central and peripheral nervous system.

(From Davidson): Numerous inherited and acquired (most are acquired) pathological processes may affect peripheral nerves, targeting either the nerve roots (radiculopathy), the nerve plexuses (plexopathy) and/or the individual nerves themselves (neuropathy). Cranial nerves 3–12 share the same tissue characteristics as peripheral nerves elsewhere and are subject to the same range of diseases. Nerve fibers of different types (motor, sensory or autonomic) and of different sizes may be variably involved. Disorders may be primarily directed at the axon, the myelin sheath (Schwann cells) or the vasa nervorum (the vascular supply of the nerves). An acute or chronic peripheral nerve disorder may be focal (affecting a single nerve: mononeuropathy), multifocal (several nerves: mononeuropathy multiplex) or generalized (polyneuropathy).

3) Mechanisms of damage: (it can be mixed in some diseases)

Mechanism		Example
Demyelination	Schwann cell damage leads to myelin sheath disruption. This causes marked slowing of conduction	GBS (Guillain–Barré syndrome) , HSMN (hereditary sensory and motor neuropathy)
Axonal degeneration	Axon damage leads to the nerve fiber dying back from the periphery. Conduction velocity initially remains normal because axonal continuity is maintained by surviving fibers. (Usually associated with atrophy, most of chronic or metabolic diseases affect axons. Once the axons are affected it's irreversible)	Toxic neuropathies
Wallerian Degeneration	Nerve section, both axon and distal myelin sheath degenerate, over several weeks. Is also called anterograde degeneration, the axon starts to degenerate distally to the area of injury (opposing the cell body direction) and takes long time to regenerate.	Trauma
Compression	Focal demyelination at the point of compression causes disruption of the myelin sheath. This occurs typically in entrapment neuropathies.	Carpel tunnel syndrome
Infarction	Microinfarction of vasa nervorum occurs in diabetes and arteritis. Just like how you get a heart attack you get a nerve attack but you have plenty of nerves overlapping so you don't get to feel the pain unless large number of nerves got infracted	Arteritis, Polyarteritis nodosa, DM, Atherosclerosis
Infiltration	Infiltration of peripheral nerves by inflammatory cells occurs in leprosy and granulomas. (nerves get damaged directly)	Infiltration Leprosy, Sarcoidosis

Nerve regeneration: occurs either by remyelination – recovering Schwann cells spin new myelin sheaths around an axon – or by axonal growth down the nerve sheath with sprouting from the axonal stump. (kumar).

Demyelination shouldn't cause atrophy, but if the disease is already severe, it might be associated with atrophy. Later on, axons will be affected, and you won't be able to differentiate or to tell the initial mechanism. >> like in GBS

Fasciculation is twitching in the motor unit (one nerve supplying group of muscle fibers)

Motor nerves (that control muscles), sensory nerves, or autonomic nerves (that control automatic functions such as heart rate, body temperature, and breathing), may be affected. More than one type of nerve may be affected at the same time (In GBS the patient has sensory/motor loss and autonomic too) . The effect could be loss of function (negative) or inappropriate gain of function (Positive).

Important notes from the doctor to start with:

- Some of the neuropathies are acute, but majority are chronic slow processing.
- Weakness isn't specific for LMN only it can happen in UMN disorders as well, but in LMN lesions there are more sensory loss, hypotonia,hyporeflexia, and muscles atrophy which you don't find in UMN lesions
- Increase the muscles tone in UMN lesions has two types 1)Spasticity related to cortical disorders 2)Rigidity related to basal ganglia disorders

-For example in Parkinson (UMN disease) patient has weakness, but with hypertonia rigidity (UMN-basal ganglia) and you can never see atrophy of the muscles (cause it's a LMN characteristic) but if the patient is too depressed and doesn't eat he will lose his muscles (late stage).

-If the patient presented with muscles atrophy in an early stage you should think of (Parkinson plus LMN together)>> ALS 1 complex (UMN+LMN+pyramidal+extrapyramidal)

- fasciculation are found in LMN diseases and it's classical for ALS

- When you have a PNS disorder or injury you use history and examination to reach your diagnosis then confirm it with EMG. In order to differentiate between LMN injury and all other PNS problems (AHC,Myopathies, NMJ disorders,..)

For example: patient came with weakness, tingling distally and it's symmetrical.

- you must exclude myopathy cause in myopathy reflexes are not affected, weakness is different it's more proximal than distal, tone will not be affected unless it's too advanced and happens late, patient's history will include pain and stop his daily activities. And lab investigations will show high CPK.
  -In proximal muscle one motor neuron supplies lots of muscle fibers unlike in distal muscles.
  -Proximal weakness is more related to myopathy and distal weakness more related to neuropathy.
- Neuromuscular junction disorders: ptosis, dysphagia, difficulty in chewing and swallowing, fatigability (at morning he is fine, by the end of the day he isn't) examination : look up, fatigubility test, Icepack test 85% accurate, or squeeze the eyes tight (sustain release of ACH and ptosis will disappear)
- Cervical cord process (spinal cord disorders in general): fast onset of symptoms. Example: sphimgomyelia (cavity inside the spinal cord) affects pain and tempreture fibers and numbness

and the tingling (always think if it's related to sphingomyelia – cervical cord process) cause it's common condition

- Hyperventilation and panic attacks cause numbness/ tingling and it's recurrent on and off unlike when it's nerve damage it's permanent. And it's regeneration takes time little as 6 weeks or long as 6 months. But also in polyneuropothy you get numbness and tingling on/off pattern but doesn't happen in seconds (HX imp)
- You must distinguish between the weakness of myopathies and NMJ disorders and Motor neuron diseases.
- Electrodiagnostic studies: nerve conduction study and electromyography can differentiate between all these categories, each has different findings. But the purpose here is to reach the diagnosis from the history and examination.

- Slide 22-23:

  -mononeuropathy: it can be medial or ulnar or radial or peroneal..etc nerve, usually related to compression problem. Some are not related to compression like in cases of DM, vascuilitis, ..etc

  -Mononeuropathy multiplex: means multiple nerves affected at the same time and asymmetrically can be on different sides or even in one side (ulnar here, medial there, sciatic, and a lot of time not explained by compression unlike the mononeuropathy, here you think more of systemic diseases you must exclude them, the patient will come with different symptoms of different nerves around the body, compression can be one of the causes but u have to exclude the other diseases in the list)

- Slide 24:

-Polyneuropathy: Distal symmetrical neuropathy, length dependant. either the axon or the myelin or all get affected.

-The important thing here to differentiate between axonal injury a dmyelination which can be done by EMG nerve conduction study but sometimes you can distinguish it clinically:

- Demyelination means myelin sheath is distructed
- Axonal means the axon itself
- So if only the myelin that is affected not the axon, the muscle will function normally and there will be no muscle atrophy. But if the axon is affected which will injure the motor neuron that controls the muscle fibers they'll atrophy and become weak (in axona injury patients they have weakness and atrophy. In myelin might have weakness but no atrophy)

-AIDP: acute inflammation demyelinating neuropathy (GBS) and if the symptoms are in chronic setting it's going to be chronic inflammation demyelinating neuropathy(CIDP).

-If someone come with progressive weakness and increases within period of two weeks this is AIDP. if more than 6 to 8 weeks this is CIDP (just the duration is the difference). The first two weeks in AIDP are the worst and treatment can different.

-Demyalination: 1-uniform (by EMG and nerve conduction study they all show slow velocity, mostly genetic disorders) 2- non uniform (velocity not similar,are slow and others aren't –patchy-, mostly acquired disorders)

- GBS is mainly demylinating but sometimes has axonal damage

- Slide 26:
  -Imp: most of the chronic diseases are axonal, most of the metabolic diseases are axonal, and most of the toxins are axonal. And most of them are subacute to chronic
  -Porphyria is acute axonal disease
  - Medications cause acutely axonal damage
- Most common cause for radicuolopathy is herniated disc and best way to diagnose it is by History and examination (follow the dermatomes and myotomes)

4) Classifications:

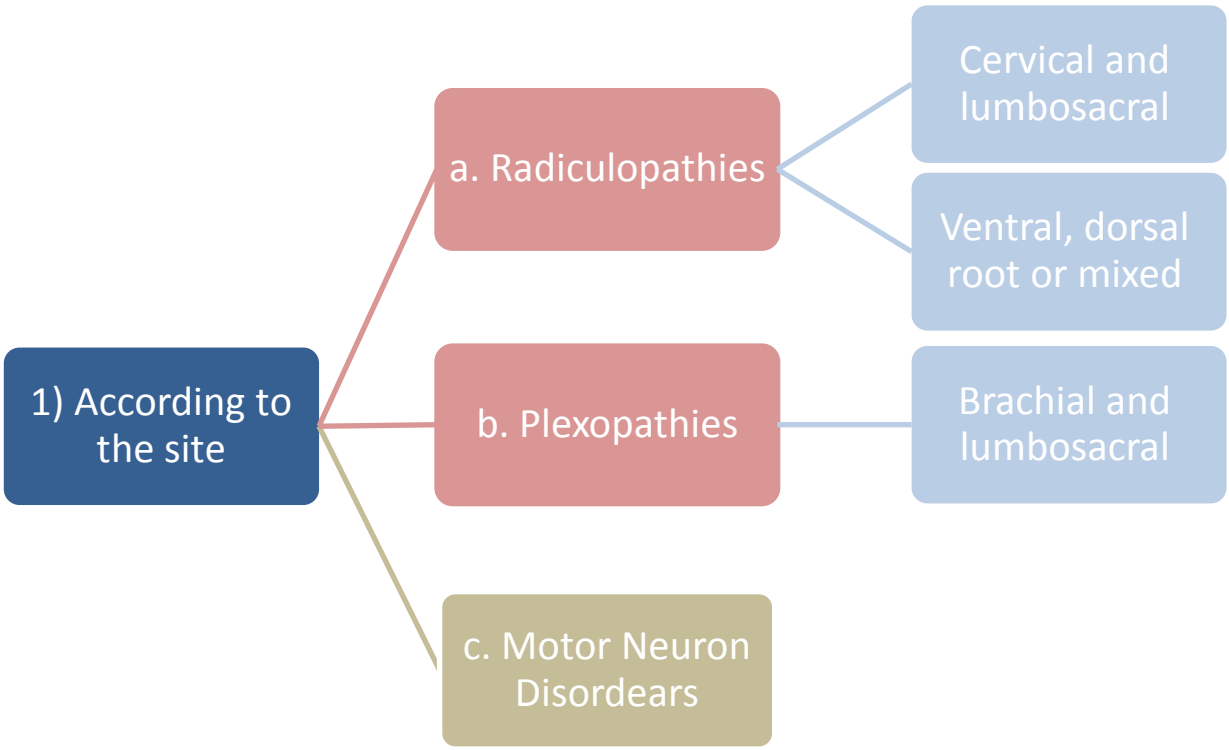
Can be classified in different ways, the commonest classification (according to the site + no. of lesions): **Classifications** according to the number and site of lesions.

According to the No. of lesions	Mononeuropathy	one nerve at a time (mono=focal)
	Mononeuritis multiplex	multiple nerves in different parts of the body (multiple mononeuropathies and or multifocal neuropathy)
	Polyneuropathy	**Symmetrical** and multiple (diffuse), **start from distal part and goes up**, the symptoms are length dependent. (Means the longest nerves get affected first) so the symptom starts from the toes up to the knees then it starts in the hands and so.
According to the site	Radiculopathy	Means disease affecting nerve roots and plexopathy.
	Myelopathy	Means disease of the cord.

- It can be classified in many ways:
  - Etiology: acquired or inherited.
  - Pathology or mechanism of damage for example: myelin, axons, or both if the disease is chronic, it can start with demyelination then affect the axon like in GBS)
  - Types of fibers that are affected (sensory, motor, autonomic or all like in GBS)
  - Site of injury (like in the figure)
    - Remember: all types of PN can have autonomic symptoms.
    - You can have two types together (e.g. polyradiculopathy, it's multiple, yet proximal not distal because of the injury position)

MND: Motor neuron disease (lesion in the spinal cord) e.g. Syringomyelia (development of a fluid-filled cavity or syrinx within the spinal cord – dissociative sensory loss)

1) Classifications according to the site



a. Radiculopathy:

Compressive: **herniated disc**, spondylosis, tumor.

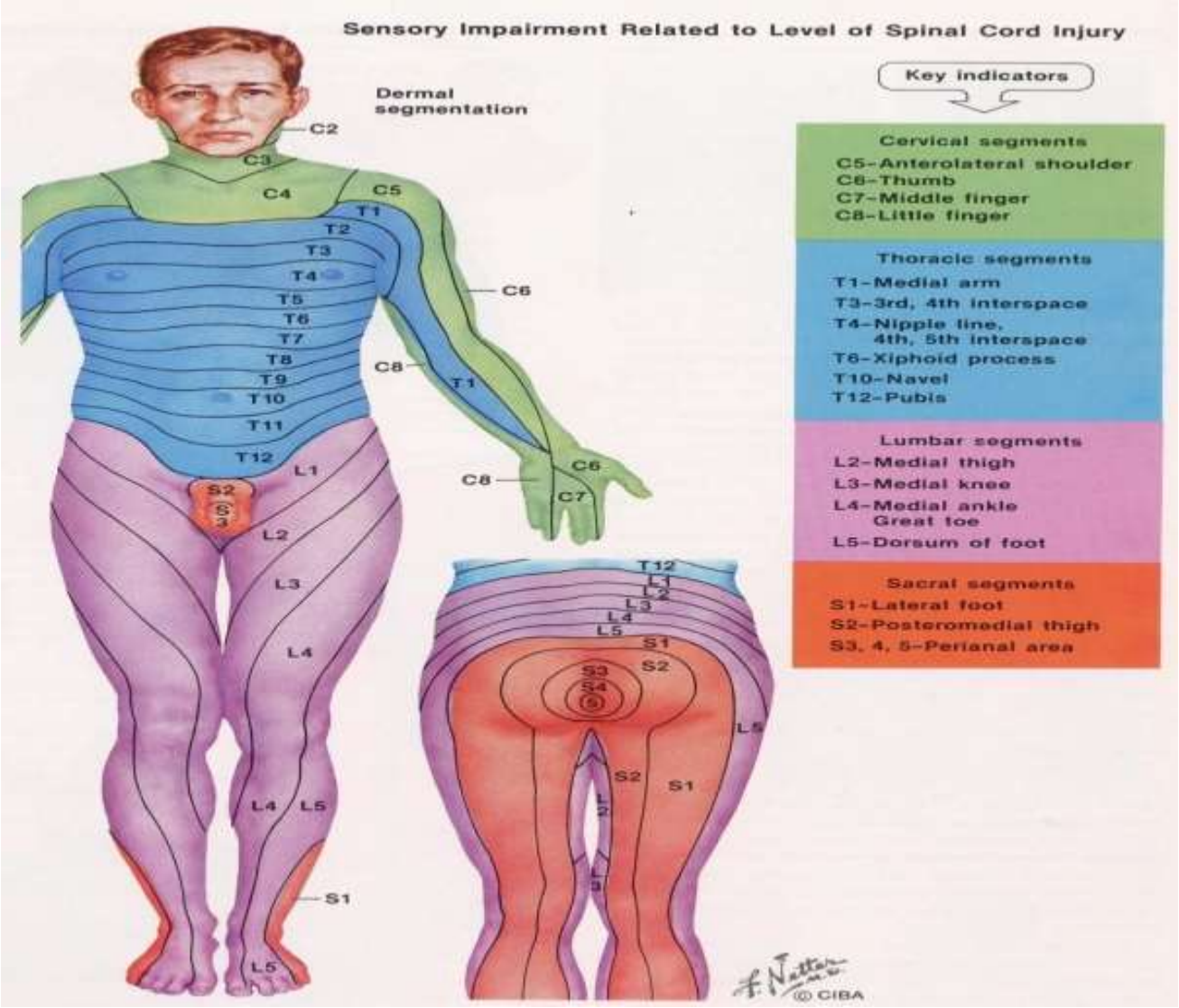
Infiltrative: tumor seeding, infection.

Inflammatory: immune-mediated.

} Different mechanisms

Dermatomes: MEMORIZE THEM 👀

A dermatome is an area of skin that is mainly supplied by a single spinal nerve. There are 8 cervical nerves (C1 being an exception with no dermatome), 12 thoracic nerves, 5 lumbar nerves and 5 sacral nerves. Each of these nerves relays sensation (including pain) from a particular region of skin to the brain. https://www.youtube.com/watch?v=mLQUFCMOvDk



- To diagnose radiculopathy with through history and examination you must know 1) dermatomes, part of skin supplied by single root 2) myotomes, the muscles supplied by it.

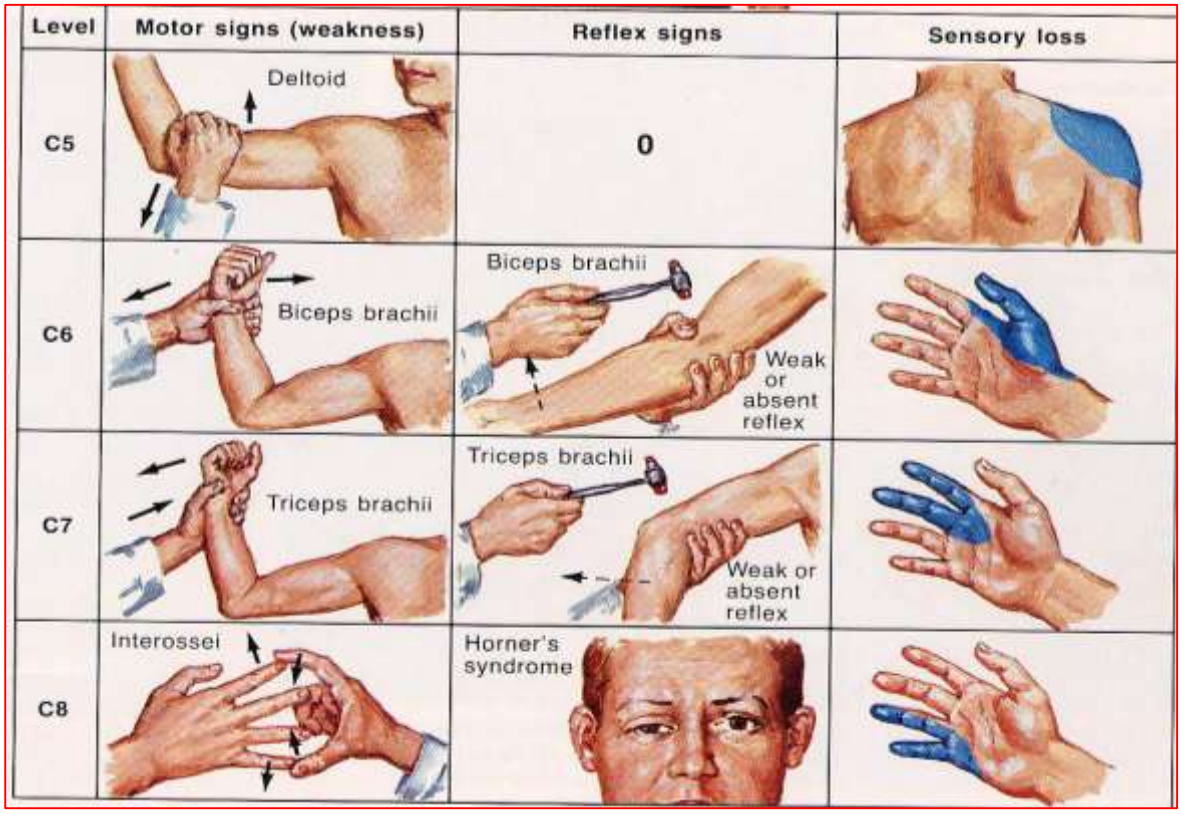
- No C1 dermatome
- C4 and T2 dermatome are contiguous on trunk
- Thumb, middle finger, and fifth digits are innervated by C6, C7, and C8, respectively
- Nipple is at T4 level
- Umbilicus is at T10 level
- Lumbar and sacral dermatome are contiguous in the posterior axial line of leg

Myotomes: MEMORIZE THEM TOO 👀

Root	Muscle	Primary function
C3	Diaphragm	Respiration
C4	Diaphragm	Respiration
C5	Deltoid	Arm abduction
C5	Biceps	Forearm flexion
C6	Brachioradialis	Forearm flexion
C7	Triceps	Forearm extension
L3	Quadriceps femoris	Knee extension
L4	Quadriceps femoris	Knee extension
L4	Tibialis anterior	Foot dorsiflexion
L5	Extensor hallucis longus	Great toe dorsiflexion
S1	Gastrocnemius	Plantar flexion

- Remember each muscle is supplied by multiple roots but in this table the main ones are mentioned to help you in diagnosing or localizing the defect.
- a reflex called: supinator operator radialis reflex can be decreased if there is a lesion at C6 and C7
- After memorizing the dermatomes and myotomes try to link things in your mind so you get the whole picture. E.g. a patient presented with abnormal sensations in his thumb and weakness while trying to flex his elbow joint → C6 is probably affected
- Generally, you rule out UMN lesions by physical examination: absence of hypertonia and hyper-reflexia, no muscles atrophy, EMG (electromyograpgies) as well.

› Cervical radiculopathy:



Examples and notes on this part by the doctor:

- Patients presented with weakness in abduction, numbness on shoulder area. Or Came with numbness on shoulder area only.

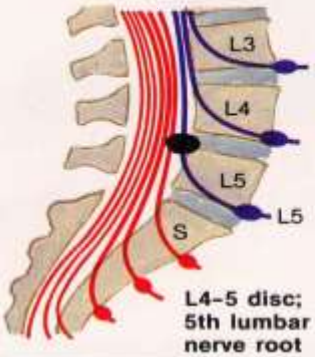
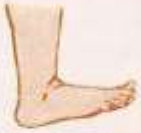
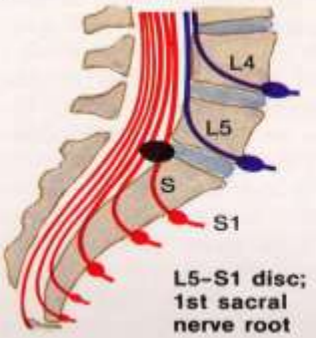
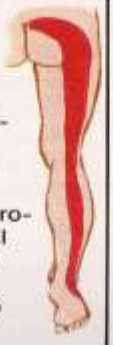
  -You think of deltoid (c5) or it can be axillary nerve. To differentiate (by examination) check the myotome of C5 which is shoulder abduction and also it supplies the biceps (flexion) so biceps reflex weak or absent. But in axillary injury only the deltoid will be affected.

- C8 gives the interossei (adduction and abduction and making a fist). Sensation: pinky and ring finger.
- C7 triceps (extension) and supplies sensation to middle finger. Weak or absent reflex of the triceps.

- C6 biceps (forearm flexion) and the sensation along the forearm laterally with thumb and index fingers. What else give sensation in this area? (Median! But median gives 3.5 fingers of the radial side, also control the flexors of the forearm and the muscles of the hands causing weakness)
- Supinator or brachioradialis reflex supplied by c6-c7 (can be decreased) you'd think of ulnar mononeuropathy too but the myotome supply is too small to distinguish ulnar clinically so you ask for EMG.

  EMJ is also done in cases to know if the cause of damage is demyelination or axonal.

› Lumber radiculopathy

Level of herniation	Pain	Numbness	Weakness	Atrophy	Reflexes
 L4–5 disc; 5th lumbar nerve root	 Over sacro-iliac joint, hip, lateral thigh and leg	 Lateral leg, first 3 toes	 Dorsifexion of great toe and foot; difficulty walking on heels; foot drop may occur	Minor	Changes uncommon in knee and ankle jerks, but internal hamstring reflex diminished or absent
 L5–S1 disc; 1st sacral nerve root	 Over sacro-iliac joint, hip, postero-lateral thigh and leg to heel	 Back of calf, lateral heel, foot and toe	Plantar flexion of foot and great toe may be affected; difficulty walking on toes	 Gastrocne-mius and soleus	 Ankle jerk diminished or absent

Doctor's notes:

- *Foot drop happens due to sciatic nerve injury or it can be L5-S1 radiculopathy*
- *All branches come from the sciatic nerve so all the muscles here will be affected, dorsiflextion, plantar flexion, eversion, inversion. What also causes foot drop in UMN lesions are strokes in MCA (you differentiate through physical examination, if it's UMN lesion you'll find hypertonia, hyperreflexia..etc)*
- *How to differentiate between sciatic nerve injury and L5S1 radiculopathy? EMG.*
- *Sciatic nerve branches in the leg: Tibial nerve(plantar flexion and inversion),common fibular nerve(dorsiflexion and eversion)*
- In lumbosacral radiculopathy L5-S1 are the most common injured ones.

(This table was skipped by the doctor)

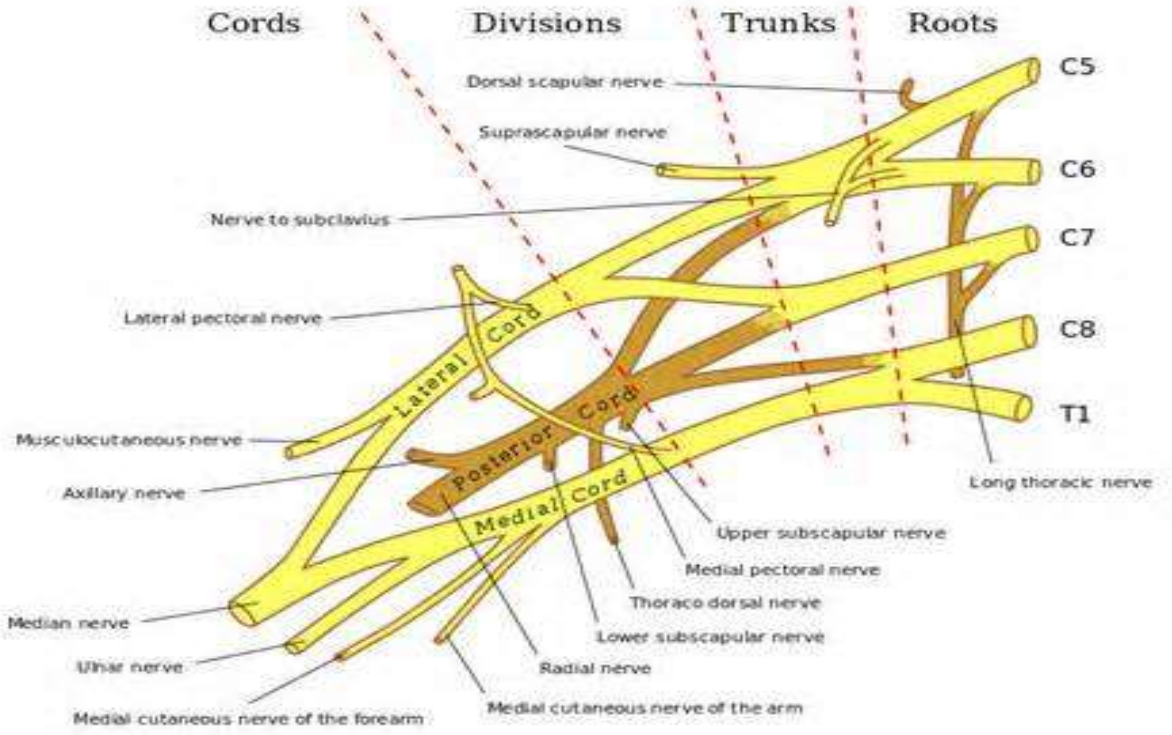
ROOT INJURY	DERMATOME PAIN	MUSCLES SUPPLIED	MOVEMENT WEAKNESS	REFLEX INVOLVED
C5	Lateral side of upper part of the arm	Deltoid and biceps brachii	Shoulder abduction, elbow flexion	Biceps
C6	Lateral side of forearm	Extensor carpi radialis longus and bravis	Wrist extensors	Brachioradialis
C7	Middle finger	Triceps and flexor carpi radialis	Flexion of elbow, extension of wrist	Triceps
C8	Medial side of forearm	Flexor digitorum superfacialis and profundus	Finger flexion	None
L1	Groin	Iliopsoas	Hip flexion	Cremaster
L2	Anterior part of thigh	Iliopsoas, sartanius, hip adductors	Hip flexion, hip adduction	Cremaster
L3	Medial side of knee	Iliopsoas, sartanius, quadriceps, hip adductors	Hip flexion, knee extension, hip adduction	Patellar
L4	Medial side of calf	Tibialis anterior, quadriceps	Foot inversion, knee extension	Patellar
L5	Lateral side of lower leg and dorsum of foot	Extensor hallusic longus, extensor digitorum longus	Toe extension, ankle dorsiflexion	None
S1	Lateral edge of foot	Gastrocnemius, saleos	Ankle plantar flexion	Ankle jerk
S2	Posterior part of thigh	Flexor digitorum longus, flexor halluces longus	Ankle plantar flexion, toe flexion	None

b. Plexopathy:

- If it's not following the root pattern, then think of plexopathy.
- In plexopathy: the defect can be anywhere BUT ANYTHING PROXIMAL TO THE LESION WILL BE SPARED.
- One important thing, nerve conduction for all sensory nerves will be normal in radiculopathy (why? Cuz the cell body is spared) But in plexopathy all sensory and motor supply are affected cause the injury is after the dorsal ganglion (where the nerve becomes mixed)
- When someone comes with mixed symptoms (sensory and motor), examine the proximal part, if intact → you're probably dealing with plexopathy rather than radiculopathy

- e.g. a patient presented with abnormal sensations in his thumb and weakness while trying to open a bottle → Median nerve
- Case: someone presents with numbness of both hands.
  -Put radiculopathy at the bottom of your differential. why? 1- bilateral at the same time , it won't push the nerve at the same time with all distribution it's not possible. 2- Nerves don't come out as one root, there are rootlets (it's not likely to compress all rootlets together at once)
  DDX: must ask about duration first if (slide 21-27)
  1- Gradual progress with a period of time >> bilateral median neuropathy (patient is working his hands alot)
  2- Cervical cord process (sphingomyelia) numbness of both hands at the same time and weakness
  3-Radicuolopathy (not very likely)
  4- Polyneuropathy (acute,chronic ,subacute)
  5-small fiber neuropathy
  6- Stroke or cranial lesion (not likely cause bilateral at the same time)

Brachial plexus:



- **Roots: C5, C6, C7, C8, T1**
- **Trunk: Upper (Roots C5 & C6), Middle (Root C7), Lower (Root C8 & T1)**
- **Division: Each trunk divides into anterior and posterior divisions**

Posterior cord (post division of all trunks)	Medial cord (anterior division of lower)	Lateral cord (anterior division of upper and middle)
all roots	C8,T1	C5,C6,C7
Radial nerve Axillary nerve	Median nerve Ulnar nerve	Median nerve Musculocutaneous nerve

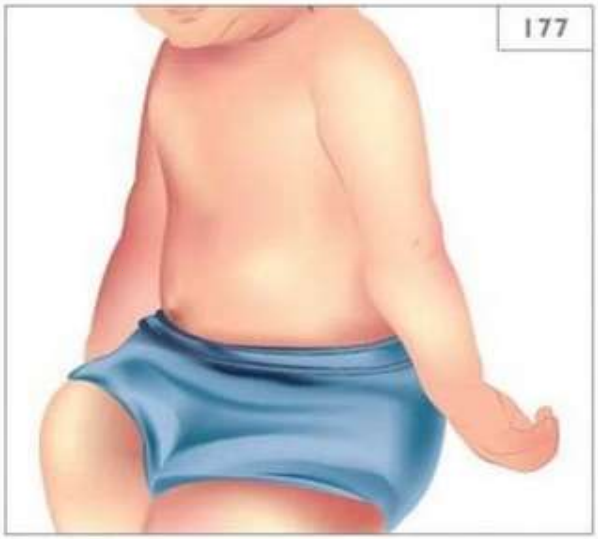
- Ulnar nerve: most common injury between medial epicondyle and olicranial process (cubital tunnel groove) causing cubital tunnel syndrome (hanging the arm on a chair and sleeping on it)
- Most of the hand muscles are supplied by the ulnar except for the thenar.

Causes of brachial plexopathy:

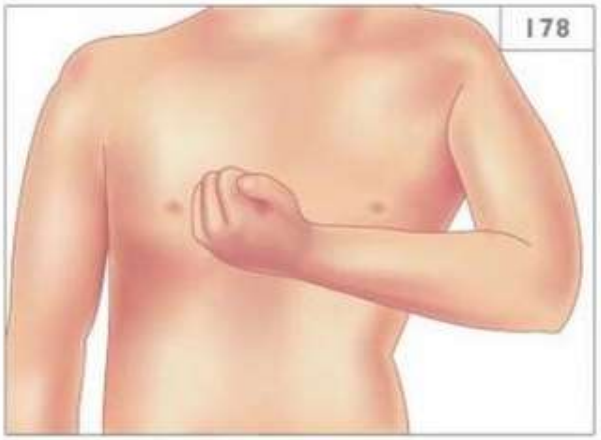
- **Trauma**
- **Tumor infiltration**
- **Infection by viral**
- **Immune-mediated**
- **Delayed effects of radiotherapy**

Brachial plexus lesions:

Erb's palsy	An upper brachial plexus lesion (C5,C6), which occurs from excessive lateral neck flexion away from the shoulder. Most commonly. It produces a very characteristic sign called Waiter's tip deformity due to loss of the lateral rotators of the shoulder, arm flexors, and hand extensor muscles.
Klumpke's paralysis	Less frequent. Caused by sudden upward pulling on an abducted arm (as when someone breaks a fall by grasping a tree branch) produces a lower brachial plexus lesion, in which the C8 and T1 are injured. The subsequent paralysis affects mainly the intrinsic muscles of the hand and the flexors of the wrist and fingers.



177 Erb's palsy.



178 Klumpke palsy.

› Lumbosacral plexus: *(check the graph in the next page)*

Causes of lumbosacral plexopathy:

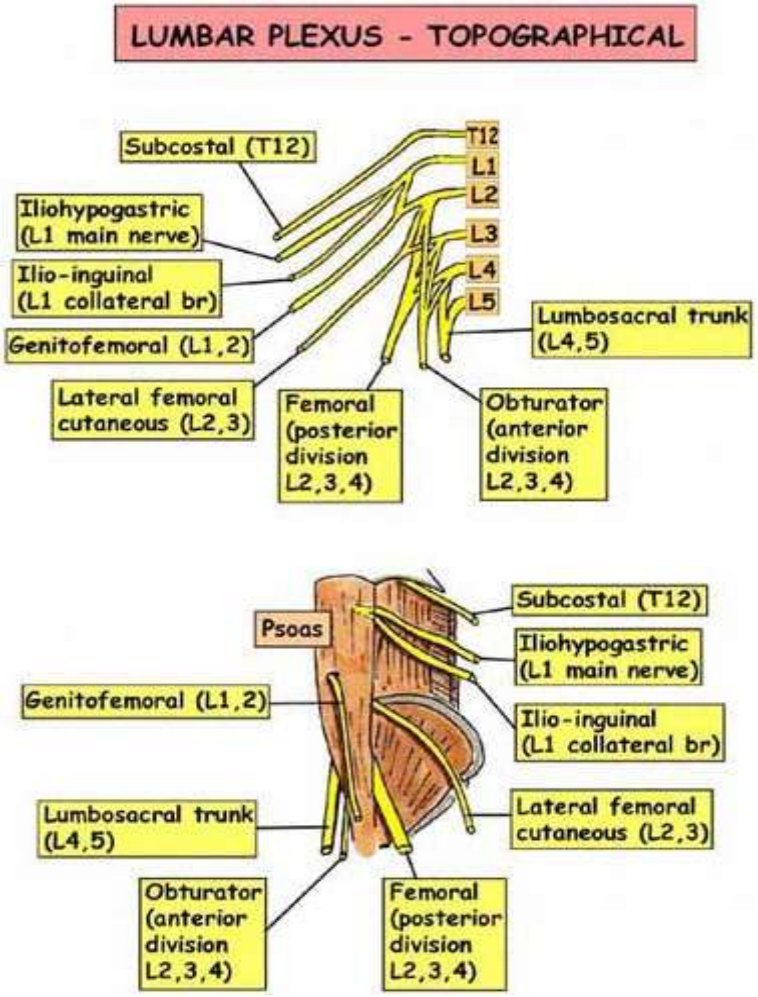
- Tumors : CA cervix, prostate, bladder, colorectal, kidney, breast, testis, ovary, sarcoma, lymphoma
- Compressed by aortic aneurysm
- Radiation plexopathy
- Plexitis : follow herpes zostor
- Diabetic amyotrophy
- Trauma (rare)
- As a manifest of mononeuropathy multiplex

Clinical manifestations:

Patients usually present with asymmetric, focal weakness, numbness, dysesthesia, and/or paresthesia in multiple contiguous lumbosacral nerve root distributions.

Patterns of weakness usually help localize the "lesion" to a more specific area within the plexus.

- Lumbar plexus lesions tend to cause weakness of hip flexion and adduction and/or knee extension.
- Lumbosacral trunk and upper sacral plexus lesions result in foot drop or flail foot depending on the extent of involvement, and weakness of knee flexion or hip abduction.

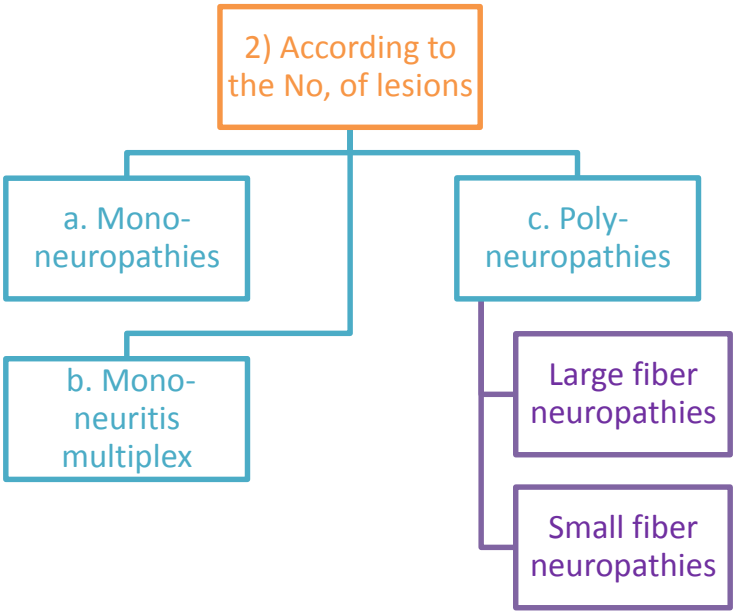


Patterns of sensory disturbance are less reliable given the difficult clinical delineation between dermatomal and named nerve sensory loss. However, in general:

- Sensory disturbance involving the anterior and medial thigh and medial leg typically represents lumbar plexus involvement.
- Sensory disturbance involving the leg, dorsum of the foot, posterior thigh, and perineum suggests a lumbosacral trunk and/or sacral plexus lesion.

(UpToDate: http://www.uptodate.com/contents/lumbosacral-plexus-syndromes)

2) According to the No. of lesions



a. Mononeuropathies

A single peripheral nerve is affected (e.g. median nerve, ulnar nerve, peroneal nerve, facial nerve etc..). The usual mechanism of damage is compression. Nerve damage by compression is either acute, e.g. due to a tourniquet, or chronic, such as in entrapment neuropathies. In both, focal demyelination predominates at the compression site, and some distal axonal degeneration occurs. Acute compression usually affects nerves exposed anatomically, e.g. the common peroneal nerve at the head of the fibula, or the ulnar nerve at the elbow. Entrapment develops in relatively tight anatomical passages, e.g. the carpal tunnel. Can be Isolated or contagious. These neuropathies are recognized largely by clinical features. Diagnosis is confirmed by nerve conduction studies.

People with these conditions can experience both weakness and numbness.

Common causes:

- Diabetes
- Vasculitis
- Infection
- Leprosy
- Neoplasm
- Brachial or lumbar
- plexopathy
- Radiation
- Sarcoidosis
- Radiculopathies

Table 21.52 Nerve compression and entrapment	
Nerve	**Entrapment/compression site**
Median	Carpal tunnel (wrist)
Ulnar	Cubital tunnel (elbow)
Radial	Spiral groove (of humerus)
Posterior interosseous	Supinator muscle (forearm)
Lateral cutaneous of thigh	Inguinal ligament
Common peroneal	Neck of fibula
Posterior tibial	Tarsal tunnel (flexor retinaculum – foot)

1. Median nerve compression: *(doctor said you don't need to know them all, only the underlined ones)*

- Carpal tunnel syndrome
- Pronator syndrome
- Anterior interosseous syndrome

Carpal tunnel syndrome

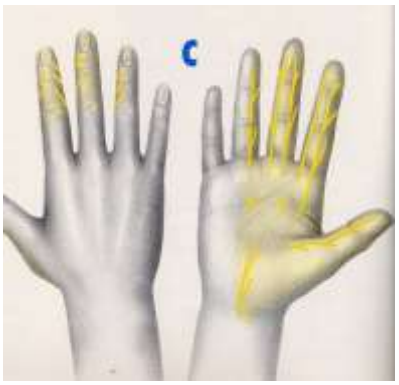
Typically is not associated with any underlying disease, however, seen in:

- hypothyroidism
- diabetes mellitus
- pregnancy (third trimester) – (self-limiting as fluid retention subsides postpartum)
- obesity
- rheumatoid disease
- acromegaly
- amyloid
- renal dialysis patients
- long activity like driving or computing might cause it.

Clinical features:

Nocturnal pain or paresthesia in the hand and/or forearm, thenar atrophy will be only in the hand (unlike Radiculopathy of C8 and T1)

Sensory loss in the palm and radial three-and-a-half fingers develops, followed by wasting of abductor pollicis brevis. Tinel's sign is often present and Phalen's test positive. Tinel's is elicited by tapping the flexor aspect of the wrist: this causes tingling and pain. In Phalen's, symptoms are reproduced on passive maximal wrist flexion.

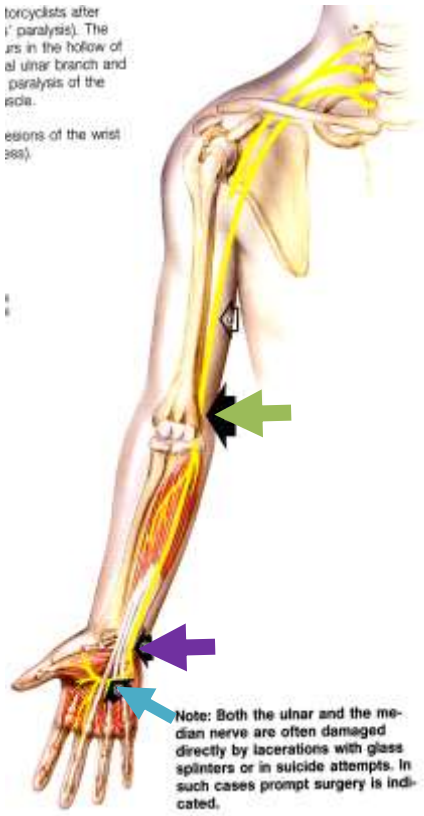


Treatment:

- Splinting – prevent wrist flexion
- Corticosteroid/anesthetic injection – give temporary relief
- Surgical decompression

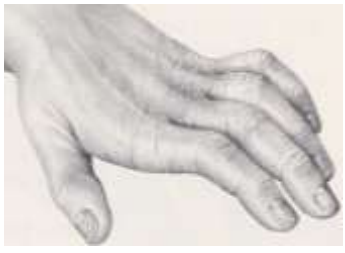
2. Ulnar Nerve:

- Lesion at condylar groove (cubital tunnel)
- Guyon's canal
- Lesion at wrist and hand

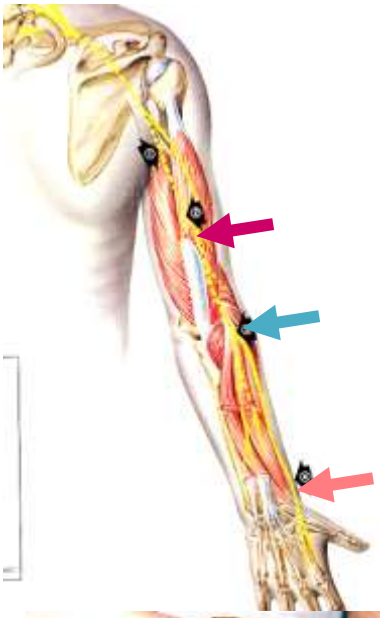


Cubital tunnel

- This follows prolonged or recurrent pressure and elbow fracture. Weakness and wasting of ulnar innervated muscles leads to clawing of the hand – hypothenar muscles, interossei and medial two lumbricals – with sensory loss in the ulnar oneand-a-half fingers.
- Decompression and transposition of the nerve at the elbow is sometimes helpful.

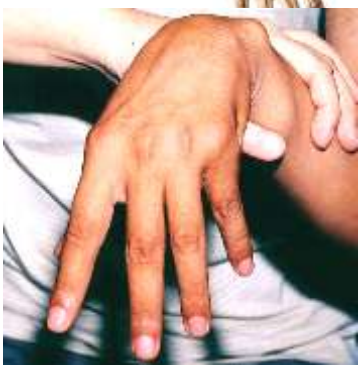


3. Radial Nerve

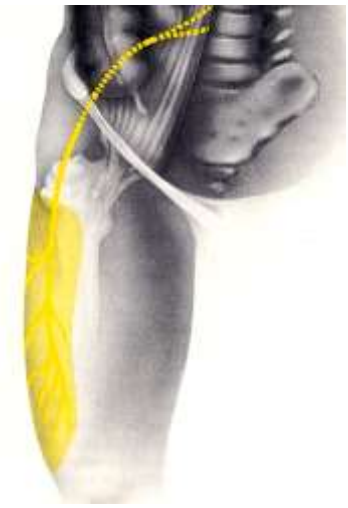


- Saturday night palsy
- Posterior interosseous syndrome (A pure motor branch of the radial nerve, no sensory loss)
- Cheiralgia paresthetica (Sensory only)

- Axillary lesion: weak triceps and radial innervated muscles.
- Mid-upper arm lesion: 'Saturday night palsy' (spiral groove or intermuscular septum): wrist drop, normal triceps, variable motor and sensory deficit (weakness of Brachioradialis and finger extension)
- Posterior interosseous : weak extensor of thumb and other fingers, no sensory loss (wrist drop, without weakness of Brachioradialis)
- Superficial radial nerve: terminal cutaneous branch.
  - Wrist drop of posterior interosseous nerve injury the sensory supply will be intact.
  - Wrist drop of the spiral groove injury both sensory and motor of wrist and fingers will be affected.
  - In lower part only sensory part of the radial will be affected at dorsum of the hand



4. Lateral femoral cutaneous



Meralgia paresthetica

Pure sensory (Common condition seen in clinics. Pure sensory loss to the inferior iliac spine area)

Doctor's notes:

- If it's sensory and motor defect at the same area (inferior iliac spine):

-It can't be femoral because the sensory branch of femoral which is the saphenous nerve extends till down so the sensation should be affected all the way down.

-But you think of radiculopathy (L2-L3) because they supply the motor and sensory part of that area but it should be assymetrical to say it's radiculopathy. And if it was pure sensory it's meralgia paresthetica.

-Plus confirm by EMG

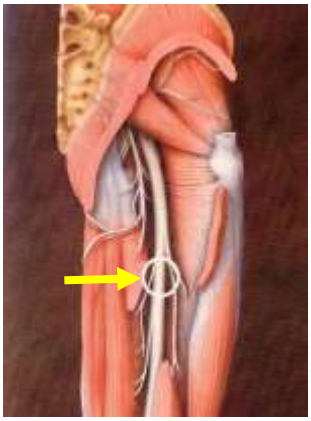
- Whenever you have a problem in sensation in one area check it from other ways it, can be different nerve, it can radiculopathy, it can't be polyneropathy here cause it's proximal defect not distal, neither mononeuritis multiplex cause only one area is involved

5. Femoral Nerve (L2,3,4)

- Mix sensorimotor
- Quadriceps femoris or knee extensor
- Weakness of hip flexor in intraabdominal lesion
- Sensory deficit over anteromedial aspect of thigh and perhaps leg
- Absent or diminished knee jerk

6. Sciatic nerve (L4, S3)

- Composed of 2 main nerves of leg: common peroneal and tibial nerve.
- Paralysis of all muscles below knee plus hamstrings and for high lesion, external rotators of thigh.
- Sensory loss below knee except anteromedial aspect of leg and foot.

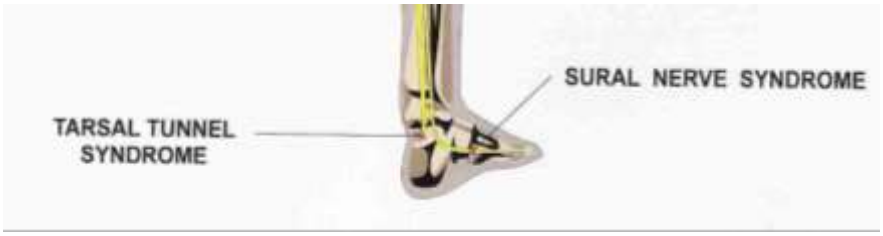


Common peroneal nerve

- Also called lateral popliteal nerve; compressed against the head of the fibula after prolonged squatting, yoga, pressure from a cast, prolonged bed rest or coma, or for no apparent reason. The ankle jerk (S1) is preserved.
- Foot-drop and weakness of ankle eversion.
- Numbness develops on the anterolateral border of the dorsum of the foot and/or lower shin.
- Paralysis of anterior and lateral compartment of leg.
- Sensory loss over dorsum of foot and toes and anterolateral aspect of leg.
- Recovery is usual, though not invariable, within several months.

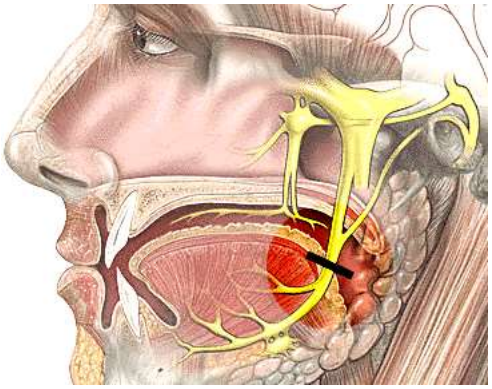
Tibial nerve

- Medial division of sciatic nerve
- Lesions at ankle
  - Tarsal tunnel syndrome
    - Pain and paresthesia in sole
    - Paralysis of intrinsic muscles of foot
    - Tenderness of Tinel's sign at flexor retinaculum
  - Sural nerve compression syndrome
    - Pure sensory
    - Numbness on lateral aspect of foot



- Tarsal tunnnel syndrome: when the tibial branch reaches the foot passing behind the medial malleulous and branches to medial nd lateral tarsal nerves, there happens the common compression which causes burning and pain and discomfort. It can happen in both feet.
- DDX: polyneruopathy
  mononeropathy if one tibial
  Keep in mind polyneuropathy can be large fibers (vibration,propioception +ve romberg test and paresthesia,weakness of the muscles) or small fibers (pain and temperature, tingling, allodynia) or mixed
  So here you think it can be:
  -Tarsal tunnel syndrome
  -Bilateral l3S4 radiculopathy
  -Or polyneuropathy with small or large fibers, it's unlikely but anything can happen

7. Facial nerve



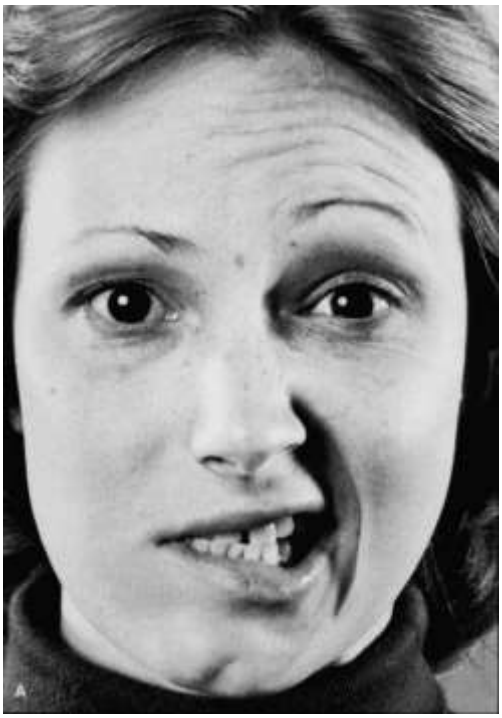
- Bell's palsy: idiopathic, HSV 1
- Ramsay Hunt syndrome : external ear pain with presence of herpes zoster vesicles in auditory canal and pinna, VZV
- Trauma: blunt impact to temporal bone
- Middle ear infection: otitis media, mastoid pain persist after acute infection resolved
- Neoplasm: rarely compressed by CPA (Cerebellopontine angle) tumor but due to surgery for tumor removal

Always remember it's a mononeuropathy

Facial nerve is LMN nerve (differentiate between upper and lower facial weakness)

Bell's palsy

- (idiopathic facial paralysis)
- Bell's palsy is **not** the result of a stroke or a transient ischemic attack (TIA). While stroke and TIA can cause facial paralysis, there is no link between Bell's palsy and either of these conditions. But sudden weakness that occurs on one side of your face should be checked by a doctor right away to rule out these more serious causes.



Clinical features:

- Postauricular pain (few days)
- Lower motor neuron facial weakness (where all muscles of facial expression are affected on the side of the lesion)
- Impaired taste
- Hyperacusis: caused by paralysis of the stapedius muscle, defined as intolerance of loud or high pitch sounds.
- Difficulty with speaking
- Dryness of the eyes and mouth (decrease lacrimation and salivation)

Management:

- Reassurance – not a stroke
- Short course of prednisolone 60 mg/day
- Prognosis:
  - complete recovery 75%
  - satisfactory 15%
  - poor function 10%

b. Mono-neuritis multiplex

Mononeuritis multiplex: sometimes they're not explained by compression. Not only involve compressive nerves, but also the non-compressive. But in mind systemic diseases.

This occurs in:

- Diabetes mellitus
- Leprosy
- Vasculitis
- Sarcoidosis
- Amyloidosis
- Malignancy
- Neurofibromatosis
- HIV
- Infection
- Guillain-Barré syndrome
- Idiopathic multifocal motor neuropathy.

Diagnosis is largely clinical, supported by electrical studies. Several nerves become affected sequentially or simultaneously, e.g. ulnar, median, radial and lateral popliteal nerves. When multifocal neuropathy is symmetrical, there is difficulty distinguishing it from polyneuropathy. Where leprosy is prevalent, e.g. in India, a single nerve lesion can be the presenting feature.

Idiopathic multifocal motor neuropathy

A distal motor neuropathy (often asymmetrical and predominantly in the hands) of unknown cause develops gradually over months with profuse fasciculation, hence confusion with motor neurone disease. Conduction block and denervation are seen electrically. Antibodies to the ganglioside GM1 are found in over 50% of cases; this is non-specific – antibodies are sometime seen in other neuropathies, e.g. Guillain–Barré syndrome. Steroids and/or cyclophosphamide and intravenous immunoglobulin slow the condition in some cases.

c. Polyneuropathy

Produces a pattern of weakness and numbness completely different from that seen in mononeuropathies. Instead of affecting the fibers of just a single peripheral nerve, polyneuropathy simultaneously affects fibers traveling in numerous peripheral nerves.

Polyneuropathy is a "**length-dependent**" neuropathy (Most length-dependent peripheral neuropathies are **chronic** and involve axonal pathology).

Polyneuropathy is a specific term that refers to a generalized, relatively homogeneous process affecting many peripheral nerves, with the distal nerves usually affected most prominently.

Because the longest nerve-fibers in the body are those that run from the lower back to the feet, in typical cases of polyneuropathy the first part of the body to become weak or numb is the feet. (However, when it reaches the knee, patient will start having symptoms in his/her hands. Why? Nerve length at knee level is approximately equal to the length innervating the hand)

Classified into:

1) Axonal	**Acute**	Porphyria[1], Axonal variant of GBS, Medications Nitrofurantoin.
	Subacute	Toxins, Nutritional, Systemic disorder: uremia, **diabetes**, hypothyroidism, HIV, lymes disease[2], paraneoplastic[3], sarcoidosis, connective tissue disease, and amyloidosis.
	Chronic	HMSN – II [4], systemic disorders, Fabry's disease[5].
2) Demyelinating (immunologic process)	**Uniform (usually genetic: ask about family Hx) – (velocity decreased in all the nerves)**	HMSN – I, HMSN – III, Refsum's[6], Krabbe's disease[7].
	Non-uniform (velocity is decreased in random sets of nerves)	Acute: AIDP[8], Diphtheria, Acute arsenic.
		Subacute or chronic: CIDP[9] and Variants.

1. Defects of enzymes needed at various steps of heme synthesis.

2. Infection that is transmitted through the bite.

3. Associated with anti-neuronal antibodies, believed to be involved in generation of signs and symptoms of neuropathies.

4. Hereditary sensorimotor neuropathies.

5. X-linked lysosomal disorder that leads to excessive deposition of neutral glycosphingolipids in the vascular endothelium of several organs and in epithelial and smooth muscle cells.

6. This is an autosomal recessive rarity. It is a treatable sensorimotor polyneuropathy with ataxia, retinal damage and deafness, due to defective phytanic acid metabolism.

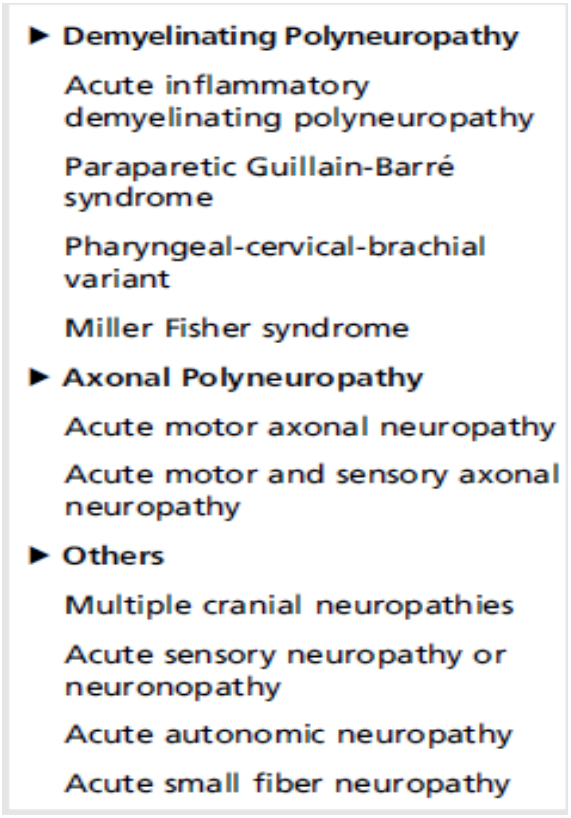
7. Autosomal recessive sphingolipidosis.

8. Acute inflammatory demyelinating polyneuropathy

9. Chronic inflammatory demyelinating polyneuropathy

Polyneuropathy (Davidson's):

Polyneuropathy is a generalized pathological process occurring in the longest peripheral nerves first, affecting the distal lower limbs before the upper limbs, with sensory symptoms and signs of an ascending 'glove and stocking' distribution. This is particularly true with axonal neuropathies where the disorder affects the metabolic processes required for axonal transport in the peripheral nerves. In inflammatory demyelinating neuropathies, the pathology may be patchier and variations from this ascending pattern occur.



Doctor's notes:

- In polyneuropathy when someone complains of symmetrical tingling: DURATION IS IMP (acute, chronic) and progression (fast or slow), Axonal or demyelinating will be distinguished by EMG. Also ask about family Hx, social HX, medications and medical history.
- Most common reason causes polyneuropathy is diabetes, next medication induced (antibioctic)
- Toxic neuropathy is one of the commonest reason in polyneuropathy, lead and arsenic are common in old people

1. Guillain-Barre Syndrome:

- Guillain-Barré syndrome (GBS) is an acute, frequently severe, and fulminant **polyradiculoneuropathy** that is autoimmune in nature.
- Males are at slightly higher risk for GBS than females, and in Western countries adults are more frequently affected than children.
- The most common acute polyneuropathy. Acute inflammatory polyneuropathy is most commonly demyelinating (acute inflammatory demyelinating neuropathy, AIDP), but occasionally axonal and probably has an autoallergic basis.
- There is a predominantly cell-mediated inflammatory response directed at the myelin protein of spinal roots, peripheral and extra-axial cranial nerves. The resulting release of inflammatory cytokines blocks nerve conduction and is followed by a destruction of the myelin sheath and the axon.
- Paralysis follows 1–3 weeks after an infection that is often trivial and seldom identified. Campylobacter jejuni and cytomegalovirus infections are well-recognized causes of severe GBS. Infecting organisms induce antibody responses against peripheral nerves.

- The patient complains of weakness of distal limb muscles and/or distal numbness. These symptoms progress proximally, over several days to 6 weeks. In some cases respiratory and facial muscles become weak, sometimes progressing to complete paralysis. Autonomic features sometimes develop.

Doctor's notes:

GBS (AIDP) is the most common condition we see.

Ten years later, it'll affect all the nerves even the proximal ones, CSF proteins will be high because it'll affect the roots and the roots are covered by protein which will reach the CSF in case of inflammation.

Characteristics of GBS: cells will be normal and CSF proteins will be high.

Subtype	Features	Electrodiagnosis	Pathology
Acute inflammatory demyelinating polyneuropathy (AIDP)	Adults affected more than children; 90% of cases in western world; recovery rapid; anti-GM1 antibodies (<50%)	Demyelinating	First attack on Schwann cell surface; widespread myelin damage, macrophage activation, and lymphocytic infiltration; variable secondary axonal damage
Acute motor axonal neuropathy (AMAN)	Children and young adults; prevalent in China and Mexico; may be seasonal; recovery rapid; anti-GD1a antibodies	Axonal	First attack at motor nodes of Ranvier; macrophage activation, few lymphocytes, frequent periaxonal macrophages; extent of axonal damage highly variable
Acute motor sensory axonal neuropathy (AMSAN)	Mostly adults; uncommon; recovery slow, often incomplete; closely related to AMAN	Axonal	Same as AMAN, but also affects sensory nerves and roots; axonal damage usually severe
M. Fisher syndrome (MFS)	Adults and children; uncommon; ophthalmoplegia, ataxia, and areflexia; anti-GQ1b antibodies (90%)	Demyelinating	Few cases examined; resembles AIDP

Diagnostic Criteria for Guillain-Barre Syndrome:

- Diagnosis is established clinically and confirmed by nerve conduction studies; these show slowing of conduction in the common demyelinating form, prolonged distal motor latency and/or conduction block. CSF protein is often raised. Differential diagnosis includes other acute paralytic illnesses, e.g. botulism, cord compression, muscle disease and myasthenia.

REQUIRED	SUPPORTIVE
1. Progressive weakness of 2 or more limbs due to neuropathy. 2. Areflexia) Absence of neurologic reflexes.(3. Disease course <4 weeks. 4. Exclusion of other causes: e.g., vasculitis (polyarteritis nodosa, SLE, Churg-Strauss syndrome), toxins (organophosphates, lead), botulism, diphtheria, porphyria, localized spinal cord or cauda equina syndrome.	1. Relatively symmetric weakness. 2. Mild sensory involvement. 3. Facial nerve or other cranial nerve involvement. 4. Absence of fever. 5. Typical CSF profile (acellular, increase in protein level) 6. Electrophysiologic evidence of demyelination.

Management of GBS (Davidson's):

During the phase of deterioration, regular monitoring of respiratory function is required, as respiratory failure may develop with little warning and require ventilatory support.

General management to protect the airway and prevent pressure sores and venous thrombosis is essential. However, plasma exchange and intravenous immunoglobulin therapy shorten the duration of ventilation and improve prognosis.

Immunotherapy:

Intravenous immunoglobulin or plasma exchange should be administered in patients who are not able to walk unaided.

In patients whose status deteriorates after initial improvement or stabilization, retreatment with either form of immunotherapy can be considered.

However, plasma exchange should not be performed in patients already treated with immunoglobulin because it would wash out the immunoglobulin still present in the blood. Also, immunoglobulin should not be used in patients already treated with plasma exchange because this sequence of treatments is not significantly better than plasma exchange alone.

Evidence for Immunotherapy in GBS management				
	Plasma Exchange (PE)	IV Immunoglobulin (IVIg)	Combined Treatments	Corticosteroids
Strong evidence supports	PE recommended in nonambulant patients within 4 weeks of onset of neuropathic symptoms. (Level A*, Class II**)	IVIg recommended in nonambulant patients within 2 weeks of onset of neuropathic symptoms. (Level A, Class II)	Sequential treatment with PE followed by IVIg does not have a greater effect than either treatment given alone. (Level A, Class I)	Steroids not recommended in the treatment of GBS. (Level A, Class I)

2. Chronic inflammatory demyelinating polyneuropathy (CIDP):

a. Multifocal motor neuropathy (MMN)
b. Lewis-Sumner syndrome, also known as multifocal acquired demyelinating sensory and motor neuropathy (MADSAM)
c. Distal demyelinating neuropathy with IgM paraprotein, with or without anti-myelin associated glycoprotein (anti-MAG)
d. Demyelinating neuropathy with IgG or IgA paraprotein
e. POEMS syndrome (osteosclerotic myeloma: Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes)
f. Sensory predominant demyelinating neuropathy
g. Demyelinating neuropathy with central nervous system demyelination
h. Demyelinating neuropathy associated with systemic disorders, including: Hepatitis B or C, HIV infection, lymphoma, diabetes mellitus, SLE/CTD, thyrotoxicosis, organ or bone marrow transplants, inherited neuropathies, nephrotic syndrome, inflammatory bowel disease

- Presents with a relapsing or progressive generalized neuropathy. Sensory, motor or autonomic nerves can be involved but the signs are predominantly motor; a variant causes only motor involvement (multifocal motor neuropathy, MMN).
- CIDP usually responds to immunosuppressive treatment, corticosteroids, methotrexate or cyclophosphamide, or to immunomodulatory treatments (plasma exchange or intravenous immunoglobulin, IVIg); MMN is best treated by IVIg.
- Some 10% of patients with acquired demyelinating polyneuropathy have an abnormal serum paraprotein, sometimes associated with a lymphoproliferative malignancy.
- Symmetrical numbness and tingling occurs in hands and feet, spreading proximally in a glove and stocking distribution. Distal weakness also ascends. Tendon reflexes are lost.
- Nerve conduction studies show either axonal degeneration or demyelination, or features of both, and no underlying cause is found.

Doctor's notes:

- 1)IVIG 2) plasma exchange. Don't the opposite cause IVIG needs 3 weeks to kick in.
- Steroids isn't recommended except in CIDP

TABLE 4-3 Chronic Inflammatory Demyelinating Polyneuropathies: Classification By Weakness and Sensory Loss Patterns

Clinical Features	Classic Chronic Inflammatory Demyelinating Polyneuropathy	Distal Acquired Demyelinating Symmetric Neuropathy	Multifocal Acquired Demyelinating Sensory and Motor Neuropathy	Multifocal Motor Neuropathy
Weakness and sensory loss	Symmetric, distal and proximal	Symmetric, mild distal	Asymmetric, mostly distal	Purely motor, asymmetric, mostly distal
Elevated CSF protein	Yes	Yes	Yes	No
M protein	Uncommon, may have IgG or IgA	Usually IgM, rarely IgG	Uncommon	Uncommon, rarely IgM
Antineural antibodies	Uncommon	Anti–myelin-associated glycoprotein (MAG) in 50% of patients	Uncommon	Anti-GM_1
Motor nerve conduction studies	Demyelination	Demyelination	Demyelination	Demyelination
Sensory nerve conduction studies	Absent or small sensory nerve action potentials (SNAPs)	Absent or small SNAPs	Absent or small SNAPs	Normal
Treatments	Prednisone, IV immunoglobulin (IVIg), plasmapheresis, immunosuppressants	Possibly rituximab Some patients without anti-MAG may respond to IVIg	IVIg, immunosuppressants	IVIg, possibly cyclophosphamide

Electrodiagnostic Criteria for CIDP:

These criteria are applied by testing the median, ulnar (stimulated below the elbow), peroneal (stimulated below the fibular head), and tibial nerves on one side of the body. During testing, limb temperature should be no less than 33°C at the palm and no less than 30°C at the external malleolus.

These criteria are applied by testing the median, ulnar (stimulated below the elbow), peroneal (stimulated below the fibular head), and tibial nerves on one side of the body. During testing, limb temperature should be no less than 33°C at the palm and no less than 30°C at the external malleolus.
Definite CIDP
At least one of the following demyelinating parameters are necessary:
≥50 percent prolongation of motor distal latency above the ULN in two nerves
≥30 percent reduction of motor conduction velocity below the LLN in two nerves
≥20 percent prolongation of F-wave latency above the ULN in two nerves, or >50 percent if the amplitude of the distal negative peak CMAP is <80 percent of the LLN
Absence of F-waves in two nerves, if these nerves have amplitudes of distal negative peak CMAPs ≥20 percent of the LLN, plus at least one other demyelinating parameter (meeting any of the definite criteria) in at least one other nerve
Partial motor conduction block, defined by a ≥50 percent amplitude reduction of the proximal negative peak CMAP relative to distal, if distal negative peak CMAP is ≥20 percent of the LLN, in two nerves, or in one nerve plus at least one other demyelinating parameter (meeting any of the definite criteria) in at least one other nerve
Abnormal temporal dispersion, defined by a >30 percent duration increase between the proximal and distal negative peak CMAP in at least two nerves
Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) increase in at least one nerve (median ≥6.6 ms, ulnar ≥6.7 ms, peroneal ≥7.6 ms, tibial ≥8.8 ms) plus at least one other demyelinating parameter (meeting any of the definite criteria) in at least one other nerve
Probable CIDP
≥30 percent amplitude reduction of the proximal negative peak CMAP relative to the distal, excluding the posterior tibial nerve, if the distal negative peak CMAP is ≥20 percent of LLN, in two nerves, or in one nerve plus at least one other demyelinating parameter (meeting any of the definite criteria) in at least one other nerve
Possible CIDP
As in "Definite CIDP" but in only one nerve

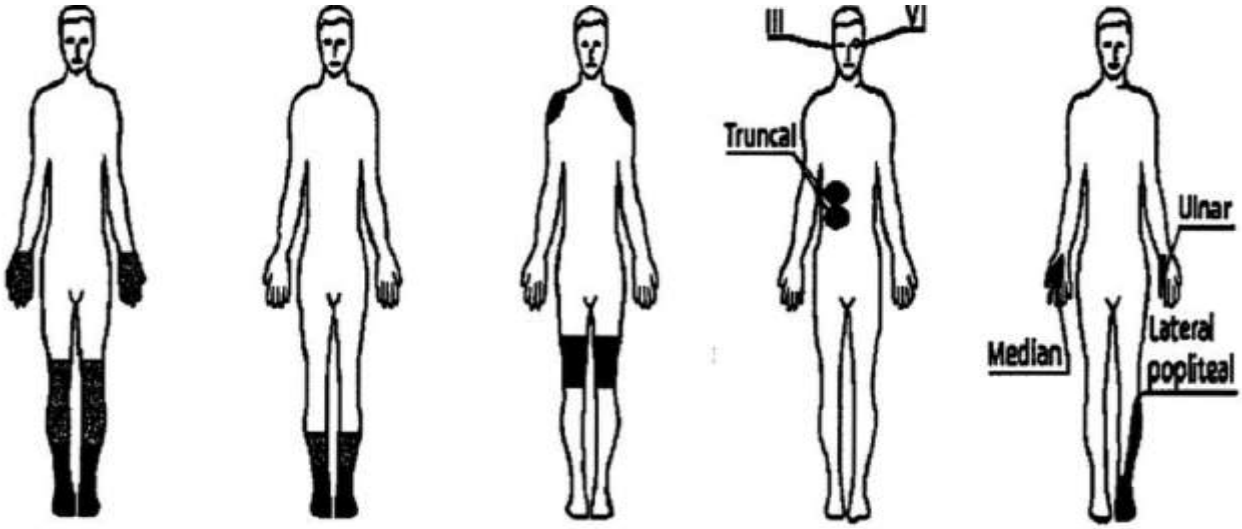
3. Cranial polyneuropathy: *(not included in the slides)*

This means multiple cranial nerve lesions. These can develop in diabetes, malignant infiltration, particularly with nasopharyngeal and breast carcinoma, lymphomas, sarcoidosis, as part of a paraneoplastic syndrome and occasionally with giant cell arteritis. Relapsing and remitting cranial polyneuropathy of unknown cause is sometimes seen in South East Asia.

4. Metabolic, toxic and vitamin deficiency neuropathies:

Metabolic neuropathies: *(not included in the slides)*

Diabetes mellitus. Several varieties of neuropathy occur:	Symmetrical sensory polyneuropathy Acute painful neuropathy Mononeuropathy and multiple mononeuropathy: - cranial nerve lesions - isolated peripheral nerve lesions (e.g. carpal tunnel syndrome) Diabetic amyotrophy Autonomic neuropathy. Everything can happen in DM (all kinds of injury and fibers and everything)
Uraemia.	Progressive sensorimotor neuropathy develops in chronic uraemia. Response to dialysis is variable; the neuropathy usually improves after transplantation. Thyroid disease. A mild chronic sensorimotor neuropathy is sometimes seen in both hyperthyroidism and hypothyroidism. Myopathy also occurs in hyperthyroidism.
Porphyria.	In acute intermittent porphyria. There are episodes of a severe, mainly proximal neuropathy in the limbs, sometimes with abdominal pain, confusion and coma. Alcohol, barbiturates and intercurrent infection can precipitate attacks.
Amyloidosis.	Polyneuropathy or multifocal neuropathy develops.



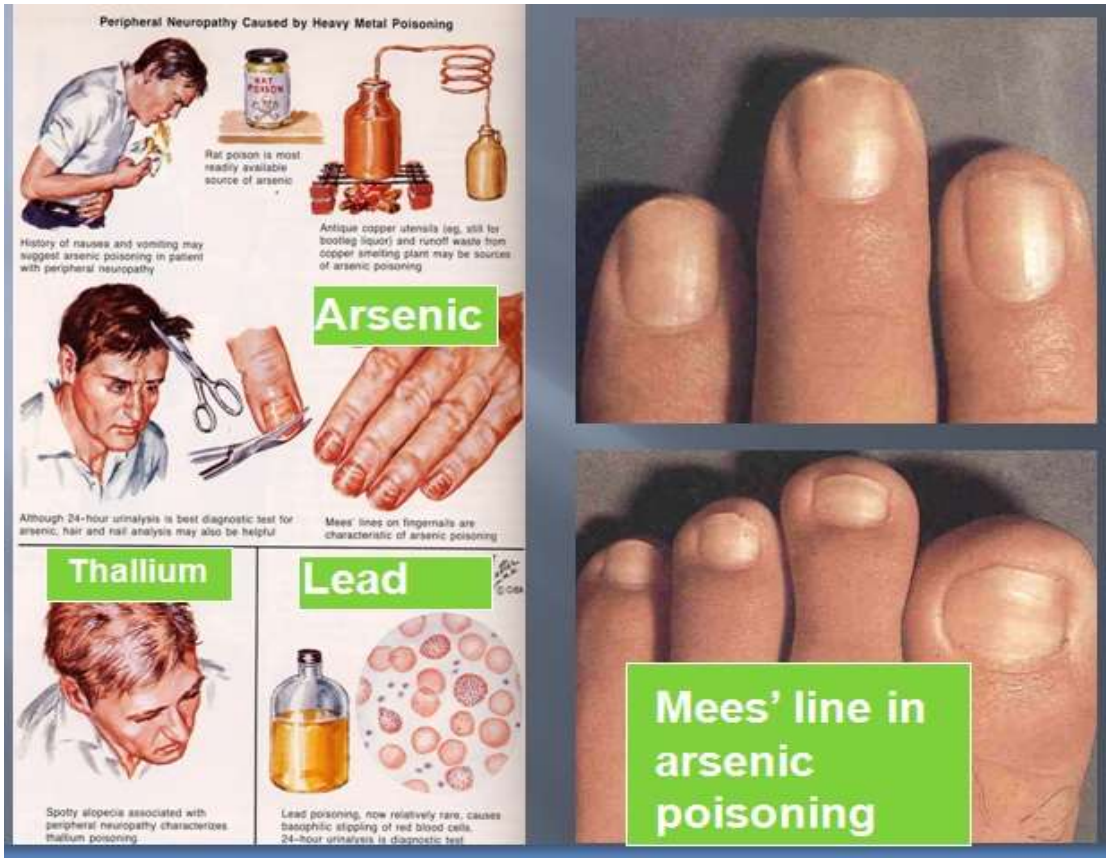
Large fiber Neuropathy	Small fiber Neuropathy	Proximal motor Neuropathy	Acute mono Neuropathies	Pressure Palsies
Sensory loss: 0→ +++ (Touch, vibration) Pain: + → +++ Tendon reflex: N → ↓↓↓ Motor deficit 0 → +++	Sensory loss: 0 → + (thermal , allodynia) Pain: + → +++ Tendon reflex: N → ↓ Motor deficit: 0	Sensory loss: 0 → + Pain: + → +++ Tendon reflex: ↓↓ Proximal Motor deficit: + → +++	Sensory loss: 0 → + Pain: + → +++ Tendon reflex: N Motor deficit: + → +++	Sensory loss in Nerve distribution: + → +++ Pain: + → ++ Tendon reflex: N Motor deficit: + → +++

Toxic neuropathies:

- Chemotherapy: anti-nucleosides, vincristine, cisplatin, paclitaxel and the podophyllotoxins
- Other medications: amiodarone, chloroquine, sulfa medications, Vit B6 intoxication
- Industrial and environmental agents: hexacarbon inhalation
- Heavy metal intoxication: arsenic, lead, mercury
- Ethanol: alcoholism

Alcohol Polyneuropathy, mainly in the lower limbs, occurs with chronic alcohol abuse. Calf pain is common. The response to thiamin treatment is variable, even with complete alcohol abstention. Recurrence and progression occur with even small amounts of alcohol.

Peripheral Neuropathy Caused by Heavy Metal Poisoning:



Vitamin deficiencies: *(not included in the slides)*

Vitamin deficiencies cause nervous system damage that is potentially reversible if treated early, and inexorably progressive if not. Deficiencies, often of multiple vitamins, develop in malnutrition.

- Thiamin (vitamin B1) Wernicke–Korsakoff syndrome
- Pyridoxine (vitamin B6)
- Vitamin B12 (cobalamin)

5. Critical illness polyneuropathy *(included in the slides, skipped by the doctor)*

Weakness is partly a consequence of improved survival in patients with multiorgan failure and sepsis, but is also a consequence of treatments administered in the ICU, including intravenous glucocorticoids and sometimes paralytic agents.

An acute, predominantly motor axonal polyneuropathy occurring in critically ill patients. Usually seen in the ICU. Patients develop flaccid generalized weakness. Movement discrepancy about pain.

Clinical features:

- Distal > proximal with muscle atrophy
- DTR (deep tendon reflex) ↓ or absent (13~100%) CIP can't be ruled out with DTR presence
- Loss of peripheral sensation to light touch and pin prick
- cranial nerves are spared

Risk factors:

- Systemic inflammatory response syndrome /or sepsis
- Steroids
- Neuromuscular blocking agents
- Aminoglycoside antibiotics
- Total parenteral nutrition
- Vasopressor support (>3d)
- Immune mechanisms (neurotoxic factor)
- Neurologic failure (GCS<10)
- Renal replacement therapy
- Low albumin and elevated glucose levels

Investigations:

1. **Electrophysiologic Studies:**

Nerve conduction studies:	**Electromyographic studies:**
- ↓ amplitude of compound motor AP - severe muscle atrophy? - ↓ amplitude of sensory nerve AP - tissue edema? - latency and velocity are unchanged - repetitive stimulation r/o N-M synapse d'z - muscle biopsy r/o myopathy	- signs of denervation - spontaneous activity with fibrillations - positive sharp waves - diaphramatic denervation: - diaphramatic needle EMG - phrenic nerve conduction study + EMG

2. **Nerve and muscle biopsy:**

Nerve biopsy:	**Muscle biopsy**
- No demyelination was found - Discrepancy between histologic and electrophysiologic studies. - Early impairment of axonal transport and transmembrane potential → Normal histological study cannot rule out CIP	- Atrophy of type II fibers: denervation - Fiber necrosis in 30% - Primary or secondary? - No clear relationship with neurophysiology - Low motor amplitudes with normal sensory neurography, and little spontaneous activity - Critical Illness Myo- and (poly)Neuropathy - CRIMYNE

3. **Additional technique**

- Quantitative EMG (fibrillation potentials will be evident on electromyography (EMG) needle examination)
- Muscle fiber excitability by direct muscle stimulation (differentiate myopathy and neuropathy):
  In patients with CIP, direct needle stimulation of muscle elicits a relatively higher amplitude response compared with the response recorded from muscle after nerve stimulation. In contrast, in critical illness myopathy, there are proportionally low direct muscle- and nerve-evoked responses.

Therapy

Neither therapy nor prevention is available

Possible prevention:	**Possible treatment**
- treatment of underlying sepsis /SIRS - glycemic control with insulin (↓40~48%) - minimize steroid and depolarizing NMBA	- intensive psychological care and reassurance - intensive physiotherapy and supportive care - intensive rehabilitation program

In survivors of CIP with mild or moderate nerve injury, recovery of muscle strength generally occurs over weeks to months. However, electrodiagnostic testing may demonstrate residual nerve dysfunction several years after initial presentation. Patients with severe CIP may remain quadriplegic.

6. Neuropathies with HIV infection

Seroconversion

- Guillain-Barre syndrome
- Chronic inflammatory demyelinating polyneuropathy (CIDP)

Symptomatic stage

- Mononeuritis multiplex axonal type (subacute or chronic)

Late symptomatic stage

- Distal symmetrical sensory polyneuropathy, most common
- Neuropathy frequently coexists with symptomatic
- Encephalopathy and myelopathy
- Toxic polyneuropathy
- Subacute asymmetrical polyneuropathy of cauda equina, caused by cytomegalovirus

7. Hereditary Sensory Motor Neuropathies *(included in the slides, skipped by the doctor)*

Type	Gene/Locus	Specific Phenotype
Autosomal dominant (AD) CMT1		
CMT1A	Dup 17p (*PMP22*)	Classic CMT1
	PMP22 (point mutation)	Classic CMT1/DSS/CHN/HNPPs
CMT1B	*MPZ*	CMT1/DSS/CHN/intermediate/CMT2
CMT1C	*LITAF*	Classic CMT1
CMT1D	*EGR2*	Classic CMT1/DSS/CHN
CMT1E	*NEFL*	CMT2 but can have slow MNCVs in CMT1 range ± early-onset severe disease
HNPP		
HNPP		
	Del 17p (*PMP22*)	Typical HNPP
	PMP22 (point mutation)	Typical HNPP
X-linked CMT1 (CMT1X)		
CMT1X	*GJB1*	Intermediate ± patchy MNCVs/male MNCVs less than female MNCVs

Autosomal recessive (AR) demyelinating CMT (CMT4)		
CMT4A	*GDAP1*	Demyelinating or axonal, usually early onset and severe/vocal cord and diaphragm paralysis described/rare AD CMT2 families described
CMT4B1	*MTMR2*	Severe CMT1/facial/bulbar/focally folded myelin
CMT4B2	*SBF2*	Severe CMT1/glaucoma/focally folded myelin
CMT4C	*SH3TC2*	Severe CMT1/scoliosis/cytoplasmic expansions
CMT4D (HMSNL)	*NDRG1*	Severe CMT1/gypsy/deafness/tongue atrophy
CMT4E	*EGR2*	Classic CMT1/DSS/CHN
CMT4F	*PRX*	CMT1/more sensory/focally folded myelin
CMT4H	*FGD4*	CMT1
CMT4J	*FIG4*	CMT1
CCFDN	*CTDP1*	CMT1/gypsy/cataracts/dysmorphic features
HMSN-Russe	10q22–q23	CMT1
CMT1	*PMP22* (point mutation)	Classic CMT1/DSS/CHN/HNPPs
CMT1	*MPZ*	CMT1/DSS/CHN/intermediate/CMT2

Type	Gene/Locus	Specific Phenotype
CMT2B	*RAB7A*	CMT2 with predominant sensory involvement and sensory complications
CMT2C	12q23–q24	CMT2 with vocal cord and respiratory involvement
CMT2D	*GARS*	CMT2 with predominant hand wasting/weakness or dHMN V
CMT2E	*NEFL*	CMT2 but can have slow MNCVs in CMT1 range ± early-onset severe disease
CMT2F	*HSPB1* (*HSP27*)	Classic CMT2 or dHMN II
CMT2G	12q12–q13.3	Classic CMT2
CMT2L	*HSPB8* (*HSP22*)	Classic CMT2 or dHMN II
CMT2	*MPZ*	CMT1/DSS/CHN/intermediate/CMT2
CMT2 (HMSNP)	3q13.1	CMT2 with proximal involvement

AR CMT2 (also called AR CMT4)		
AR CMT2A	*LMNA*	CMT2 proximal involvement and rapid progression described/also causes muscular dystrophy/cardiomyopathy/lipodystrophy
AR CMT2B	19q13.1–13.3	Typical CMT2
AR CMT2	*GDAP1*	CMT1 or CMT2 usually early onset and severe/vocal cord and diaphragm paralysis described/rare AD CMT2 families described
Dominant intermediate CMT (DI-CMT)		
DI-CMTA	10q24.1–25.1	Typical CMT
DI-CMTB	*DNM2*	Typical CMT
DI-CMTC	*YARS*	Typical CMT
Hereditary neuralgic amyotrophy (HNA)		
HNA	*SEPT9*	Recurrent neuralgic amyotrophy

Pseudoneuropathy *(might be mistaken as neuropathies / DDX)*

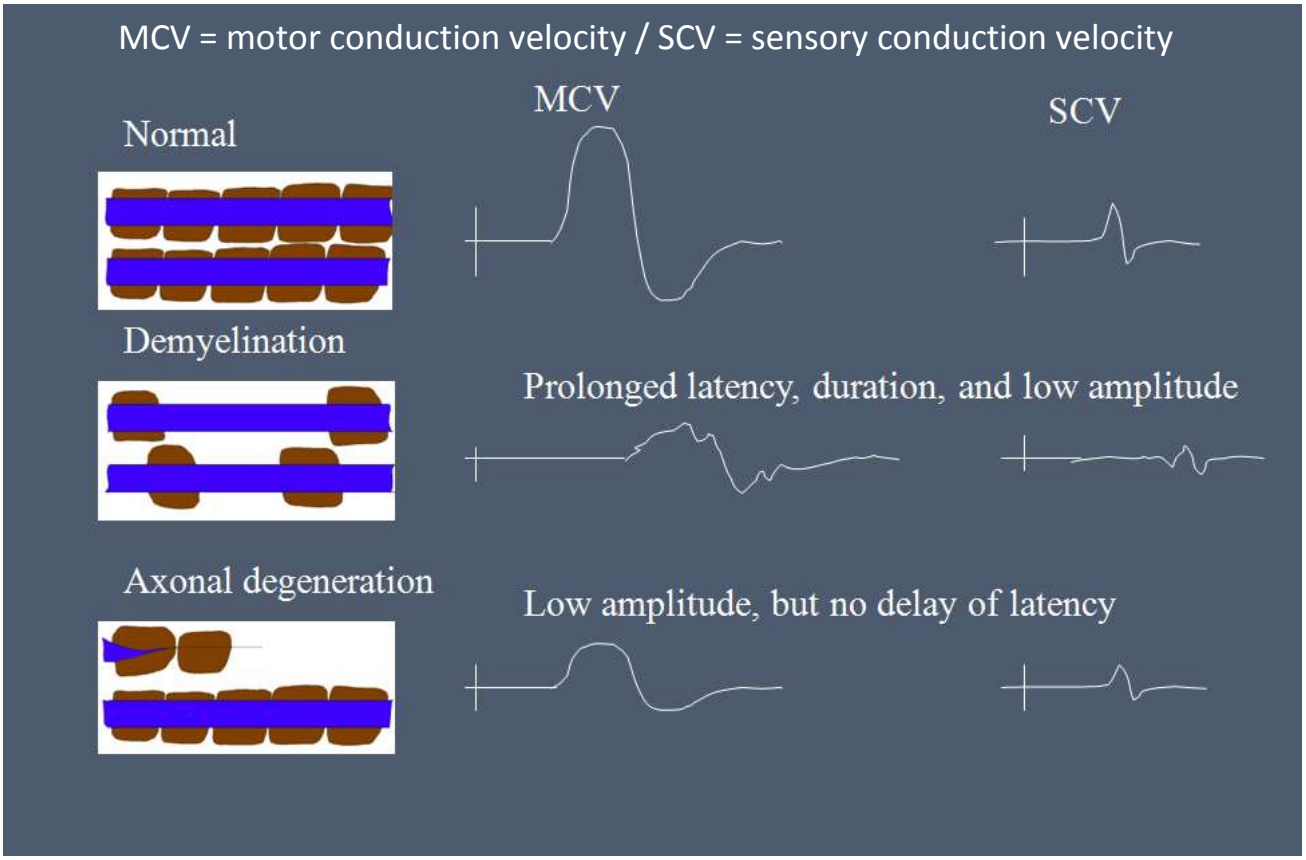
- Hyperventilation
- Myopathy
- Neuromuscular junction diseases
- Motor neuron diseases
- Psychogenic
- Cervical cord process

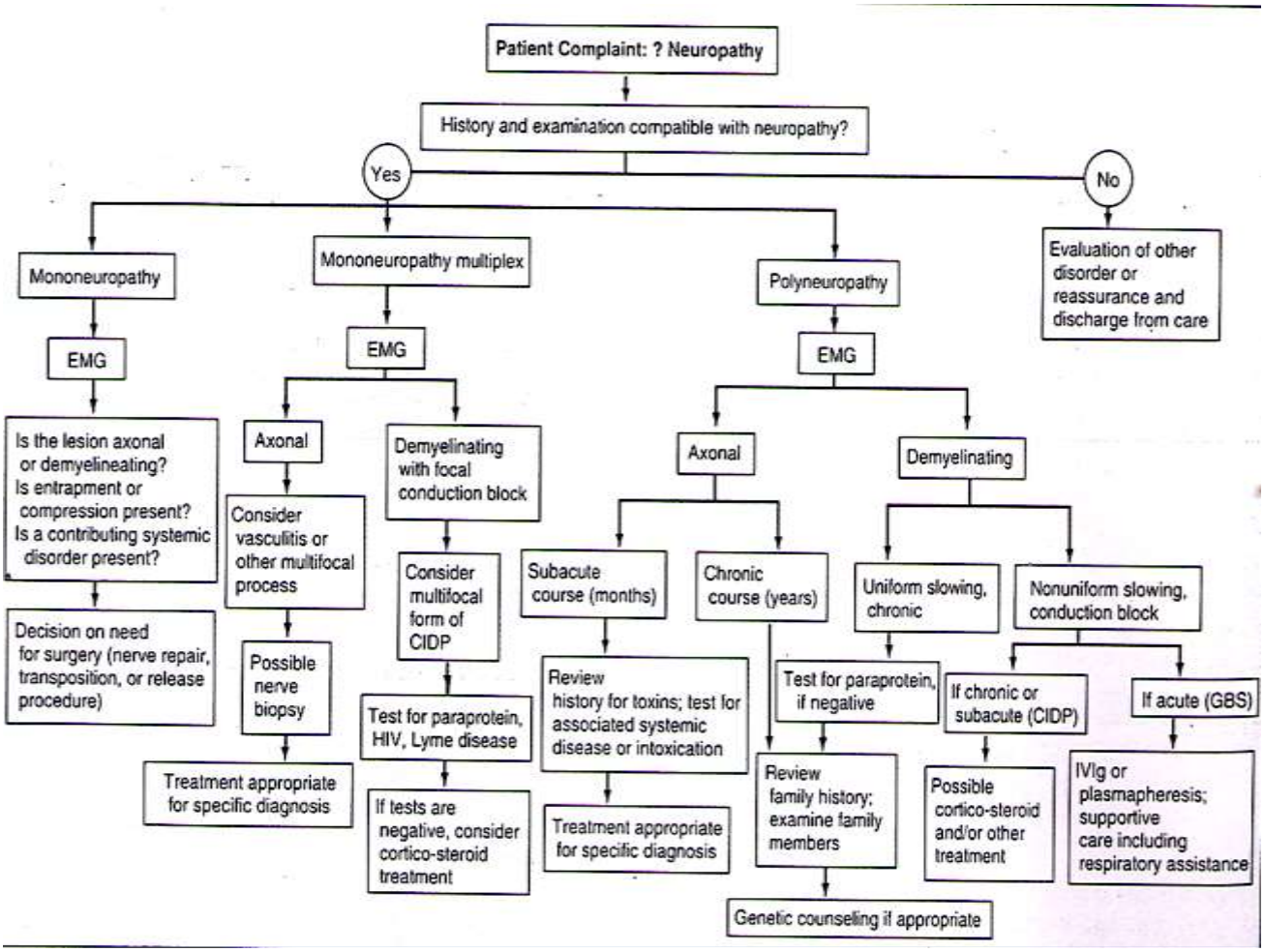
Investigations: (from Davidson's)

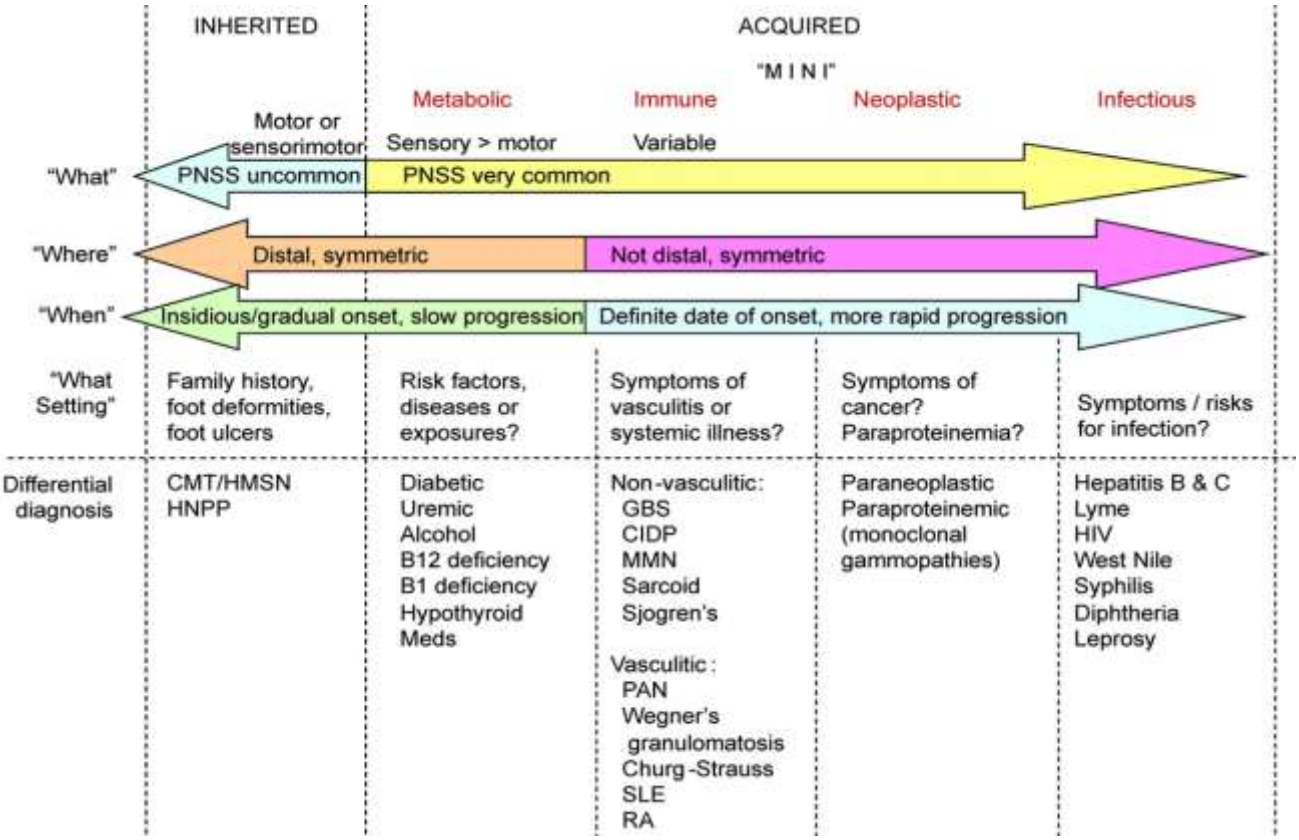
26.112 Investigation of peripheral neuropathy

	First-line tests	Second-line tests	Occasionally useful tests
Haematology	Full blood count ESR B_{12} and folate		
Biochemistry	Urea, electrolytes, calcium Creatinine Liver function tests Blood glucose ± tolerance test/HbA_{1c} Thyroid function tests Plasma protein electrophoresis	Serum lipids, lipoproteins Cryoglobulins Toxic metal and drug screen Prostate-specific antigen Urinary porphyrins Urinary Bence Jones protein Faecal occult blood	Vitamin assays (e.g. vitamin E) Phytanic acid (Refsum's disease)
Immunology	Venereal Diseases Research Laboratory (VDRL) test Serum autoantibodies (antinuclear factor, dsDNA, rheumatoid factor, extractable nuclear antigens)	Antiganglioside antibodies Antineuronal antibodies	
Other	Nerve conduction/EMG EMG: Electro myography	Genetic screening tests (hereditary neuropathies, Friedreich's ataxia) Chest X-ray/CT Mammogram Abdominal imaging	Nerve biopsy

Nerve Conduction Studies (NCS):




Patient Complaint: ? Neuropathy
History and examination compatible with neuropathy?
Yes
No
Evaluation of other disorder or reassurance and discharge from care
Mononeuropathy
Mononeuropathy multiplex
Polyneuropathy
EMG
EMG
EMG
Is the lesion axonal or demyelineating? Is entrapment or compression present? Is a contributing systemic disorder present?
Decision on need for surgery (nerve repair, transposition, or release procedure)
Axonal
Demyelinating with focal conduction block
Consider vasculitis or other multifocal process
Possible nerve biopsy
Treatment appropriate for specific diagnosis
Consider multifocal form of CIDP
Test for paraprotein, HIV, Lyme disease
If tests are negative, consider cortico-steroid treatment
Axonal
Demyelinating
Subacute course (months)
Chronic course (years)
Uniform slowing, chronic
Nonuniform slowing, conduction block
Review history for toxins; test for associated systemic disease or intoxication
Treatment appropriate for specific diagnosis
Test for paraprotein, if negative
Review family history; examine family members
Genetic counseling if appropriate
If chronic or subacute (CIDP)
If acute (GBS)
Possible cortico-steroid and/or other treatment
IVIg or plasmapheresis; supportive care including respiratory assistance


INHERITED
ACQUIRED
"MINI"
Metabolic
Immune
Neoplastic
Infectious
Motor or sensorimotor
Sensory > motor
Variable
"What"
PNSS uncommon
PNSS very common
"Where"
Distal, symmetric
Not distal, symmetric
"When"
Insidious/gradual onset, slow progression
Definite date of onset, more rapid progression
"What Setting"
Family history, foot deformities, foot ulcers
Risk factors, diseases or exposures?
Symptoms of vasculitis or systemic illness?
Symptoms of cancer? Paraproteinemia?
Symptoms / risks for infection?
Differential diagnosis
CMT/HMSN
HNPP
Diabetic
Uremic
Alcohol
B12 deficiency
B1 deficiency
Hypothyroid
Meds
Non-vasculitic:
GBS
CIDP
MMN
Sarcoid
Sjogren's
Vasculitic:
PAN
Wegner's granulomatosis
Churg-Strauss
SLE
RA
Paraneoplastic
Paraproteinemic (monoclonal gammopathies)
Hepatitis B & C
Lyme
HIV
West Nile
Syphilis
Diphtheria
Leprosy

SUMMARY

1. Neuropathies are classified according to the site of lesion into:

- Radiculopathies: knowing the distribution of dermatoms and myotoms help you localizing the lesion.
- Plexopathies: Brachial (C5,6,7,8,T1), Lumbosacral

2. According to the No. of lesions

- Mononeuropathies: Median nerve (carpel tunnel) Ulnar nerve (cubital tunnel) Radial nerve, Lateral femoral cutaneous (Meralgia paresthetica), Femoral nerve, Sciatic nerve (common peroneal, tibial), Fasial nerve (Bell's pulsy)
- Mononeuritis multiplex: Idiopathic multifocal motor neuropathy
- Polyneuropathies:
  - Guillain-Barre Syndrome (AIDP)
  - CIDP
  - Cranial neuropathies
  - Metabolic, toxic and vitamin deficiency neuropathies
  - Critical ill polyneuropathies
  - Neuropathies with HIV infection
  - HSMN

Questions

1) **Patient came to the ER complaining of numbness and weakness for 3 days in his feet then gradually reached his knees and now and he is having the same symptoms in his hands. what is the diagnosis?**

   a. AIDP
   b. CIDP
   c. L5-S1 radiculopathy

2) What type of injury?

   a. Demyelination
   b. Axonal injury

3) How do you proceed with the management if you are still not sure about your diagnosis?

If I'm not sure I still treat the patient as demyelinatig DBG because if I didn't he'll develop further complications. I'll ask for EMG and nerve conduction study to confirm my diagnosis.