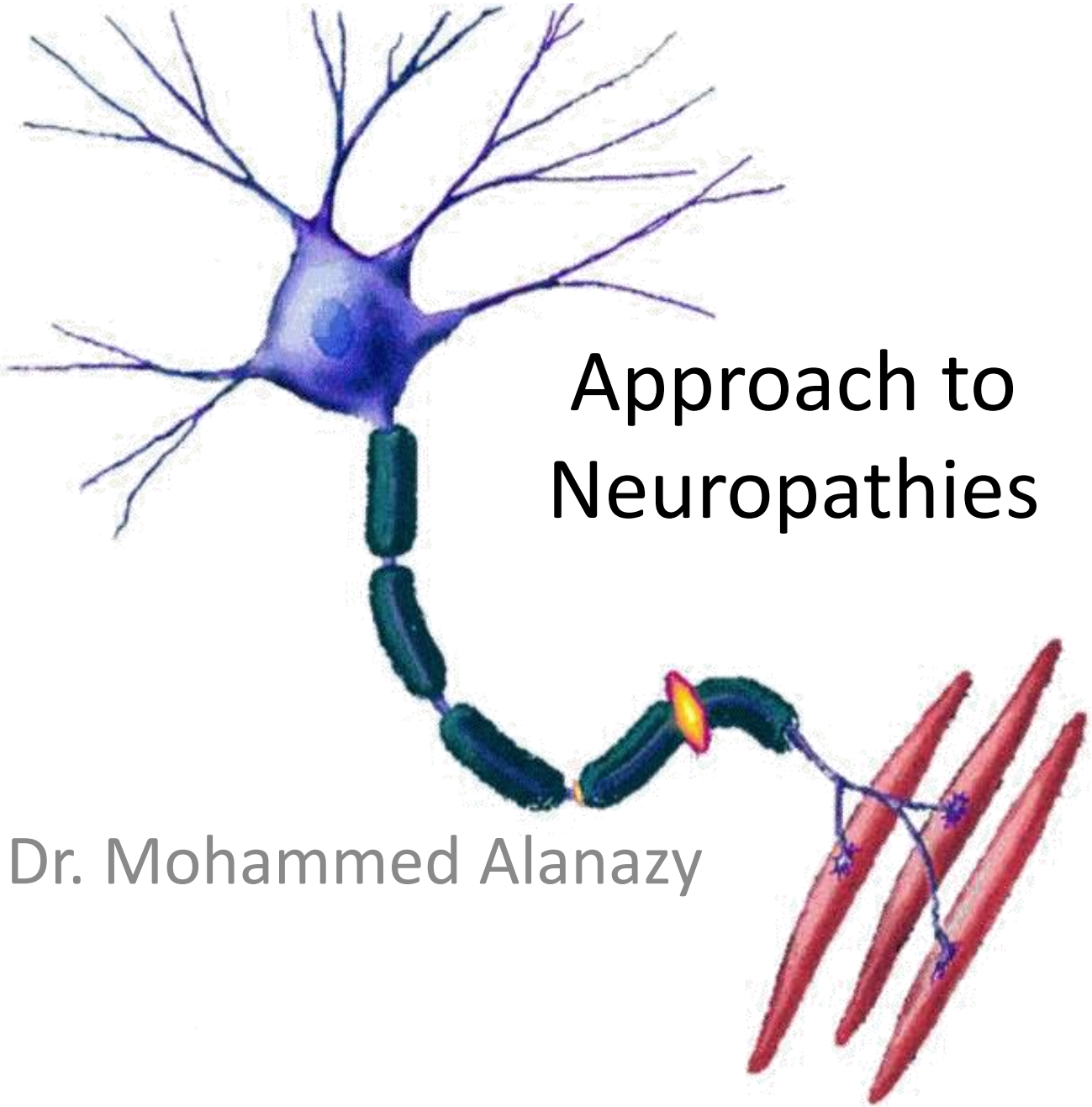
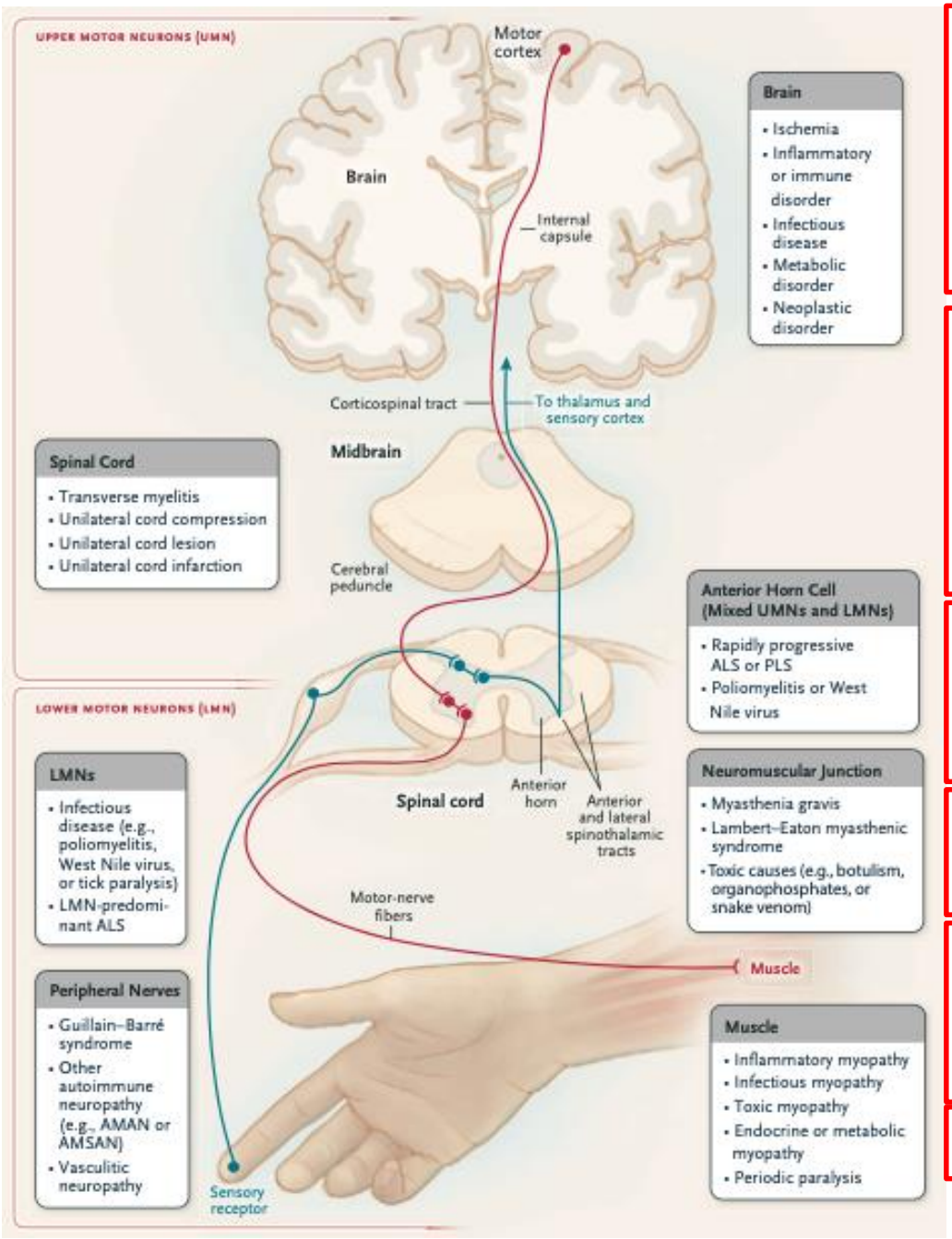


Approach to Neuropathies

Dr. Mohammed Alanazy

Goals and objectives

- Obtain informative history from a patient with peripheral neuropathy.
- Use clinical information to recognize different patterns of peripheral neuropathy
- Provide differential diagnosis for each pattern



Cortex = weakness, sensory, Aphasia, Dysarthria, Hemianopia, Apraxia, Agnosia, Alexia, Agraphia, Asterognosis, Graphesthesia, Dementia, memory, Decrease LOC, Seizures, UMN sings

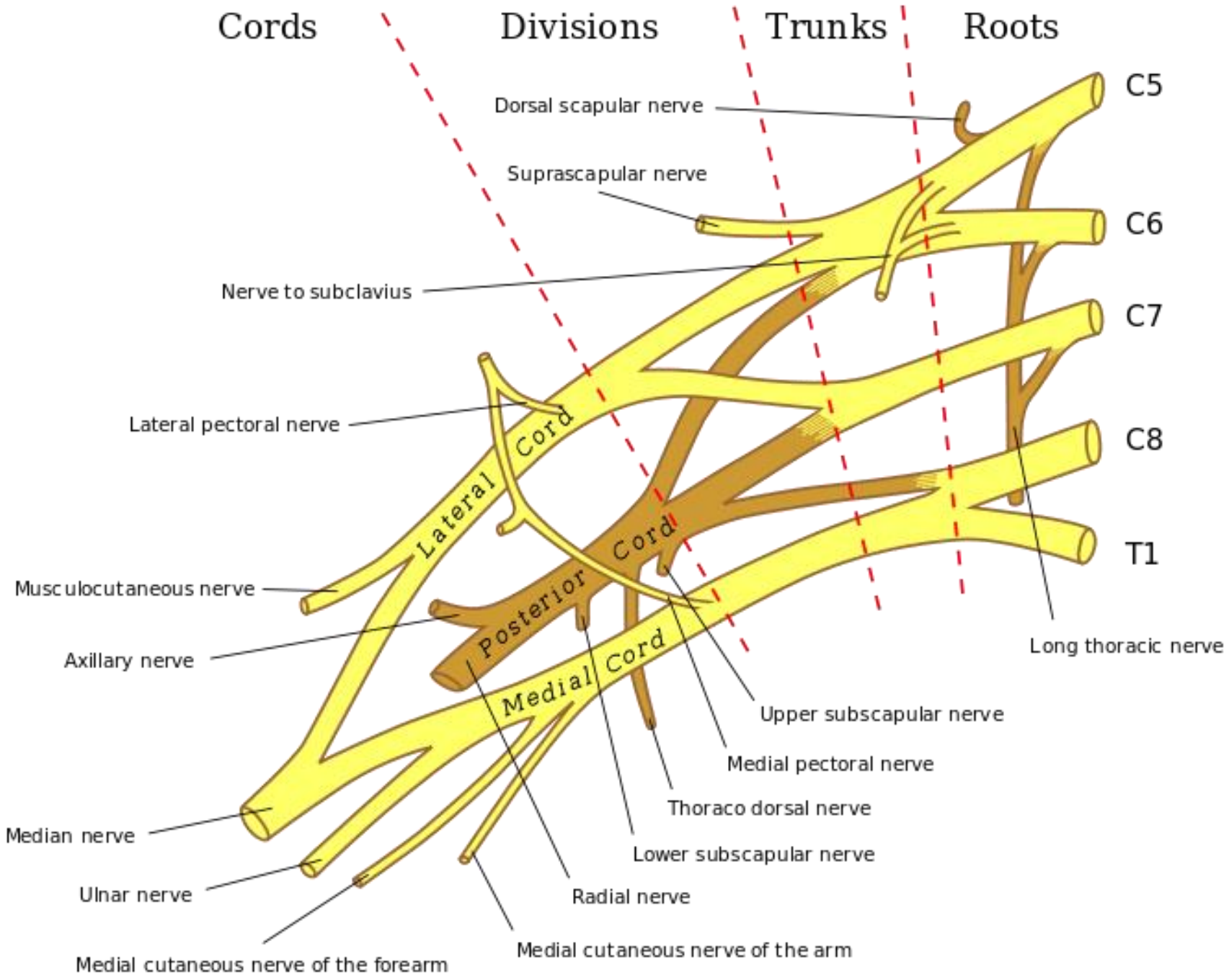
Brainstem = weakness, sensory, CN dysfunction (diplopia, vertigo, tongue weakness, dysphagia, dysarthria, LMN facial) crossed features, ataxia, Decrease LOC, UMN signs

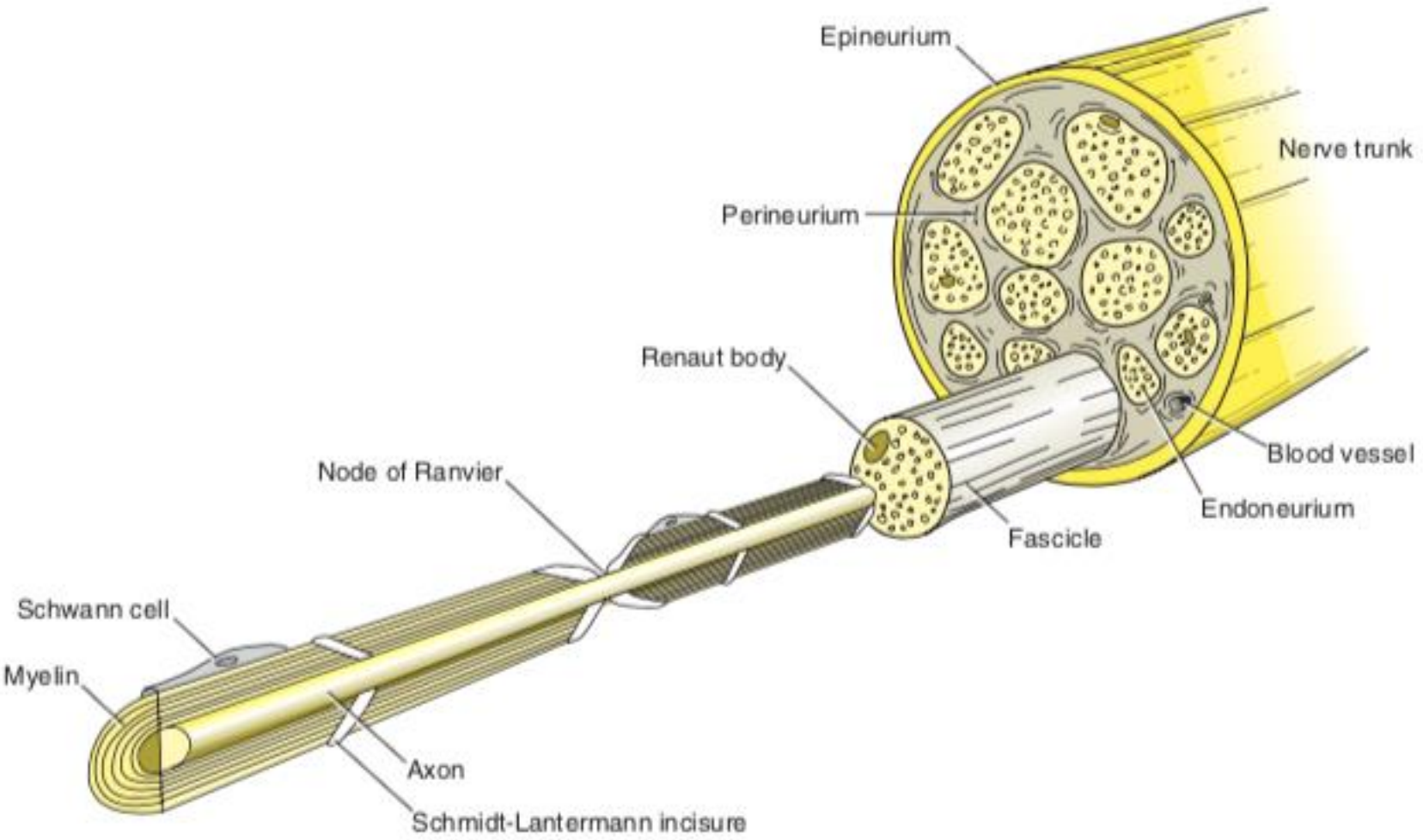
Spinal cord = weakness, sensory, crossed features, sensory ataxia, sphincter dysfunction

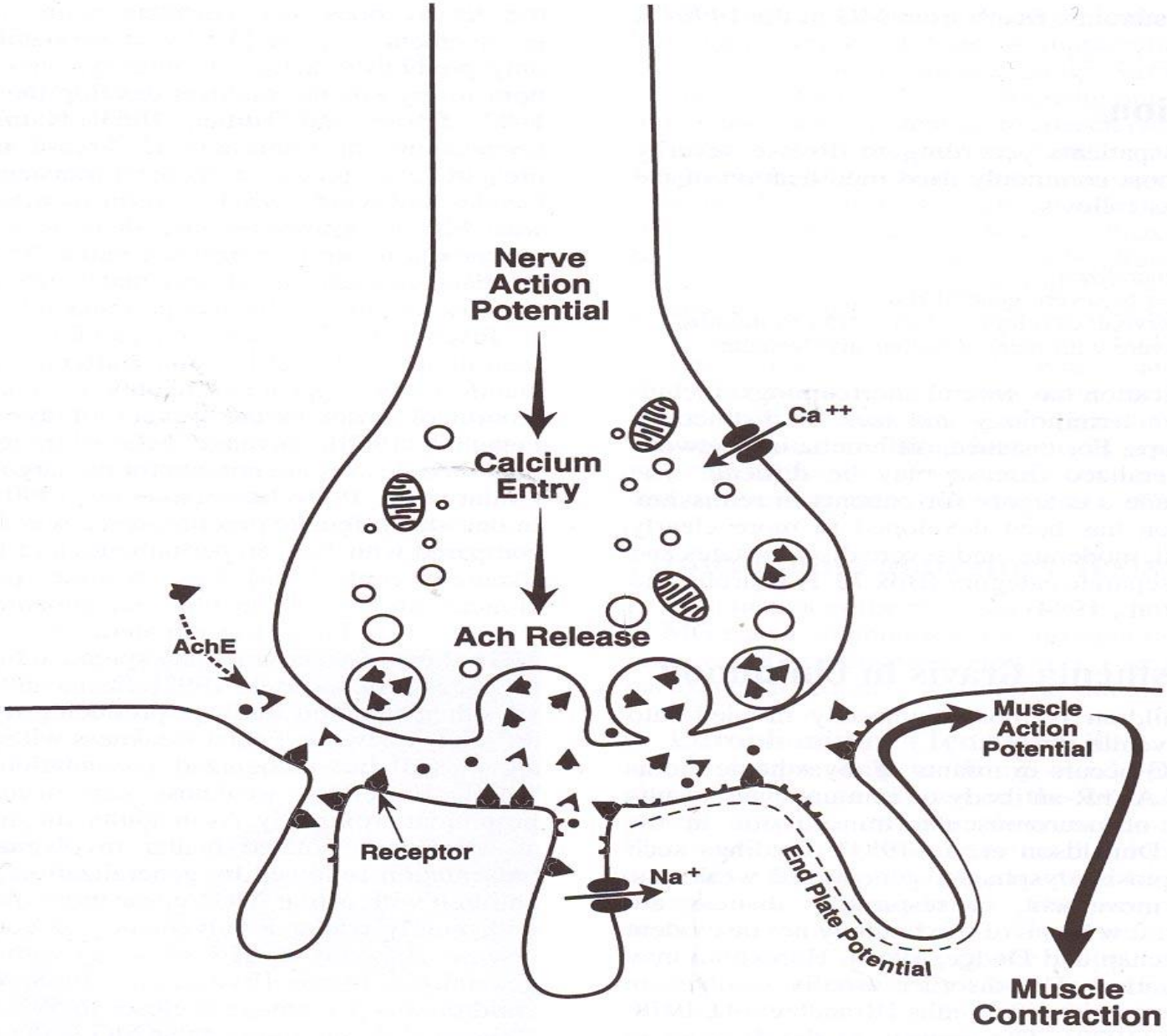
AHC = weakness, atrophy, fasciculations, LMN signs

Root, plexus, peripheral nerve = weakness, atrophy, fasciculations, sensory, pain, LMN signs

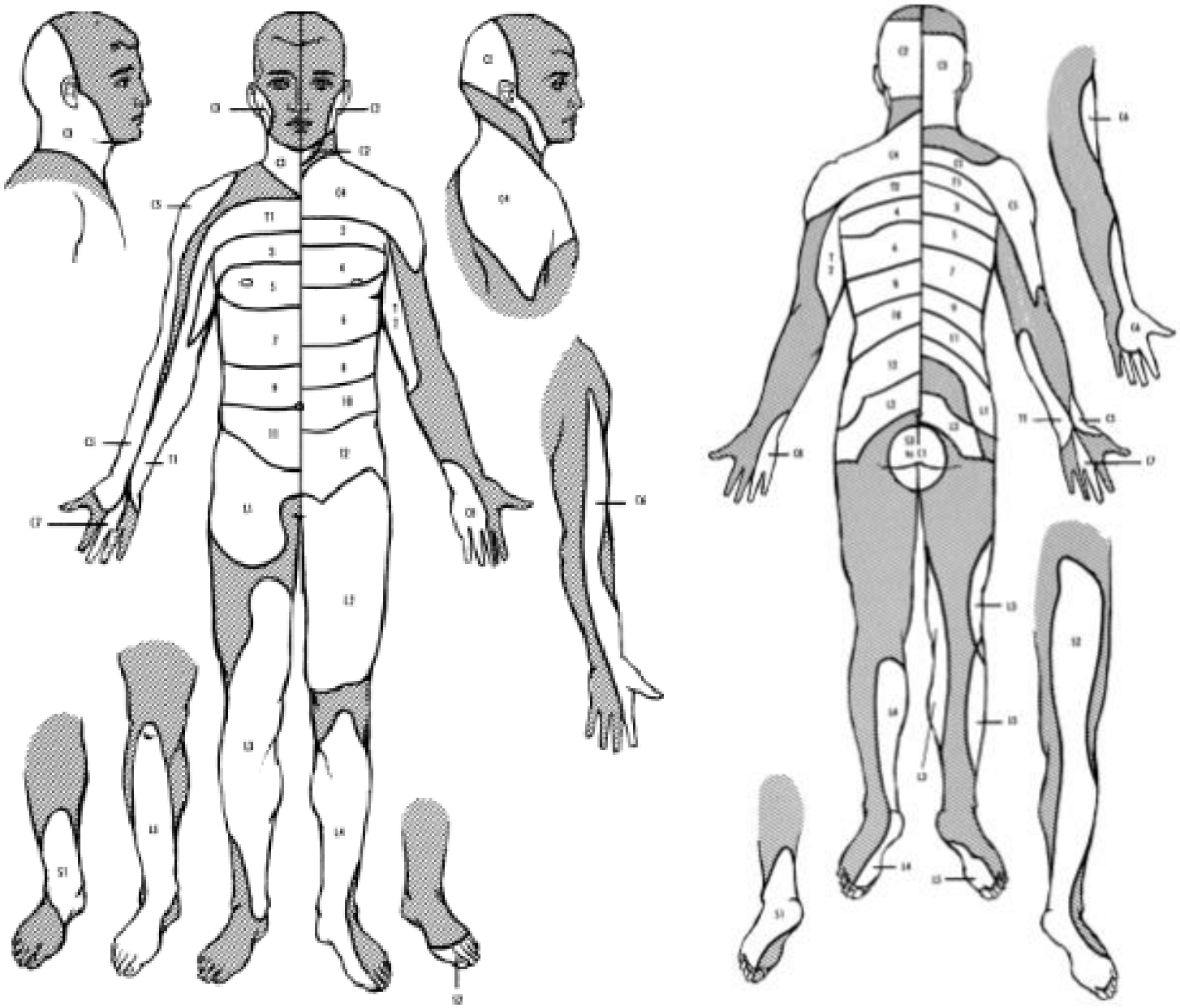
Muscle & NMJ = weakness, LMN signs

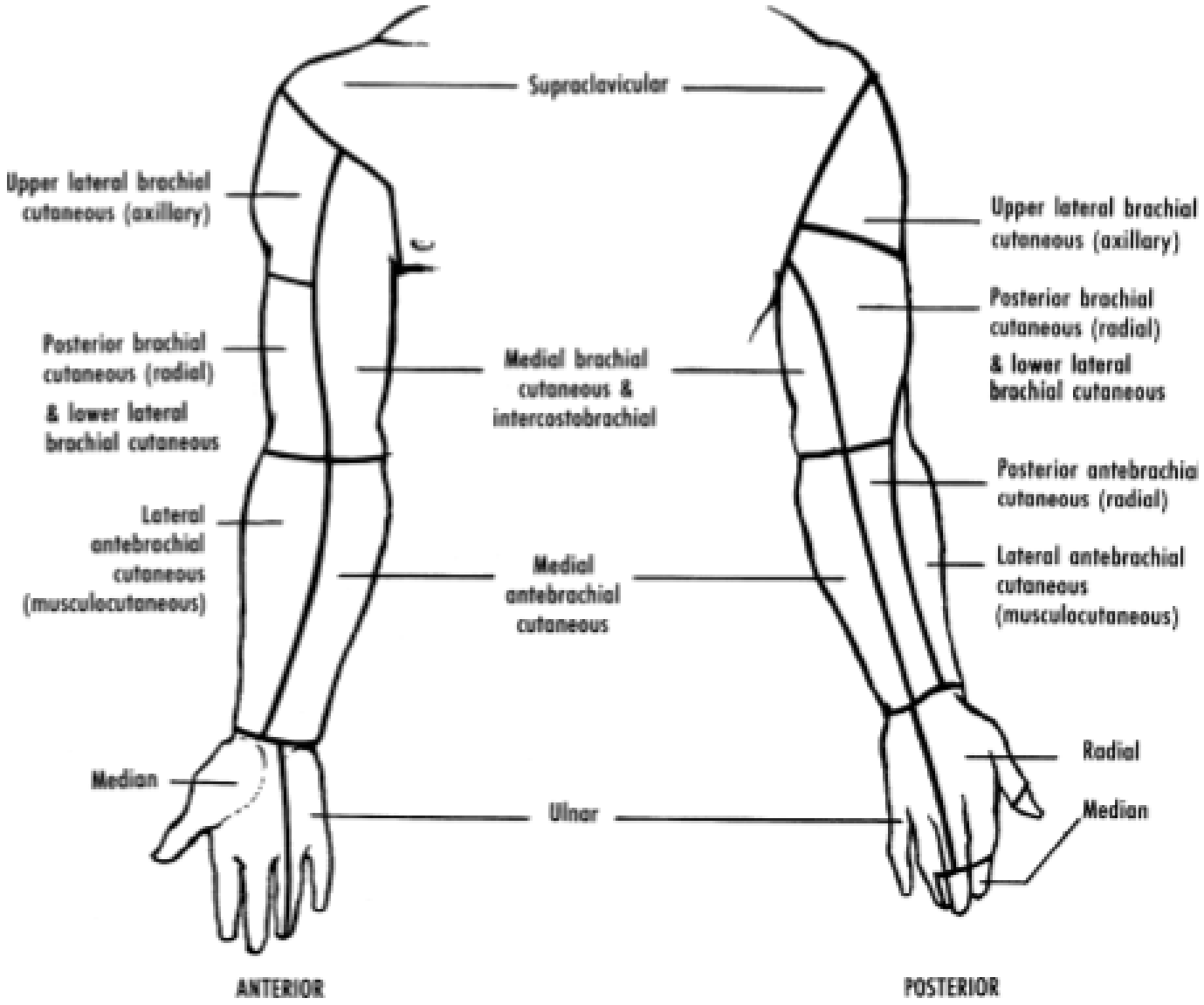

Cords
Divisions
Trunks
Roots
C5
C6
C7
C8
T1
Dorsal scapular nerve
Suprascapular nerve
Nerve to subclavius
Lateral pectoral nerve
Musculocutaneous nerve
Axillary nerve
Median nerve
Ulnar nerve
Medial cutaneous nerve of the forearm
Medial cutaneous nerve of the arm
Radial nerve
Lower subscapular nerve
Thoraco dorsal nerve
Medial pectoral nerve
Upper subscapular nerve
Long thoracic nerve
Lateral Cord
Posterior Cord
Medial Cord

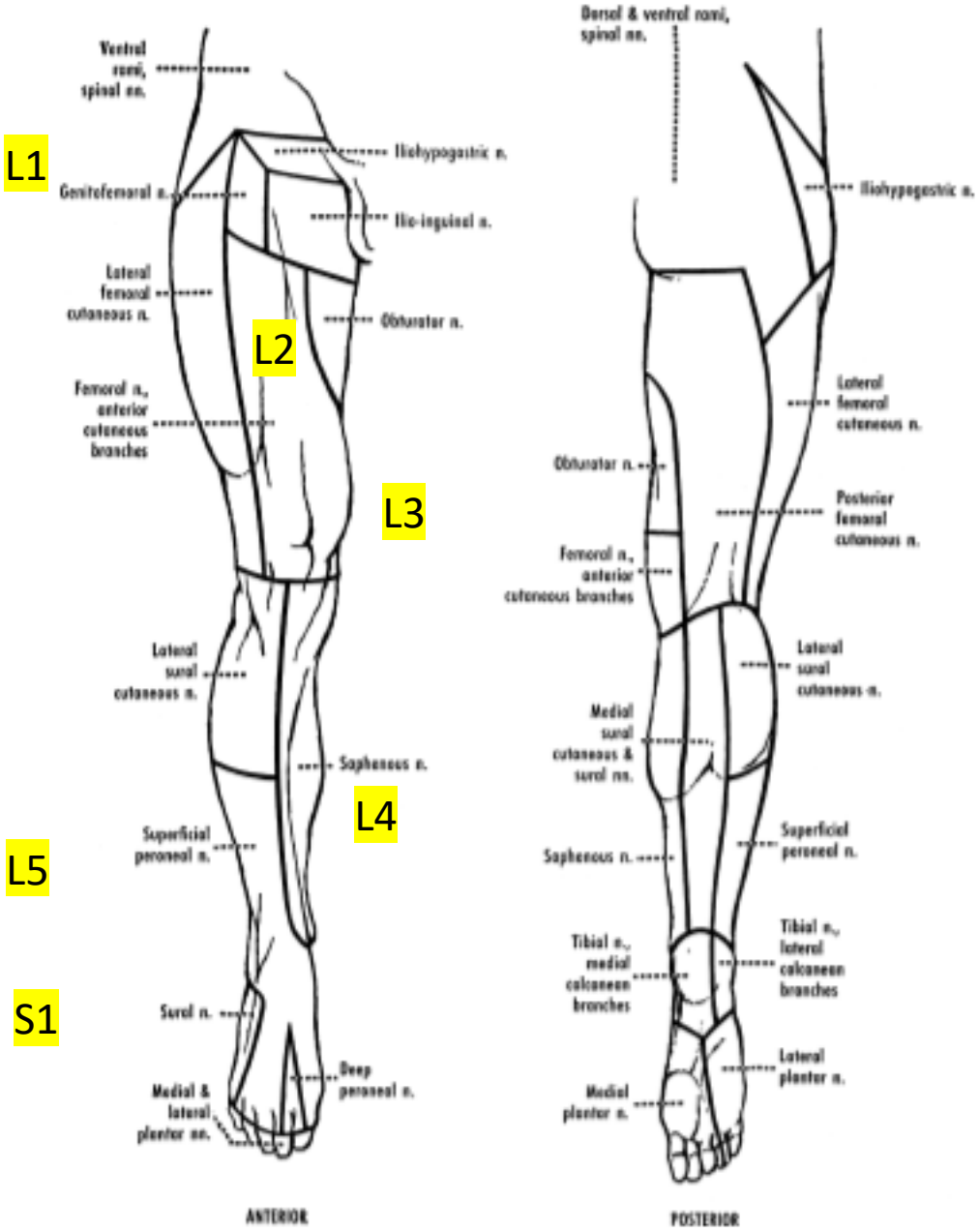

Epineurium
Nerve trunk
Perineurium
Renaut body
Blood vessel
Node of Ranvier
Endoneurium
Fascicle
Schwann cell
Myelin
Axon
Schmidt-Lantermann incisure


Nerve
Action
Potential
Ca ++
Calcium
Entry
Ach Release
AchE
Muscle
Action
Potential
Receptor
Na +
End Plate Potential
Muscle
Contraction

Dermatomes

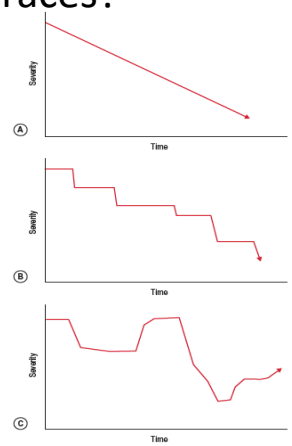



Supraclavicular
Upper lateral brachial cutaneous (axillary)
Posterior brachial cutaneous (radial) & lower lateral brachial cutaneous
Lateral antebrachial cutaneous (musculocutaneous)
Median
Medial brachial cutaneous & intercostobrachial
Medial antebrachial cutaneous
Ulnar
ANTERIOR
Upper lateral brachial cutaneous (axillary)
Posterior brachial cutaneous (radial) & lower lateral brachial cutaneous
Posterior antebrachial cutaneous (radial)
Lateral antebrachial cutaneous (musculocutaneous)
Radial
Median
POSTERIOR


L1
L2
L3
L4
L5
S1
Ventral rami, spinal nn.
Iliohypogastric n.
Genitofemoral n.
Ilio-inguinal n.
Lateral femoral cutaneous n.
Obturator n.
Femoral n., anterior cutaneous branches
Lateral sural cutaneous n.
Saphenous n.
Superficial peroneal n.
Sural n.
Deep peroneal n.
Medial & lateral plantar nn.
ANTERIOR
Dorsal & ventral rami, spinal nn.
Iliohypogastric n.
Lateral femoral cutaneous n.
Obturator n.
Posterior femoral cutaneous n.
Femoral n., anterior cutaneous branches
Lateral sural cutaneous n.
Medial sural cutaneous & sural nn.
Saphenous n.
Superficial peroneal n.
Tibial n., medial calcaneal branches
Tibial n., lateral calcaneal branches
Lateral plantar n.
Medial plantar n.
POSTERIOR

History

- Symptoms
  - Sensory: Tingling, pins & needles, burning, stabbing, shooting, prickling, dead, icy, hot, clumsy, wooden, walking on sponges or cotton.
  - Motor : Weakness , cramps, twitches (fasciculations)
  - Distal weakness
    - Turning keys, opening jars, doing up buttons
    - Tripping, stepping over curbs, uneven ground
  - Proximal weakness
    - Standing from sitting, walking up or down stairs
    - Shaving, combing hair, brushing teeth
  - Autonomic: anhydrosis, excessive sweating, orthostatic light-headedness, impotence, dry mouth, early satiety, blurred vision in bright light
- Onset
  - Timing: <4 weeks, 4-8 weeks, >8 weeks, chronic
  - Sudden, gradual, etc
  - Were you a reasonable athlete as a child? Did you finish last in foot races? Were you able to skate or play soccer?
- Duration
- Progression
  - Chronic progression
  - Acute deterioration to nadir then stability or improvement



	Negative	Positive
Motor	Weakness Fatigue Hyporeflexia or areflexia Hypotonia Orthopedic deformities (e.g., pes cavus, hammer toes)	Fasciculations Cramps Myokymia Restless legs "Tightness"
Sensory		
Large fiber	Decreased vibration sensation Decreased joint position sensation Hyporeflexia or areflexia Ataxia Hypotonia	"Tingling" "Pins and needles"
Small fiber	Decreased pain sensation Decreased temperature sensation	"Burning" "Jabbing" "Shooting"
Autonomic	Hypotension Arrhythmia Decreased sweating Impotence Urinary retention	Hypertension Arrhythmia Increased sweating

Past history and comorbidities

- Diabetes (glucose intolerance)
- Thyroid disease
- Renal failure / hepatic failure
- Malignancies
- Connective tissue disease e.g. SLE, RA, Sjogren, etc.
- Previous cervical or lumbar disc disease
- Previous entrapment neuropathies
  - Multiple entrapments (consider HNPP, amyloidosis)
- Orthopedic procedures on feet and ankles
- Bariatric surgery

Family History

- Detailed family history
  - Walking difficulty, use of cane or wheelchair
  - Postural or foot deformities
- Probe history of disabled or possibly affected individuals
- Do not necessarily accept what diagnoses other individuals have

Social History

- Exposure to alcohol
- Occupation
- Tobacco
- Recreational drugs (Nitrous oxide)
- Vitamin and herb use

Occupation	Neuropathy
Dentists	Nitrous oxide
Painters, glue sniffers	Hexacarbons
Farmers	Organophophates
Welders	Lead
Jewelers	Arsenic
Plastic industry	Acrylamide

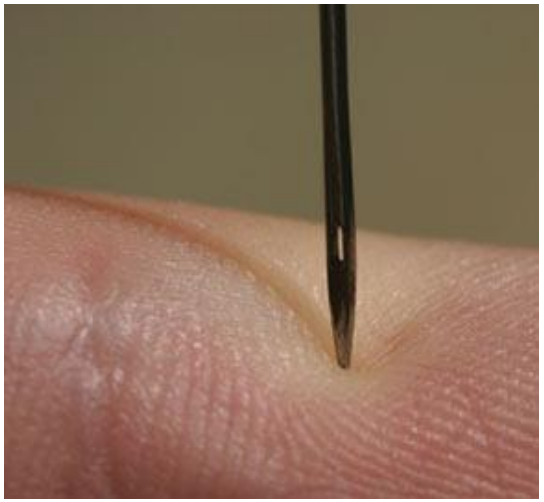
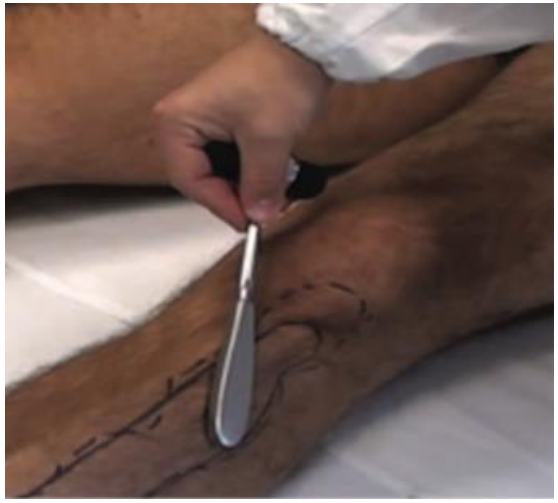
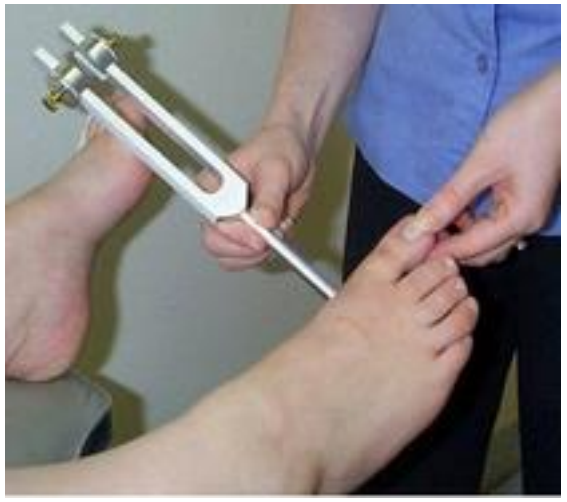
Review of Systems

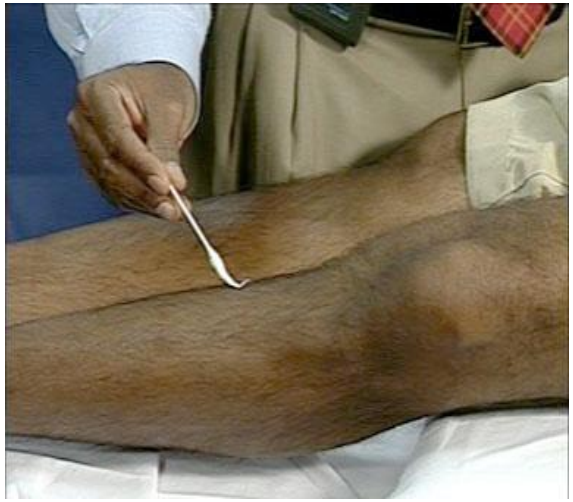
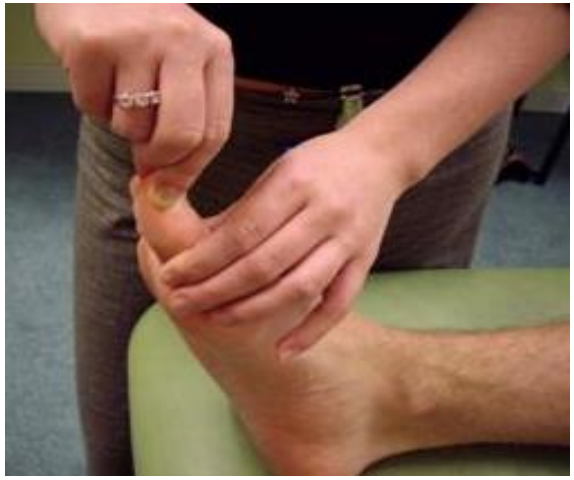
- Other neurological symptoms that may indicate CNS involvement as well.
- Systemic symptoms
  - Joint pain, stiffness and swelling
  - Fever
  - Skin rash
  - Other systems

Neurological examination

- Confirm localization (LMN vs UMN, myopathy vs neuropathy)
- Recognize pattern of neuropathy
  - Motor vs sensory vs sensorymotor
  - Proximal vs distal
  - Symmetric vs asymmetric
- Recognize features of hereditary neuropathy
- Recognize features that narrows the differential diagnosis.
  - Purpura and levido reticularis
- Autonomic features
  - BP & HR supine and standing
  - Pupillary reaction to light and accommodation
- Other
  - Skin: trophic changes (such as thin, shiny, and discolored skin)
  - ulcerations or amputations.
  - peripheral pulses.

Neuro exam…

Approach

1. Recognition of a clinical pattern.
2. There are 6 key questions the clinician should consider in arriving at the pattern that fits the patient best.
3. Most neuropathy and neuronopathy patients can be placed into one of 10 patterns.

Approach – 6 questions

1- What systems are involved?

2- What is the distribution of weakness?

3- What is the nature of the sensory involvement?

4- Is there evidence of UMN involvement?

5- What is the temporal evolution?

6- Is there evidence for a hereditary neuropathy?

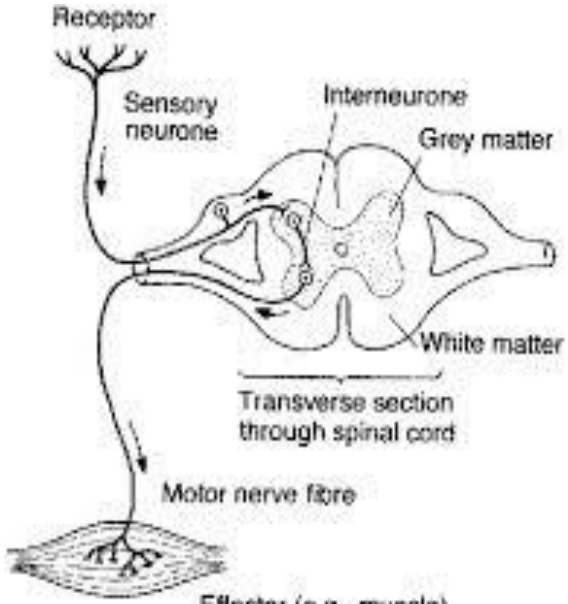
1- What Systems are Involved?

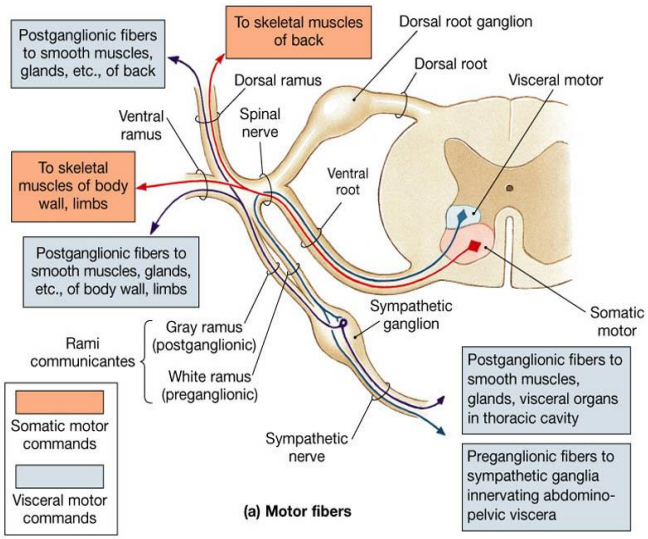
a. Motor: localized to AHC, motor nerve roots, motor nerves, NMJ, muscle.

a. Sensory: DRG, sensory nerve roots, small fibers, thalamus, sensory cortex.

a. Autonomic: autonomic nerves, gray/white communicants

a. or combinations

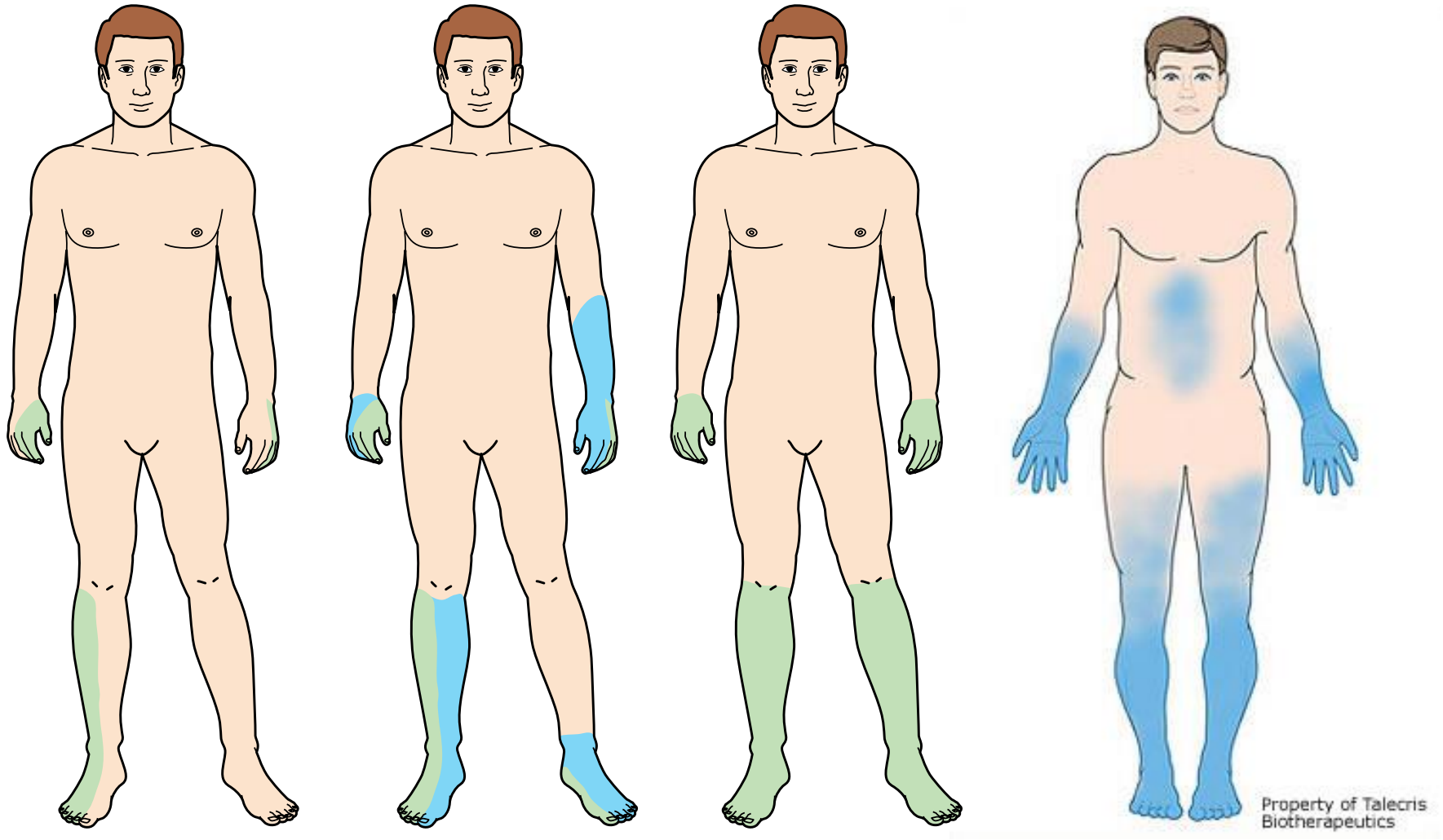




2- What is the Distribution of Weakness?

a. Proximal
b. Distal
c. Proximal > distal
d. Distal > proximal
e. Focal
f. Multifocal

Symmetric vs Asymmetric


Property of Talecris
Biotherapeutics

Asymmetric/focal weakness

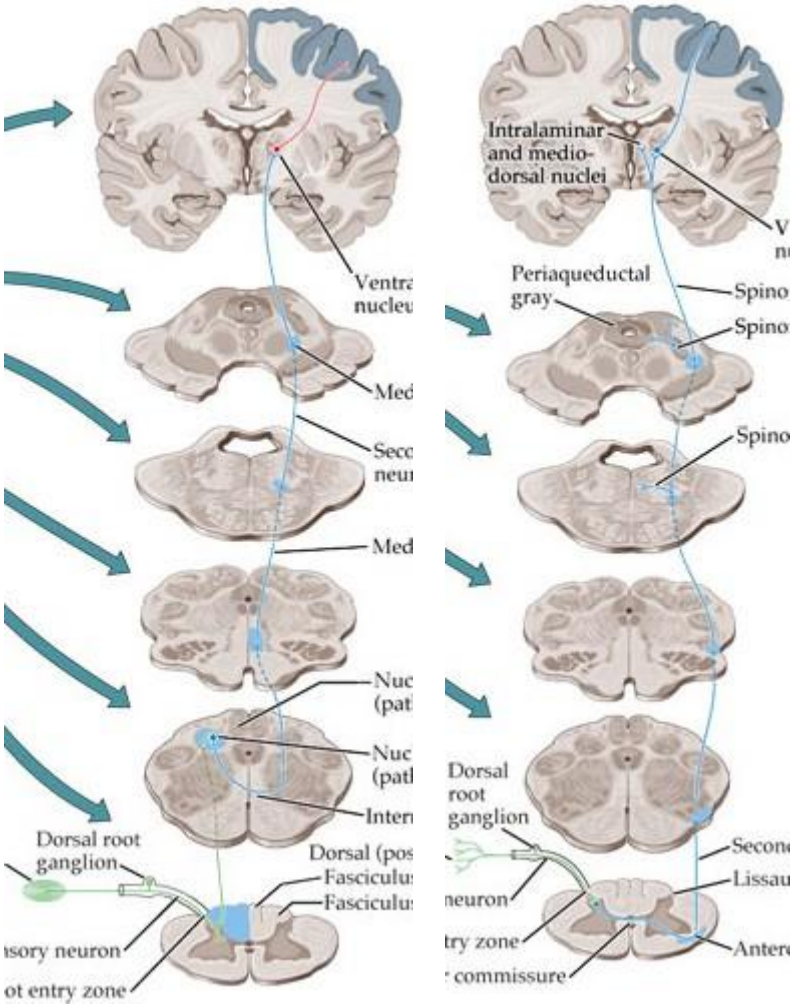
- Radiculopathy
- Plexopathy
- Mononeuropathy
- Multiple mononeuropathies
- Motor neuron disease
- Hereditary e.g. HNPP
- MADSAM
- MMNCB
- Infections

Symmetric weakness

- GBS & CIDP
- Metabolic
  - Diabetic peripheral neuropathy, uremic, endocrine, etc.
- Toxic
  - ETOH, chemo, etc.
- Infections
  - HIV
- Vitamin deficiency
  - B1, 6, 12, folic acid, copper, vit E, etc.
- Hereditary
  - CMT, HSAN, etc
- etc

3- What is the Nature of the Sensory Involvement?

- Pain (burning, stabbing), impaired PP & temperature → small fiber
- Tingling, weakness, ataxia, imbalance, impaired vibration and proprioception→ large fiber
  - Most neuropathies involve both small and large fibers.
- Severe proprioceptive loss
  - Ganglionopathy: loss of all sensory modalities and reflexes
  - Central: dorsal column
    - Generally less profound proprioceptive loss



4- Is there evidence of upper motor neuron involvement?

a. Without sensory loss (ALS,PLS)

b. With sensory loss (vit B12 or folate def, copper, vit E, Friedreich's ataxia, etc)

5- What is the temporal evolution?

a. Acute (days to 4 weeks)

b. Subacute (4–8 weeks)

c. Chronic (>8 weeks)

d. Preceding events, infections, drugs, toxins

6- Is there evidence for a hereditary neuropathy?

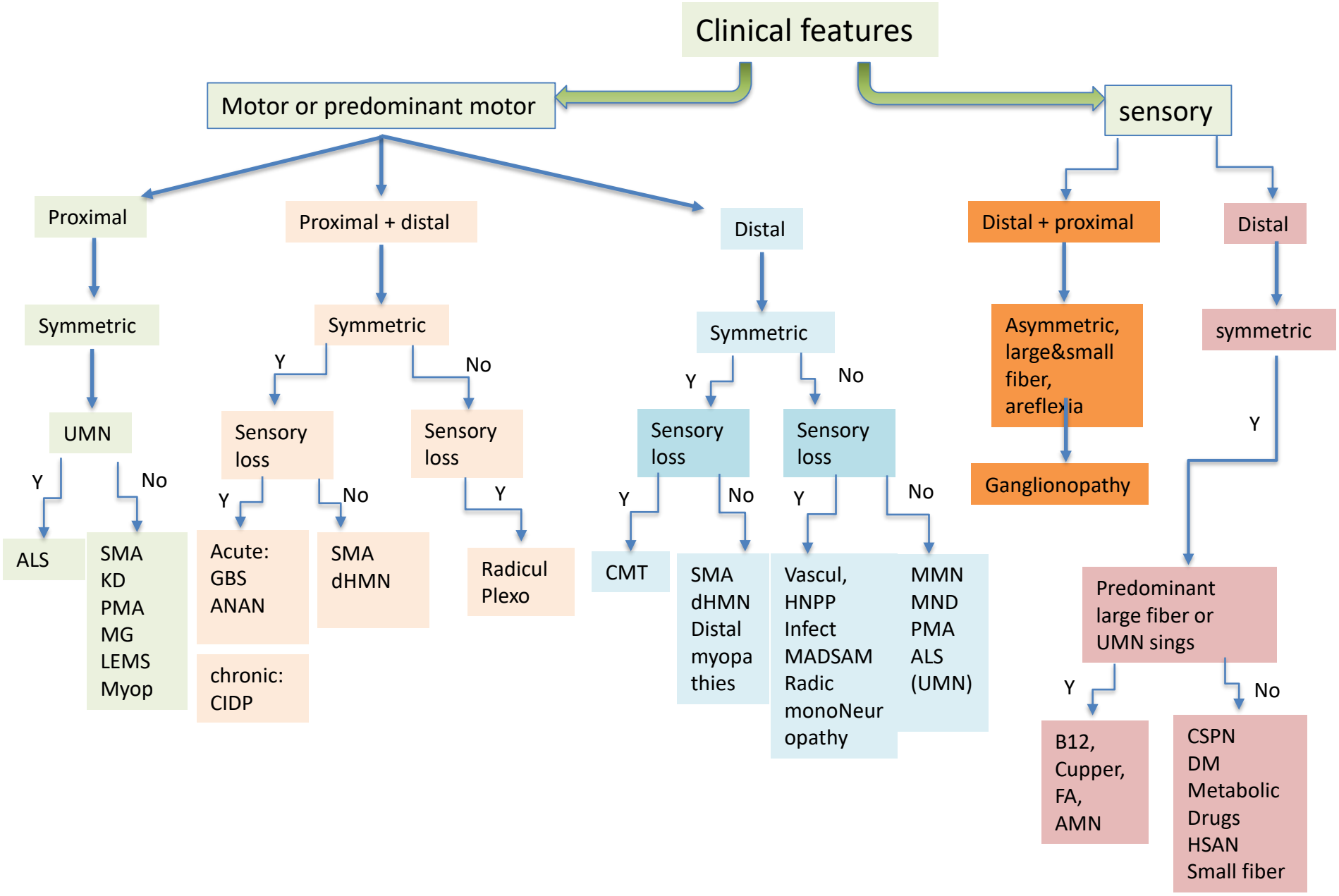
a. Family history of neuropathy

b. Skeletal deformities

c. Lack of sensory symptoms despite sensory signs

Ten patterns of neuropathic disorders

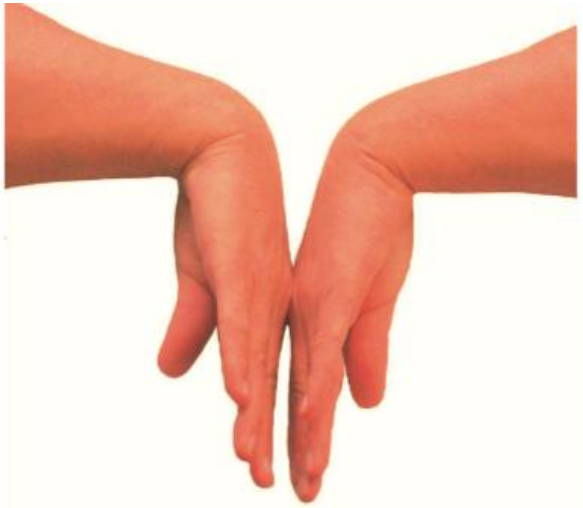
	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 1: symmetric proximal and distal weakness with sensory loss	+	+		+	+				GBS/CIDP
Pattern 2: distal sensory loss with/ without weakness		+		+	+				CSPN, metabolic, drugs, hereditary
Pattern 3: distal weakness with sensory loss		+	+		+				Multiple: vasculitis, HNPP, MADSAM, infection Single: mononeuropathy, radiculopathy
Pattern 4: asymmetric proximal and distal weakness with sensory loss	+	+	+		+				Polyradiculopathy, plexopathy
Pattern 5: asymmetric distal weakness without sensory loss		+	+				±		LMN and UMN – ALS Pure UMN – PLS Pure LMN – MMN, PMA, BAD, LAD, MAMA
Pattern 6: symmetric sensory loss and upper motor neuron signs		+		+	+	+	+		B_{12} deficiency, copper deficiency, Friedreich ataxia, adrenomyeloneuropathy
Pattern 7[a]: symmetric weakness without sensory loss	±	+		+					Proximal and distal SMA Distal Hereditary motor neuropathy
Pattern 8[a]: focal midline proximal symmetric weakness	+ Neck/extensor + Bulbar			+ +			+ +		ALS
Pattern 9: asymmetric proprioceptive loss without weakness			+		+	+			Sensory neuronopathy (ganglionopathy)
Pattern 10: autonomic dysfunction								+	HSAN, diabetes, GBS, amyloid, porphyria, Fabry


Clinical features
Motor or predominant motor
sensory
Proximal
Proximal + distal
Distal
Distal + proximal
Distal
Symmetric
Symmetric
Symmetric
Asymmetric, large&small fiber, areflexia
symmetric
UMN
Sensory loss
Sensory loss
Sensory loss
Sensory loss
Ganglionopathy
Y
No
Y
No
Y
No
Y
No
Y
No
Y
No
Y
ALS
SMA
KD
PMA
MG
LEMS
Myop
Acute:
GBS
ANAN
chronic:
CIDP
SMA
dHMN
Radicul
Plexo
CMT
SMA
dHMN
Distal
myopa
thies
Vascul,
HNPP
Infect
MADSAM
Radic
monoNeur
opathy
MMN
MND
PMA
ALS
(UMN)
Predominant large fiber or UMN sings
Y
No
B12,
Cupper,
FA,
AMN
CSPN
DM
Metabolic
Drugs
HSAN
Small fiber

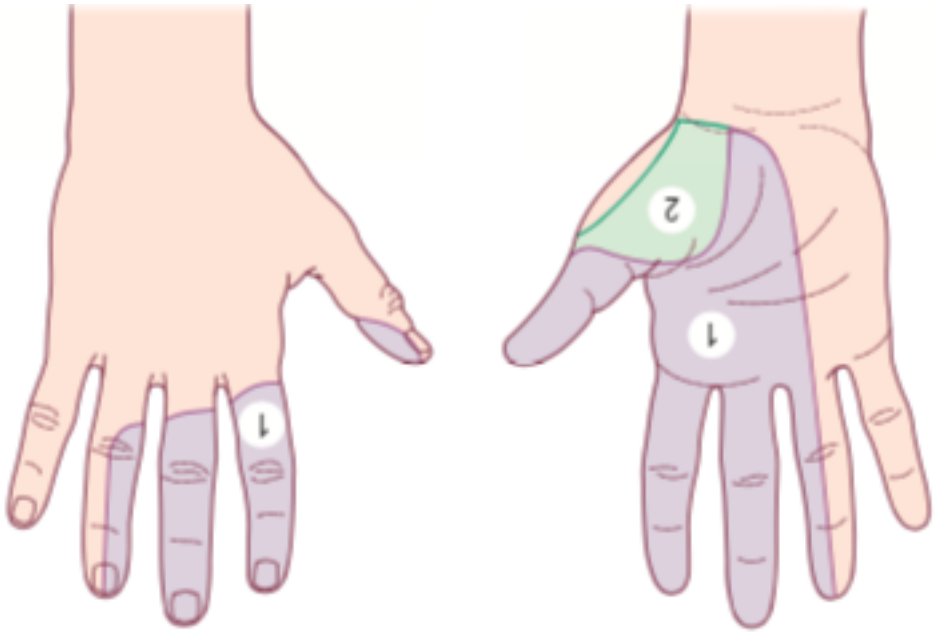
What is the pattern?

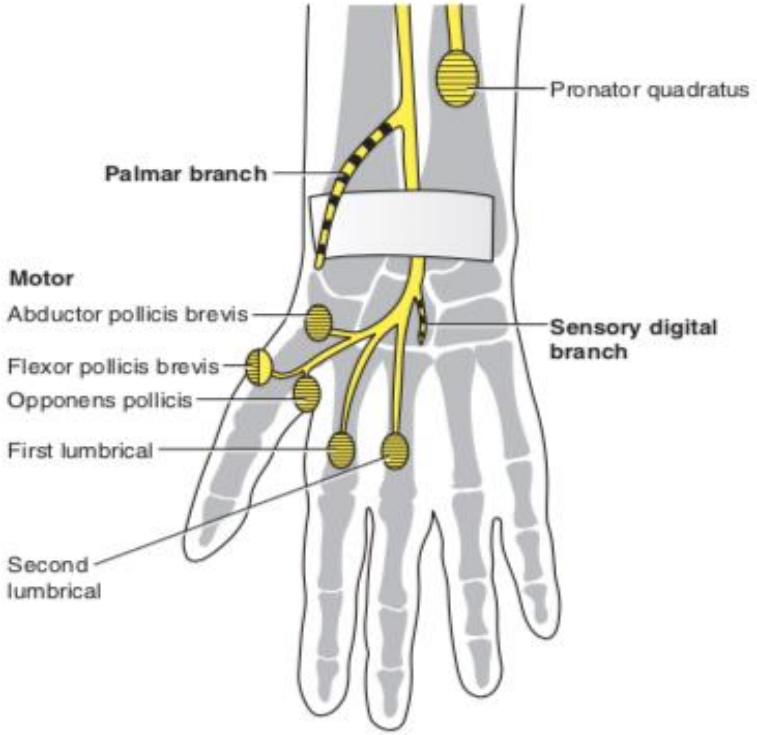
A 67-year-old woman was referred for clumsiness, tingling, and pain in both hands of several months' duration, but the right was worse than left and was affected for a longer time that she could not remember. Symptoms were most prominent at night, often awakening her from sleep, or during hand use such as driving.

- Examination showed slight wasting of the right thenar eminence.
- Thumb abduction was weak on the right and normal on the left.
- Reflexes were normal.
- Sensation was slightly reduced over the finger pads of the thumb, index, middle, and ring fingers bilaterally.
- There was no Tinel's sign at the wrist on either side. A Phalen's maneuver elicited tingling in the middle finger bilaterally after 30 seconds.



	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 3: distal weakness with sensory loss		+	+		+				Multiple: vasculitis, HNPP, MADSAM, infection Single: mononeuropathy, radiculopathy

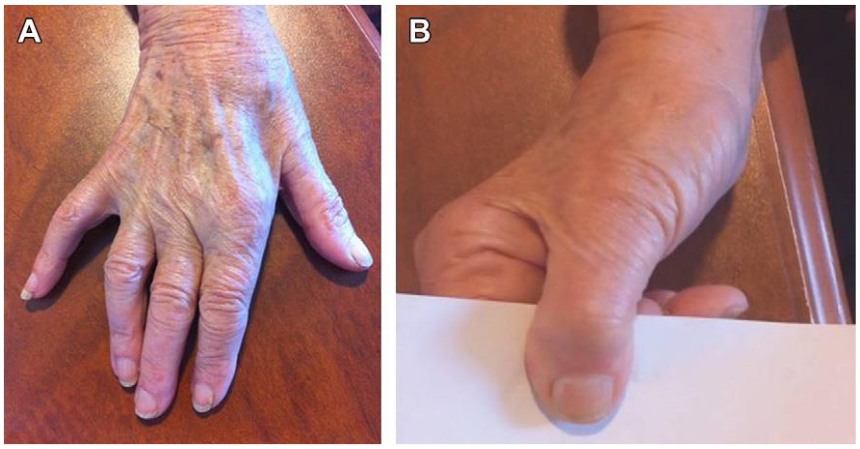

1
2
1

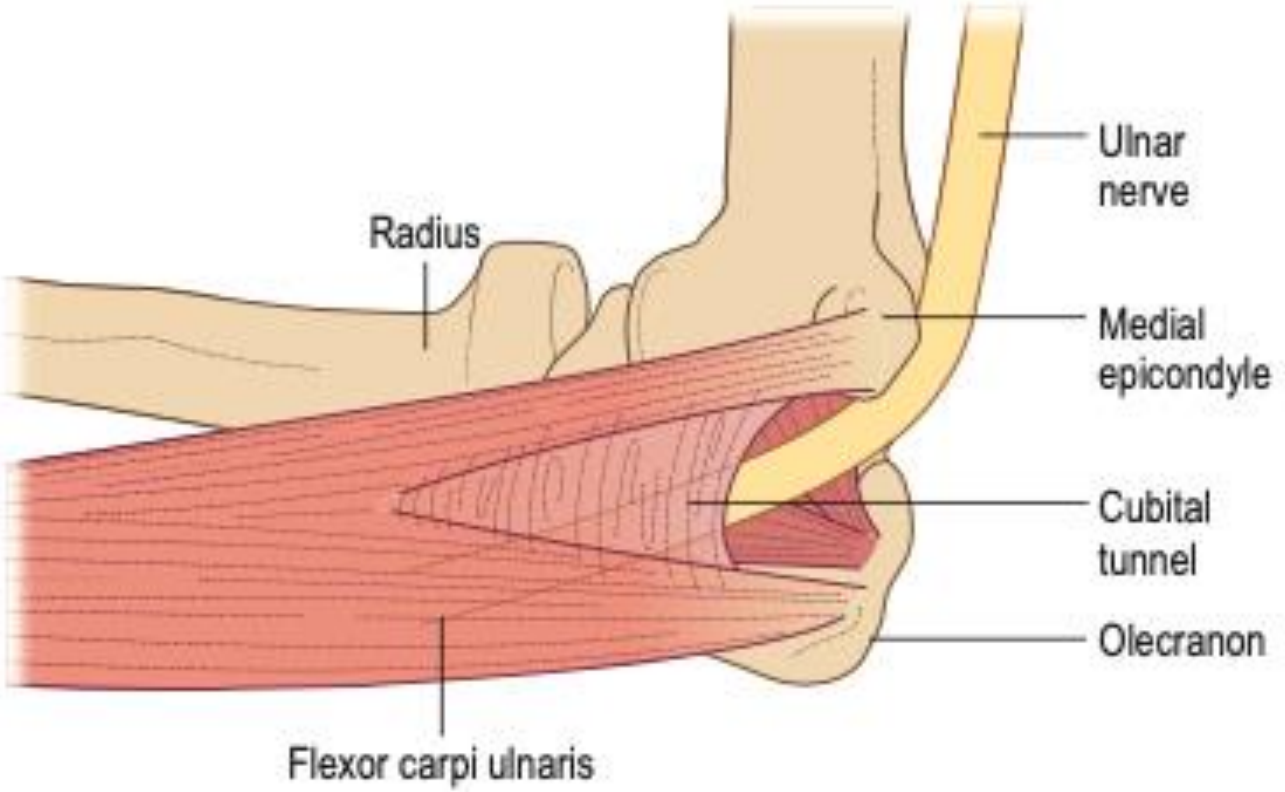

Pronator quadratus
Palmar branch
Motor
Abductor pollicis brevis
Flexor pollicis brevis
Opponens pollicis
First lumbrical
Second lumbrical
Sensory digital branch

What is the pattern?

- A 65-year-old woman presented with a 3-month history of right-hand numbness, grip weakness, and vague elbow pain. Examination demonstrated diminished sensation on the medial hand and fourth and fifth digits, and weakness of finger abduction and adduction, associated with intrinsic hand muscle atrophy.

	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 3: distal weakness with sensory loss		+	+		+				Multiple: vasculitis, HNPP, MADSAM, infection Single: mononeuropathy, radiculopathy


A
B

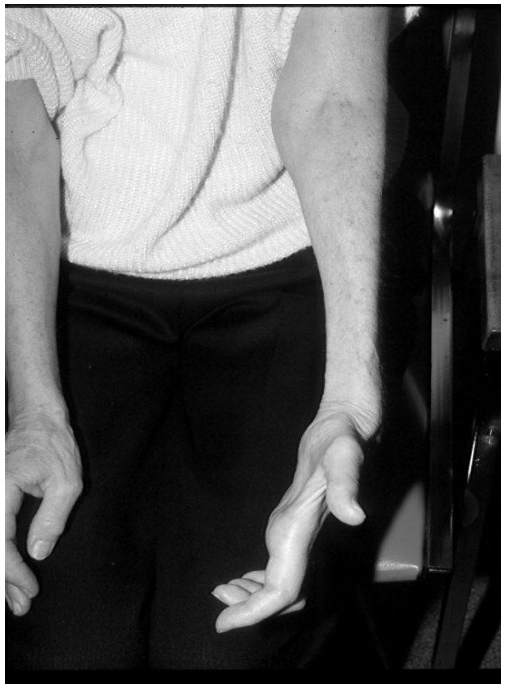


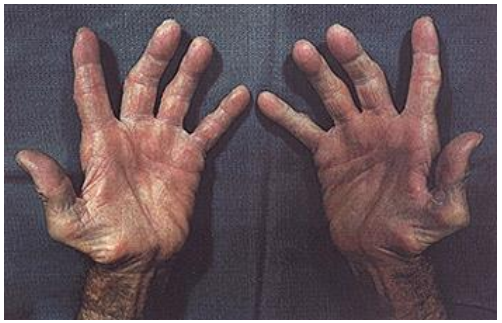
- Ulnar neuropathy at the elbow usually occurs as a result of chronic mechanical compression or stretch, either at the groove or at the cubital tunnel.

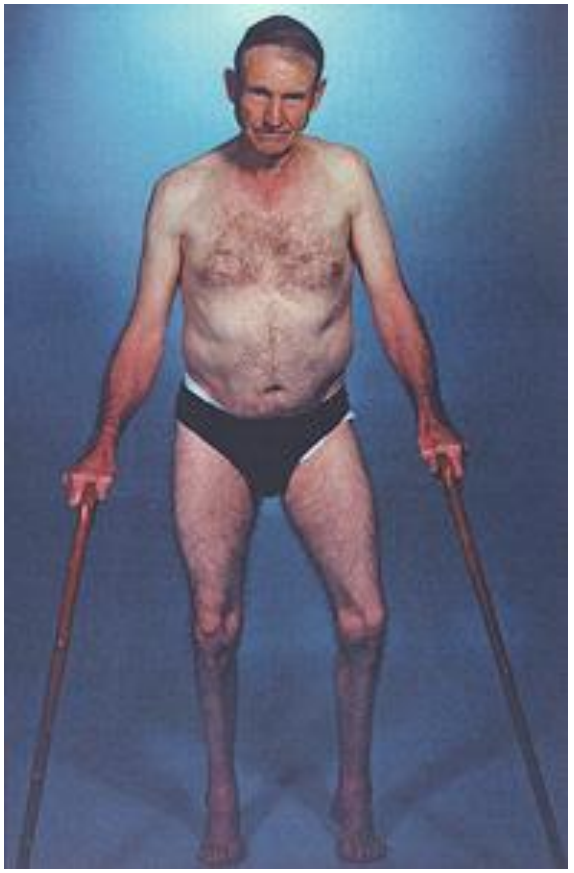
What is the pattern?

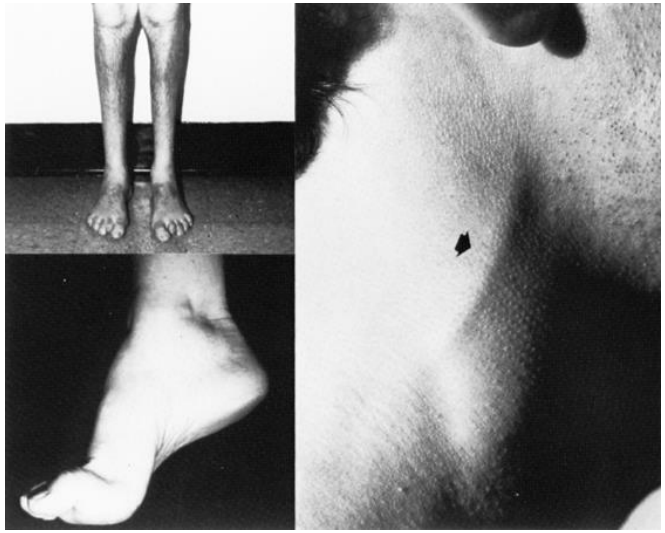
- A 25-year-old man complaining of weakness since early childhood. He remembers being unable to keep up with his peers when running. He is currently only able to walk if wearing ankle-foot orthosis due to bilateral foot drop. He denied sensory symptoms and denied family history of neuropathy
- Neurological examination showed
  - symmetric severe weakness in distal leg muscles with power of 1-2/5 with bilateral drop foot.
  - Proximal leg muscles were 4/5 as well as intrinsic hand muscles.
  - Proximal upper limb muscles were normal.
- Reflexes were absent.
- Vibration and proprioception sensation were absent over the toes and medial malleoli bilaterally and Pinprick and temperature were decreased to the knees and wrists
- Bilateral Pes cavus and hammer toes

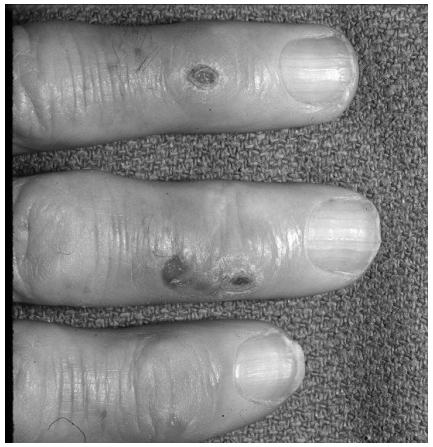
	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 2: distal sensory loss with/ without weakness		+		+	+				CSPN, metabolic, drugs, hereditary

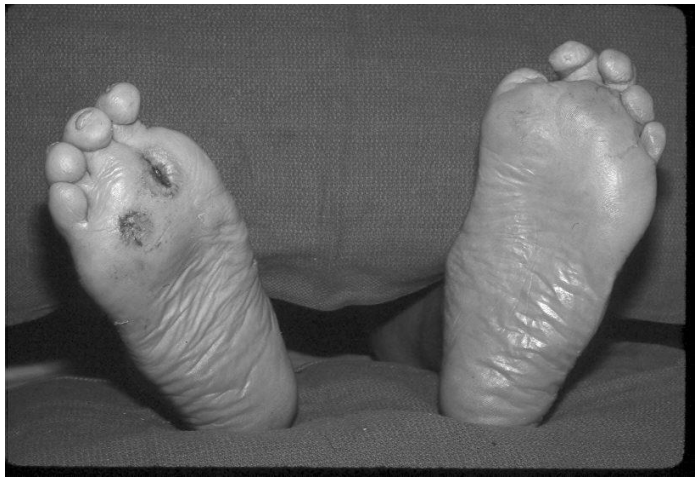












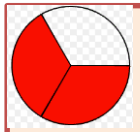
What is the pattern here?

- A 42-year-old man insidiously developed numbness and tingling in the toes, progressing up to the ankles over the past 2 years. He describes burning pain in his feet, mainly at night. He recently started noticing symptoms of numbness and tingling in distal fingers. He denies weakness. No family history.
- Examination showed
  - normal strength
  - decreased pinprick and light touch sensations to the mid leg level and distal fingers.
  - Vibration was absent at the toes and decreased at the ankles, and proprioception is normal at the toes.
  - Reflexes are normal in the arms and at the knees but ankle reflexes are absent.
  - Gait is normal
  - No skeletal deformities

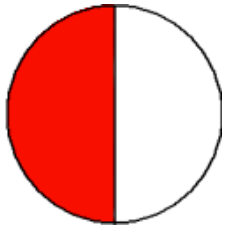
	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 2: distal sensory loss with/ without weakness		+		+	+				CSPN, metabolic, drugs, hereditary

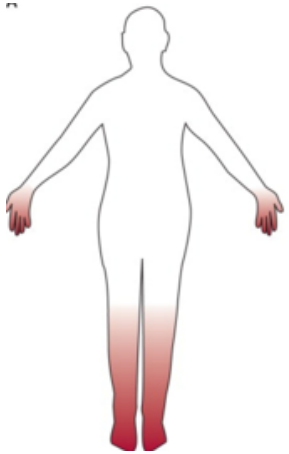
Diabetic neuropathy: Classification

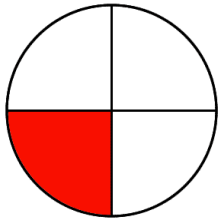
- Symmetric:
  - Distal symmetric polyneuropathy (DSPN)
    - Sensory or sensory motor
  - Small fiber neuropathy
  - Autonomic neuropathy
  - Diabetic neuropathic cachexia
  - Treatment-induced diabetic neuropathy
- Asymmetric/focal and multifocal:
  - Diabetic radiculoplexopathy (amyotrophy)
  - Truncal neuropathies (thoracic radiculopathy)
  - Cranial neuropathies
  - Mononeuropathies, mostly CTS

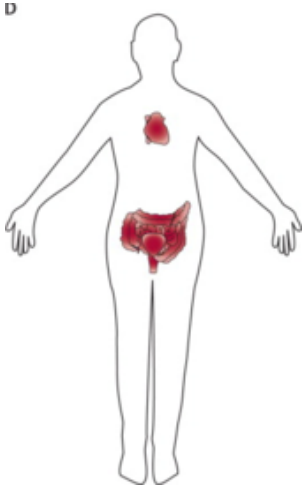


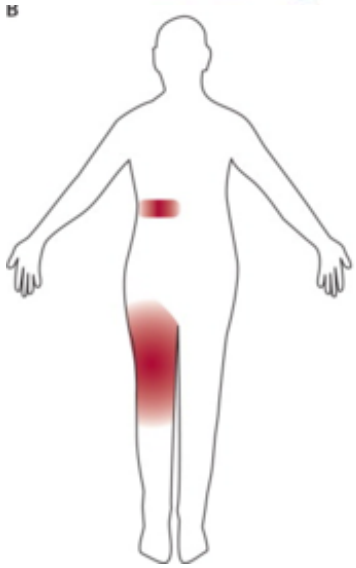
66% of patients with DM had subclinical or clinical evidence of a peripheral neuropathy



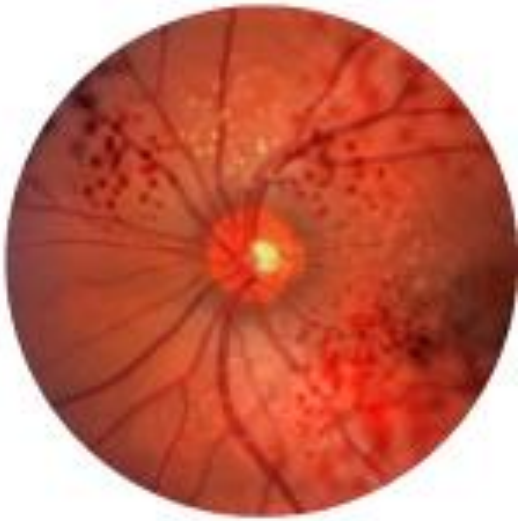








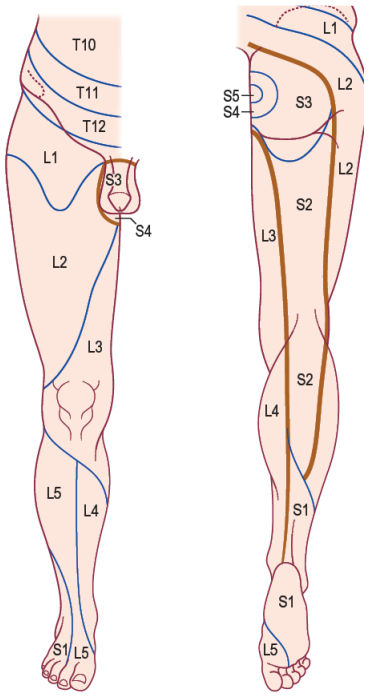
The occurrence of neuropathy correlates with:

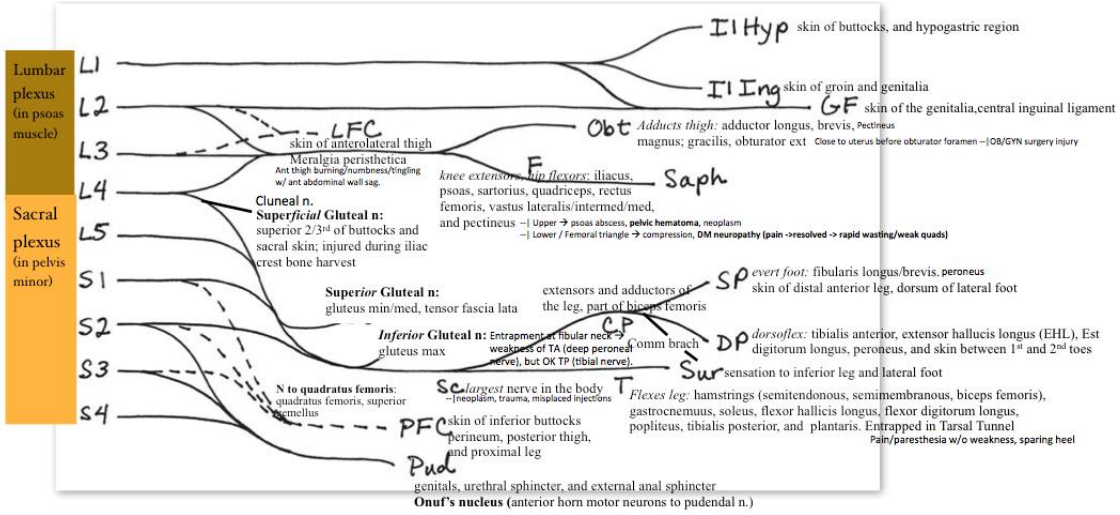


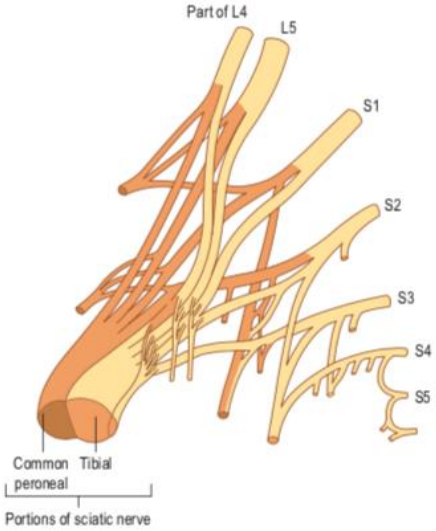
What is the pattern in this case?

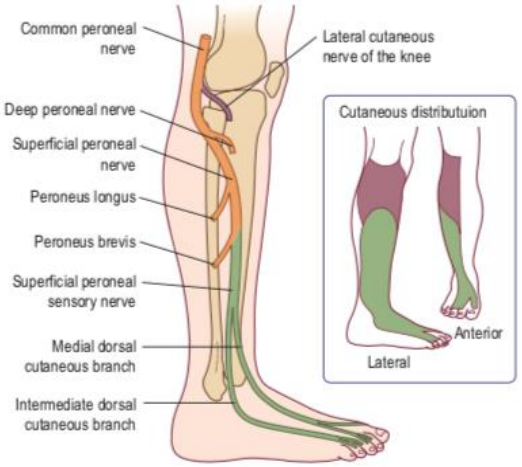
- A 36-year-old man
- Eight weeks ago, he had bent down to lift a chair and developed acute pain in the right back and buttock with radiating paresthesia into the calf and lateral foot.
- Neurologic examination:
  - normal muscle bulk and tone in the lower extremities.
  - Straight-leg raising elicited pain and paresthesia into the right leg at 45 degrees.
  - Power: weakness in right **hip extension**, **knee flexion**, and **ankle plantar flexion**
  - Sensory examination: mild sensory loss on the right sole and lateral foot.
  - DTR: right ankle reflex was absent, other DTRs were normal

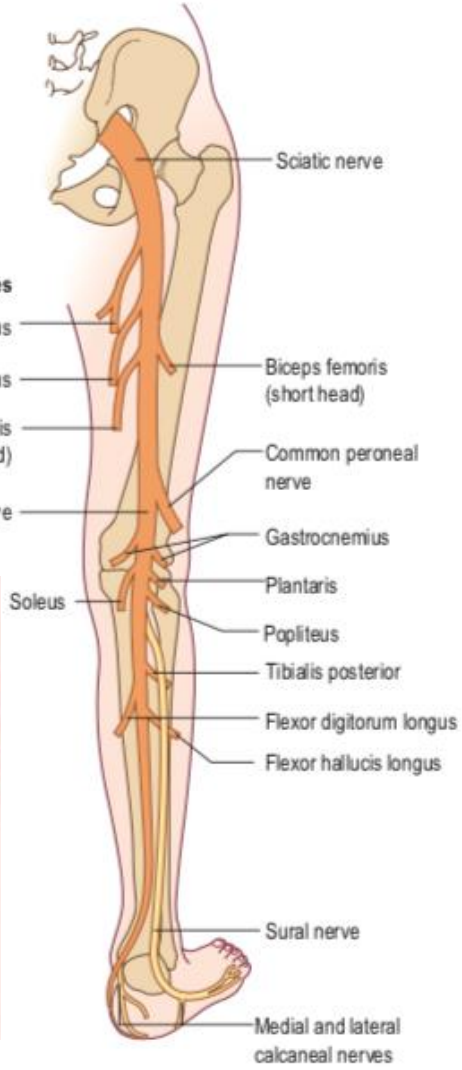
	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 4: asymmetric proximal and distal weakness with sensory loss	+	+	+		+				Polyradiculopathy, plexopathy

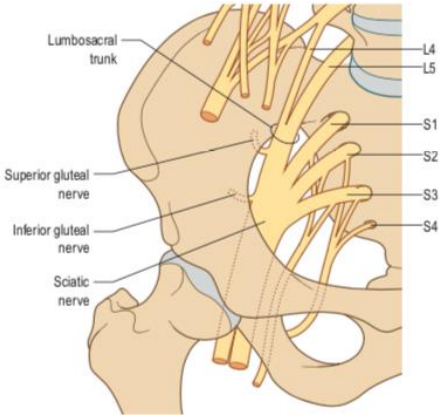


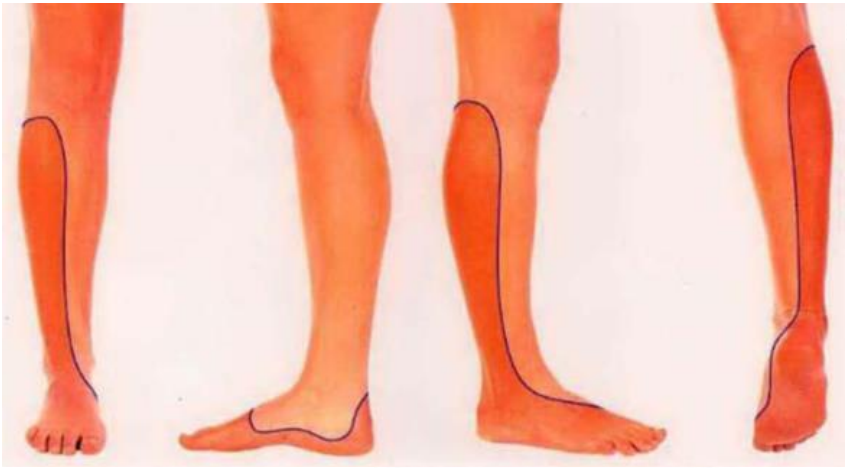



Part of L4
L5
S1
S2
S3
S4
S5
Common peroneal
Tibial
Portions of sciatic nerve


Common peroneal nerve
Lateral cutaneous nerve of the knee
Deep peroneal nerve
Superficial peroneal nerve
Peroneus longus
Peroneus brevis
Superficial peroneal sensory nerve
Medial dorsal cutaneous branch
Intermediate dorsal cutaneous branch
Cutaneous distributuion
Anterior
Lateral

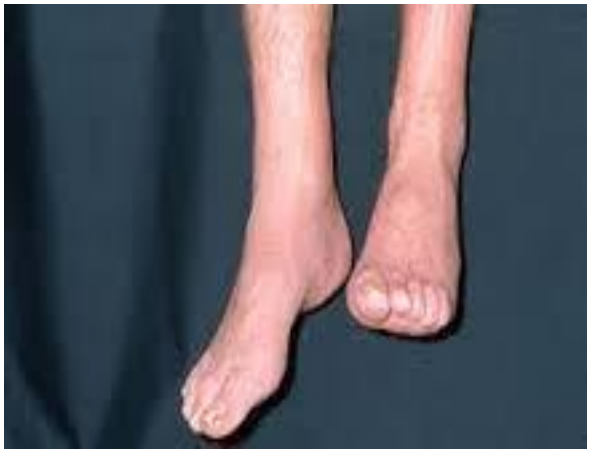

Hamstring muscles
Semimembranosus
Semitendinosus
Biceps femoris (long head)
Tibial nerve
Soleus
Sciatic nerve
Biceps femoris (short head)
Common peroneal nerve
Gastrocnemius
Plantaris
Popliteus
Tibialis posterior
Flexor digitorum longus
Flexor hallucis longus
Sural nerve
Medial and lateral calcaneal nerves

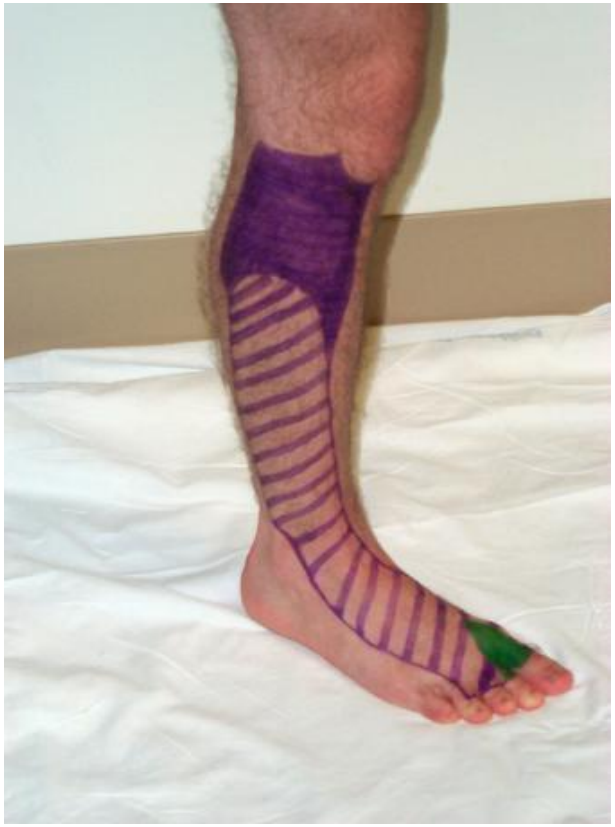

Lumbosacral trunk
L4
L5
S1
S2
S3
S4
Superior gluteal nerve
Inferior gluteal nerve
Sciatic nerve



What is the pattern?

- A 56-year-old man was referred for a persistent foot drop 3 weeks after coronary artery bypass surgery. Shortly after awakening from anesthesia, the patient noted difficulty dorsiflexing his right foot and toes. In addition, there was a pins-and-needles sensation over the dorsum of the right foot. He noted that when he was walking, his right foot would slap with each step. There was no pain, and the left leg was unaffected.
- On examination, muscle bulk and tone were normal and symmetric in both legs. There was marked weakness of right ankle and toe dorsiflexion (1/5) as well as ankle eversion (2/5). Foot inversion, ankle and toe plantar flexion, knee flexion, and all movements around the hip were normal. Deep tendon reflexes were intact and symmetric.
- Sensory examination showed a well-demarcated loss of sensation to pinprick and temperature over the dorsum of the right foot extending into the lateral calf. Sensation over the right lateral knee was normal, as was sensation over the lateral foot, sole of the foot, and medial calf.





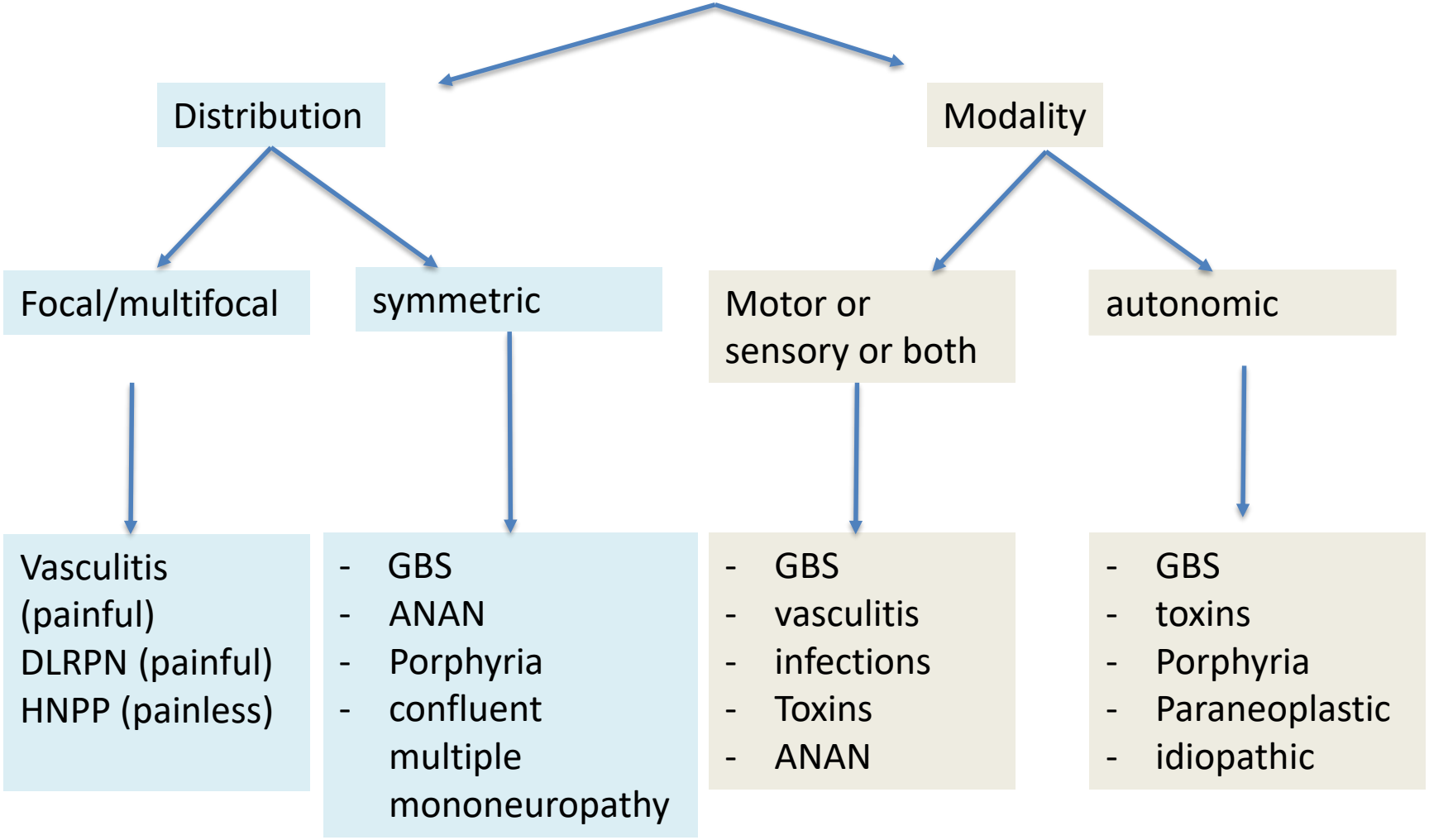
	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 3: distal weakness with sensory loss		+	+		+				Multiple: vasculitis, HNPP, MADSAM, infection Single: mononeuropathy, radiculopathy

What is the pattern in this case?

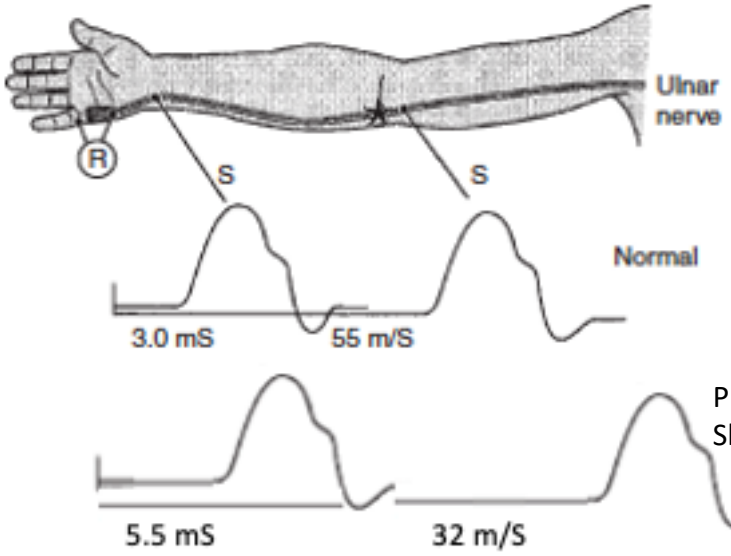
- A 25 year-old woman developed numbness and tingling of the feet and hands followed by progressive leg more than arm muscle weakness over the last week. She experienced a diarrheal illness 3 weeks ago that had resolved within 10 days.
- Examination showed marked bifacial weakness
- Muscle power in the lower limbs was 2/5 and in the upper limbs 3/5, with equal proximal and distal weakness. She could not stand up or walk with assistance.
- DTR were absent.
- She had normal pinprick, light touch and proprioception but vibration was reduced at the toes.

	Weakness								
	Proximal	Distal	Asymmetric	Symmetric	Sensory Symptoms	Severe Proprioceptive Loss	UMN Signs	Autonomic Symptoms/ Signs	Diagnosis
Pattern 1: symmetric proximal and distal weakness with sensory loss	+	+		+	+				GBS/CIDP

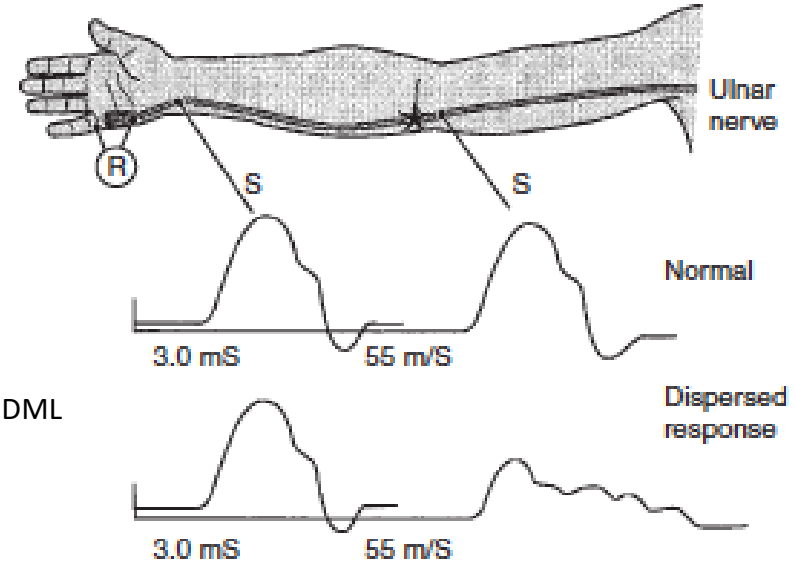
Acute neuropathy

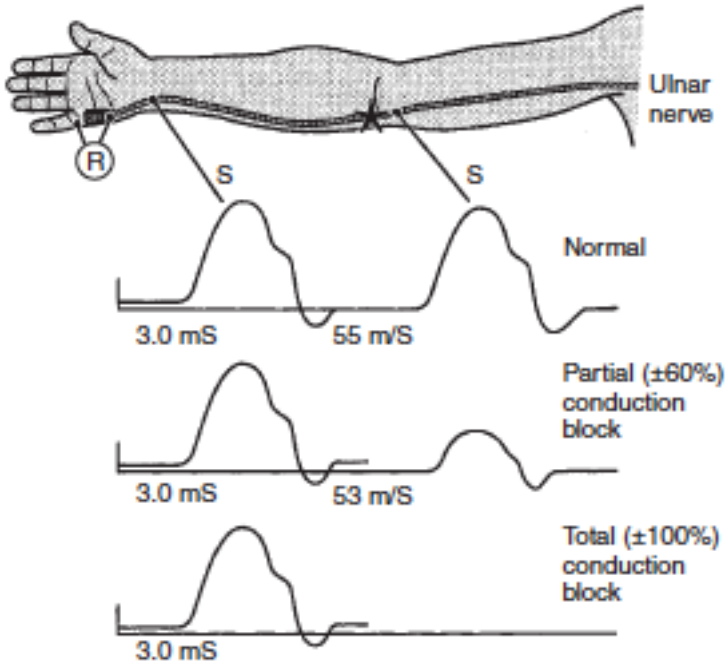


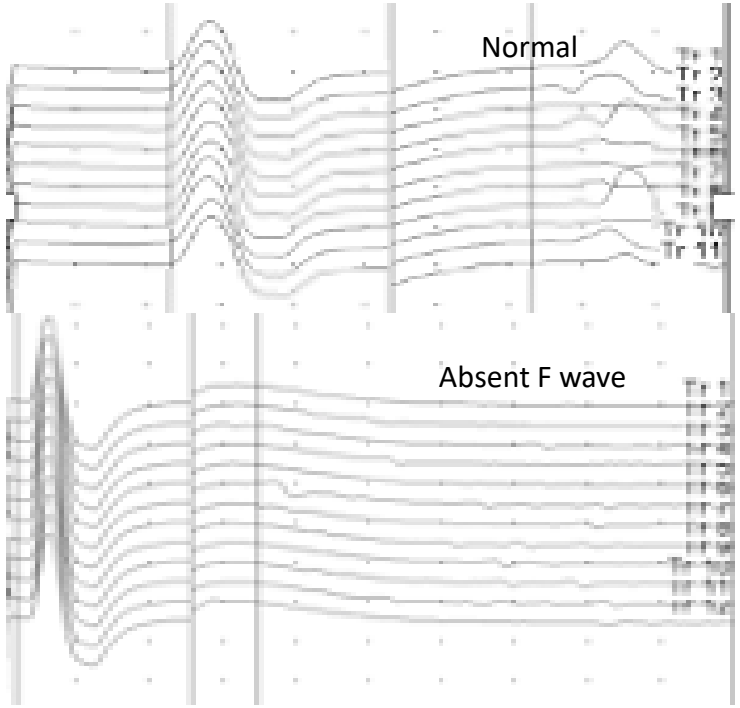
- CBC = normal,
- vitamin B12 level = normal
- Serum glucose and A1c – normal
- SPEP – normal
- CK = normal, TSH = normal, lactate = normal
- Forced vital capacity was 2.0 liters.
- CSF: cells count = 0 & protein = 82 mg/dl.
  - cyto-albuminologic dissociation
- NCS
  - Next slide



Prolonged DML
Slowed CV







Treatment

- IVIG or Plasmapheresis
- Supportive therapy

- Monitor progression and prevent and manage potentially fatal complications, especially:
  - Regularly monitor pulmonary
  - Regularly check for autonomic dysfunction
  - Check for swallowing dysfunction
  - Recognize and treat pain
  - Prevent and treat infections and pulmonary embolism
  - Prevent cornea ulceration due to facial weakness
  - Prevent decubitus and contractures