Peripheral neuropathies

435 medicine teamwork

[Important | Notes | Davidson's | Article | Editing file]

lecture objectives:

⇨ Not giving.

★ This work is based on the article the Dr shared; which he regarded as "*More than enough*".

★ Lecture summary.

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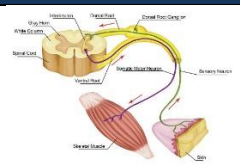
References: Article & Davidson's

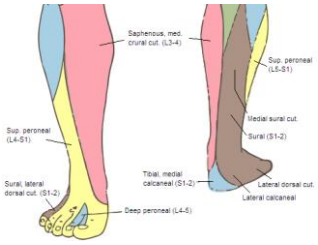
Introduction:

Nervous system: This is just for you to understand.

CNS	PNS
Brain and spinal cord. (Not our concerns in this lecture).	 Everything else <u>starting from</u> the anterior horn cell, roots, cervical and lumbosacral plexi, peripheral nerves and their divisions.
	PNS anatomical division:
	• **Anterior horn cell** (motor neuron) (diseases affecting AHC are clinically separated from peripheral neuropathies, they're called <u>motor neuron disorders</u>). • **Ventral root** (pure motor). • **Dorsal root ganglion.** • **Dorsal root** (pure sensory). • **Plexus.** (e.g. Brachial plexus) • **Peripheral nerves.** • **Neuromuscular junctions.** • **Muscles.** • **End organ receptor / small fiber neuropathy.** ● Involved in peripheral neuropathy

Dermatomes of the foot: the dr. said the dermatomes are important & he mainly concentered on the foot dermatomes.

- A dermatome is an area of skin that is mainly supplied by a single spinal nerve. There are 8 cervical nerves, 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.



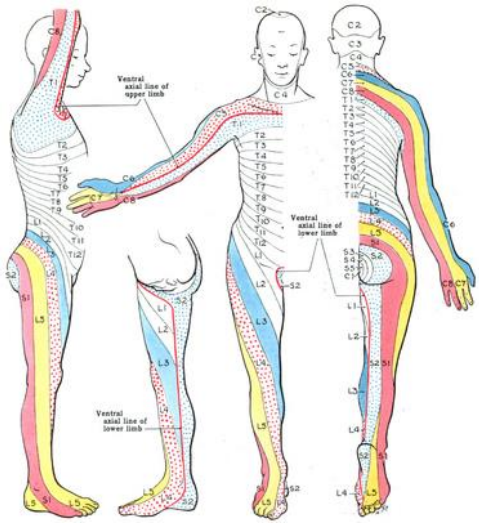
Lateral side of the bottom of the foot = S1 = sural
saphenous nerve = Medial of the foot = area of L4
L5 = superficial peroneal

Myotomes

- 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 reflex (associated with brachioradialis) 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.

TABLE 1: DERMATOMES	
C1	Top of head
C2	Face
C3	Lateral neck
C4	Lower neck and top of shoulder
C5	Shoulder to base of thumb outside of arm
C6	Front of shoulder, down arm, into thumb and back of hand
C7	Back of shoulder, down back of arm, into back of hand
C8	Little finger and wrist
T1	Inside elbow down to wrist
L1	Back and over trochanter
L2	Back and anterior thigh to knee
L3	Back, upper buttocks, anterior thigh and knee, inner lower leg
L4	Inner buttocks, outer thigh inside of leg, and dorsum of foot and big toe
L5	Buttock, back, side of thigh, lateral leg, dorsum of foot, inner half of sole of foot, and second and third toes
S1, S2	Buttock, posterior thigh and lower leg
S3	Groin and inner thigh to the knee
S4	Genitals

TABLE 2: MYOTOMES	
C1, C2	Cervical flexion
C3	Cervical side flexion
C4	Scapula elevation
C5	Shoulder abduction
C6	Elbow flexion and wrist extension
C7	Elbow extension and wrist flexion
C8	Thumb extension
T1	Finger abduction
L1, L2	Hip flexion
L3	Knee extension
L4	Ankle dorsiflexion
L5	Big toe extension
S1	Ankle plantiflexion
S2	Knee flexion



Peripheral neuropathies:

Concepts:

- Peripheral neuropathy is a disorder that occurs when your PNS malfunction because they're damaged or destroyed.
- Disorders of the peripheral nervous system are common and may affect the motor, sensory or autonomic components, either in isolation or combination.
- **The site of pathology may be:**
    - **Nerve root** (radiculopathy).
    - **Nerve plexus** (plexopathy)
    - **Nerve** (neuropathy).
        - Neuropathies may present as **mononeuropathy** (single nerve affected), **multiple mononeuropathies** ('mononeuritis multiplex') or a **symmetrical**. Cranial nerves 3–12 share the same tissue characteristics as peripheral nerves elsewhere and are subject to the same range of diseases.

Pathophysiology:

- Damage may occur to the nerve cell body (axon) or the myelin sheath (schwann cell), leading to axonal or demyelinating neuropathies.
    - The distinction is requiring neurophysiology (nerve conduction studies and electromyography), and it is very important as only demyelinating disorders are usually susceptible to treatment.

Neuropathies can occur in association with many systemic diseases, toxins and drugs.

Pathological classifications:

Neuropathic disorders				
Neuronopathy (Pure; pure sensory or pure motor or autonomic)			**Peripheral neuropathy** (mixed "sensorimotor")	
Sensory (ganglionopathies)	**Motor** (motor neuron disease)	**Autonomic**	**Myelinopathies**	**Axonopathies**
			e.g. GBS (Guillain–Barré syndrome)	e.g. Toxic neuropathies

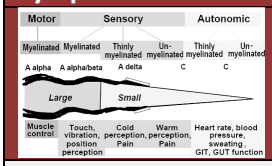
Etiological classifications:

Acquired	Hereditary
Dysmetabolic states:	**Charcot-marie-tooth disease and related disorders**
• **Diabetes mellitus** • **Neuropathy** related to renal disease • **Vitamin deficiency states** (eg, **vitamin b12 deficiency**)	
Immune mediated:	**Hereditary sensory and autonomic neuropathy**
• **Guillain-barre syndrome (GBS)** • **Vasculitis** e.g. (polyarteritis nodosa) • **Sarcoidosis**	
Infectious	**Hereditary neuropathy with liability to pressure palsy (hnpp)**
• **Herpes zoster** • **HIV**	
Cancer related	**Familial amyloidosis**
• **Malignant infiltration** e.g (lymphoma) • **Primary amyloidosis**	
Drugs/ toxins	**Motor neuron disease**
• **Chemotherapy induced** e.g. (cisplatin)	

• **Other drugs** e.g. (amiodarone, INH) • **Heavy metals and industrial toxins** e.g. (lead)	
Mechanical/compressive	
• **Radiculopathy** • **Mononeuropathy**	
Unknown etiology	
• **Cryptogenic sensory and sensorimotor neuropathy** • **Amyotrophic lateral sclerosis (ALS)**	

Clinical features:

Every nerve in your peripheral system has a specific function, so symptoms depend on the type of nerves affected. You should ask about these signs and symptoms in your OSCE exam

Symptoms		
	Loss of function "Negative"	Altered function "positive"
Motor	Wasting Hypotonia Weakness: **Proximal weakness:** difficulty to rise arm (to brush the teeth, comb the hair), as well as problems climbing stairs or rising from a chair. **Distal weakness:** dragging of the foot while walking, لمن يرفع رجله تسقط Hyporeflexia Orthopedic deformity	Fasciculations Cramps
Sensory (Large Fibers)	↓ Vibration, ↓ proprioception, Hyporeflexia Sensory ataxia	Paresthesias
Sensory (Small fibers)	↓ Pain ↓ Temperature	Dysesthesias Allodynia
Autonomic Nerves	↓ Sweating Hypotension Urinary retention Impotence Vascular color changes	↑ Sweating Hypertension

Investigations:

- The investigations required reflect the wide spectrum of causes. Neurophysiological tests are key in discriminating between demyelinating and axonal neuropathies, and in identifying entrapment neuropathies.
- Most neuropathies are of the chronic axonal type.

26.101 Investigation of peripheral neuropathy

Initial tests

- Glucose (fasting)
- Erythrocyte sedimentation rate, C-reactive protein
- Full blood count
- Urea and electrolytes
- Liver function tests
- Serum protein electrophoresis
- Vitamin B_{12}, folate
- ANA, ANCA
- Chest X-ray
- HIV testing

If initial tests are negative

- Nerve conduction studies
- Vitamins E and A
- Genetic testing (see Box 26.99)
- Lyme serology (p. 335)
- Serum ACE
- Serum amyloid

(ACE = angiotensin-converting enzyme; ANCA = antineutrophil cytoplasmic antibody; ANA = antineutrophil antibody)

Pattern-recognition approach to neuropathy: the most IMP part of the lecture!

The whole idea of this lecture is to apply the 3-6-10-step clinical approach to neuropathy: 3 goals, 6 key questions, 10 phenotypic patterns.

3 goals:

1. To determine the **location** of the lesion.
2. To know the **cause** of the lesion.
3. To determine whether the **therapy** is possible?

6 Questions: Easily defined clinical patterns of involvement are used to identify patients in need of neurologic consultation, whenever you're confronted with a case of peripheral neuropathy it is very necessary to ask yourself these 6 key questions.

1. What systems are involved?

A. **Motor:** AHC, motor root, peripheral nerves (only motor fibers).
B. **Sensory:** Peripheral nerves (only sensory fibers), dorsal root ganglia, dorsal column.
C. **Autonomic.**
D. **Combinations.**

2. What is the distribution of weakness?

A. **Only distal versus proximal and distal**
B. **Focal/asymmetric versus symmetric**

The distribution of the patient's weakness is crucial for an accurate diagnosis, thus 2 questions should be asked: (1) does the weakness only involve the distal extremity or is it both proximal and distal? and (2) is the weakness focal and asymmetric or is it symmetric? The finding of weakness in both proximal and distal muscle groups in a symmetric fashion is the hallmark for acquired immune demyelinating polyneuropathies **(i.e. GBS) and the chronic form (CIPD).**

3. What is the nature of the sensory involvement?

A. **Severe pain/burning or stabbing**
B. **Severe proprioceptive loss.**
E. Is the involved nerve fiber small or large? Small → Pain & temperature, Large → Vibration & joint position.

When taking the history from a patient with a peripheral neuropathy, it is important to determine whether the patient has loss of sensation (numbness), altered sensation (tingling), or pain. Sometimes patients may find it difficult to distinguish between uncomfortable tingling sensations (dysesthesias) and pain. Neuropathic pain can be burning, dull, and poorly localized (protopathic pain), presumably transmitted by polymodal c nociceptor fibers, or sharp and lancinating (epicritic pain), relayed by delta fibers. If severe pain is one of the patient's symptoms, certain peripheral neuropathies should be considered most commonly: **cryptogenic sensory neuropathy, diabetes mellitus, GBS & vasculitis.**

4. Is there evidence of upper motor neuron involvement?

A. **Without sensory loss**
B. **With sensory loss**

Think about Myelopathies, B12 deficiency

	Upper motor neuron lesion	Lower motor neuron lesion
Inspection	Normal	Wasting, fasciculation
Tone	Increased with clonus	Normal or decreased, no clonus
Pattern of weakness	Preferentially affects extensors in arms, flexors in leg. Hemiparesis, paraparesis or tetraparesis.	Typically focal, in distribution of nerve root or peripheral nerve, with associated sensory changes
Deep tendon reflexes	Increased	Decreased/absent
Plantar response	Extensor (Babinski sign)	Flexor

5. What is the temporal evolution?

A. **Acute** (days to 4 weeks)

B. **Subacute** (4–8 weeks)
   ✓ Acute or subacute think about GBS
C. **Chronic** (>8 weeks)
D. **Preceding events, 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, Very bad sensory loss that they don't mention it & found on examination.

In patients with a chronic, very slowly progressive distal weakness over many years, with very little in the way of sensory symptoms, the clinician should pay particular attention to the family history and inquire about foot deformities in immediate relatives. Patients with hereditary neuropathy often will present with significant foot drop, with no sensory symptoms, but significant vibration loss in the toes. On examining the patient, the clinician must look carefully at the **feet for arch and toe abnormalities (high or flat arches, hammer toes), and look at the spine for scoliosis.** In suspicious cases, it may be necessary to perform both neurologic and electrophysiologic studies on family members

10 Phenotypic patterns:

One can classify neuropathic disorders into several patterns based on sensory and motor involvement and the distribution of signs. Each syndrome has a limited differential diagnosis. A final diagnosis is arrived at by using other clues such as the temporal course, presence of other disease states, family history, and information from laboratory studies.

Pattern1: Symmetrical proximal & distal weakness with sensory loss

■ **Inflammatory demyelinating polyneuropathy e.g. (GBS)**

Guillain–Barré syndrome (GBS) is an immune-mediated condition (triggered by acute bacteria enteric infection).

- **Abrupt onset** (within less than 4 weeks) with rapidly ascending weakness/paralysis of all four extremities; frequently progresses to involve respiratory, facial, and bulbar muscles.
- Usually **symmetric** (but not always)
- Weakness:
  - Mild or severe.
  - Progresses from distal to central muscles.
- **If generalized paralysis is present, it can lead to respiratory arrest.**
- Extremities may be painful, usually show sensory loss on examination.
- Sphincter control and mentation are typically spared.
- Autonomic features (e.g., arrhythmias, tachycardia, postural hypotension) are dangerous complications.

Pattern2: Symmetrical distal sensory loss with or without weakness.

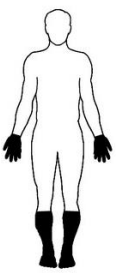
■ **DM** diabetes is the most common cause of neuropathy

Frequently asymptomatic. The most common clinical signs (during examination) are,

- **'Glove and stocking' impairment of all modalities of sensation (especially vibration)**
- Loss of tendon reflexes in the lower limbs.

In symptomatic patients, sensory abnormalities are predominant. Symptoms (patient complain) include,

- Paraesthesiae in the feet (and, rarely, in the hands)
- Pain in the lower limbs (dull, aching and/or sharp, worse at night, and mainly felt on the anterior aspect of the legs)
- Burning sensations in the soles of the feet.
- Abnormal gait (commonly wide-based) often associated with a sense of numbness in the feet.

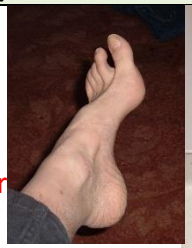
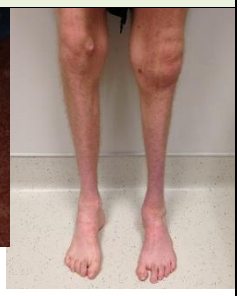


- Weakness and atrophy, in particular of the interosseous muscles, may develop, leading to,
  - Structural changes in the foot with loss of lateral and transverse arches.
  - Clawing of the toes and exposure of the metatarsal heads.
- This results in increased pressure on the plantar aspects of the metatarsal heads, with the development of callus skin at these and other pressure points.
- Electrophysiological tests demonstrate slowing of both motor and sensory conduction, and tests of vibration sensitivity and thermal thresholds are abnormal.
- **Note: autonomic neuropathy is common in diabetics & is not necessarily associated with peripheral somatic neuropathy. Parasympathetic or sympathetic nerves may be predominantly affected in one or more visceral systems. (e.g. postural hypotension, erectile dysfunction.)**

■ CSPN (predominantly sensory polyneuropathy with no identifiable cause)

■ Drugs induced peripheral neuropathy.

■ **Charcot-Marie-Tooth (hereditary)**

Charcot–Marie–Tooth disease (CMT) is an umbrella term for the inherited neuropathies. This group of syndromes has different clinical and genetic features. The most common CMT is the autosomal dominantly inherited CMT type 1. Common signs are distal wasting (**'inverted champagne bottle' legs**), often with **pes cavus (high arched)**, and predominantly motor involvement.

Other signs:

- Muscle weakness (especially in the foot and leg)
- Other foot deformities (hammertoes "curled toes")
- Muscle wasting (shrinking and weakness) in the legs
- Curved spine (scoliosis)
- Loss of pain sensitivity (upon examination)

Pattern3: Asymmetric distal weakness with sensory loss.

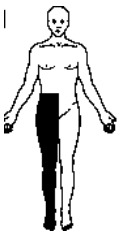
Multiple lesions:	■ Vasculitis ■ Hereditary Neuropathy with Liability to Pressure Palsy (HNPP) ■ Infection	
Single lesion:	■ **Radiculopathy**	Spinal **root** lesions (radiculopathy) **Pain is a key finding**. This affects a group of muscles supplied by a spinal root (myotome) and a sensory area supplied by a spinal root (dermatome). **Therefore, the distribution of affected areas can help differentiate this from a peripheral neuropathy or a plexopathy.** Patients may present with weakness, atrophy, and sensory deficits in a dermatomal pattern; may include fasciculations and diminished deep tendon reflexes. **Etiology** • Compressive: herniated disc, spondylosis, tumor. • Infiltrative: tumor seeding, infection. • Inflammatory: immune-mediated.

Pattern4: Asymmetric proximal & distal weakness with sensory loss

■ **Plexopathy**

Deficits (motor and sensory) involve more than one nerve. Findings are variable depending on which part of the plexus is involved. Trauma is the most common cause overall, especially for the brachial plexus. A postsurgical hematoma in the pelvis is a more common cause in lumbosacral 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? Because 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.

Plexuses that are commonly involved include:

- Brachial plexus—Erb–Duchenne type is the more common (upper trunk—C5–6 roots). Lower trunk (C8-T1) is less common.
- Lumbosacral plexus (L5-S3)

Pattern 5: Asymmetric distal weakness without sensory loss.

With UMN:	Without UMN:
■ **ALS (Amyotrophic lateral sclerosis)**  A disorder affecting the anterior horn cells and corticospinal tracts at many levels. **Corticobulbar involvement is common as well**. **The presence of upper and lower motor neuron signs is a hallmark of ALS.** Note that only the motor system is involved. Signs & symptoms: • Progressive weakness in legs & arms. • Trouble with swallowing or speaking. • Frequent muscle twitching & spams. **Onset is usually between 50 and 70 years of age.** Occurrence of ALS before age 40 is uncommon. Only 10% of cases are familial, with the remainder being sporadic. Prognosis is dismal: 80% mortality rate at 5 years; 100% mortality rate at 10 years.	MMN (Multifocal motor neuropathy)

Pattern 6: Symmetric sensory loss & upper motor neuron signs with proprioceptive loss.

■ **B12 deficiency (Subacute combined degeneration of the cord)**

Usually with underlying disorder that interferes with B12 absorption → Pernicious anemia

Signs & symptoms:

- Tingling, numbness & weakness in legs, arms & trunk.
- Change in mental status.
- Diminished sensations → Sensory ataxia.
- Positive Babinski sign
- Positive Rhomberg sign

Treatment: Reversible with B12 replacement

■ ALD (Adrenoleukodystrophy)

Pattern 7: Symmetric weakness proximal & distal without sensory loss.

■ SMA (spinal muscular atrophy)

Pattern 8: Focal midline proximal symmetric weakness with upper motor neurons.

■ ALS

Pattern 9: Asymmetric proprioceptive loss without weakness.

■ Ganglionopathy

Pattern 10: Autonomic dysfunction.

■ (seen in DM & GBS)

Entrapment syndrome: الدكتور خلال الشرح شرح كيسنز ومنها وحدة فيها النار نوروباثي فمروا هالجزئية

- Focal compression or entrapment is the usual cause of a mononeuropathy.
- Symptoms and signs of entrapment neuropathy are listed in Box 26.102. Entrapment neuropathies may affect anyone, but diabetes, excess alcohol or toxins, or genetic syndromes may be predisposing causes. Unless axonal loss has occurred, entrapment neuropathies will recover, provided the primary cause is removed, either by avoiding the precipitation of activity or by surgical decompression.

26.102 Symptoms and signs in common entrapment neuropathies

Nerve	Symptoms	Muscle weakness/ muscle-wasting	Area of sensory loss
Median (at wrist) (carpal tunnel syndrome)	Pain and paraesthesia on palmar aspect of hands and fingers, waking the patient from sleep. Pain may extend to arm and shoulder	Abductor pollicis brevis	Lateral palm and thumb, index, middle and lateral half 4th finger
Ulnar (at elbow)	Paraesthesia on medial border of hand, wasting and weakness of hand muscles	All small hand muscles, excluding abductor pollicis brevis	Medial palm and little finger, and medial half 4th finger
Radial	Weakness of extension of wrist and fingers, often precipitated by sleeping in abnormal posture, e.g. arm over back of chair	Wrist and finger extensors, supinator	Dorsum of thumb
Common peroneal	Foot drop, trauma to head of fibula	Dorsiflexion and eversion of foot	Nil or dorsum of foot
Lateral cutaneous nerve of the thigh (meralgia paraesthetica)	Tingling and dysaesthesia on lateral border of thigh	Nil	Lateral border of thigh

Key-words:

- Proximal weakness + Distal weakness + Symmetric + Sensory symptoms = **inflammatory** (GBS or CIPD – with acute presentation).
- Proximal weakness + Distal weakness + Asymmetric + Sensory symptoms = **Radiculopathy** (nerve roots supply multiple proximal and distal muscles
  - C7 nerve root supplies which muscle in the arm? Triceps, extensor digitorum communis (weakness → finger drop).
- Distal weakness + Symmetric + Sensory symptoms = **Metabolic** (vitamin deficiency), **Diabetic neuropathy**, **Idiopathic**.
  - length dependent, numbness, and شوية weakness.
- Distal weakness + Asymmetric + Sensory symptoms = **vasculitis with nerve infarct** (that's why it's asymmetric), **compressive**
- Upper motor neuron signs? **Cord involvement** (Myelopathy: deficiency or compressive) or motor neuron disease such as **ALS** that gives proximal & distal weakness.
- Autonomic symptoms = **Autonomic neuropathy**.
- Severe proprioceptive loss = **dorsal root ganglia** or **spinal cord** (dorsal column).

★ **Pattern recognition summary (from the article)**

MCQs

1) A 55 years old female presented with sensory loss and incoordination in both upper and lower limbs for 5 months. Her neurological examination showed normal muscle power and absent reflexes. She had sensory loss to pinprick, vibration and position in both upper and lower limbs. Which one of the following localization describe pattern is associated with?

A. Anterior horn cell
B. Diffuse Peripheral Nerves
C. Dorsal root ganglia
D. Neuromuscular Junction

2) A 18 years old male presented with weakness and numbness for 5 years. On examination he had high arched feet. Reflexes was absent. Sensory examination showed abnormal sensation to pinprick and vibration. Muscle power was 2/5 distally, 4/5 proximally in lower limbs. And 3/5 distally, 5/5 proximally in upper limbs.

Which one of the following is the most appropriate description for his neuropathy?

A. Diabetic Neuropathy
B. Inherited Neuropathy
C. Toxic Neuropathy
D. Vitamin B12 Deficiency

Answer key:

1 (C) | 2 (B)