Peripheral Neuropathy

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Introduction

- Classification
- Approach to PN
- Pathology
- Mononeurpathies
- Polyneuropathies:
  - Hereditary
  - Acquired
- Plexus lesions

Classification

- Anatomical:
  - Peripheral nerve lesion
  - Root & plexus
- Pathological:
  - Demyelinating
  - Axonal
- Etiology
  - Hereditary
  - Acquired

Clinical History

- Time course:
  Acute: GBS, diphtheria, porphyria.
  Gradual: CIDP, hereditary, metabolic
- Age of onset: HPN, Cancer,
- Medical history: as DM, collagen diseases
- Drug & alcohol history: As chemotherapy ,
- FH
- Occupational history: as painters, manual work, exposures to heavy metals.

Differential Diagnosis of Neuropathies by Clinical Course

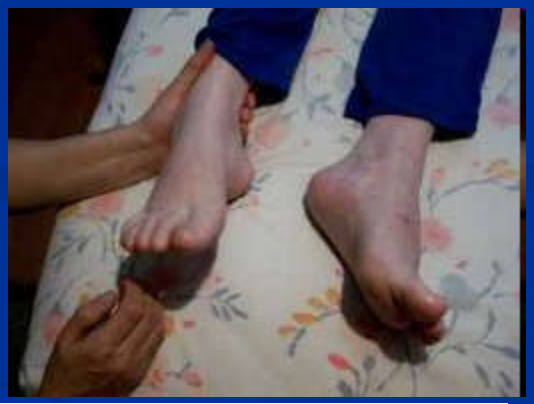
Relapsing/ remitting course	Chronic course/ insidious onset	Subacute onset (weeks to months)	Acute onset (within days)
Guillain-Barré syndrome	Hereditary motor sensory neuropathies	Maintained exposure to toxic agents/medications	Guillain-Barré syndrome
CIDP	Dominantly inherited sensory neuropathy	Persisting nutritional deficiency	Acute intermittent porphyria
HIV/AIDS	CIDP	Abnormal metabolic state	Critical illness polyneuropathy
Toxic		Paraneoplastic syndrome	Diphtheric neuropathy
Porphyria		CIDP	Thallium toxicity

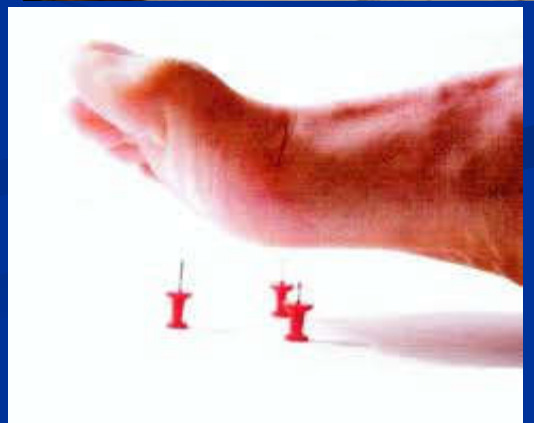
Symptoms

Motor	*Sensory*	*Autonomic*
Weakness	Paresthesia	Postural hypotension
Cramps	Dysesthesia	B/B dysfunction
Fasciculation	Pain	Impotence
	Loss of sensation	Impaired sweating

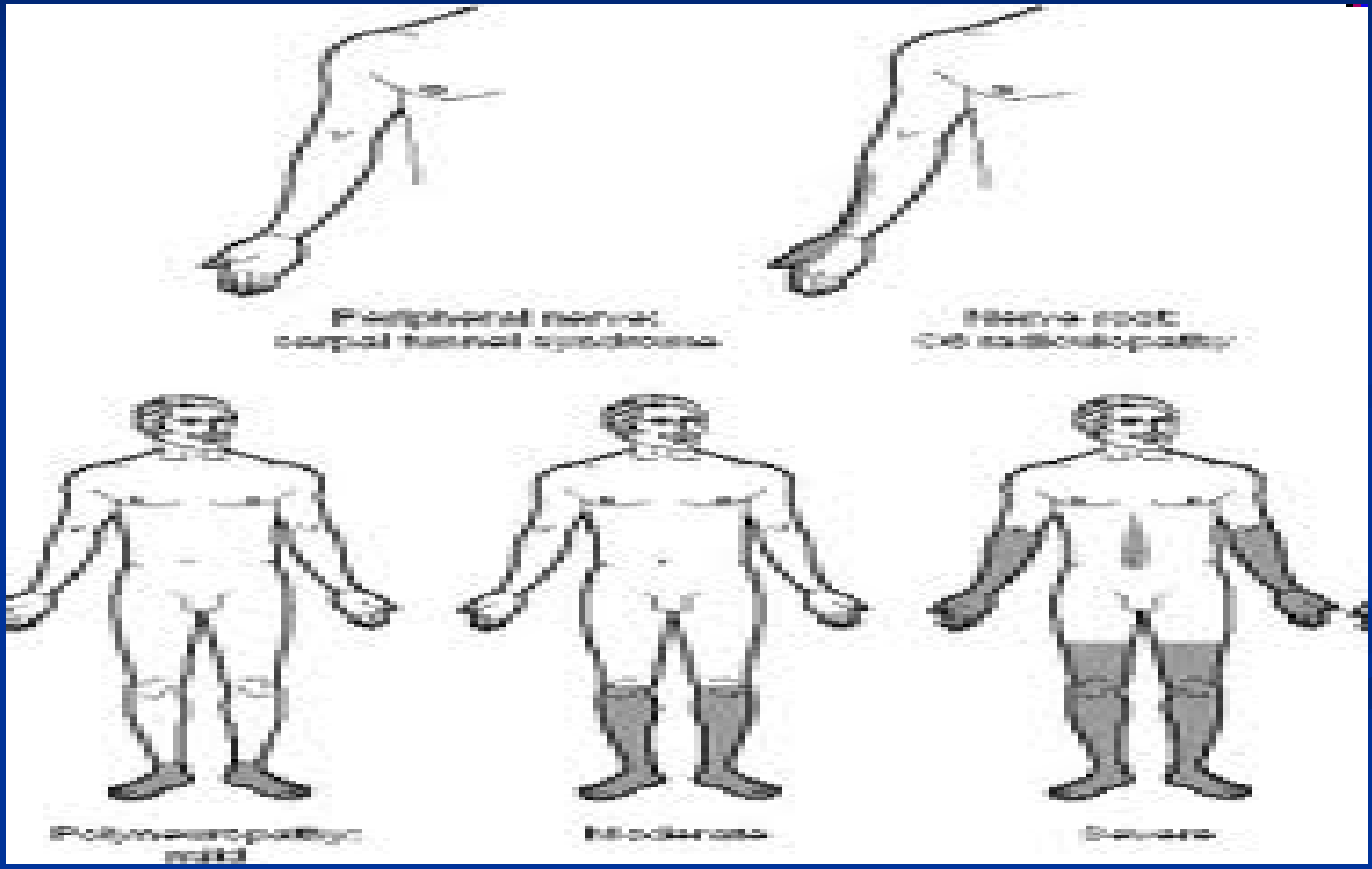
Complaint

Weakness
Pain
Burning
Thick soles
Walking on stones
Tingling
Imbalance





Distribution of numbness or weakness in peripheral neuropathy



Physical Examination

- Localize the deficit:
  - Mononeuropathy
    - Mononeuropathy multiplex
    - Polyneuropathy
- Motor; Sensory; Autonomic:
  - Predominantly motor
    - Predominantly Sensory
    - Autonomic involvement

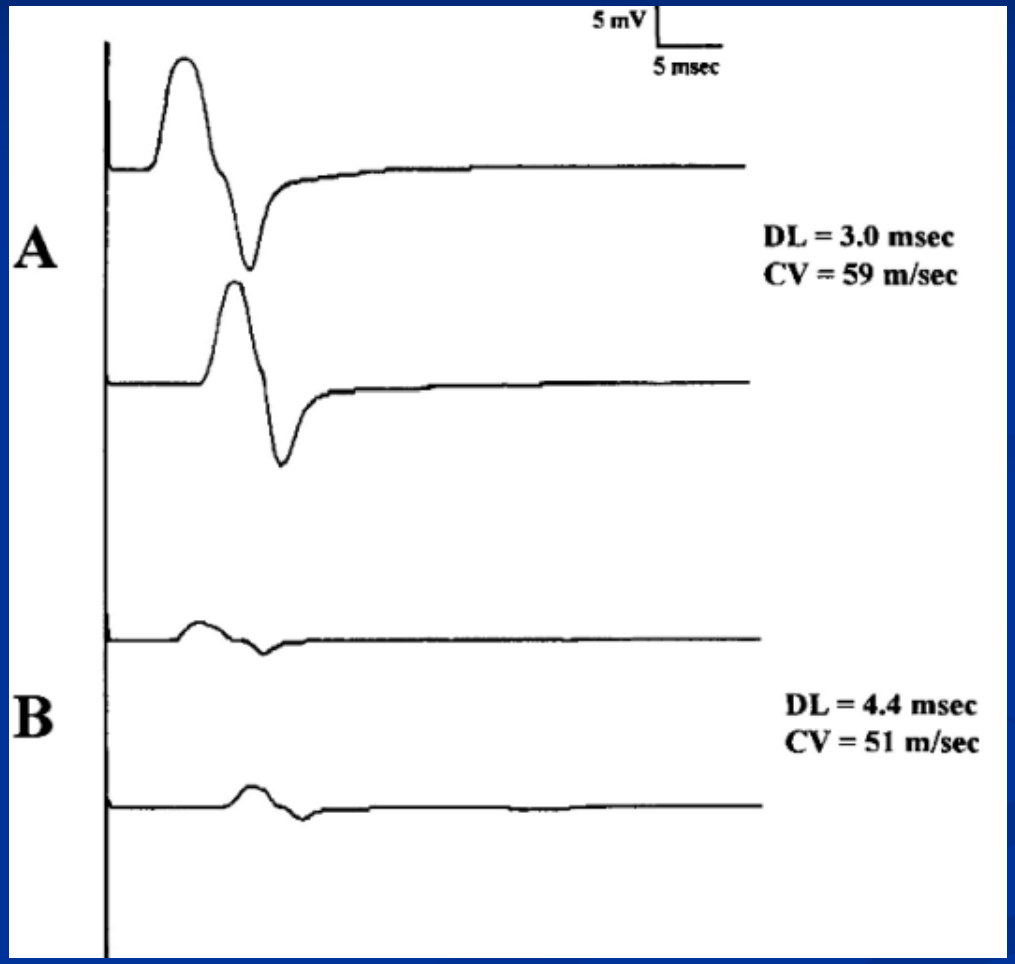
Causes of Neuropathy

- Inflammatory (blood vessels or myelin)
- Hereditary (Charcot Marie Tooth)
- Metabolic (diabetes, liver, kidney)
- Toxic (alcohol, chemical exposure)
- Vitamin deficiency (B12, D, Thiamine…)
- Drug related (chemo drugs)
- Related to tumor (paraneoplastic)

Pathology

(1) Axonal Loss:
Most common
DM, RF, Hereditary
Distal weakness
Absent reflexes
Distal sensory loss
NCS
Partial recovery

NCS of axonal neuropathy



Causes of axonal neuropathy

Box 6: Chronic axonal neuropathies

- Drugs or toxins
  - alcohol
  - chemotherapeutic agents—for example, vincristine, cisplatinum
  - organophosphate
  - phenytoin
  - antibiotics—for example, metronidazole, dapsone
  - statins
- Infections
  - leprosy
  - Borrelia
  - HIV, HTLV1
- Connective tissue diseases
  - Sjogren's syndrome
  - systemic lupus erythematosus
  - rheumatoid arthritis
- Metabolic
  - diabetes
- Paraneoplastic
  - lung, ovarian carcinoma
- Inherited
  - CMT 2 and X
  - familial amyloid neuropathies
- Vitamins
  - vitamin B12
  - vitamin E
  - pyridoxine toxicity
- Endocrine
  - hypothyroidism
- Paraprotein
  - myeloma
  - Waldenstrom's disease
  - benign monoclonal gammopathies

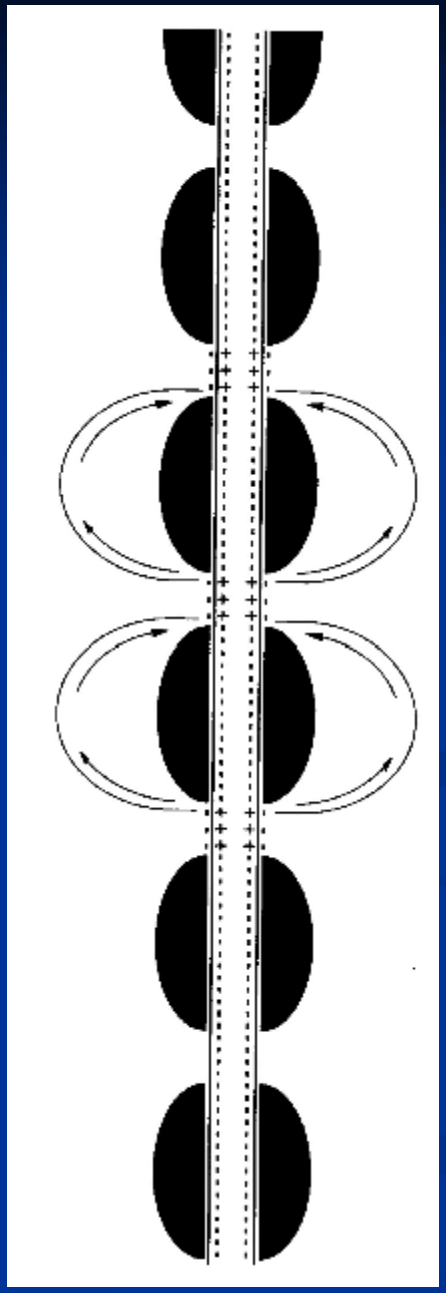
(2) Myelin loss:

- Hereditary
- Immune-mediated neuropathies (GBS)
- compression
- Weakness
- Absent reflexes
- Better prognosis
- NCS
- Onion bulb

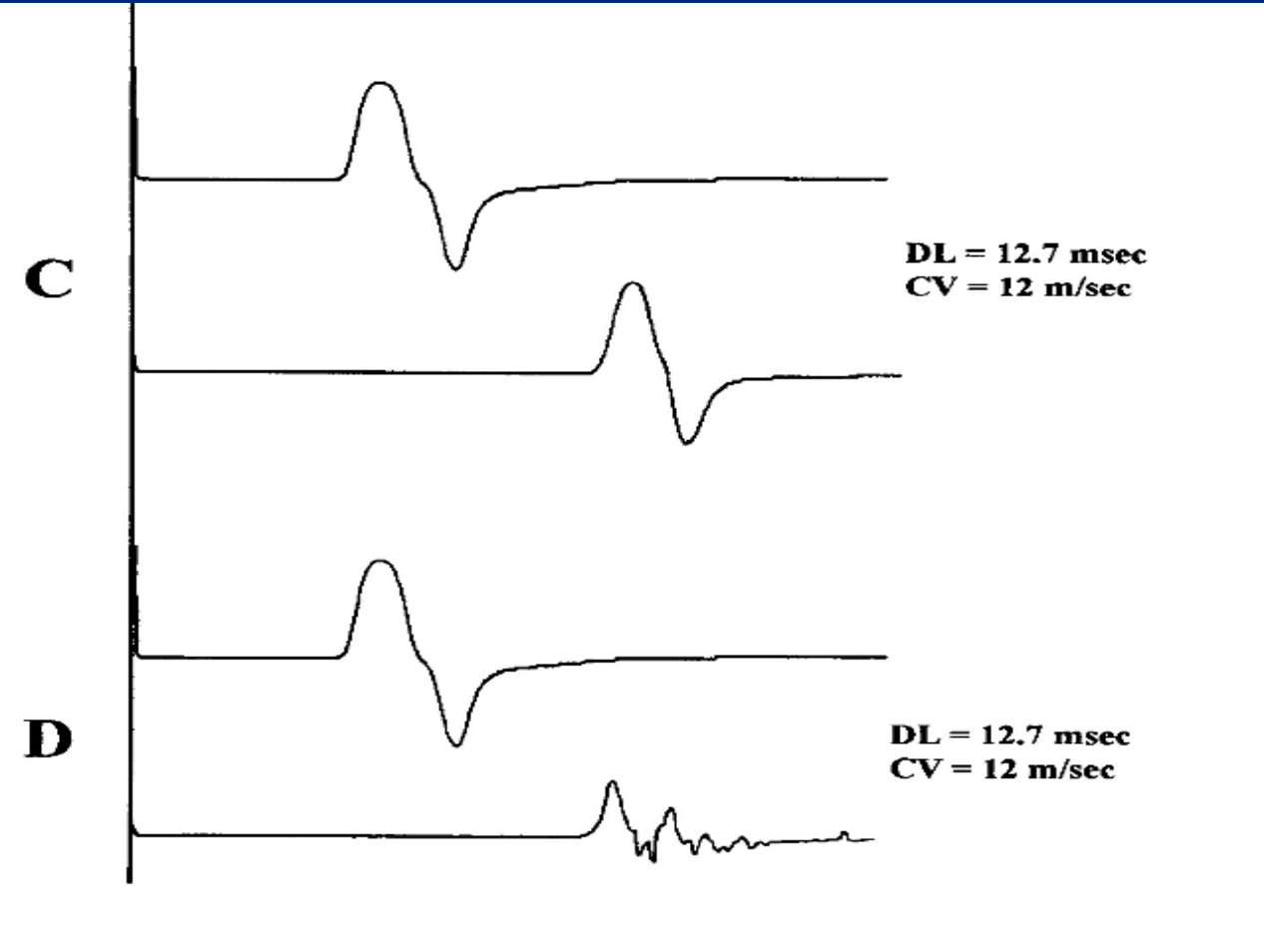
Causes of demyelinating neuropathy

Box 2: Demyelinating neuropathies

- Acute
  - Guillain Barre syndrome (GBS)
- Chronic
  - chronic inflammatory demyelinating polyradiculo-neuropathy (CIDP)
  - paraproteinemia related
  - amiodarone toxicity
  - Refsum's disease
  - Charcot-Marie-Tooth (CMT) types 1, X and AR CMT 1
  - metachromatic leucodystrophy
  - statins



NCS of demyelinating neuropathy

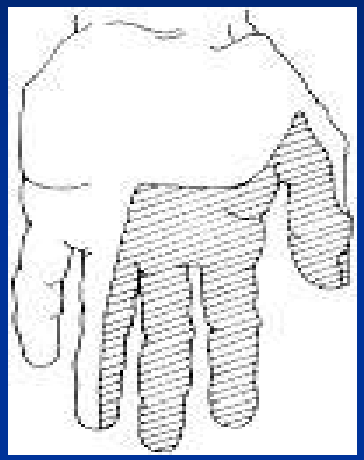


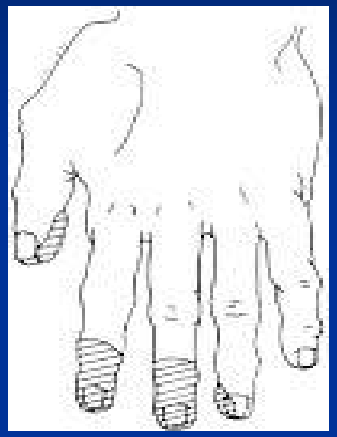
Mononeuropathies

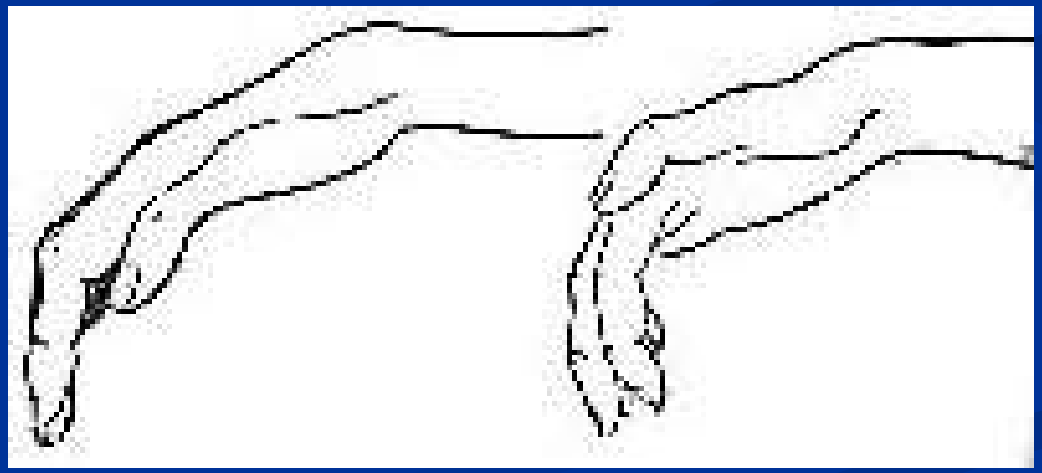
(1) Median Neuropathy

- Most common
- CTS: Most common
- Women 3:1, DM, rheumatoid arthritis, hypothyroidism, pregnancy
- Nocturnal numbness or pain
- Dropping things: APB weekness
- + Tinel's, phalen's signs
- NCS/EMG
- Splinting vs. surgical decompression

Median Nerve lesion

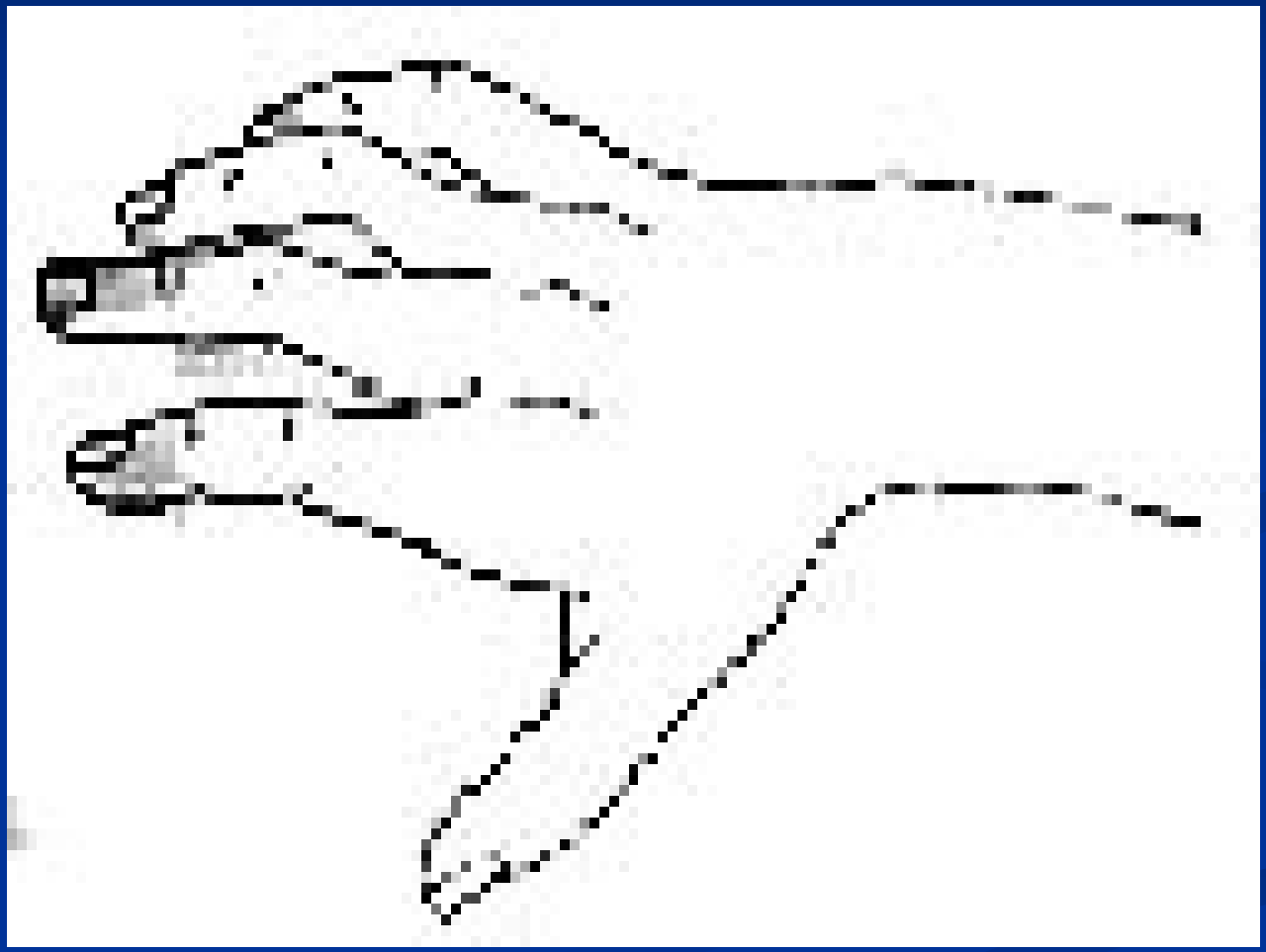






(2) Ulnar Neuropathy

- Elbow
  Trauma, bone deformity, leprosy, idiopathic
- Elbow pain
- Intrinsic hand muscle weakness
- Paresthesia
- NCS/EMG
- Conservative vs. surgery



(3) Radial Neuropathy

- Humerus fracture
- Pressure palsy
- Crutches
- Wrist drop, other extensors
- Triceps & brachialis reflexes
- Dorsal sensory loss
- NCS/EMG

(4) Common Peroneal Neuropathy

- Compression:
  Coma, prolonged bed rest, crossed legs
- Trauma
- Systemic disorders:
  HNPP, DM, Leprosy
- Foot drop, steppage gait
- NCS/EMG
- Conservative ttt & physiotherapy

Polyneuropathies

Diagnostic Approach

- The differential diagnosis of peripheral neuropathy is significantly narrowed by a focused clinical assessment that addresses several key issues –
  - Does the patient actually have a neuropathy?
  - What is the pattern of involvement?
  - Is the neuropathy focal, multifocal or symmetric?
  - If the neuropathy is symmetric, is it proximal or distal?

Does the patient actually have a neuropathy?

- Causes of generalized weakness include motor neuron disease, disorders of the neuromuscular junction and myopathy.
- Peripheral neuropathy can also be mimicked by myelopathy, syringomyelia or dorsal column disorders, such as tabes dorsalis.
- Hysterical symptoms can sometimes mimic a neuropathy.

Is the neuropathy focal, multifocal or symmetric?

- Focal neuropathies include common compressive neuropathies such as carpal tunnel syndrome, ulnar neuropathy at the elbow or peroneal neuropathy at the fibular head

- A multifocal neuropathy suggests a mononeuritis multiplex that may be caused, for example, by vasculitis or diabetes

If the neuropathy is symmetric, is it proximal or distal?

- Most toxic and metabolic neuropathies present as a distal symmetric or dying-back process.
- Proximal sensory neuropathies are rare and include porphyria.
- Predominantly motor neuropathies are often proximal and include acquired inflammatory neuropathies such as Guillain-Barré syndrome.
  - An exception is lead neuropathy, which initially affects motor fibers in radial and peroneal distributions.

Differential diagnosis of wasting of small muscles of the hands.

- *Lesions of the AHCs*

(A) lesions of acute onset e.g poliomyelitis, Acute cord compression AHCs

(B) Lesions of slow onset e.g. MND:.

- *Syringomyelia:*
- *Spinal cord tumours.*
- *Syphilitic meningomyelitis or in arachnoiditis*
- *Lesions of spinal nerves "Root avulsion".*
- *Lesion of brachial plexus.*
- *Lesions of peripheral nerves (median and ulnar)*
- *Muscle lesions*
- *Trophic disorders*

Physical Examination

- **The motor examination includes a search for fasciculations or cramps, or loss of muscle bulk.**
- **Tone is normal or reduced**
- **The pattern of weakness helps narrow the diagnosis: symmetric or asymmetric, distal or proximal, and confined to a particular nerve, plexus or root level**
- **Deep tendon reflexes are reduced or absent.**
- **Gait :high steppage gait , stamping gait .**

- Proximal weakness results in an inability to squat or to rise unassisted from a chair
- The general physical examination can provide evidence of orthostatic hypotension without a compensatory rise in heart rate when autonomic fibers are involved.
- Respiratory rate and vital capacity should be evaluated in Guillain-Barré syndrome to assess for respiratory compromise.

- The presence of lymphadenopathy, hepatomegaly or splenomegaly, and skin lesions may provide evidence of systemic disease.

Hereditary Neuropathies

(1) Charcot-Maries-Tooth

Distal weakness

Wasting

Absent reflexes

Pes cavus

Demyelinating (CMT1); Axonal (CMT2)

AD, AR, X-linked

(2) Friedreich's Ataxia:
AR
Trinucleotide repeat (9q13-21)
Sensory loss
Absent reflexes

(3) HNPP:
AD
Simple or multiple mononeuropathies at compression sites

Acquired Neuropathies

(1) Acute Idiopathic Inflammatory Polyneuropathy (GBS or AIDP

- Clinical Features:
  Acute to subacute
  Preceding febrile illness (Flue, GI, Vaccine..)

Proximal & ascending symmetrical weakness

Respiratory involvement

Sensory complaints (subjective)

Absent reflexes

Autonomic : hypotension and arrhythmias, sphincter intact and if affected only transient

CN may be involved

4 w progression 4 w stationary 4 w regression

Diagnosis and treatment

- Clinical features
- investigation
  - ↑ CSF protein
  - Normal CSF cell count (<10)
  - NCS:
  - Slow motor velocity
- treatment:
  - Plasmapharesis, IVIG
  - Symptomatic: Respiratory, DVT, Autonomic, Nutrition….and physiotherapy
- Prognosis: good

(2) Chronic inflammatory Demyelinating Polyneuropathy (CIDP)

- Chronic progressive or relapsing course
- Similar to GBS
- Similar CSF
- Electrodiagnosis:
  Demyelinating & axonal
- Steroids
- Plasma exchange, IVIG
- Immunosuppression

Diabetic peripheral neuropathy

- DM is one of the most common causes of disableing polyneuropathy.
- DPN was present in 66% of IDDM and 59% NIDDM.
- However only 20% are symptomatic

Etiology of DPN

- ***Hyperglycemic –polyol-myoinositol hypothesis***:

Glucose— Hexokinase Glucose 6 phosphate→ Krebs's cycle

In diabetics glucose inter to polyol pathway with excess production of sorbitol and increase of intracellular myoinositol

This result in defective of **Na/ K ATPase** activity leading to reduction of axonal transport

Other theories

- **Microangiopathy:**
- **Structural change at the node of Ranvier**: **ATPase** deficiency increase of Na lead to detachment of myelin and dying back of axon
- **Vsaculitic neuropathy**: lymphocytic inflammatory vasculopathy as in painful proximal diabetic neuropathy.
- **Nerve growth factor deficiency**:

  Skin of foot of diabetics show marked reduction of **NGF** which responsible on small sensory fiber neuropathy.

Classification of diabetic neuropathy

- Two classification systems for diabetic neuropathy are the Thomas system and the symmetrical-versus-asymmetrical system.
- The Thomas system (modified) is as follows:

The Thomas system classification

- Hyperglycemic neuropathy
- Generalized symmetrical polyneuropathies
- Sensory neuropathy
- Sensorimotor neuropathy
- Autonomic neuropathy
- Focal and multifocal neuropathies
- Superimposed chronic inflammatory demyelinating polyneuropathy

Distal symmetrical sensorimotor polyneuropathy

- Distal symmetrical sensorimotor polyneuropathy is most common for of diabetic neuropathy and defined according to the following 3 key criteria**:**

1. The patient must have diabetes mellitus consistent with a widely accepted definition.
2. Severity of polyneuropathy should be correlate with duration and severity of diabetes.
3. Other causes of sensorimotor polyneuropathy must be excluded

Asymmetrical neuropathies include the following:

- Median neuropathy of the wrist (carpal tunnel syndrome)
- Other single or multiple limb mononeuropathies
- Thoracic radiculoneuropathy
- Lumbosacral radiculoplexus neuropathy
- Cervical radiculoplexus neuropathy

Clinical features of diabetic polyneuropathy

- **Mainly sensory** :paraesthesiae and pain
- Deep sensation affection and sensory ataxia
- "Neuropathic Arthoropathy"

  most affected joint tarsometatarsal then metatharsophalengial joint
- Unrecognized fractures
- Ulcers
- **If** prominent motor features must suspect **CIDP**

Acute painful diabetic neuropathy

- Acute or subacute burning lower limb pain with marked **cutanous hyperalgesia**, with **no** definite **distal sensory loss**, and **slight reduction of ankle jerk**
- So may confusing as **psychogenic condition** specially that **70%** of cases associated with **depression**
- Most of cases associated with **rapid weight loss**
- And usually follow tight gylcemic control

Diabetic truncal radiculoneuropathy

- Attacks of truncal pain with no specific sensory disturbance of abdomen
- Occur in fifth to seventh decades female with type2 DM
- Focal abdominal wall paralysis and increase of abdominal protuberance
- Marked weigh loss ?????

Diabetic proximal neuropathy

- The disorders range from familiar extreme of **acute asymmetrical painful proximal weakness within days to painless symmetrical proximal weakness occur over weeks or months**
- The disorders carry many terms as: **Diabetic** (myelopahty, amyotrophy, myopathy, radiculopathy, lumber radiculopathy, or neuropahtic cachexia).

Clinical features

- Occur in fifth to seventh decades in type2 DM
- Anterior thigh muscle pain usually first presenting symptoms
- Characteristic involvement of ***quadriceps*** weakness
- Lost knee jerks
- Extensor planter
- In spite of unilateral onset **50%** of cases bilateral affection within few weeks
- Marked weight loss
- Increase of CSF protein ???

Mononeuropathy and cranial neuropathy

- **Mononeuropathy**: as CTS
- **Cranial neuropathy** :

Either ischemic or vasculitic ???

Most common affected nerves are ocular nerves third, sixths and less common fourth

Other nerves may be affected specially facial and usually preceded by pain around ear ????

Autonomic neuropathy

- Is the most serious and disabling neuropathy with DM

- Most of functional abnormalities of organ as kidney, heart, retina , bladder ect…. Are due to sympathetic denervation of these organs .

Sweating abnormalities

- Abnormal sweating is the first presenting symptoms of autonomic neuropathy which precede other symptoms by many years as:

1. **Defective sweating** in foot
2. **Gustatory sweating** which highly characteristic symptoms of diabetic autonomic neuropathy.

Orthostatic hypotension

- ↓of systolic Bp >30 mmHg or diastolic > 10 with setting position
- Features:

1. Headedness, dizziness with longstanding or when patient awake from sleep
2. Gray mistiness of vision follow by curious pain in back of neck and shoulders " **coat hanger**" distribution and later loss of consciousness
3. **Orthostatic hypotension worse** with of **insulin** due to reduction of peripheral vascular resistance with insulin

Thank you