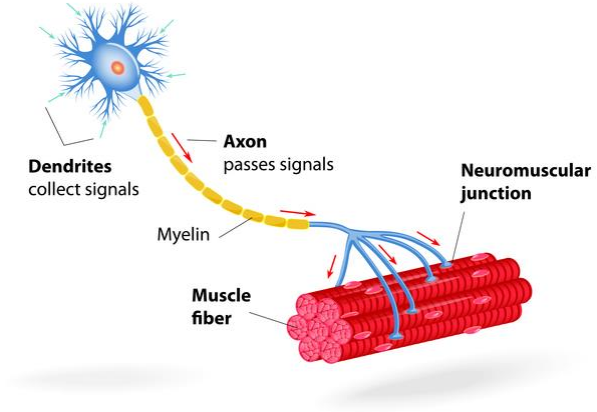
SUBSAHARAN REGIONAL TRAINING COURSE 11
ACCRA, GHANA 4-7 SEPTEMBER 2019

NEUROPATHIES AND MYOPATHIES IN THE ADULT AND ELDERLY



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OUTLINE

- When will you see a patient with a neuropathy or myopathy?
- Definition of neuropathies and myopathies
- Causes of neuropathies and myopathies in the adult and elderly patient
- Examination of the patient presenting with neuropathies and myopathies
- Investigating a patient with neuropathies and myopathies
- Management

Reasons for seeking medical attention

- PAIN
- Abnormal gait
- Falls
- Overt muscle weakness
- Muscle cramps
- Muscle stiffness

WHAT IS PAIN?

Definitions of pain

- • Pain is a complex unpleasant phenomenon composed of sensory experiences that include time, space, intensity, emotion, cognition, and motivation
- • Pain is an unpleasant or emotional experience originating in real or potential damaged tissue
- • Pain is an unpleasant phenomenon that is uniquely experienced by each individual; it cannot be adequately defined, identified, or measured by an observer

Definition of Pain

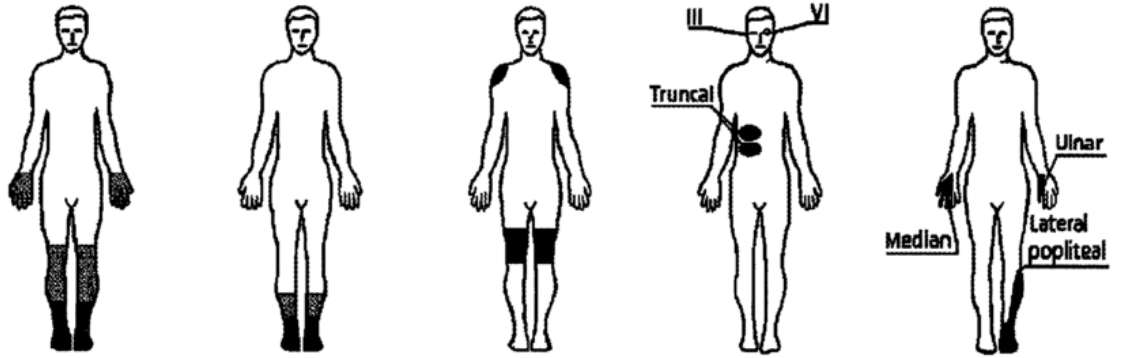
International Association for the Study of Pain

- An unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage
- Sensory, emotional, cognitive, and behavioral components that are interrelated with environmental, developmental, socio-cultural, and contextual factors

Neuropathy? Myopathy?

Features suggestive of neuropathy:

- Sensory loss may be present
- Fasciculations may be present
- There may be cranial nerve involvement
- There may be dysautonomia



Large-fibre neuropathy	Small-fibre 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: +→ +++

Definition of Neuropathy

- Generalized term including disorders of any cause affecting PNS
- May involve **sensory** nerves, **motor** nerves, or both
- May affect one nerve (**mononeuropathy**), several nerves together (**polyneuropathy**) or several nerves not contiguous (**Mononeuropathy multiplex**)
- Further classified into those that primarily affect the cell body (e.g., **neuronopathy or ganglionopathy**), myelin (**myelinopathy**), and the axon (**axonopathy**)

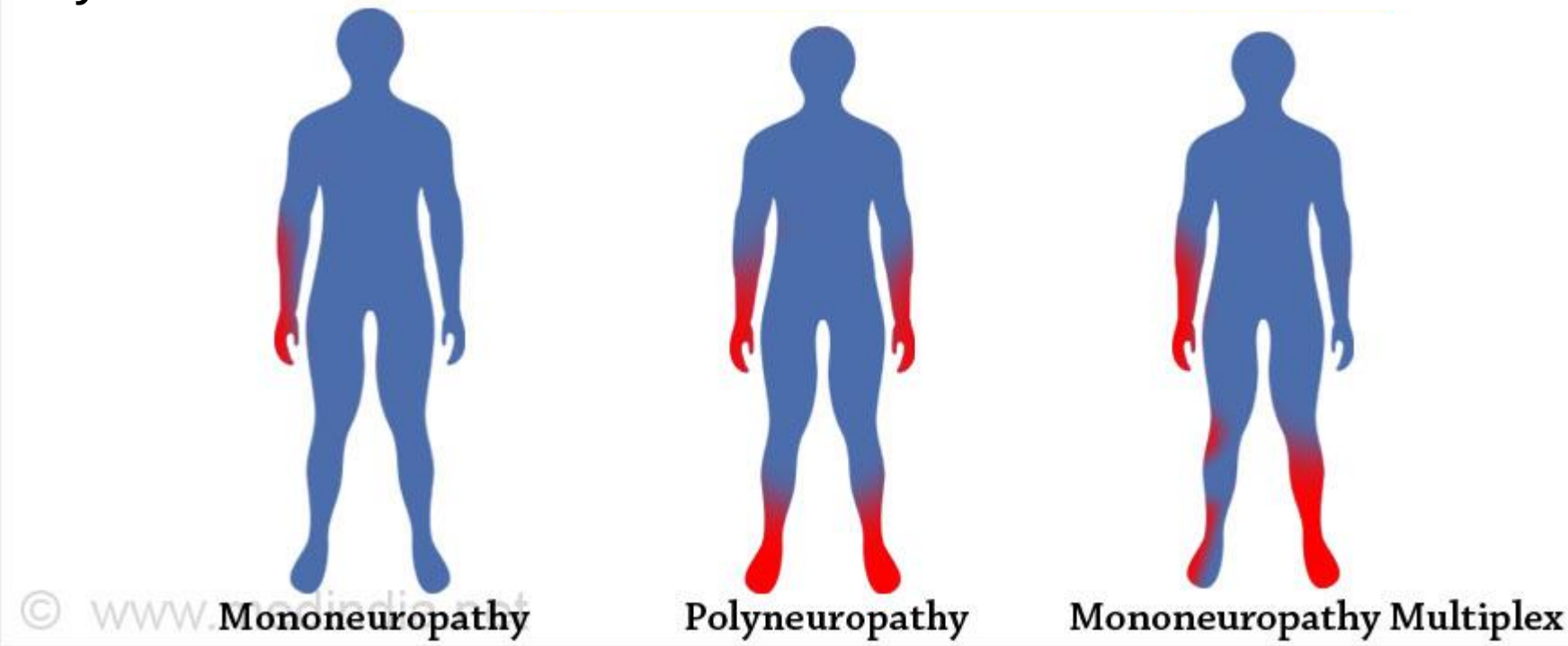
Most common causes

Disease	Prevalence
Diabetes[1 2]	11-41% (depending on duration, type, and control)
Paraproteinaemia[2 3]	9-10%
Alcohol misuse[1]	7%
Renal failure[1]	4%
Vitamin B-12 deficiency[1]	3.6%
HIV infection[1]	16% (depending on the population studied, usually much lower)
Chronic idiopathic axonal neuropathy[4]	10-40% of different hospital series

BMJ 2010:341:c6100

Patterns of neuropathy

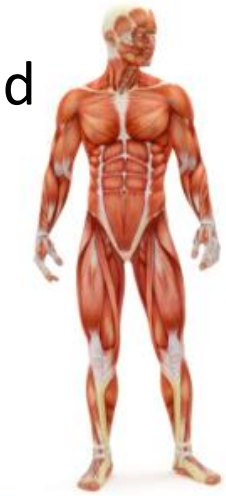
- Mononeuropathy
- Multiple mononeuropathy
- Polyneuropathy



Neuropathy? Myopathy?

Features suggestive of myopathy:

- The sensory supply should be preserved
- The reflexes should be preserved – can be absent in severe muscle disease
- Weakness predominantly **proximal**
- There should be no fasciculations
- There may be myocardial involvement (skeletal myopathies tend to be associated with cardiomyopathy)
- The muscles involved may be painful and tender(as in myositis)
- There may be muscle contractures, requiring splints



Neuropathy? Myopathy?

	Muscle bulk	Tone	Strength	DTR	Plantars	sensation	fasicualtion
UMN	N	⇑	N	⇑	⇑	N	-
Ant horn cell	Prox wasting	⇓	Prox weakness	⇓⇓	⇓	N	+
P nerve	Distal wasting	⇓	Distal weakness	Distal ⇓	⇓	⇓	rarely
NMJ	N	N	fatigues	N- ⇑	⇓	N	-
Muscle	selective	⇓	⇓	⇓	⇓	N	-

Causes of Neuropathies and Myopathies

- **NEUROPATHIES**
  - **Inflammatory**
  - **Infectious**
  - **Hereditary**
  - **Acquired Toxic/Metabolic**
  - **Traumatic**
  - **Neoplasms**

- **MYOPATHIES**
  - **Denervation**
  - **Dystrophies**
  - **Ion Channel**
  - **Congenital**
  - **Genetic Metabolic**
  - **Inflammatory**
  - **Toxic**
  - **Neuro-Muscular Junction**
  - **Neoplasms**

The clinical response to sensory nerve injury

	Loss of function "- symptoms"	Disordered function "+ symptoms"
Sensory "Large Fiber"	↓ Vibration ↓ Proprioception Hyporeflexia Sensory ataxia	Paresthesias
Sensory "Small Fiber"	↓ Pain ↓ Temperature	Dysesthesias Allodynia

The clinical response to motor nerve injury

	Loss of function “- symptoms”	Disturbed function “+ symptoms”
Motor nerves Large fibre	Wasting Hypotonia Weakness Hyporeflexia Orthopedic deformity	Fasciculation Cramps

The clinical response to autonomic nerve injury

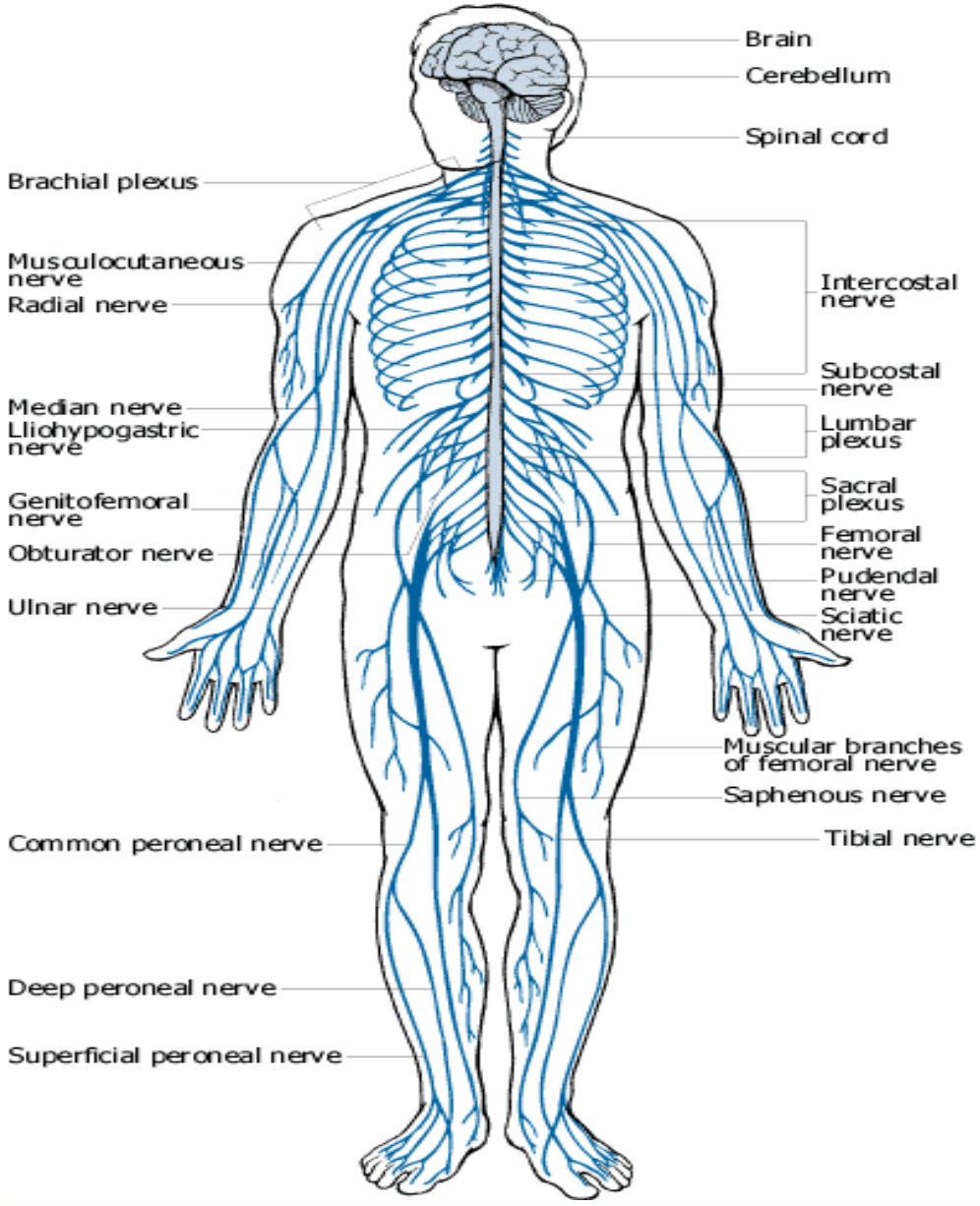
	Loss of function "- symptoms"	Disturbed function "+ symptoms"
Autonomic nerves	↓ Sweating Hypotension Urinary retention Impotence Vascular color changes	↑ Sweating Hypertension

The 3 principal questions …

#1. Where is the lesion?

#2. What is the etiology?

#3. What is the treatment?



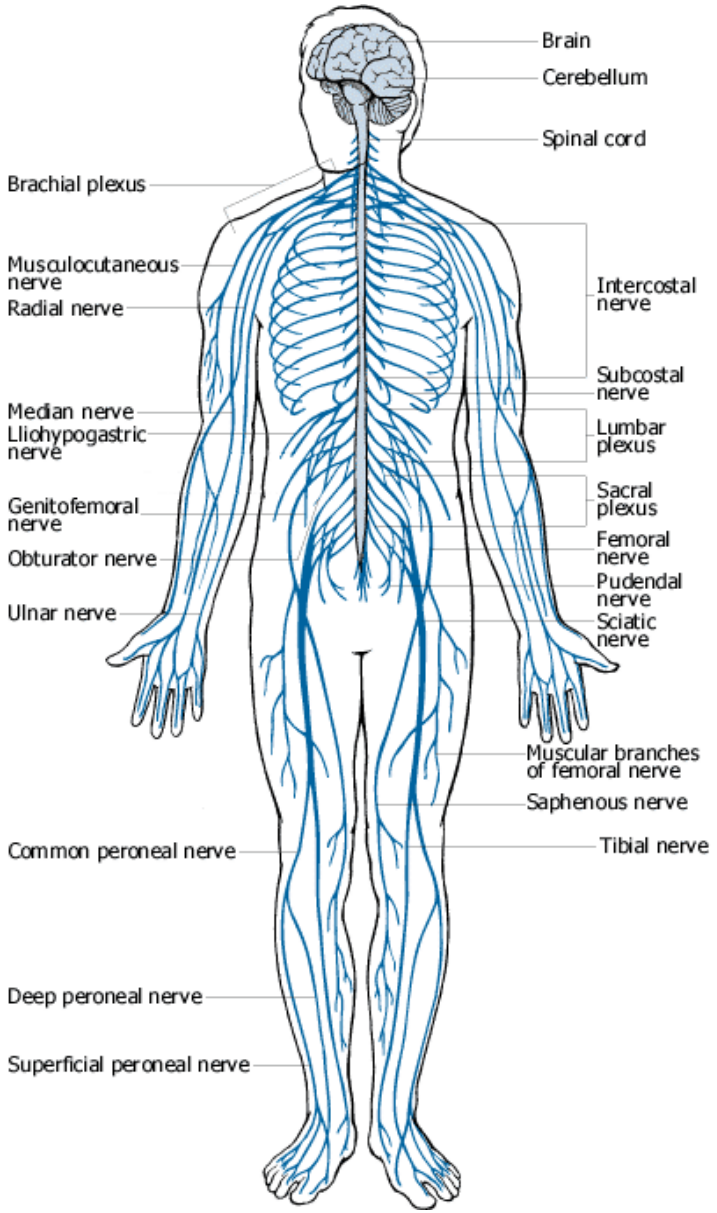
www.ama-assn.org/ama/pub/category/7172.html

The *patterns* of peripheral neuropathy…

- **Mononeuropathy?**

- **Polyneuropathy?**
  - **multiple nerves**
  - **contiguous**
  - **typically length dependent (“stocking-glove”)**

Polyneuropathy is common! 2.4% (8% over 55 yr)



www.ama-assn.org/_ama/pub/category/17220.html

Pathogenic Mechanism of Peripheral Nerve Damage

- Several changes are identified but are not disease specific:
  - Segmental Degeneration
  - Wallerian Degeneration
  - Axonal Degeneration
- Myelin sheath is the most susceptible to damage. It can break down as a primary process affecting Schwann Cells, myelin itself, or secondarily to the diseases affecting axon.

Mononeuropathy

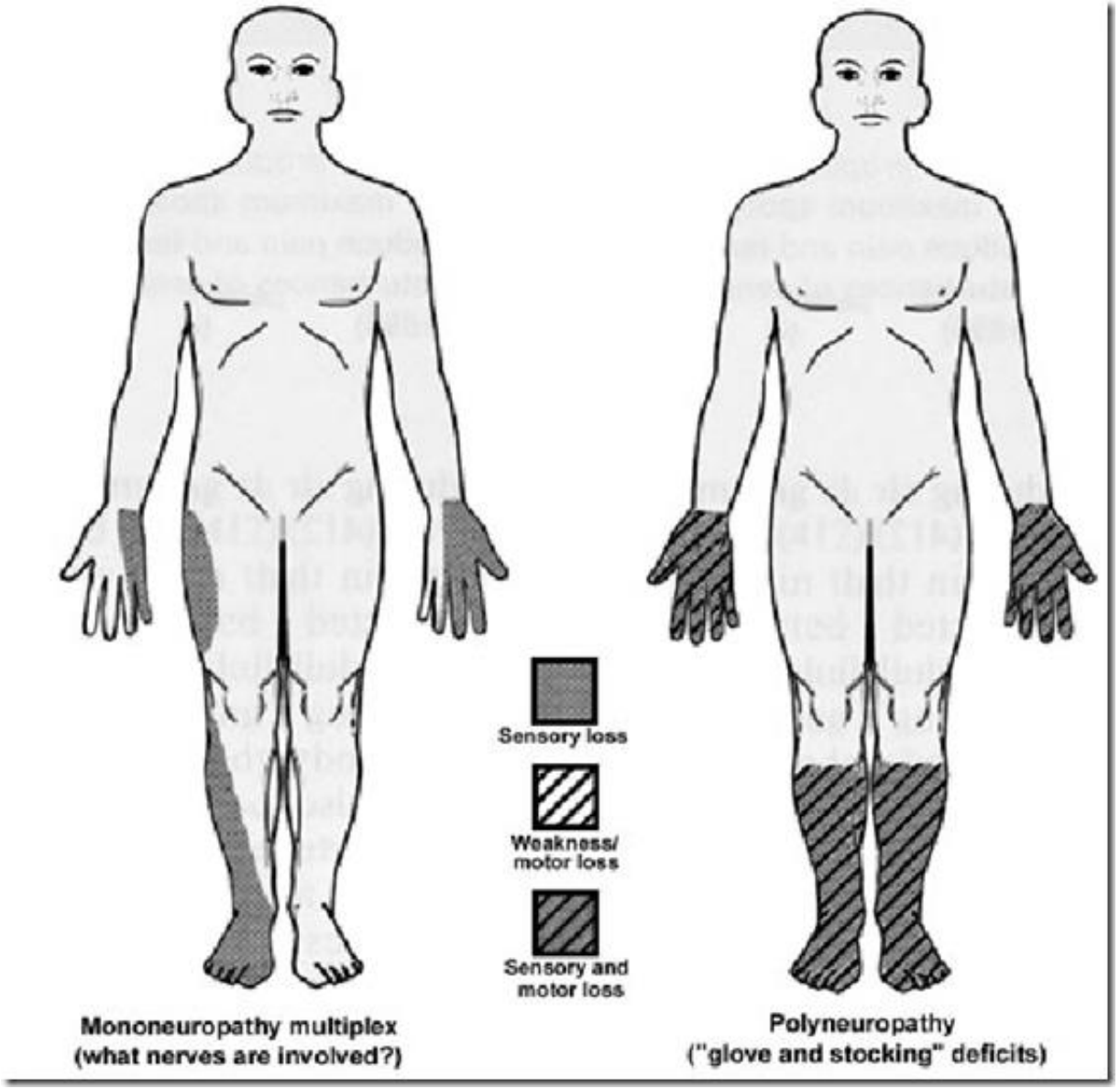
- Focal involvement of a single nerve and implies a local process:
- Direct trauma
- compression or entrapment
- vascular lesions
- neoplastic compression or infiltration

Mononeuropathy multiplex

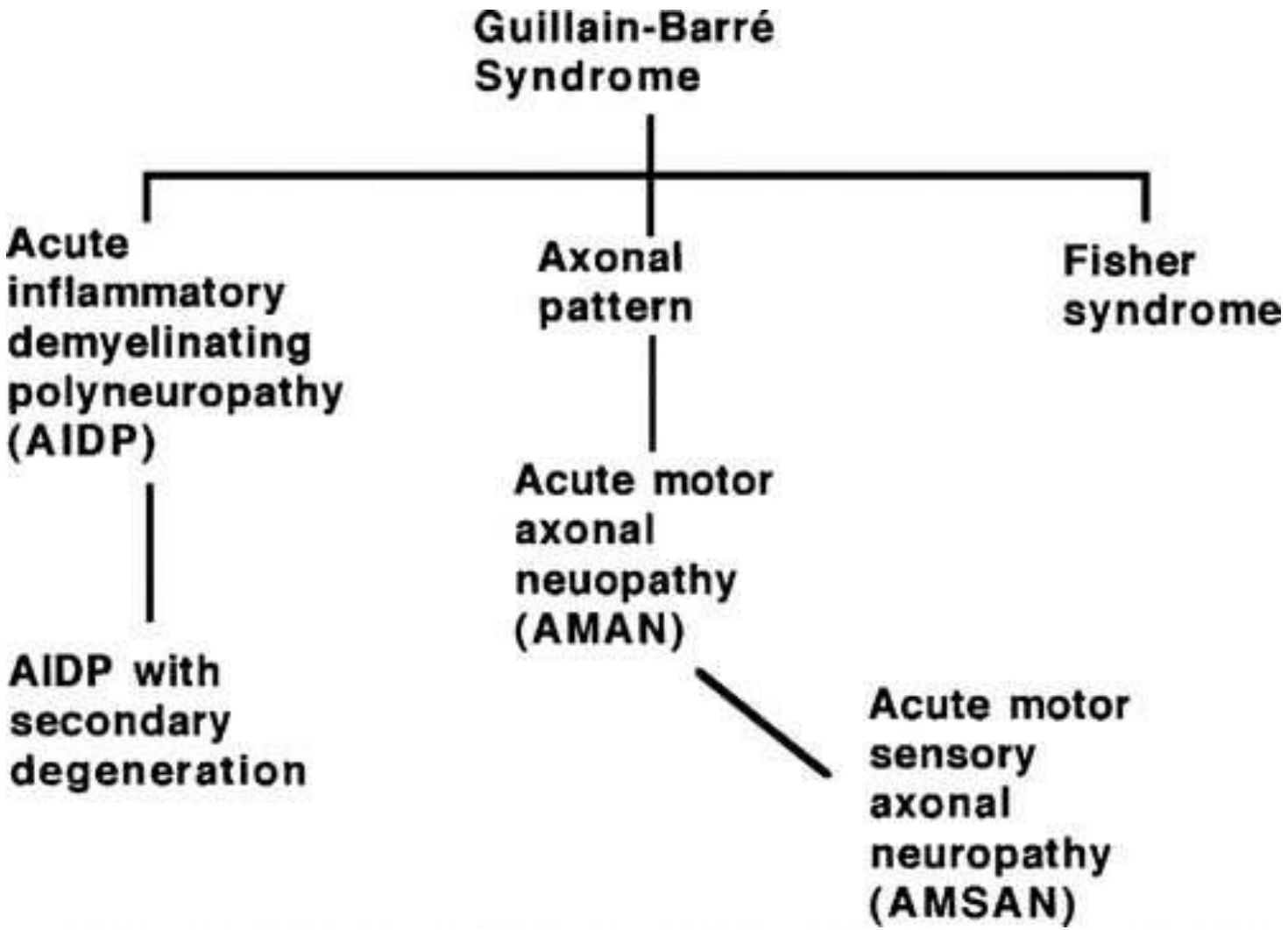
- simultaneous /sequential damage to **multiple noncontiguous nerves.**
- Ischemia caused by vasculitis
- Microangiopathy in diabetes mellitus
- Less common causes : Granulomatous, leukemic, or neoplastic infiltration, Hansen's disease (leprosy) and sarcoidosis.

Polyneuropathy

- Characterized by symmetrical, distal motor and sensory deficits that have a graded increase in severity distally and by distal attenuation of reflexes,
- Rarely predominantly proximal:(E.g: acute intermittent porphyria).
- The sensory deficits generally follow a length-dependent stocking-glove pattern


Sensory loss
Weakness/
motor loss
Sensory and
motor loss
Mononeuropathy multiplex
(what nerves are involved?)
Polyneuropathy
("glove and stocking" deficits)

ACUTE INFLAMMATORY DEMYELINATING POLYNEUROPATHY



Axonopathies

- By far the majority of the toxic, metabolic and endocrine causes
- NCVs: CMAPs ↓ 80% lower limit of normal w/o or min velocity or distal motor latency change.
- Legs>> arms.
- EMG: Signs of denervation (acute, chronic) and reinnervation

Myelinopathies

- **Rarer than axonopathies**
- Clues: hypertrophic nerves on exam (not usually found)

  global arreflexia

  weakness without wasting

  motor >> sensory deficits

  NCS can discriminate inherited from acquired

- NCS: Distal motor latency prolonged — Conduction velocities slowed

  May have conduction block

  EMG: Reduced recruitment w/o much denervation

Clues for diagnosis

Constitutional symptoms

•Weight loss, malaise, and anorexia.

- DM
- hypothyroidism
- chronic renal failure
- liver disease
- intestinal malabsorption
- malignancy
- connective tissue diseases

- [HIV]
- drug use
- Vitamin B6 toxicity
- alcohol and dietary habits

Conditions Associated with Painful Peripheral Neuropathy

- Diabetes and Pre-Diabetes
- Alcohol neuropathy
- Chemotherapy
  - Platinum-based
- Paraproteinemia
- Vasculitis and Connective Tissue Diseases
- Heavy metals and other toxins
- HIV
- Amyloidosis
- Porphyria

Proximal Symmetric Motor Polyneuropathies

- Guillain-Barré syndrome
- Chronic inflammatory demyelinating polyradiculoneuropathy
- Diabetes mellitus
- Porphyria
- Osteosclerotic myeloma
- Waldenstrom's macroglobulinemia
- Monoclonal gammopathy of undetermined significance
- Acute arsenic polyneuropathy
- Lymphoma
- Diphtheria
- HIV/AIDS
- Lyme disease
- Hypothyroidism
- Vincristine (Oncovin, Vincosar PFS) toxicity

Cryptogenic (Idiopathic) Sensory and Sensorimotor Polyneuropathy

- CSPN – diagnosis of exclusion
- 6^{th} or 7^{th} decade of life
- Distal numbness, tingling, often burning pain that begins in feet and eventually involves the fingers and hands
- Both small and large fibre loss on neurological exam and EDx

History

- The temporal course of a neuropathy varies, based on the etiology.
  - With trauma or ischemic infarction, the onset will be acute, with the most severe symptoms at onset.
  - Inflammatory and some metabolic neuropathies have a subacute course extending over days to weeks.
  - A chronic course over weeks to months is the hallmark of most toxic and metabolic neuropathies.

History

- A chronic, slowly progressive neuropathy over many years occurs with most hereditary neuropathies or with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

- Neuropathies with a relapsing and remitting course include CIDP, acute porphyria, Refsum's disease, hereditary neuropathy with liability to pressure palsies (HNPP), familial brachial plexus neuropathy, and repeated episodes of toxin exposure.

History

- Ischemic neuropathies often have pain as a prominent feature.
- Small-fiber neuropathies often present with burning pain, lightning-like or lancinating pain, aching, or uncomfortable paresthesias (dysesthesias).

History

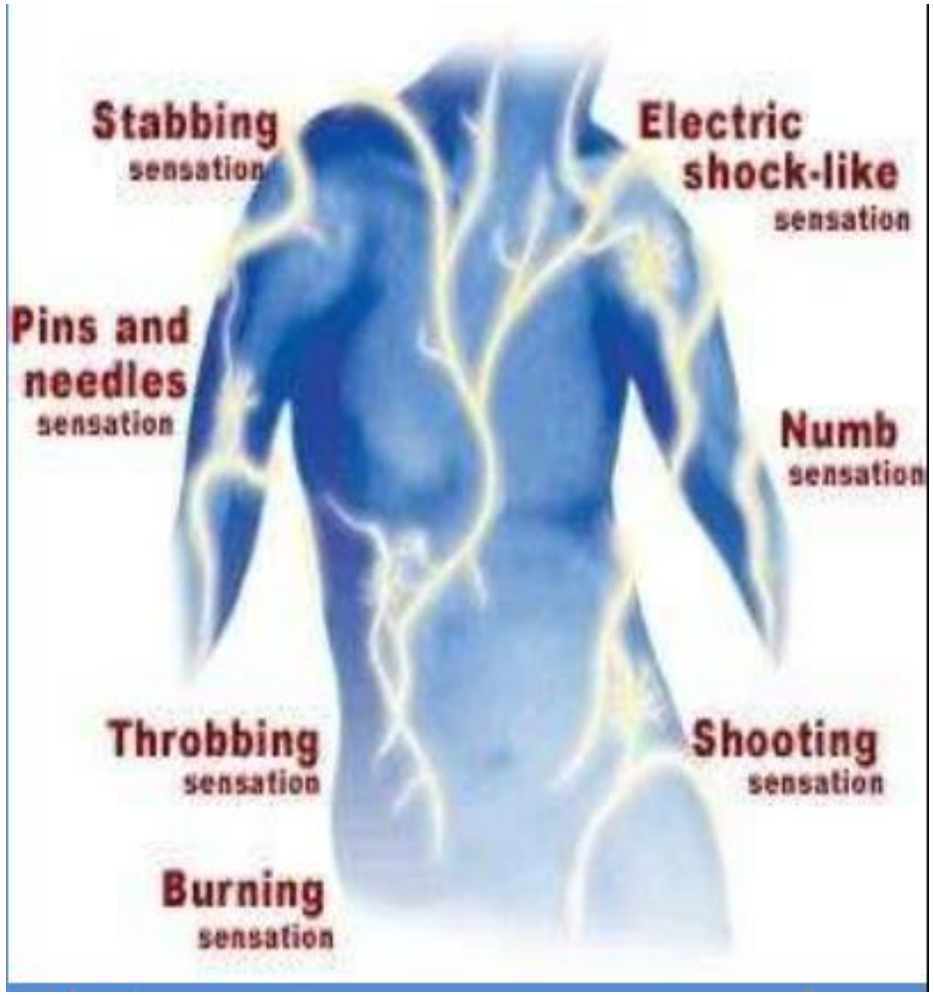
- Peripheral neuropathy can present as restless leg syndrome.

- Proximal involvement may result in difficulty climbing stairs, getting out of a chair, lifting and bulbar involvement can also be seen

History

- The clinical assessment should include:
  - careful past medical history, looking for systemic diseases that can be associated with neuropathy, such as diabetes or hypothyroidism.

Descriptives in neuropathies



Medications Causing Neuropathies

❑**AXONAL**

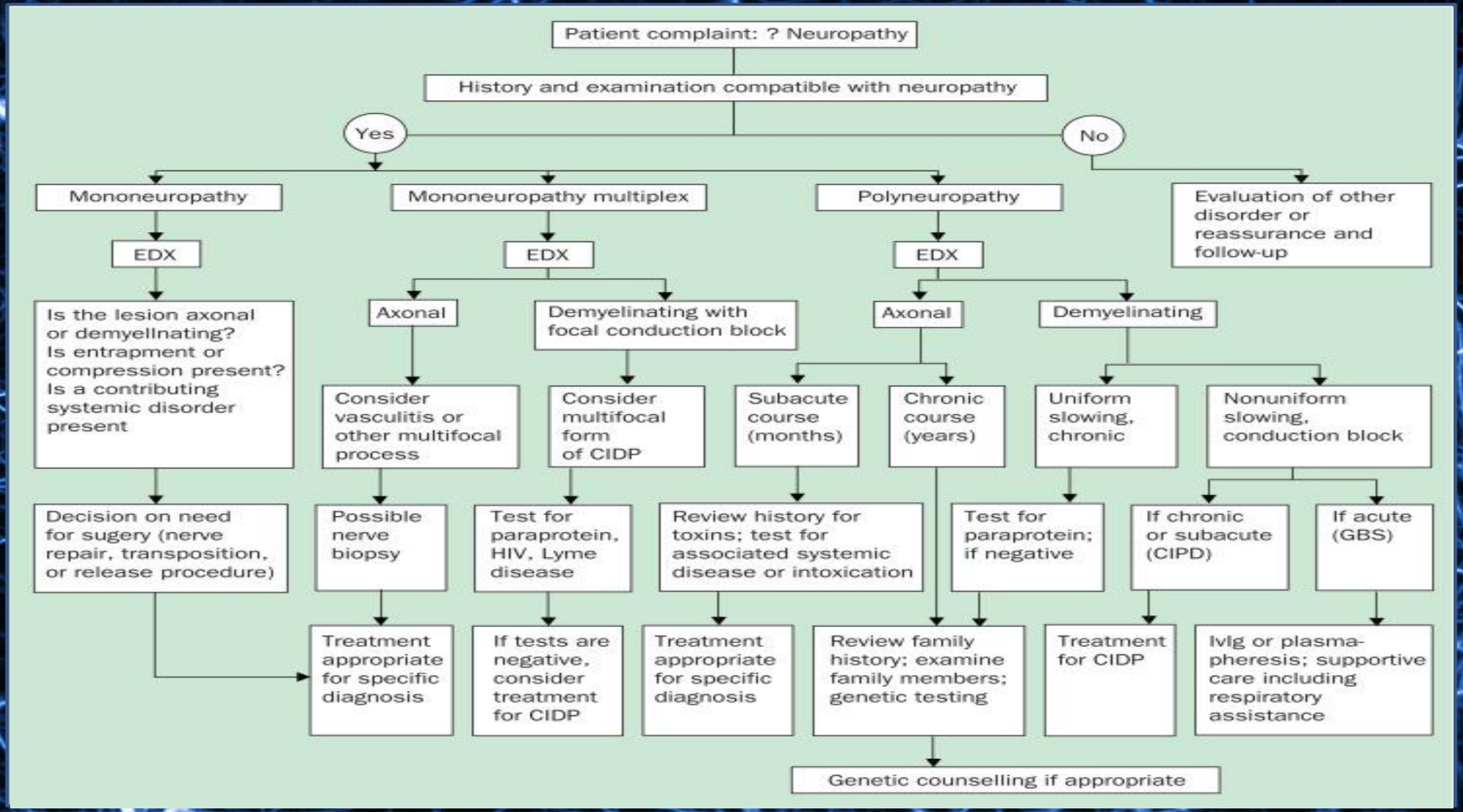
- Vincristine
- Paclitaxel
- Nitrous oxide
- Colchicine
- Isoniazid
- Hydralazine
- Metronidazole
- Pyridoxine
- Didanosine
- Lithium
- Alfa interferon
- Dapsone
- Phenytoin
- Cimetidine
- Disulfiram
- Chloroquine
- Ethambutol
- Amitriptyline

❑**DEMYELINATING**

- Amiodarone
- Chloroquine
- Suramin
- Gold

❑**NEURONOPATHY**

- Thalidomide
- Cisplatin
- Pyridoxine


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

Treatment

- Medical management
- – Analgesics
- – antiepileptic drugs, including gabapentin, phenytoin, and carbamazepine
- – some classes of antidepressants, including tricyclics such as amitriptyline.
- – local anesthetics such as lidocaine or topical patches/ Capsaicin
- containing lidocaine
- – Codeine/oxycodone

Myopathies

- Neuromuscular disorder entity in which muscle weakness is the predominant symptom occurs because of **Muscle fibre** dysfunction.

Incidence

- Worldwide incidence of all inheritable myopathies is about 14%
- • Overall incidence of muscular dystrophy is about 63 per 1 million.
- • Worldwide incidence of inflammatory myopathies is about 5–10 per 100,000 people.
- More common in women
- • Corticosteroid myopathy is the most common endocrine myopathy and endocrine disorders
- are more common in women
- • Incidence of metabolic myopathies – increasing

Symptoms of myopathy

- Muscle pain and fatigue; exercise intolerance
- • Proximal and symmetric weakness
- – Waddling gait; difficulty of rising from
- sitting, climbing stairs; Gower’s sign
- – Hyperextension of the knee
- – Increased lordosis of the lumbar spine, scoliosis
- – Contractures, tight Achilles tendons
- • Myopathic face
- • Muscle atrophy; pseudohypertrophy
- • Myotonia
- • Tendon reflexes are normal or depressed

Clinical Examination

- Thorough clinical examination!
- Observation – look for muscle atrophy, deformities
- Strength testing
- Functional testing
    - –– Stand up from a chair
    - –– Walk
    - –– Step up on a low stool
- REFLEXES and SENSATION

Types of muscle diseases

Hereditary muscle diseases

– Denervation atrophy

– Muscle dystrophies

– Muscle channelopathies

– Mitochondrial myopathies

– Metabolic myopathies

Acquired muscle diseases

– Inflammatory myopathies

– Endocrine and toxic myopathies

– Infectious muscle diseases

Types of myopathies

- Inflammatory Myopathies
- – Polymyositis
- – Dermatomyositis
- – Inclusion body myositis
- – Viral
- • Muscular dystrophies
- – Duchenne muscular
- – Limb-girdle
- – Congenital
- – Fasioscapulohumeral
- – Oculopharyngeal
- – Emery – Dreifuss
- – Distal (Welander)
- • Myotonic Syndromes
- – Myotonic dystrophy
- – Inherited
- – Schwarz-Jampel
- – Drug-induced

Dermatomyositis	Polymyositis	Incusion body myositis
Sub acute progressive weakness	Sub acute progressive weakness	Slowly progressive weakness,
proximal>distal	proximal>distal	proximal and distal.
Children and adults, women	adults, women	adults, mostly men
Characteristic rash and periorbital heliotrope.		
Electromyogram myopathic potentials, spontaneous	myopathic potentials, spontaneous	myopathic potentials, spontaneous activity
Elevated serum creatine kinase activity.	Elevated serum creatine kinase activity	Mildly elevated serum creatine kinase or normal.
inflammatory myopathy affecting chiefly the perimysium with perifascicular atrophy	inflammatory myopathy chiefly the endomysium	: inflammatory myopathy affecting chiefly the endomysium, but chronic and has

Endocrine myopathies

- Thyrotoxic myopathies
- Cushing syndrome and steroid myopathy
- Myopathy associated with parathyroid disorders.

Toxic myopathies

- Myotonic disorders
- Necrotizing myopathies
- Acute muscle necrosis
- Mitochontrial myopathy
- Hypokalemic myopathy
- Inflammatory myopathy
- Autophagic myopathy
- Focal myopathy
- Envenomation myopathy

Muscle Channelopathies

Na channelopathies	Cl channelopathies	Ca channelopathies
Hyperkalemic periodic paralysis	Myotonia congenita (Thomsen and Becker type)	Malignant hyperthermia
Paramyotonia congenita		Hypokalemic periodic paralysis
Potassium aggravated myotonia		

TREATMENT

- There is no single treatment for myopathy.
- Treatment of the symptoms to specific cause – targeting treatments.
- Drug therapy
- Physical therapy
- Bracing for support,
- Surgery
- Massage

TAKE HOME POINTS

- THERE IS NO SUBSTITUTE TO A THOROUGH INTERVIEW AND EXAMINATION
- The examination is targeted to differentiate between nerve or muscle dysfunction
- Treatment is dependent on the cause – the underlying pathology needs to be addressed – often the management is only symptomatic.


THANK
YOU