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

NEUROPATHIES AND MYOPATHIES
IN THE ADULT AND ELDERLY

AO CHARWAY-FELLI, MD, PhD
37 Military Hospital
• 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
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
- Diabetes\(^1\)\(^2\)

- Paraproteinaemia\(^2\)\(^3\)
- Alcohol misuse\(^1\)
- Renal failure\(^1\)
- Vitamin B-12 deficiency\(^1\)
- HIV infection\(^1\)

- Chronic idiopathic axonal neuropathy\(^4\)

- Prevalence
  - 11-41% (depending on duration, type, and control)
  - 9-10%
  - 7%
  - 4%
  - 3.6%
  - 16% (depending on the population studied, usually much lower)
  - 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?

<table>
<thead>
<tr>
<th></th>
<th>Muscle bulk</th>
<th>Tone</th>
<th>Strength</th>
<th>DTR</th>
<th>Plantars</th>
<th>sensation</th>
<th>fasicaualtion</th>
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<tbody>
<tr>
<td>UMN</td>
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<td>N</td>
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<td>↑</td>
<td>N</td>
<td>-</td>
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<tr>
<td>Ant horn cell</td>
<td>Prox wasting</td>
<td>↓</td>
<td>Prox weakness</td>
<td>↓↓</td>
<td>↓</td>
<td>N</td>
<td>+</td>
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<tr>
<td>P nerve</td>
<td>Distal wasting</td>
<td>↓</td>
<td>Distal weakness</td>
<td>↓↓</td>
<td>↓</td>
<td>↓</td>
<td>rarely</td>
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<td>NMJ</td>
<td>N</td>
<td>N</td>
<td>fatigues</td>
<td>N- ↑</td>
<td>↓</td>
<td>N</td>
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<tr>
<td>Muscle</td>
<td>selective</td>
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<td>N</td>
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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

<table>
<thead>
<tr>
<th>Sensory “Large Fiber”</th>
<th>Loss of function “- symptoms”</th>
<th>Disordered function “+ symptoms”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibration</td>
<td>Hyporeflexia</td>
<td>Paresthesias</td>
</tr>
<tr>
<td>Proprioception</td>
<td>Sensory ataxia</td>
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<td>↓</td>
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</table>

<table>
<thead>
<tr>
<th>Sensory “Small Fiber”</th>
<th>Loss of function “- symptoms”</th>
<th>Disordered function “+ symptoms”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Dysesthesias</td>
<td></td>
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<tr>
<td>Temperature</td>
<td>Allodynia</td>
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<td>↓</td>
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</table>
The clinical response to motor nerve injury

<table>
<thead>
<tr>
<th></th>
<th>Loss of function “- symptoms”</th>
<th>Disturbed function “+ symptoms”</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor nerves</strong></td>
<td>Wasting</td>
<td>Fasciculation</td>
</tr>
<tr>
<td><strong>Large fibre</strong></td>
<td>Hypotonia</td>
<td>Cramps</td>
</tr>
<tr>
<td></td>
<td>Weakness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyporeflexia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Orthopedic deformity</td>
<td></td>
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</tbody>
</table>
The clinical response to autonomic nerve injury

<table>
<thead>
<tr>
<th></th>
<th>Loss of function “- symptoms”</th>
<th>Disturbed function “+ symptoms”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomic nerves</td>
<td>↓ Sweating, Hypotension, Urinary retention, Impotence, Vascular color changes</td>
<td>↑ Sweating, Hypertension</td>
</tr>
</tbody>
</table>
The 3 principal questions …

#1. Where is the lesion?
#2. What is the etiology?
#3. What is the treatment?
The *patterns* of peripheral neuropathy...

- Mononeuropathy?
- Polyneuropathy?
  multiple nerves
  contiguous
  typically length dependent
  ("stocking-glove")

*Polyneuropathy is common!* 2.4%
*(8% over 55 yr)*
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
ACUTE INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Guillain-Barré Syndrome

- Acute inflammatory demyelinating polyneuropathy (AIDP)
  - AIDP with secondary degeneration
- Axonal pattern
  - Acute motor axonal neuropathy (AMAN)
  - Acute motor sensory axonal neuropathy (AMSAN)
- Fisher syndrome
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
<table>
<thead>
<tr>
<th>Proximal Symmetric Motor Polyneuropathies</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Guillain-Barré syndrome</td>
</tr>
<tr>
<td>– Acute arsenic polyneuropathy</td>
</tr>
<tr>
<td>– Chronic inflammatory demyelinating</td>
</tr>
<tr>
<td>polyradiculoneuropathy</td>
</tr>
<tr>
<td>– Lymphoma</td>
</tr>
<tr>
<td>– Diphtheria</td>
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<tr>
<td>– HIV/AIDS</td>
</tr>
<tr>
<td>– Lyme disease</td>
</tr>
<tr>
<td>– Hypothyroidism</td>
</tr>
<tr>
<td>– Porphyria</td>
</tr>
<tr>
<td>– Vincristine (Oncovin, Vincosar PFS)</td>
</tr>
<tr>
<td>– Osteosclerotic myeloma</td>
</tr>
<tr>
<td>– Hypothyroidism</td>
</tr>
<tr>
<td>– Waldenstrom’s macroglobulinemia</td>
</tr>
<tr>
<td>– Vincristine toxicity</td>
</tr>
<tr>
<td>– Monoclonal gammopathy of undetermined</td>
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<td>– Monoclonal gammopathy of undetermined</td>
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<tr>
<td>significance</td>
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<tr>
<td>– Monoclonal gammopathy of undetermined</td>
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<td>significance</td>
</tr>
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</table>
Cryptogenic (Idiopathic) Sensory and Sensorimotor Polyneuropathy

- CSPN – diagnosis of exclusion
- 6\textsuperscript{th} or 7\textsuperscript{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).
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

- Stabbing sensation
- Electric shock-like sensation
- Pins and needles sensation
- Numb sensation
- Throbbing sensation
- Shooting sensation
- Burning sensation
Medications Causing Neuropathies

❑ AXONAL
- Vincristine
- Paclitaxel
- Nitrous oxide
- Colchicine
- Isoniazid
- Hydralazine
- Metronidazole
- Pyridoxine
- Didanosine
- Lithium

❑ DEMENTINATING
- Alfa interferon
- Dapsone
- Phenytoin
- Cimetidine
- Disulfiram
- Chloroquine
- Ethambutol
- Amitriptyline

❑ NEURONOPATHY
- Amiodarone
- Chloroquine
- Suramin
- Gold
- Thalidomide
- Cisplatin
- Pyridoxine
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
- Muscular dystrophies
  - Fasioscapulohumeral
  - Oculopharyngeal
  - Emery – Dreifuss
  - Distal (Welander)
- Myotonic Syndromes
  - Myotonic dystrophy
  - Inherited
  - Schwarz-Jampel
  - Drug-induced
<table>
<thead>
<tr>
<th>Dermatomyositis</th>
<th>Polymyositis</th>
<th>Incusion body myositis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub acute progressive weakness</td>
<td>Sub acute progressive weakness</td>
<td>Slowly progressive weakness,</td>
</tr>
<tr>
<td>proximal&gt;distal</td>
<td>proximal&gt;distal</td>
<td>proximal and distal.</td>
</tr>
<tr>
<td>Children and adults, women</td>
<td>adults, women</td>
<td>adults, mostly men</td>
</tr>
<tr>
<td>Characteristic rash and periorbital heliotrope.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Electromyogram myopathic potentials, spontaneous</td>
<td>myopathic potentials, spontaneous</td>
<td>myopathic potentials, spontaneous activity</td>
</tr>
<tr>
<td>Elevated serum creatine kinase activity.</td>
<td>Elevated serum creatine kinase activity</td>
<td>Mildly elevated serum creatine kinase or normal.</td>
</tr>
<tr>
<td>inflammatory myopathy affecting chiefly the perimysium with perifascicular atrophy.</td>
<td>inflammatory myopathy chiefly the endomysium</td>
<td>: inflammatory myopathy affecting chiefly the endomysium, but chronic and has...</td>
</tr>
</tbody>
</table>
Endocrine myopathies

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

- Myotonic disorders
- Necrotizing myopathies
- Acute muscle necrosis
- Mitochondrial myopathy
- Hypokalemic myopathy
- Inflammatory myopathy
- Autophagic myopathy
- Focal myopathy
- Envenomation myopathy
# Muscle Channelopathies

<table>
<thead>
<tr>
<th>Na channelopathies</th>
<th>Cl channelopathies</th>
<th>Ca channelopathies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperkalemic periodic paralysis</td>
<td>Myotonia congenita (Thomsen and Becker type)</td>
<td>Malignant hyperthermia</td>
</tr>
<tr>
<td>Paramyotonia congenita</td>
<td></td>
<td>Hypokalemic periodic paralysis</td>
</tr>
<tr>
<td>Potassium aggravated myotonia</td>
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</tbody>
</table>
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.