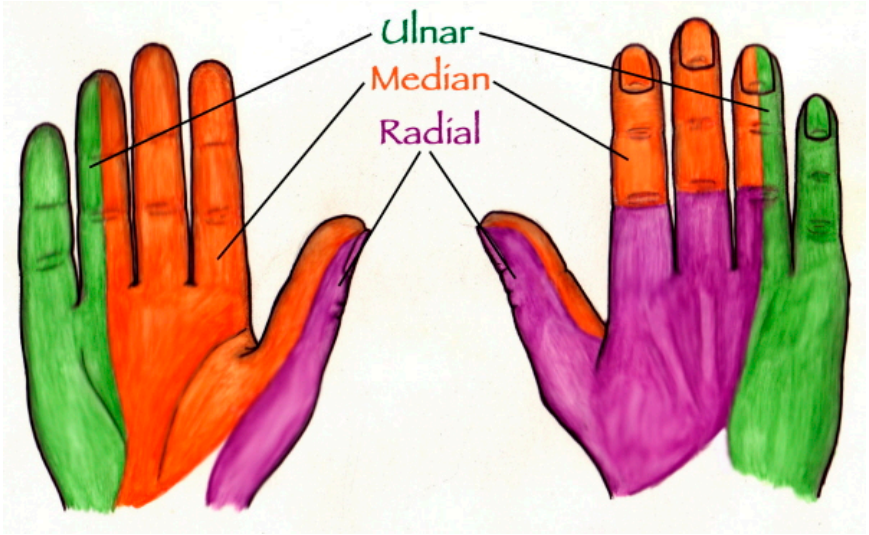
Nerves and Muscles diseases

Diagnosis and management

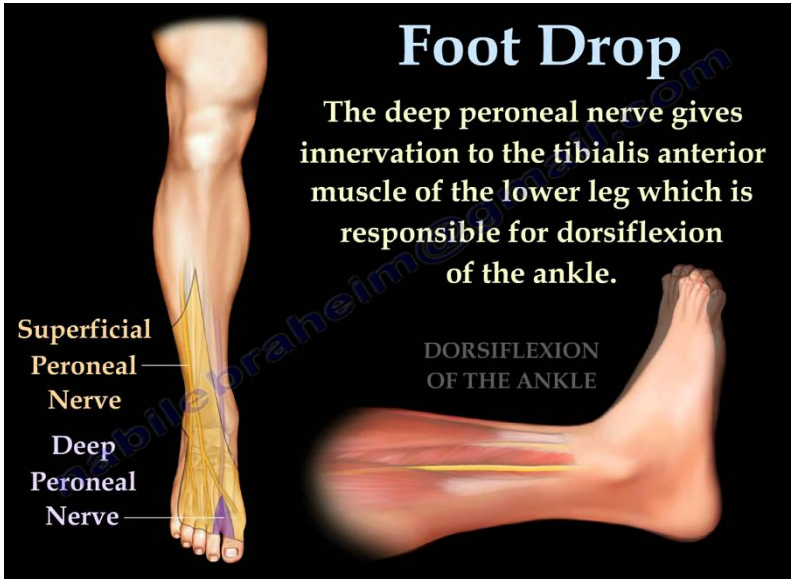
NEUROPATHY

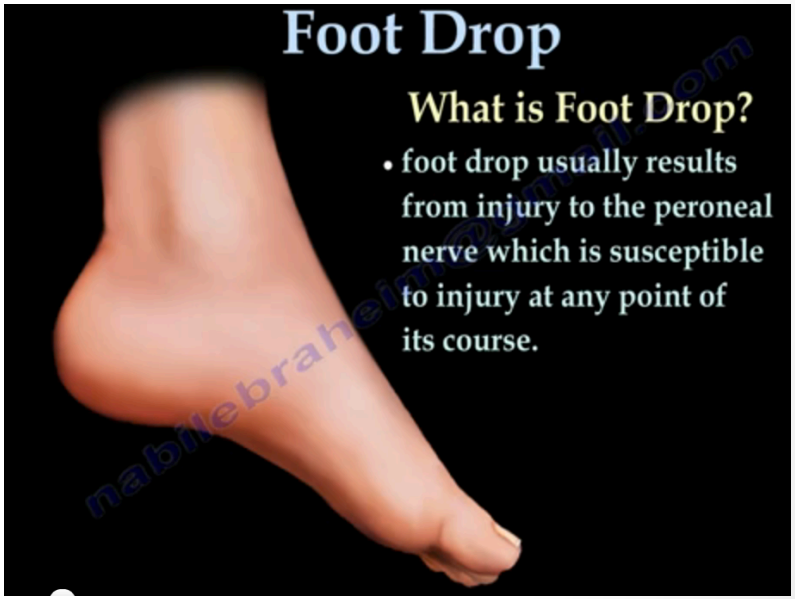
- distal weakness
- concomitant sensory symptoms + signs
- reflexes lost early
- +/- fasciculations
- no contractures
- not associated with myocardial dysfunction nor muscle tenderness

Mononeuropathy



Mononeuropathy



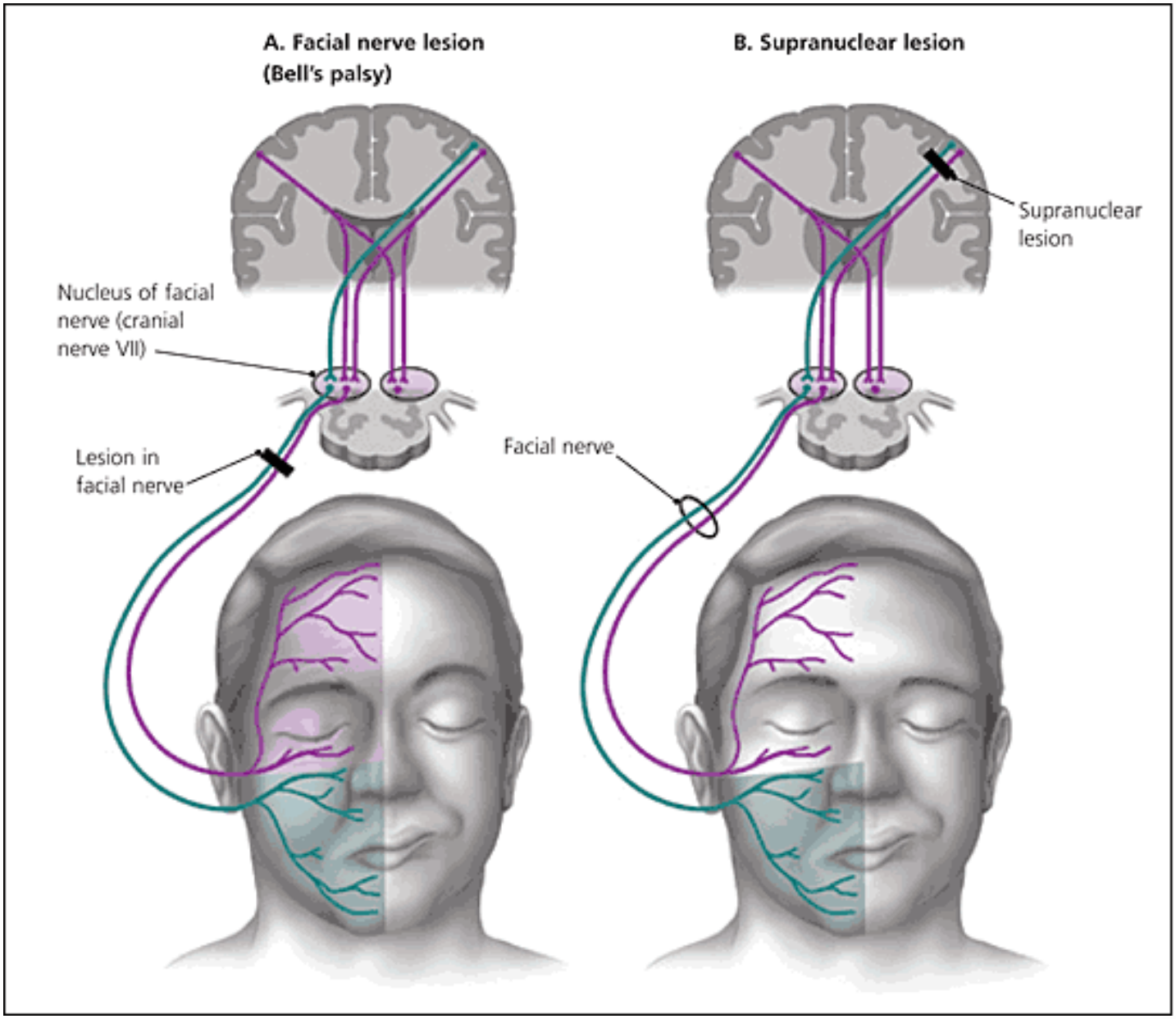


Neuropathy:

- 1/ mononeuropathy - trauma or compression – deficits reflect the anatomic distribution of the nerve (for example carpal tunnel syndrome)
- 2/ polyneuropathy: symmetrical, featuring weakness, numbness, pins-and –needles, burning pain, it usually begins in the hands and feet (“stocking and glove” pattern) and may progress to the arms and legs, loss or decrease of reflexes,
- autonomic disturbances (orthostatic hypotension, incontinence, impotence, sweating abnormalities)
- Causes: diabetes mellitus, uraemia, hypothyroidism, rheumatologic disease, medications (chemotherapy), toxins (alcohol) vitamins deficiencies (B vitamin) , hereditary neuropathies (**Charcot–Marie–Tooth disease**)

FACIAL NERVE (N. VII) PARALYSIS:

- The pathway of the facial nerve is long and relatively convoluted, and so there are a number of causes that may result in facial nerve paralysis.
- The most common is Bell's palsy, an idiopathic disease that may only be diagnosed by exclusion.
- Facial nerve paralysis may be divided into supranuclear and infranuclear lesions.


A. Facial nerve lesion
(Bell's palsy)
B. Supranuclear lesion
Supranuclear
lesion
Nucleus of facial
nerve (cranial
nerve VII)
Lesion in
facial nerve
Facial nerve
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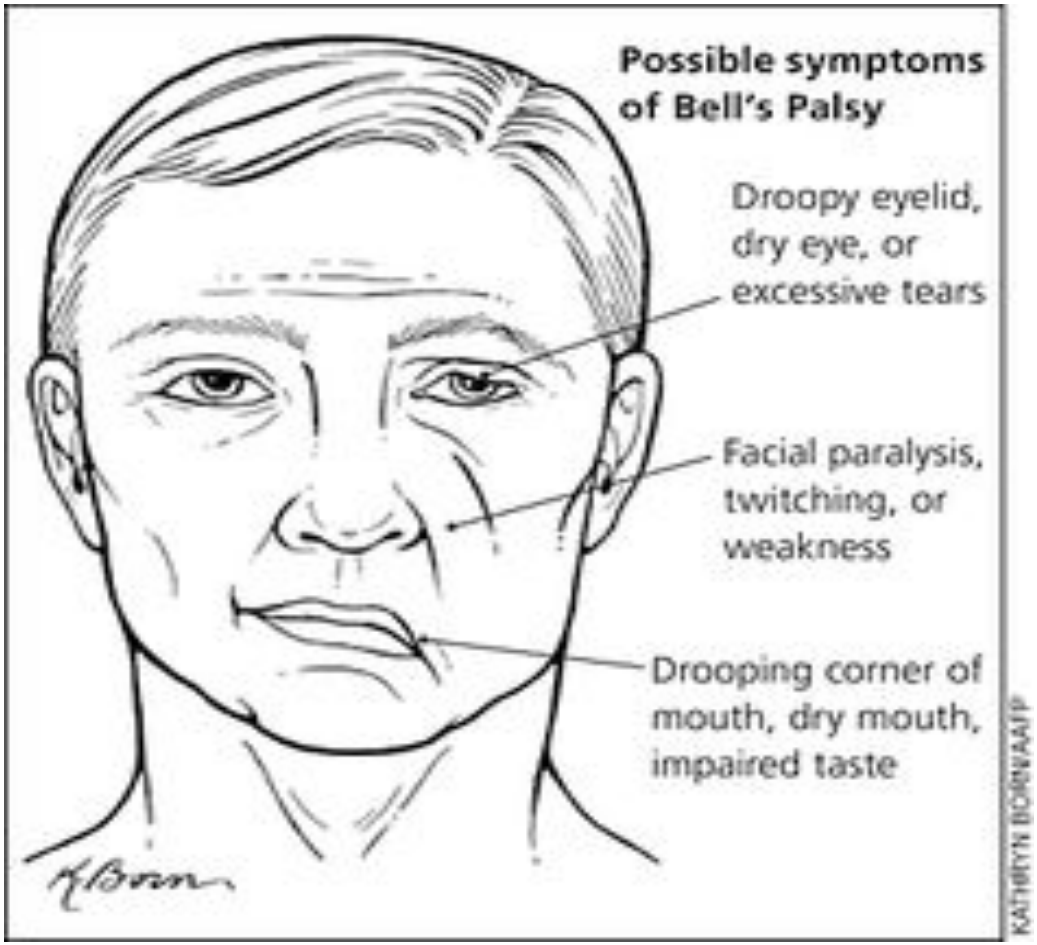
SUPRANUCLEAR and nuclear lesions- central facial palsy can be caused by a lacunar infarct

INFRANUCLEAR LESIONS

- characterised by unilateral facial weakness, loss of taste, hyperacusis and decreased salivation and tear secretion. Symptoms may develop over several hours.
- Acute facial pain radiating from the ear may precede the onset of other symptoms.


Possible symptoms of Bell's Palsy
Droopy eyelid, dry eye, or excessive tears
Facial paralysis, twitching, or weakness
Drooping corner of mouth, dry mouth, impaired taste
KBorn
KATHRYN BORN/AAFP

Causes:

- Herpes,
- Otitis media,
- Lyme disease (caused by Borrelia burgdorferi infection- specially in endemic areas)
- Fractures of the temporal bone
- Diabetes mellitus, sarcoidosis,
- Moebius syndrome (extremely rare)- is a bilateral facial paralysis resulting from the underdevelopment of the VII cranial nerve (facial nerve), which is present at birth. The VI cranial nerve is also affected, so people with Moebius syndrome cannot form facial expression or move their eyes from side to side.

Investigation and diagnosis:

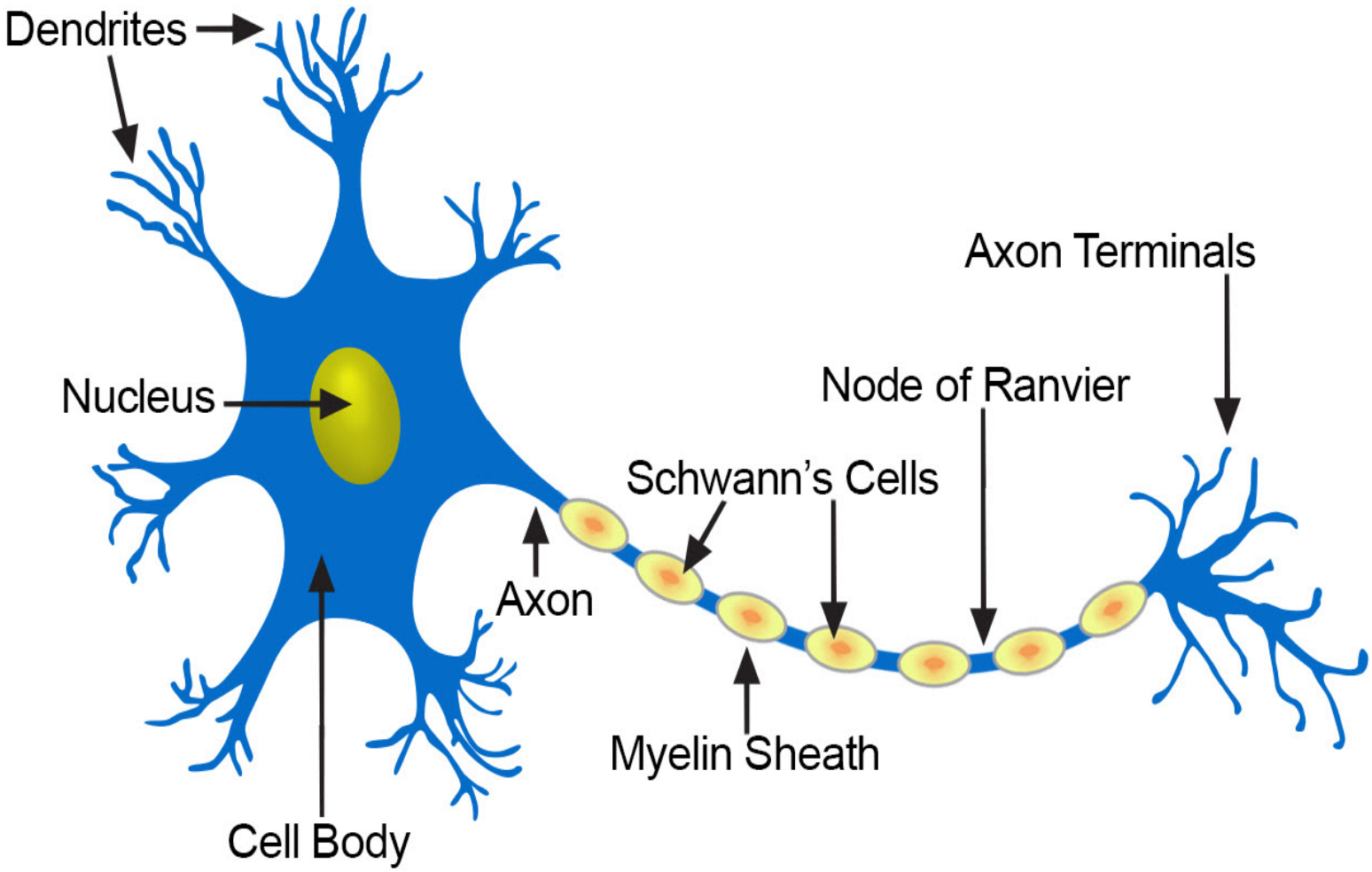
- Medical history, neurological examination, laryngological examination with audiometry and tympanometry
- Blood tests , Borrelia, CT of temporal bone,
- Treatment: steroids, vit B, rehabilitation

Guillain–Barré syndrome (GBS)

- Acute polyneuropathy
- rapid-onset muscle weakness as a result of damage to the peripheral nervous system , also changes in sensation or pain is reported by the patient - both sides equally, cranial nerve is involved in 50%
- the symptoms develop over half a day to two weeks to reach the maximum, then plateau phase then improvement
- during the acute phase, the disorder can be life-threatening with about a quarter developing weakness of the breathing muscles and requiring mechanical ventilation

- Some are affected by changes in the function of the autonomic nervous system, which can lead to dangerous abnormalities in heart rate and blood pressure
- This is autoimmune disease caused by the body's immune system mistakenly attacking the peripheral nerves and damaging their myelin insulation (very often is triggered by an infection of upper respiratory system or diarrhoea 3-6 weeks before or vaccination) .
- Molecular mimicry - the production of antibodies after an infection - the immune system is reacting to microbial substances but the resultant antibodies also react with substances occurring naturally in the body.
- Causes: Campylobacter jejuni, CMV, Varicella zoster, Mycoplasma pneumoniae, influenza virus, Zika-virus

Structure of a Typical Neuron



Different types of Guillain–Barré syndrome feature different types of immune attack:

- 1/ the demyelinating variant (AIDP) features damage to the myelin sheath by white blood cells (T lymphocytes and macrophages) this process is preceded by activation of a group of blood proteins known as complement
- 2/ the axonal variant is mediated by IgG antibodies and complement against the cell membrane covering the axon without direct lymphocyte involvement

DIAGNOSIS:

- 1/ The signs and symptoms (rapid development of muscle paralysis, absent reflexes, neurological examination : reduced power and reduced or absent tendon reflexes (hypo or areflexia)
- 2/ examination of cerebrospinal fluid : "albuminocytological dissociation" - increased of spinal fluid protein concentration but a normal cell count
- Despite this, the CSF is unremarkable in 50% of people with Guillain–Barré syndrome in the first few days of symptoms, and 80% after the first week; therefore, normal results do not exclude the condition

- 3/ nerve conduction studies and electromyography – demielinization or/and axonal abnormalities But in the first two weeks, these investigations may not show any abnormality so neurophysiology studies are not required for the diagnosis
- 4/ MRI of the spinal cord - enhancement of the nerve roots

Type	Symptoms	Population affected	Nerve conduction studies	Antiganglioside antibodies
Acute inflammatory demyelinating polyneuropathy (AIDP)	Sensory symptoms and muscle weakness, often with cranial nerve weakness and autonomic involvement	Most common in Europe and North America	Demyelinating polyneuropathy (↓CV)	No clear association
Acute motor axonal neuropathy (AMAN)	Isolated muscle weakness without sensory symptoms in less than 10%; cranial nerve involvement uncommon	Rare in Europe and North America, substantial proportion (30–65%) in Asia and Central and South America; sometimes called "Chinese paralytic syndrome"	Axonal polyneuropathy (↓ amplitude) , normal sensory action potential	GM1a/b, GD1a & GalNac–GD1a
Acute motor and sensory axonal neuropathy (AMSAN)	Severe muscle weakness similar to AMAN but with sensory loss			
Miller Fisher syndrome	Ataxia, eye muscle weakness (ophtalmoplegia), areflexia but usually no limb weakness	This variant occurs more commonly in men than in women (2:1 ratio). Cases typically occur in the spring and the average age of occurrence is 43 years old	Generally normal, sometimes discrete changes in sensory conduction or H-reflex detected	GQ1b, GT1a

Treatment:

- 1/ Immunotherapy: plasmapheresis and intravenous immunoglobulins (IVIg) both are equally effective, but IVIg is usually used first in practice
- IVIg total therapy 2g/kg - 0,4 g/kg/ x 5 doses
- 2/ Pain medication
- 3/ Rehabilitation
- 4/ Mechanical ventilation /Intensive care - in case of Respiratory failure

MYOPATHY

- usually proximal weakness
- usually no sensory deficit
- reflexes preserved until late
- fasciculation absent
- contractures usually present
- may be associated with myocardial dysfunction or muscle tenderness

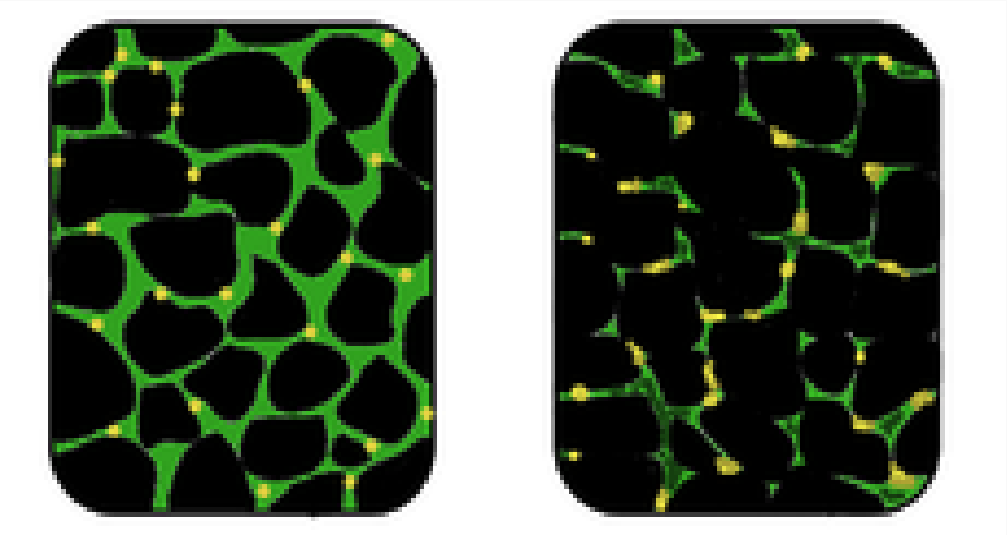
Inherited forms of myopathy:

- Muscular dystrophies
- Myotonia
- Congenital myopathies with microscopic changes (nemaline myopathy- with nemaline rods, minicore myopathy, centronuclear myopathy)
- Mitochondrial myopathy - defects in mitochondria, which provide a critical source of energy for muscle
- Metabolic myopathies (glycogenosis, lipidoses)

Duchenne muscular dystrophy (DMD) Becker's muscular dystrophy (BMD)

- The pattern of BMD symptom development resembles that of DMD but with a later, and much slower rate of progression.
- an X-linked recessive inherited disorder (carrier females, affected boys)
- a mutation of the dystrophin gene at locus Xp21, located on the short arm of the X chromosome
- which codes for the protein dystrophin
- Dystrophin is an important component within muscle tissue that provides structural stability to the dystroglycan complex of the cell membrane.

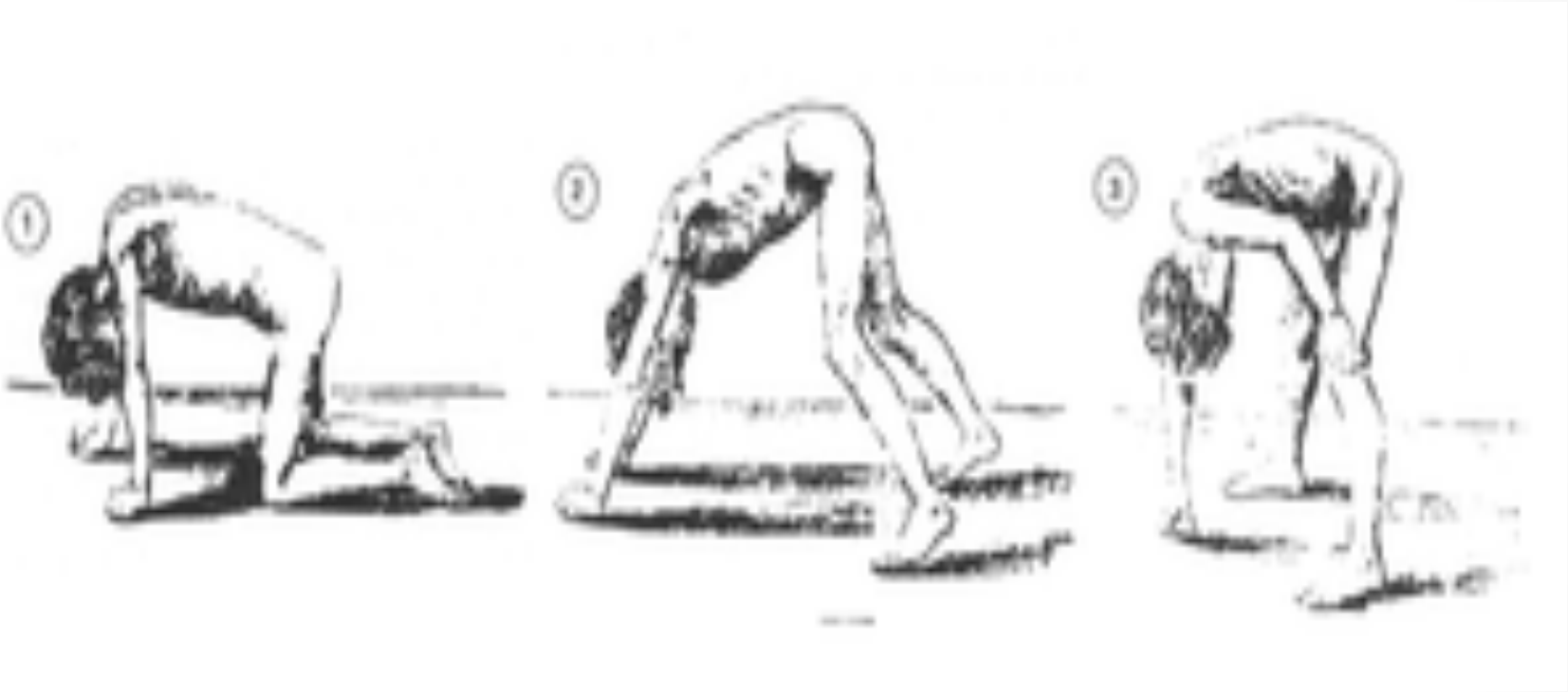
Muscular Dystrophy



In affected muscle (right) the tissue becomes disorganized and the concentration of dystrophin (green) is greatly reduced, compared to normal muscle (left)

Signs:

- Boys are affected, first signs about 3 - 4 years of old
- Frequent falls
- Fatigue
- Difficulty with motor skills (running, hopping, jumping)
- Trouble getting up from lying or sitting position
- A positive Gower's sign reflects the more severe impairment of the lower extremities muscles. The child helps himself to get up with upper extremities: first by rising to stand on his arms and knees, and then "walking" his hands up his legs to stand upright.



Gowers' sign

- Lumbar hyperlordosis
- Muscle contractures of Achilles tendon
- Progressive difficulty walking
- Muscle fibre deformities
- Pseudohypertrophy (enlarging) of tongue and calf muscles. The muscle tissue is eventually replaced by fat and connective tissue, hence the term pseudohypertrophy.
- Higher risk of neurobehavioral disorders (e.g., ADHD), learning disorders (dyslexia), and non-progressive weaknesses in specific cognitive skills (in particular short-term verbal memory), which are believed to be the result of absent or dysfunctional dystrophin in the brain.

- Eventual loss of ability to walk (usually by the age of 12)
- Skeletal deformities (scoliosis)
- Abnormal heart muscle (dilated cardiomyopathy)
- Congestive heart failure or irregular heart rhythm (arrhythmia) – Echocardiography and ECG is required
- Respiratory disorders, including pneumonia and swallowing with food or fluid passing into the lungs (in late stages of the disease)

DIAGNOSIS:

- DNA test: The muscle-specific isoform of the dystrophin gene is composed of 79 exons, and DNA testing and analysis can usually identify the specific type of mutation of the exon or exons that are affected. DNA testing confirms the diagnosis in most cases.
- Prenatal test possible
- Muscle biopsy
- Creatinine kinase (CPK-MM) levels in the bloodstream are extremely high
- EMG – myogenic changes but not specific for DMD

Treatment :

- Treatment is generally aimed at controlling the onset of symptoms to maximize the quality of life, and include the following:
- corticosteroids increase energy and strength and defer severity of some symptoms
- Mild physical activity such as swimming is encouraged; inactivity can worsen the muscle disease
- Physical therapy is helpful to maintain muscle strength, flexibility, and function
- Orthopedic appliances (such as braces and wheelchairs) may improve mobility and the ability for self-care. Form-fitting removable leg braces that hold the ankle in place during sleep can defer the onset of contractures
- Appropriate respiratory support as the disease progresses is important
- Cardiologic care (echo, ECG, Holter ECG)

Acguired forms of myopathy:

- external substance induced myopathy : drug induced (statins, glucocorticoid), alcoholic, other toxic agents
- dermatomyositis
- polymyositis

Feature	Neuropathic	Myopathic
Distribution of weakness	Distal	Proximal
Reflexes	Absent	Usually Present
Sensory loss	Usually present	Absent
Atrophy	Present	Absent until late
CPK	Normal	Elevated
Nerve conduction Velocity	Usually decreased	Normal
EMG	Fibrillations and fasciculations	Small motor units
Muscle biopsy	Group atrophy	Irregular, necrotic fibers

MYASTENIA GRAVIS:

- fluctuating muscle weakness and fatigue
- In the most common cases, muscle weakness is caused by circulating antibodies that block acetylcholine receptors at the postsynaptic neuromuscular junction, inhibiting the excitatory effects of the neurotransmitter acetylcholine on nicotinic receptors at neuromuscular junctions.

Myasthenia gravis signs:

- Apokamnosis - The muscle weakness becomes progressively worse during periods of physical activity, and improves after periods of rest.
- In about two-thirds of individuals, the initial symptom of MG is related to the muscles around the eye. There may be eyelid drooping (ptosis- weakness of levator palperbae superioris) and double vision (diplopia due to weakness of the extraocular muscles)
- Dysphagia, dysarthria, hypophonia
- Facial weakness- manifesting as inability to hold the mouth closed (the "hanging jaw sign")
- In a myasthenic crisis - a paralysis of the respiratory muscles

Myasthenia gravis diagnosis:

- Serology - test for antibodies against the acetylcholine receptor, or antibodies against the MuSK protein
- CT MR of mediastinum - Myasthenia associated with thymoma
- EMG- single fibre test

Myasthenia gravis management:

- acetylcholinesterase inhibitors to directly improve muscle function and immunosuppressant drugs to reduce the autoimmune process.
- Thymectomy is a surgical method to treat MG.
- Myasthenia crisis- plasmapheresis, IVIg

Weakness due to motor neuron disease :

- SMA (spinal muscular atrophy)
- Autosomal recessive disease caused by a genetic defect in the SMN1 gene, which encodes SMN SMN is apparently selectively necessary for survival of motor neurons, as diminished abundance of the protein results in loss of function of neuronal cells in the anterior horn of the spinal cord and subsequent system-wide muscle wasting
- Areflexia
- Muscle weakness, poor muscle tone- “Floppy baby syndrome”
- Difficulty achieving developmental milestones, difficulty sitting/ standing/walking
- Loss of strength of the respiratory muscles: weak cough, weak cry (infants)
- Fasciculation
- serum creatine kinase (CK) may be normal or increased
- genetic testing will show bi-allelic deletion of exon 7 of the SMN1 gene

Thank You