PERIPHERAL NERVOUS SYSTEM DISORDERS

Weakness (+/- sensory deficits) with NO UMN signs—
no hyperreflexia, no clonus, no upgoing toes
1. ANTERIOR HORN CELL
   A. Spinal Muscular Atrophy (SMA) (genetic),
   B. Poliomyelitis (acquired)

2. Peripheral nerve

3. Neuromuscular junction

4. Muscle
Figure 27.5 Neuromuscular disorders

Disorders of the anterior horn cell
- Spinal muscular atrophy
- Poliomyelitis

Disorders of the peripheral nerve
- Hereditary motor sensory neuropathies
- Acute post-infectious polyneuropathy (Guillain-Barré)
- Bell palsy

Disorders of neuromuscular transmission
- Myasthenia gravis

Muscle disorders
- Muscle dystrophies
  - Duchenne/Becker/congenital
- Inflammatory myopathies
- Benign acute myositis
- Polymyositis/dermatomyositis
- Myotonic disorders
  - Dystrophia myotonica
- Metabolic myopathies
- Congenital myopathies

(a) (b)

Figure 27.6 (a,b) Gowers sign. The child needs to turn prone to rise (the key, early feature of Gowers sign), then uses his hands to climb up on his knees before standing (late feature), because of poor hip girdle fixation and/or proximal muscle weakness. Any child continuing to turn prone to rise after 3 years of age is likely to have a neuromuscular condition.
- **Anterior horn cell** – there are signs of denervation:
- **Neuropathy** – often distal nerves affected.
- **Myopathy** – there is weakness (often proximal)
- **Neuromuscular junction** – fatigue
Investigations Myopathy:

- Serum creatine phosphokinase – markedly elevated in Duchenne and Becker muscular dystrophy and inflammatory myopathies

- Muscle biopsy, needle or open – modern histochemical techniques often enable a definitive diagnosis

- DNA testing – to identify abnormal genes
Neuropathy:

- **Nerve conduction studies** – to identify delayed motor and sensory nerve conduction velocities seen in neuropathy
- **DNA testing** – for abnormal genes
- **EMG** (electromyography) helps in differentiating myopathic from neuropathic disorders, e.g. fatiguability on repetitive nerve stimulation in myasthenia.
DNA TESTS

- DNA available for
- spinal muscular atrophy (SMA),
- Duchenne muscular dystrophy,
- myotonic dystrophy, the
- congenital muscular dystrophies and
- hereditary neuropathies.

- allows antenatal testing and genetic counselling and often obviates the need for the discomfort of peripheral neurophysiology
A. Spinal muscular atrophy (SMA)

Type 1 SMA - Werdnig-Hoffman

- Prenatal – decreased fetal movements
- Neonatal / early infancy
  - severe hypotonia
  - breathing / swallowing difficulties
  - absent reflexes
  - tongue fasciculations
  - no face / eye weakness
- Motor milestones: never sit
- Autosomal recessive - SMN (survival motor neuron) gene mutation, chromosome 5
Spinal muscular atrophy

- This is an autosomal recessive.
- due to mutations in the survival motor neurone (SMN) gene.
- degeneration of the anterior horn cells,
- leading to progressive weakness and wasting of skeletal muscles.
SMA Muscle biopsy reveals grouped atrophy
Spinal muscular atrophy type 1 (Werdnig–Hoffmann disease)

- Presenting in early infancy
- Diminished fetal movements are often noticed during pregnancy.
- And there may be arthrogryposis.
- Absent deep tendon reflexes
- Intercostal recession
- Fasciculation of the tongue.
- These children never sit unaided.
- Death is from respiratory failure within about 12 months.
Milder forms

- There are of the disorder with a later onset. Children with
- type 2 spinal muscular atrophy can sit, but never walk independently.
- type 3 (Kugelberg–Welander) do walk and can present later in life.
Acute post-infectious polyneuropathy (Guillain–Barré syndrome)

- 2–3 weeks after an upper respiratory tract infection or gastroenteritis.
- The disorder is probably due to the formation of antibody attaching itself to protein components of myelin.
- Ascending symmetrical weakness with loss of reflexes.
- Autonomic involvement.
- Sensory symptoms, usually in the distal limbs.
- Involvement of bulbar muscles leads to difficulty with chewing and swallowing and the risk of aspiration.
B. Poliomyelitis (infantile paralysis)

- viral infection -> destruction of anterior horn cells
- flaccid asymmetric paralysis, usually legs
- may involve face (bulbar muscles)
- decreased or absent reflexes
GBS

- Respiratory depression may require artificial ventilation.
- The maximum muscle weakness may occur only 2–4 weeks after the onset of illness.
- Although full recovery may be expected in 95% of cases, this may take up to 2 years
GBS Ix:

- The **CSF protein** is characteristically markedly raised, but this may not be seen until the second week of illness.
- The CSF white cell count is not raised.
- Nerve conduction velocities are reduced.
GBS Management

- supportive, particularly of respiration.
- Corticosteroids have no beneficial effect and may delay recovery.
- immunoglobulin infusion. If this is not successful, plasma exchange may be effective.
Bell palsy

- Bell palsy and facial nerve palsies. Bell palsy is an isolated lower motor neurone paresis of the VIIth cranial nerve leading to facial weakness.
Myasthenia gravis

- This presents as abnormal muscle fatiguability which improves with rest or anticholinesterase drugs.
Juvenile myasthenia

- This is similar to adult autoimmune myasthenia
- is due to binding of antibody to acetylcholine receptors on the post-junctional synaptic membrane.
- This gives a reduction of the number of functional receptors.
Juvenile myasthenia

- Presentation is usually after 10 years of age with
  - ophthalmoplegia and ptosis,
  - loss of facial expression and
difficulty chewing.
- Generalised, especially proximal, weakness may be seen.
Diagnosis

- improvement following the administration of intravenous edrophonium (less used now)
- acetylcholine receptor antibodies (seen in 60–80%).
- EMG
Treatment

- **neostigmine** or pyridostigmine acetylcholinesterase inhibitors.
- **immunosuppressive** therapy with prednisolone or azathioprine is of value.
- **Plasma exchange** is used for crises.
- **Thymectomy:** is considered if a thymoma is present, or if the response to medical therapy is unsatisfactory.
Muscular Dystrophy

- Duchenne MD
  - X-linked (only boys)
    - Onset typically preschool age
    - PROXIMAL muscle weakness – Gower sign +
    - Face and eye weakness NOT present
    - Pseudohypertrophy of calf (gastroc) muscles
    - Toe walking
    - Gait lordotic and wide based (waddling)
    - Wheelchair bound by early-to-mid teens
    - Progressive dilated cardiomyopathy eventually occurs
    - Death by late teens to early 20s
      - respiratory failure due to weakness, immobility and scoliosis
- Becker MD
  - slowly progressive muscular dystrophy
  - onset after preschool (elementary or later)
  - prognosis more variable
    - may live past middle age
    - may self-ambulate without a wheelchair for may decades
  - progressive dilated cardiomyopathy occurs
    - may result in end-stage cardiac failure
Pseudohypertrophy of Calf muscles

Gower Sign
Diagnosis of both Duchenne vs. Becker MD:
- Elevated CPK (>10,000 DMD, < 10,000 BMD)
- Genetic mutation analysis*
  - X-linked Xp21
  - Mutated Dystrophin gene product (in skeletal and cardiac muscle)
  - 2/3 symptomatic patients have positive genetic mutation, 1/3 patients negative test
- Muscle biopsy - Dystrophin staining
  - Dystrophin **absent** in Duchenne MD
  - Dystrophin **reduced** in Becker MD
  - Normal in all other muscle disorders

Optimal management:
- Preserve ambulation with orthotics
- OT/PT to minimize contractures
- When non-ambulatory, prevention of scoliosis with:
  - proper fitting wheelchair, spinal fusion if necessary
B. **Infant Botulism (6 weeks – 6 months)**

- **Toxin** of the bacteria *clostridium botulinum* (which grows in the intestine) irreversibly binds to the acetylcholine receptor at the NMJ

- **Symptoms:**
  - poor feeding, poor suck, absent gag, weak cry
  - descending paralysis, hypotonia, head lag
  - reflexes reduced
  - constipation
  - respiratory compromise, apnea
Infant Botulism

- Source of C. botulinum spores
  - Soil
  - Foods
    - honey
    - corn syrups

- Diagnosis
  - Isolation of organism or toxin in stool

- Treatment
  - Botulism immune globulin (BIG)
Myotonic disorders

- Myotonia is delayed relaxation after sustained muscle contraction. It can be identified clinically and on electromyography.
Dystrophia myotonica

- dominantly inherited.
- nucleotide triplet repeat expansion,
- so this means there can be anticipation through
Dystrophia myotonica

- **Newborns:**
- **Mother:**
  - This manifests as slow release of handshake or difficulty releasing the tightly clasped fist.
- **Older children** can present with myopathic facies, learning difficulties and myotonia.
- **Adults** develop cataracts and males develop baldness and testicular atrophy.
- Death is usually due to cardiomyopathy.
Figure 27.11 Dystrophia myotonica in an 8-year-old who has marked facial weakness and moderately severe learning difficulties.
Treatment considerations for SMAs:

- aggressive and early respiratory toilet
- assisted ventilation for most type 1 + many type 2
- physical therapy to avoid / minimize contractures
- encouragement of full educational pursuits—intellect unaffected