Motor dysfunction I: Motor unit and myopathic disease

- Myopathic: problems with the muscle
- Neurogenic: problems with the motor neuron and ‘pre’ motor neuron

- 4 examples of motor dysfunction
  – Muscular dystrophy(ies)
  – Amyotrophic Lateral Sclerosis (ALS)
  – Multiple Sclerosis
  – Cerebral Palsy

Characteristic of the disease depends on which component of motor unit affected

- Nerve cell body: motor unit disease
- Motor neuron axon/neuromuscular junction: peripheral neuropathy
- Muscle degeneration: myopathy

- Different clinical implications for different sources of disease

Criteria for distinguishing neurogenic versus myopathic diseases

- Myopathic
  – main symptom = muscular weakness/wasting (atrophy)
    • leads to difficulty walking, lifting, etc.
  – also myotonia, myalgia, cramps
- Neurogenic diseases have these characteristics also, though
  – tendon reflexes lost
  – gradual weakening
  – fasciculations (visible twitches)
‘Upper’ and ‘Lower’ motor neurons

- **Used clinically (historically)**
  - lower motor neurons directly innervate muscle
  - ‘upper’ motor neurons originate in higher brain regions and synapse with ‘lower’ motor neurons in spinal cord
    - technically ‘premotor’ neurons (but don’t confuse with premotor cortex neurons!)
- **Each produces distinctive symptoms**
  - upper: spasticity, overactive tendon reflex (msr), Babinski sign
  - lower: atrophy, fasciculations, loss of tendon reflex, hypotonia

Clinical and lab tests often needed to distinguish the two

- **EMG**
  - rest
  - low contr.
  - max contr.

- **BIOPSY**
  - See histochemistry differences
  - Type I and II fibres usually equal and distributed randomly
    - neuropathy: can see clustering, size changes
    - myopathy: can see damage

Clinical and lab tests often needed to distinguish the two
Neuropathies: symptom mechanisms

- **Motor neuron disease**: affects motor neurons leaving sensory neurons intact
  - selective lesioning of corticospinal tracts
  - fasciculation caused by something beyond spinal cord (axon? terminals? NM junction?)
- **Peripheral neuropathies affect sensory and motor functions**
  - often have *paresthesias* (numbness, tingling, etc)
- **May be categorized as ‘demyelinating’ or ‘axonal’**
  - demyelinating more common

Demyelination: causes ‘negative’ symptoms

- can’t conduct nerve impulse as well
  - lower conduction velocity, conduction block, impaired high impulse frequencies

- leads to slowing of conduction velocity
  - no node (of what?) jumping, smaller diameter
  - attenuates action potential
- lose synchrony of conduction if at different velocities
  - can lead to reflex problems, odd sensations

**Record action potentials to determine conduction velocity**

**Ion channel differences**

- Axonal Normal
- Axonal Partially demyelinated
- Axonal Demyelinated

Lower conduction velocity, conduction block, impaired high impulse frequencies

- Attenuates action potential

- Lose synchrony of conduction if at different velocities
  - Can lead to reflex problems, odd sensations

**Ion channel differences**
Causes

• viral: certain viruses can affect motor nerves selectively (eg, poliomyelitis)
  – virus may induce autoimmune disorder (eg, guillain-barré syndrome…and counting…)
• neonatal hypoxia (eg, cerebral palsy)
• unknown (eg, multiple sclerosis)
• genetic (eg, muscular dystrophies)

Case 1: Duchenne Muscular Dystrophy

• Description
  – Muscular dystrophies are genetic disorders characterized by progressive muscle wasting and weakness that begin with microscopic changes in the muscle
  – As muscles degenerate over time, the person’s muscle strength declines.
  – Patients begin to show signs of muscle weakness as early as age 3. The disease gradually weakens the skeletal or voluntary muscles, those in the arms, legs and trunk. By the early teens or even earlier, the heart and respiratory muscles may also be affected.


• Symptoms (boys only)
  – Children with the disorder are often late in learning to walk
    • clumsy, unsteady gait, difficulty raising arms, walk on toes
  – lose the ability to walk sometime between ages 7 and 12
  – in teen years, activities involving the arms, legs or trunk require assistance or mechanical support
  – often develop fixations of the joints, known as contractures

Gowers manoeuvre: distinct way of getting up with weak legs.
**Causes**
- In 1986, researchers identified the gene that, when flawed (mutation) causes DMD. In 1987, the protein associated with this gene was identified and named dystrophin.
  - lack of dystrophin affects cytoskeleton

**Treatment**
- Physical therapy for contractures (knees, hips, feet, elbows, wrists, fingers) & spinal curvatures
  - Range-of-motion and back straightening exercises
  - Braces on the hands and lower legs
  - Tendon release surgery, spine-straightening surgery
- Medications to slow muscle degeneration
  - Catabolic steroids (prednisone)
    - has side effects: weight gain, bone loss, psychological distress
- Braces, wheelchair (eventually)
- Future: stem cell therapy

**Case 2: Amyotrophic Lateral Sclerosis**

**Amyotrophic:** neurogenic muscle atrophy, **Lateral sclerosis:** hardening of lateral CS tracts

**Description**
- upper and lower motor neuron disease
- motor neurons undergo shrinkage, caused by altered cytoskeleton
  - they ennervate less and less musculature, and those muscles atrophy
- mean onset age: 56-63
• **Symptoms**
  – initially, muscle weakness and stiffness
    • Usually the first muscles affected are those in the hands, arms and legs. (lateral CS tracts)
    • Speech problems, such as slurring, hoarseness, or decreased volume may also occur (dysarthria)
  – Motor neuron signs (normal sensation): atrophy, hyperactive msr, hyper/hypotonia, Babinski’s sign, spasticity, fasciculations

• **Causes**
  – exact causes of the neural degeneration is unknown
  – 5 to 10 % can be attributed to heredity
    • There are multiple genes in which, if mutated, may cause ALS
  – suspects: viruses, neurotoxins, heavy metals, DNA defects (especially in familial ALS), immune system abnormalities, and enzyme abnormalities

• **Treatment**
  – Motor deficits only. Sensory and cognitive function intact
  – Treatment focuses on relieving symptoms and maintaining an optimal quality of life
  – Medications for spasticity, discomfort, pain
  – Physical therapy for cramping, contractures

• **Prognosis**
  – Fifty percent of patients die within 3 years of diagnosis, 20% live 5 years, and 10% live 10 years, 20% longer
Case 3: Multiple sclerosis

**Description**
- In MS, myelin is lost in multiple areas, leaving scar tissue called sclerosis.
  - damaged areas are also known as plaques or lesions
  - Sometimes the nerve fiber itself is damaged or broken
- Most people with MS are diagnosed between the ages of 20 and 50.
  - Two to three times as many women as men have MS
- MS is a chronic, unpredictable neurological disease
- The majority of people with MS do not become severely disabled

**Symptoms**
- Wide range of unpredictable symptoms, vary from person to person, time to time
  - can affect vision, speech, balance, bladder function, coordination, dizziness, pain, tremors can be problems
- Different types
  1) Relapsing-Remitting: flareups then remission (most common - 85%)
  2) primary-progressive: slow continuous worsening (10%)
  3) secondary-progressive: 1) followed by 2)
  4) progressive relapsing: continuous with flareups (rare)

**Causes**
- It is believed that MS is an autoimmune disease
  - In the case of MS, myelin is attacked
- Unknown what triggers the improper autoimmune reaction
- Several factors are involved
  - Genetics
  - Gender
  - Environmental Triggers
    - Possibilities include viruses, trauma, and heavy metals
• **Treatment**
  – Medications can treat relapsing forms of MS:
    1) Synthetic interferons (Avonex, Betaseron)
       • Host cells infected with a virus produce interferons.
         Induces neighbouring cells to synthesize a protein
         that inhibits intracellular viral replication. First line of
         defense against viral infection
    2) Glatiramer Acetate (Copaxone)
       • a synthetic protein that simulates myelin basic protein
         • this drug seems to block myelin-damaging T-cells by
           acting as a myelin decoy
    3) Mitoxantrone (Novantrone)
       • suppressing the activity of T cells, B cells, and
         macrophages that are thought to lead
         the attack on the myelin sheath.

• **Case 4: Cerebral Palsy**
  • **Description (not a disease, actually)**
    – describes a non-progressive medical condition
      that affects control of the muscles, muscle tone
      • Cerebral means anything in the head and palsy refers
        to anything wrong with control of the muscles or joints
        in the body
    – different types
      • Spastic (high tone), ~50%
      • ataxic (low tone)
      • athetoid (mixed tone) ~25%

• **Symptoms**
  – Movement symptoms depend on type
    • Affects limbs, face, mouth, head
  – Learning disabilities in 25-50% of CP children
    • slower rate of learning
  – Seizures in about 50% of children

Source: http://hsc.virginia.edu/cmctutorials/cp/type/type.html
• **Causes**
  – Injury to the brain before, during, or shortly after birth. In many cases, no one knows for sure what caused the brain injury or what may have been done to prevent the injury.
    • neonatal/perinatal: insufficient oxygen (hypoxia) and/or insufficient blood (ischemia) is a major cause of damage to the newborn infant’s brain
      – a hypoxic-ischemic injury
    • prenatal: maternal infection or accident, maternal medical condition such as high blood pressure or diabetes

• **Treatments**
  – Exercise and its favourable impact factors
    • cardio-pulmonary conditioning, muscle strength building and coordination, obesity control, a general sense of well being
    • research needed into detrimental effects, if any
  – Therapies
    • physical, recreational, speech, occupational
  – Adapted objects, communication & mobility aids

**Next class of topics (from periphery to central):**
• Cerebellar motor disorders
• Basal ganglia motor disorders
• Paralysis research