

Neurology

Lecture 4
Pathologies: Parkinson's, CVA,
CMT, ALS

Parkinsonism

Parkinsonism is a syndrome that has features of tremor, rigidity, bradykinesia, and altered postural reflexes – due to brain nigrostriatal dopamine deficiency. The most common cause of Parkinsonism is Parkinson's disease.

- Chronic progressive CNS syndrome of extrapyramidal system due to continuous degeneration of dopaminergic cells in the substantia nigra and depletion of dopamine in the corpus striatum.
- Develop 4 cardinal features - bradykinesia, rigidity, resting tremor and akinesia
- Most commonly develops around 60 years
- Cause is unknown.

- Main pathological process is degeneration of melanin containing dopaminergic neurones of substantia nigra in basal ganglia.
- Onset is insidious – initial symptoms are variable and often missed, but can include apathetic facial expression, softening of voice, muscular weakness and cramps, tremor, foot dystonia

Four major neurological signs:

- **Tremor** – more evident at rest – “pill rolling”; unilateral tremor at rest of one limb is most common presenting complaint; frequency of 4 to 6 Hz; usually resolves on activity; up to 30% do not have tremor initially.
- **Rigidity** – best seen in wrist and elbow – jerky rigidity to motion when examined – “cogwheel rigidity”; may complain of muscle soreness and general aches; can be unilateral or bilateral.
- **Akinesia** – difficulty in initiating movement.
- **Bradykinesia** – slowness of movement (combined with akinesia --> responsible for most of disability seen in Parkinson's disease).

- **Gait:**
Slow to start walking; stride length reduced; festination (rapid short accelerating steps); problems in stopping and changing sequential movements; less arm swing; poor balance when turning; difficulty crossing obstacles; less toe elevation at heel strike; increase in stance phase and double support phase duration; increased variability of gait; more difficulty walking when performing simultaneous motor or cognitive tasks. Gait abnormalities increase risk for falling.

Involvement of foot:

- Foot dystonia (sustained muscle contraction --> twisting, repetitive patterned movement or an abnormal posture) triggered by walking and relieved by rest can occur in up to a third of those with PD.
- Dystonia of the lower limb is the presenting feature in up to 1-3% of those with PD – most of these involve the foot.
- Significant changes in plantar pressure patterns are also seen in those in mild to moderate disease, with a tendency to higher forefoot loading and a medial shift in the load, which may be related to strategies to reduce unsteadiness of gait.
- **Gait retraining:**
 - gait can be improved by guidance of a visible pattern on the ground.
 - visual clues on the ground have been shown to improve gait parameters (Bagley et al, 1991). The cues consisted of yellow coloured rods with a height of 2cm, 45cm apart.

Management

- Two approaches to drug management:
 - 1) Decrease cholinergic activity by anticholinergic/antimuscarinic drugs.
 - 2) Increase dopaminergic activity by dopaminergic drugs.

Drugs:

- Levodopa – improves most features of Parkinsons; first line drug; may cause nausea; postural hypotension; dyskinesia's.
- Dopamine agonists (bromocriptine, pergolide, ropinirole) – less effective than levodopa, but less likely to cause dyskinesia; may cause nausea, hypotension.
- Anticholinergics (eg benzhexol) – second line drug for tremor but not rest of Parkinsons (symptoms can substantially worsen if drug is rapidly withdrawn).
- COMT inhibitors (eg entacapone, talcapone) - second line drug.
- Amantadine – has mild anti-parkinsonism effects.

Cerebrovascular Accident (Strokes)

- Common acute nonconvulsive focal neurological clinical syndrome due to ischaemia or haemorrhage – not necessarily a diagnosis, but a symptom of an underlying aetiological diagnosis. Occurs when oxygen supply to brain is suddenly stopped.
- Risk factors include
 - age (2/3rd > 65yrs);
 - male;
 - cigarette smoking;
 - hypertension; diabetes mellitus; dyslipidaemia; obesity;
 - sedentary lifestyle/lack of physical exercise;
 - alcohol consumption; oral contraceptives; polycythemia; atrial fibrillation; family history; history of prior stroke or transient ischaemic attack.

Types:

- Ischaemic strokes – thrombotic brain infarct (45-65%); embolic brain infarct (10-20%).
- Haemorrhagic strokes – intracerebral haemorrhage (5-15%); subarachnoid haemorrhage (5-10%).
- Unknown, combined, other strokes – up to 10%.
- 70% present with hemiparesis, 20% with aphasia; abrupt onset.

- The clinical features of ischaemic strokes usually depend on which artery is involved.
- a) *Middle cerebral artery (MCA)*:
 - Most common pattern; extent of clinical signs will depend on collateral circulation and site of occlusion; usually embolic.
 - Contralateral hemiparesis and hemisensory loss (usually severe) – mainly face and arms; eyes deviate to side of infarct; feet and legs less affected than arms; aphasia if dominant hemisphere is affected; may later develop confusional states (if left hemisphere) or depressive states (if right hemisphere).

- b) Anterior cerebral artery:
Collateral circulation is often adequate, so less common; face not normally involved; eyes deviate towards side of lesion; hemiplegia, motor and sensory deficits of contralateral limb (sensory loss affects leg more than arm). If paracentral lobe --> mainly leg and foot affected with hemiparesis and hemisensory loss. If frontal and parietal lobe --> inability to correctly identify objects; apathy and personality changes.
- c) Posterior cerebral artery:
Contralateral homonymous hemianopia; hemisensory loss; thalamic pain visual agnosia; impairment of memory.
- d) Internal carotid artery:
Contralateral hemiparesis and hemisensory loss; partial loss of sight; half have history of TIAs.

- e) Verteobasilar artery:
Imbalance, vertigo, vomiting, nystagmus; lack of co-ordination; ipsilateral pain and temperature sensory loss on face and contralateral loss in rest of body; ipsilateral ataxia; Horner's syndrome.
- f) Lacunar stroke:
Common in those with hypertension; due to occlusion of small arterioles or single deep perforating artery --> small deep cystic infarcts (lacunar infarcts). Four common clinical types – a motor hemiparesis stroke (pure motor stroke); a hemisensory stroke; a dysarthria and arm involvement; and an ataxia with crural paresis (there are other less common types).

- **Haemorrhagic strokes:**
Sudden severe 'explosive' headache with loss of consciousness; grand mal seizure; severe confusional state (often fluctuating); bradycardia.
- Limb synergy patterns: These are patterns of mass movement of the limbs that occur after injury to the cerebral voluntary movement system (not just in CVA's) – limb assumes a flexion or extension synergy pattern:
- Lower extremity flexion synergy pattern --> pelvic protraction, pelvic depression, hip flexion, hip abduction, hip external rotation, knee flexion, ankle dorsiflexion, foot inversion, toe and hallux dorsiflexion.
 - Lower extremity extension synergy pattern --> pelvic retraction, pelvic elevation, hip extension, hip adduction, hip internal rotation, knee extension, ankle plantarflexion, foot inversion toe and hallux plantarflexion.

Management

- Acute – medical emergency - stabilise patient, protect airway; assessment by CT or MRI to determine if ischaemic or haemorrhagic; IV tissue plasminogen activator; adequate oxygen; followed by early mobilisation, adequate hydration, bowel program, prevent pressure sores, prevention of emboli, reduction of oedema .

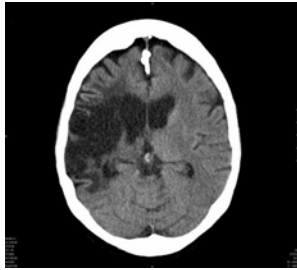
Post-acute – rehabilitation therapy (physiotherapy, occupational therapy, speech therapy), social services, evaluate for depression, management of risk factors; pharmacological (aspirin).

Involvement of the foot:
There are three hemiplegic movement patterns that influence control and alignment of the foot:

- 1. Characterised by severe loss of motor control. Weight is born largely by unaffected leg --> centre of gravity shifted toward that leg. Affected side has flexed knee, plantarflexed ankle, weight is born by forefoot, midtarsal and subtalar joints pronate; poor toe clearance during swing; muscle contractures.
- 2. Characterised by an incomplete pattern of motor function recovery, an inability to sequence muscle firing and the presence hypertonicity. Affected side tends to have a genu recurvatum (but retraining may have corrected this); forefoot makes initial contact during stance; lack of ankle dorsiflexion and early forefoot contact --> midtarsal joint collapse and subtalar joint pronation; claw toes due to extensor substitution; elevates pelvis to initiate swing --> toe clearance; during swing foot supinates and adducts during to firing of anterior and posterior tibial muscles
- 3. Characterised by an abnormality of muscle co-activation, an inability to selectively fire the appropriate initiation patterns and the inability to stop firing patterns once they are activated. Do not have control of agonist and antagonist muscles. Ankle is plantarflexed and rearfoot is supinated during swing --> lateral border contacts ground first – if rigid --> foot remains inverted. If flexible --> midtarsal joint collapses; claw toes develop.

Problems of foot

- Weakness of some muscle groups and spasticity of others;
- loss of mobility due to foot pathology; joint hypermobility and poor alignment due to proximal influences; muscle contractures; lack of ankle dorsiflexion
- Swelling with pitting oedema (sometimes pain) is common in paralysed leg --> may further limit movement. Swelling may be due to gravity in dependant limb, lack of contraction of muscle, DVT, cardiac failure, hypoalbuminuria or reflex sympathetic dystrophy.
- Feeling of coldness in limb occurs in some (arm more frequent than leg) Ankle-foot orthoses are usually used to improve the gait of those with hemiparetic gait, however an inappropriate AFO can make walking more difficult.



Old right middle cerebral artery stroke

Hereditary Motor and Sensory Neuropathy

- Hereditary Motor-Sensor Neuropathy is also known as Charcot-Marie-Tooth Disease
- There are many forms of CMT disease, including CMT1, CMT2, CMT3, CMT4

Charcot-Marie-Tooth Disease (CMT) Hereditary Motor and Sensory Neuropathy **Type I**

- CMT the most commonly inherited neurological disorder and is found world-wide in all races and ethnic groups.
- Type 1 hereditary motor and sensory neuropathy (HMSN) is an inherited disorder characterised by degeneration of the posterior columns of the spinal cord, loss of anterior horn cells with degeneration of the spinocerebellar tracts, demyelination of peripheral nerves.
- Clinical features: Usually onset is around 5 years (first concern may be difficulty fitting shoes). Characterised by atrophy of the peroneals and intrinsic muscles with a pes cavus foot - may present with pain under lateral forefoot. Pes cavus develops as muscle weakness primarily affects peroneus brevis and tibialis anterior with peroneus longus being spared - plantarflexion of first ray.

■ HMSN/CMT Type 2: Peroneal Muscle Atrophy

Characterised by axonal degeneration of peripheral nerves and is clinically similar to CMT. Foot plantarflexors are involved to a greater extent than CMT, due to profound distal muscle weakness and wasting - develop 'stork legs'. Develop a 'flail foot' that may be in varus or valgus

- **HMSN/CMT Type 3: Dejerine-Sottas Disease**
Autosomal recessive. Characterised by hypertrophic interstitial neuropathy and is pathologically similar to CMT. Begins in infancy. Motor milestones are delayed and sensation is impaired – reflexes absent. Develop pes cavus and drop foot deformities. Spinal deformities, so usually confined to wheelchair.

■ HMSN/CMT Type 4: Refsum's Disease

Characterised by anorexia, gait abnormalities, ichthyosis, night blindness, eye complications, hearing deficits, polyneuropathy with distal muscle weakness and muscular atrophy. Loss of sensation and pes cavus are common.



- Mild cases are often misdiagnosed as pes cavus and not investigated further.
- Initial symptoms are the peroneal brevis weakness and a 'foot slap' with falls and tripping. Patients generally notice a feeling of weakness in the legs.
- Progressive loss of vibration sensation and proprioception.
- Rearfoot and first ray are usually initially flexible, later becomes fixed.
- Gait: Steppage Type

Diagnosis Overview

- Good History including family history
- evidence of foot deformities, such as:
 - high arches, hammertoes, inverted heel, flat feet.Other orthopedic problems, such as mild scoliosis or hip dysplasia, may also be present. A specific sign that may be found in patients with CMT1 is nerve enlargement that may be felt or even seen through the skin. These enlarged nerves, called hypertrophic nerves, are caused by abnormally thickened myelin sheaths.

Further Studies

- nerve conduction studies and electromyography (EMG).
- Nerve biopsy to confirm diagnosis

- Treatment:
 - conservative management of symptoms of pes cavus
 - surgical correction of foot deformity.

Amyotrophic Lateral Sclerosis (ALS) (Lou Gehrig's Disease)



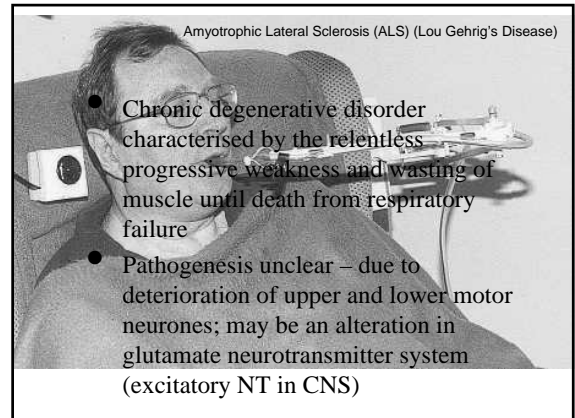
- <http://www.youtube.com/watch?v=N90k0H11Oyg&feature=related>
- <http://goldbamboo.com/topic-t1064-a1-6Amyotrophic Lateral Sclerosis.html>
- <http://www.youtube.com/watch?v=yZeWWJHTV1g>

Upper/Lower MN

- The voluntary motor system consists of two primary groups of neurons: upper motor neurons and lower motor neurons.
- Upper motor neurons: originate in the pyramidal cells of the motor cortex, cerebellum and brainstem and modulate the activity of the lower motor neurons (ie. the neuron from the motor cortex to the ventral horn of the spinal cord)
- Lower motor neurons: are found either in the anterior horn of the spinal cord (grey matter) or the cranial nerve nuclei of the brainstem. (ie. the second order neurones)
- The axons of both groups extend through peripheral nerves to skeletal muscles

Classification

- 1) Upper motor neuron diseases:
1: primary lateral sclerosis; 2: spastic paresis; 3: spastic paraplegia
- 2) Combined upper and lower motor neuron disease: amyotrophic lateral sclerosis (ALS)
- 3) Lower motor neuron disease:
1: spinal muscular atrophies; 2: x-linked spinobulbar muscular atrophy; 3: poliomyelitis



Clinical features of ALS

- Initially complain of muscular weakness, usually asymmetrically affecting one limb
- Also fasciculations and atrophy (lower motor neuron signs) – 20-40% the lower limb (usually the foot dorsiflexors) --> spreads proximally and to other limb; Cramps may precede weakness.
- Develop spasticity, hyporeflexia (lower motor neurons), hyperreflexia and atrophy

Treatment for ALS

- Supportive (emotional, psychological and family) and symptomatic
- Riluzole (sodium channel blocker that inhibit release of glutamate) may prolong survival; Baclofen/quinine for muscle cramps
- Physiotherapy (exercises); speech therapy; dietician; occupational therapy (adaptive equipment, wheelchair and aids)
- Gastrostomy tube if ability to chew and swallow affected

