o Dementia → PD, Lewy Bodies, Frontotemporal, Vascular, Prion

Neurodegenerative Diseases

o Motor Neuron Disease

Neurodegenerative Diseases

- Umbrella term for disorders characterised by progressive neuronal loss

Dementia

- Clinical syndrome defined by:
  - Acquired loss of higher mental function, affecting two or more cognitive domains (e.g.: episodic memory, language etc)
  - Of sufficient severity to significantly cause social or occupational impairment
  - Occurring in clear consciousness (i.e.: not just delirium)
- Mild Cognitive Impairment (MCI): intermediate states between normal cognition and dementia (basically a pre-dementia state)

Causes of Dementia- Degeneration

- **Alzheimer's Disease:**
  - Commonest cause of dementia
  - Technically a definitive diagnosis can only be made by histopathology, but key clinical features and diagnostic investigations can usually give a pretty accurate diagnosis during the patient's lifetime.
- **Dementia with Lewy Bodies**
  - Characterised by visual hallucinations (often of people or animals or the sense of a 'presence', fluctuating cognition with variation in attention and alertness, sleep disorders (especially REM sleep behaviour disorder), dysautonomia and Parkinsonism.
  - Memory loss may not occur in the early stages
  - Delusions and transient loss of consciousness occur
  - Cognitive features dominate, later on Parkinsonism may evolve (it is typically mild)
- **Frontotemporal Dementia**
  - A group of neurodegenerative disorders characterised by frontal lobe and temporal lobe atrophy on MRI and at post-mortem
  - Onset is usually below the age of 65 and there is often a family history
  - Three distinct presentations, depending on which anatomical region is affected first:
    - Frontal Presentation: personality change, emotional blunting, apathy, disinhibition, carelessness, behavioural change (although memory is perfectly preserved)
    - Temporal Presentation: progressive impairment of language function. There are two types within this categorisation:
      - Involvement of left temporal lobe: semantic dementia with progressive loss of word-findingability. Speech is fluent but lacking in meaningful content and the person has difficulty comprehending language
      - Post-Sylvian atrophy: progressive non-fluent aphasia with loss of verbal fluency
- **Vascular Dementia:**
  - Can be progressive and similar to AD (can also co-exist with AD)
  - There is either a history of TIAs, or the dementia follows a succession of cerebrovascular events, or the dementia has a stepwise course
  - Common additional features: apraxic gait disorder, pyramidal signs, and urinary incontinence
  - Typically, an MRI will show widespread small vessel disease
- **Prion Diseases:**
  - Transmissible neurodegenerative disorders (caused by accumulation of misfolded native prion protein)
  - CJD: commonest prion disease, may be sporadic, iatrogenic or familial. Rapidly progressing cognitive decline
  - Variant CJD: young adults, neuropsychiatric symptoms followed by ataxia and dementia with myoclonus and chorea

Two other important neurodegenerative diseases (which are mentioned elsewhere)

- Huntington's Disease
- Parkinson's Disease

MOTOR NEURON DISEASE

- Degeneration of motor neurons in motor cortex, cranial nerve nuclei and anterior horn cells. You get progressive weakness, eventually resulting in death due to respiratory failure
- Average age of presentation is 50-75 years
- Upper *and* lower motor neurons are affected, BUT there is *no* sensory loss or sphincter disturbance ****THIS IS THE DISTINGUISHING FEATURE OF MND (as opposed to MS or polyneuropathy)****
- Motor neuron disease *never* affects CNs 3, 4 and 6, therefore it *never* affects eye movements ****THIS IS THE DISTINGUISHING FEATURE OF MND (as opposed to Myasthenia)****
- No one really knows why MND occurs, however there may be some viral component to it

More about MND

- Umbrella Term for a number of different disorders:
  - Amyotrophic Lateral Sclerosis (ALS): UMN and LMN features which usually start in one limb (e.g.: the hand becomes weakened and wasted and there are fasciculations). It then spreads
  - Progressive Muscular Atrophy: pure LMN weakness with wasting and fasciculations. Usually contained to one limb
  - Primary Lateral Sclerosis: rarest form of MND. Features include tetraparesis and pseudobulbar palsy
  - Bulbar Palsy:
    - Palsy of the tongue, the muscles for chewing and swallowing, and the facial muscles
    - Palsy occurs due to a loss of function of the motor nuclei in the medulla
    - LMN lesions occur; flaccid, fasciculating tongue, absent jaw jerk, speech is hoarse/nasal/quiet
    - Causes: MND, Guillain-Barre, Polio, Syringobulbia, brainstem tumours, central pontine myelinolysis (CPM)
  - Pseudobulbar Palsy:
    - UMN lesions of the muscles of eating, swallowing and talking
    - Due to bilateral lesions above the midpons
    - Signs: spastic jaw, increased jaw jerk, 'Donald duck speech', random weeping or giggling not associated with mood alterations ('emotional incontinence')
- Features:
  - >40 years old
  - Stumbling gait
  - Weak grip
  - LMN & UMN signs
  - (aspirational pneumonia can occur)
- Treatment
  - Palliative (5 year prognosis)
  - Treat the symptoms such as Riluzole (antiglutamate drug which sometimes helps to slow the progression of the disease), Propantheline or Amytriptiline for drooling etc