Pathology of the Central Nervous System

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II. Major disease categories

- V – Vascular
- I – Infectious
- T – Traumatic
- A – Autoimmune
- M – Metabolic
- I – Iatrogenic / Idiopathic
- N – Neoplastic
- C – Congenital / Genetic
- D – Degenerative

CEREBROVASCULAR DISEASE, INTRACRANIAL HAEMORRHAGE
CNS INFECTIONS
INTRACRANIAL HAEMORRHAGE
DEMYELINATING DISEASES
STORAGE DISEASES, VITAMIN DEFICIENCIES, ALCOHOLIC ENCEPHALOPATHY
CNS TUMOURS
MALFORMATIONS, NEUROCUTANEOUS SYNDROMES
NEURODEGENERATIVE DISEASES
PARKINSON DISEASE
ALZHEIMER DISEASE
HUNTINGTON CHOREA
Neurodegenerative disease
- Alzheimer disease
- Parkinson disease

Metabolic CNS disease
- Alcohol

Neurodegenerative Diseases

- Progressive loss of specific groups of neurons or brain areas
- >65y higher incidence
- Main syndromes
  - 1. Dementia: e.g. Alzheimer disease
  - 2. Movement disorders:
    - Parkinson disease (substantia nigra neurones)
    - Huntington chorea (basal ganglia)
  - 3. Motor weakness: e.g. Motor neurone disease
  - 4. Others: e.g. Spinocerebellar degenerations, Friedreich’s ataxia etc.
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Alzheimer Disease

- Aging population
- 20% in > 80 yrs age group
- “Early onset” group
- Genetic basis
  - Chromosome 21 – APP (amyloid precursor protein) → production of AB (beta amyloid)
  - Chromosome 19 – Apo E4 subtype (isoform) → tau hyperphosphorylation
- Clinical – progressive cognitive decline; immobility; pneumonia
Gross morphology
- Smaller, atrophied brain
- Temporal lobe most affected, also frontal and parietal regions

AD: Pathology
- Abnormal protein deposition (Hippocampus, neocortex)
  - Amyloid plaques (senile plaques, extracellular)
  - Neurofibrillary tangles – tau protein (within neurons)
  - Neuronal damage and loss

Parkinson disease

- >45y
- Pathology
  - 1. Loss of nerve cells from substantia nigra (midbrain):
    - Contain neuromelanin
    - Reduced dopamine to the basal ganglia
  - 2. Lewy bodies in neurones
- Genetics
  - Disorder of α-synuclein gene → accumulation of abnormal protein: Lewy bodies
- Clinical:
  - Rigidity
  - Slowing of voluntary movements
  - Rest tremor
Loss of pigment from substantia nigra

Lewy body

http://library.med.utah.edu/WebPath/jpeg5/CNS182.jpg
Huntington disease (chorea)

- Autosomal-dominant
- Mutation in *Huntingtin* gene → increased trinucleotide repeats → Huntingtin protein accumulates in neurones of striatum (caudate nucleus, putamen), cortex → Atrophy, neuronal inclusions
- Clinical:
  - Personality alterations, cognitive decline
  - Abnormal movements
  - 15 -20 yrs average duration
  - Death from aspiration pneumonia, heart disease
Summary: Neurodegenerative Diseases

- Specific groups of neurons/areas of brain
  - Alzheimer disease (Cognitive – Dementia)
  - Parkinson disease (Movement)
  - Huntington disease (Movement)
- Accumulation of abnormal proteins
  - Within neurons
  - Extracellular (A beta protein)
  - Neuronal damage and loss → clinical manifestations
- May have genetic predisposition

Alcohol and the brain

1. **Fetal alcohol syndrome**
   - Growth retardation, cerebral malformations
2. **Acute intoxication** → respiratory depression → death!
3. **Chronic alcoholism**
   - Cerebral cortical atrophy
   - Cerebellar atrophy
   - Wernicke encephalopathy (thiamine deficiency)
   - Korsakoff’s psychosis
Alcohol and Korsakoff’s Psychosis

- Korsakoff’s syndrome (= Korsakoff’s dementia, Korsakoff’s psychosis)
  - Lack of thiamine (vitamin B1) in the brain
  - Damage to the medial thalamus, mammillary bodies
  - Generalised cerebral atrophy

- Risk factors:
  - Chronic alcohol abuse
  - Severe malnutrition

Pathology:
- Neuronal damage and loss
- Gliosis
- Haemorrhage in mammillary bodies

Atrophy of cerebellar vermis

Haemorrhage in mamillary bodies
Acknowledgements

Unless otherwise specified, illustrations used in this presentation are from Robbins and Cotran Pathology Textbook (Elsevier); Histology for Pathologists