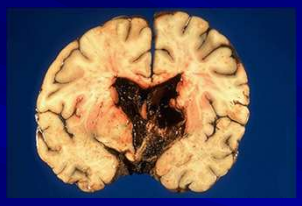
Pathology of the Central Nervous System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II. Major disease categories

- V – Vascular — CEREBROVASCULAR DISEASE, INTRACRANIAL HAEMORRHAGE
- I – Infectious — CNS INFECTIONS
- T – Traumatic — INTRACRANIAL HAEMORRHAGE
- A – Autoimmun — DEMYELINATING DISEASES
- M – Metabolic — STORAGE DISEASES, VITAMIN DEFICIENCIES, ALCOHOLIC ENCEPHALOPATHY
- I – Iatrogenic / Idiopathic
- N – Neoplastic — CNS TUMOURS

- C – Congenital / Genetic — MALFORMATIONS, NEUROCUTANEOUS SYNDROMES
- D – Degenerative — 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 : eg. Alzheimer disease
  - 2. Movement disorders :
    - Parkinson disease (substantia nigra neurones)
    - Huntington chorea (basal ganglia)
  - 3. Motor weakness : eg. Motor neurone disease
  - 4. Others : eg. Spinocerebellar degenerations, Friedreich's ataxia etc.

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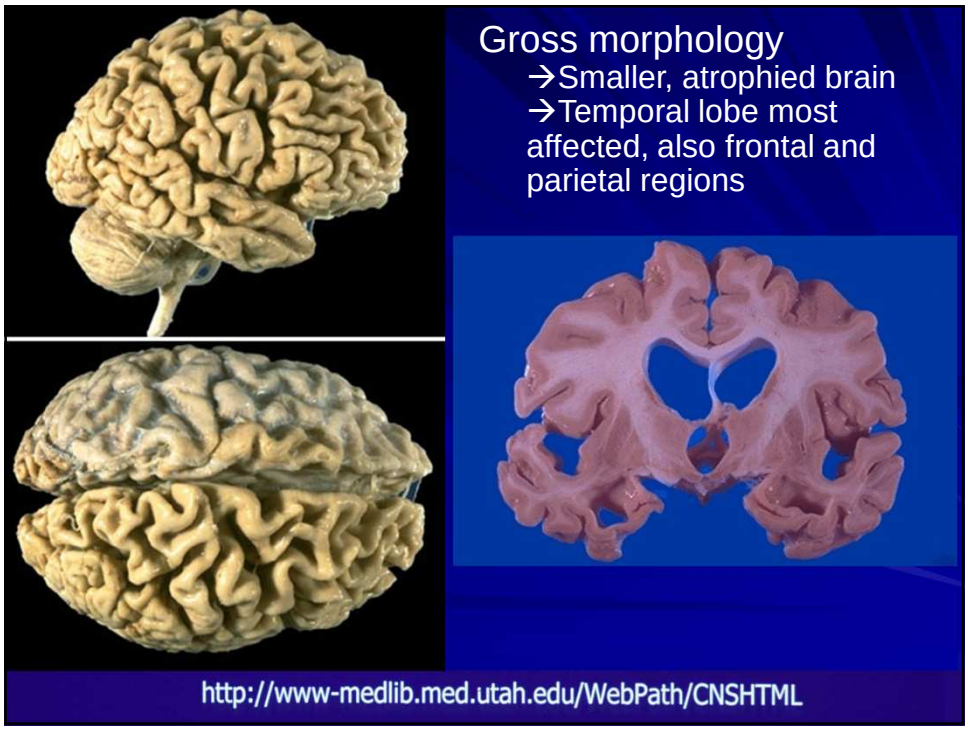
Alzheimer Disease

- Aging population
- 20% in > 80 yrs age group
- "Early onset" group
- Genetic basis

- Chromosome 21 – APP (amyloid precursor protein) → production of AB (beta amyloid)

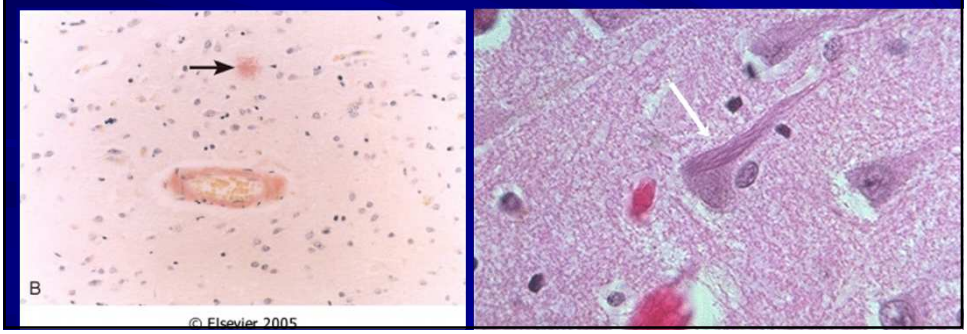
- Chromosome 19 – Apo E4 subtype (isoform)→ tau hyperphosphorylation

-Clinical – progressive cognitive decline ; immobility; pneumonia

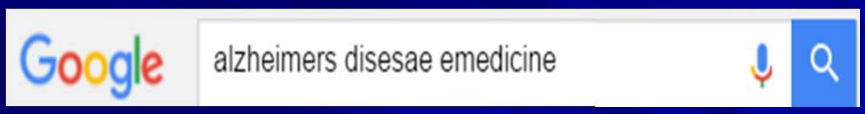


AD: Pathology

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

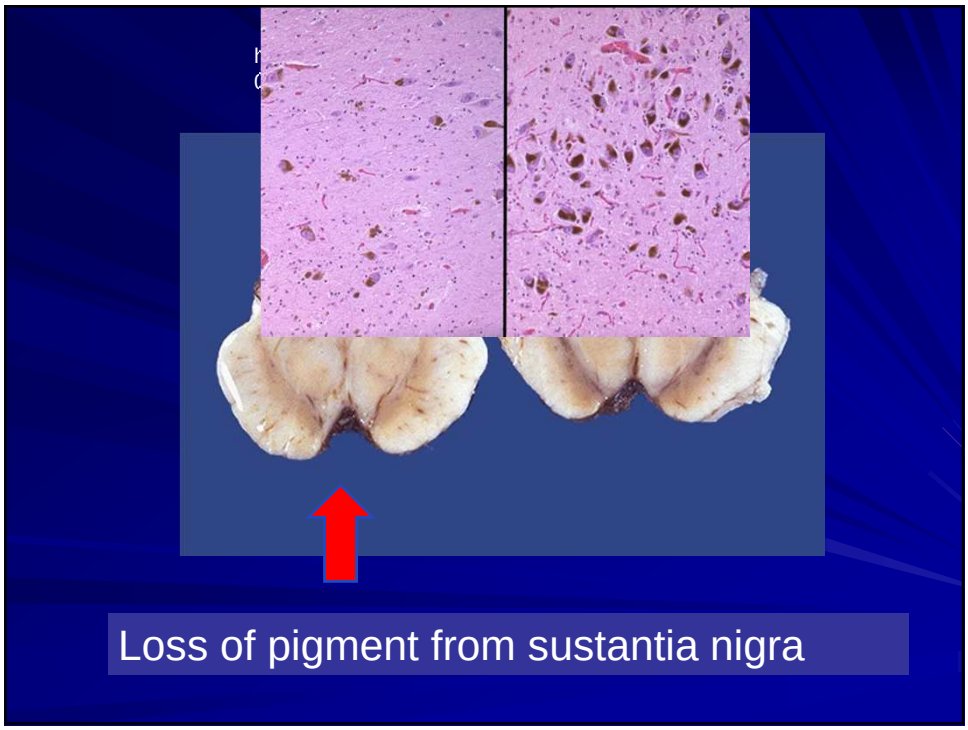


http://emedicine.medscape.com/article/1134817-overview

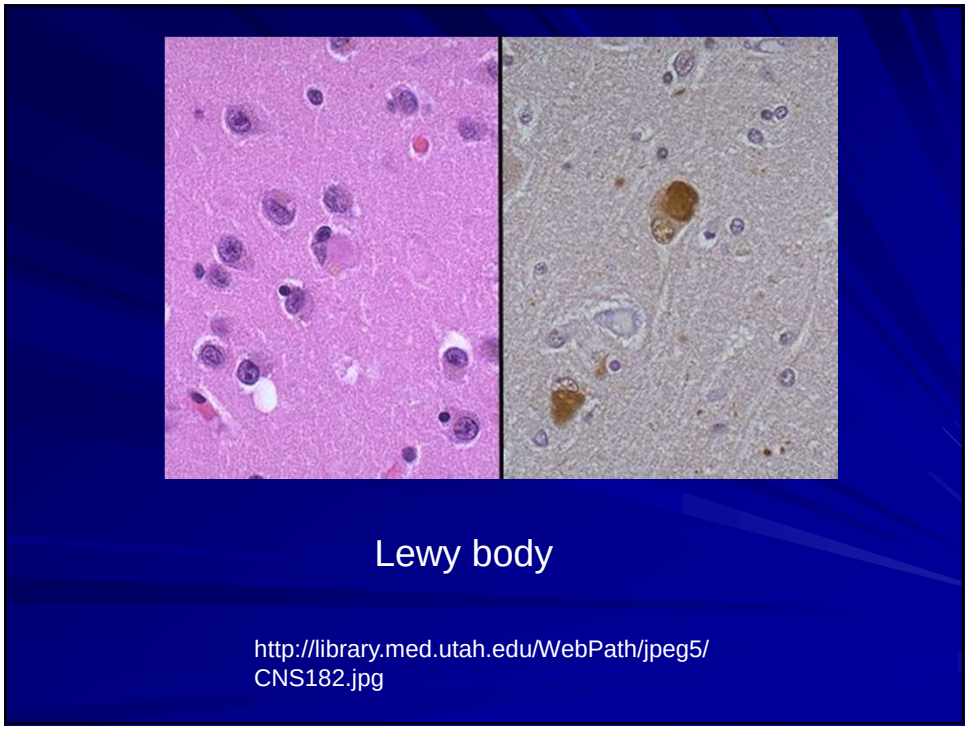


Parkinson disease

- >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 sustantia nigra



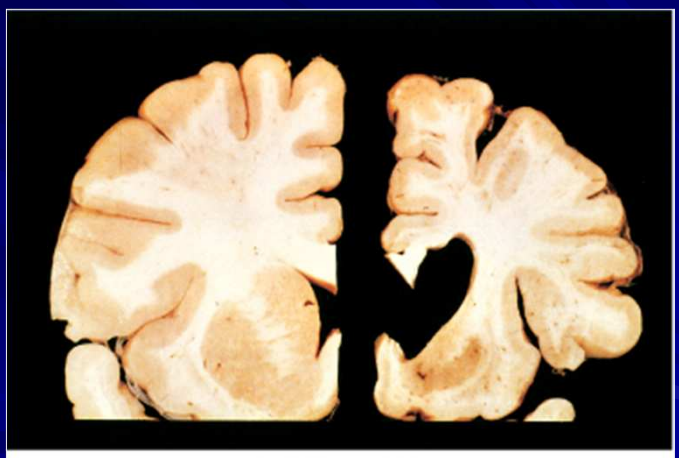
Lewy body

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

HD



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 manfestations
- May have genetic predisposition

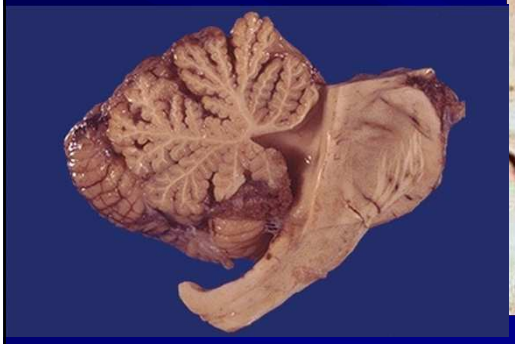
Alcohol and the brain

- 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

http://library.med.utah.edu/WebPath/jpeg5/CNS081.jpg

Haemorrhage in mamillary bodies

http://yassermetwally.files.wordpress.com/2008/03/ver3.jpg

Acknowledgements

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