Notes on Dementia

Dementia is a progressive decline in cognitive function due to damage or disease in the body beyond what might be expected from normal aging.

<table>
<thead>
<tr>
<th></th>
<th>Early onset dementia (aged &lt;65 years)</th>
<th>Late onset dementia (aged &gt;65 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's Disease</td>
<td>34%</td>
<td>60%</td>
</tr>
<tr>
<td>Vascular Dementia</td>
<td>18%</td>
<td>20%</td>
</tr>
<tr>
<td>Lewy Body Dementia</td>
<td>8%</td>
<td>15%</td>
</tr>
<tr>
<td>Fronto-Temporal Dementia</td>
<td>14%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Alcohol Related Dementia</td>
<td>12%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Other</td>
<td>14%</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>

Alzheimer's Disease (AD)

Risk factors – age, sex F:M (2:1)

Aetiology

Genetics
- Rare to find familial autosomal dominant pattern, tend to present with earlier age of onset
- Chromosome 21 mutations in gene encoding for amyloid precursor protein (APP)
- Recognised association with Down’s Syndrome (Trisomy 21)
- and Alzheimer’s Disease (~100% develop the typical histopathological lesions of AD)
- Chromosome 14 (early onset AD)
- Chromosome 19 (later onset AD)

Environmental
- Head trauma
- Aluminium toxicity (controversial)

Clinical features
- Insidious onset
- Presents with memory failure, accompanied by lability of mood, anxiety, depression or apathy, impaired attention
- Abnormal disinhibited behaviour with agitation (esp. at night)
- Confusion and wandering at night
- 3 phases -  
  - first, predominantly memory problems  
  - second, general cognitive decline, psychotic symptoms  
  - third, terminal phase, neurological signs, primitive reflexes and double incontinence

**Prognosis**
- Deterioration to death within 2-5 years of hospital admission

**Vascular/Multi-infarct dementia**

**Risk factors**
- Anything vascular e.g., Hypertension, diabetes, AF, IHD, carotid stenosis, smoking, high cholesterol, M>F

**Aetiology**
- Multiple emboli from extracranial arteries, ischaemia and infarction, multiple micro-infarcts, cystic necrosis and gliosis

**Clinical features**
- Acute onset with stepwise deterioration  
- Fluctuating cognitive impairment  
- Depression and emotional incontinence  
- Focal neurological deficits  
- Personality and insight can be preserved until late

**Prognosis**
- Slightly longer than AD  
- Death in 4-5 years and 50% of these from IHD

**Lewy Body Dementia (LBD)**

**Aetiology**
- Abnormal accumulation of ubiquitin  
- Linked to Parkinsonism

**Clinical features**
- Fluctuating cognitive impairment  
- Parkinsonism  
- Dementia milder than AD  
- Hallucinations more prominent  
- Visuospatial problems prominent  
- Susceptibility to neuroleptics  
- Falls

**Prognosis**
- Fluctuating, variable course with duration of ~7 years
**Fronto-Temporal Dementia**

Includes Pick’s disease

**Aetiology**
- High familial incidence, mutation on Chromosome 17 (in the tau gene) occurs in some families.

**Clinical features**
- Personality change from disinhibition and impulsivity to inertia
- Neglect
- Rigidity and inflexibility
- Hyperorality
- Utilisation behaviour
- Stereotypies and rituals
- Memory can be variable
- Spatially unaffected
- Language disorders including perseveration and mutism, naming disorders
- Motor neurone disease
- EEG is normal

**Prognosis**
- Slow deterioration of functions, 8-11 years

**Alcohol Related Dementia**

**Aetiology**
- Cortical shrinkage/ventricular enlargement, especially frontal lobes

**Clinical Features**
- Poor memory
- Impaired speed and attention
- Visuospatial deficits
- Frontal lobe problems
- Psychotic symptoms
- Korsakoff’s Syndrome – chronic amnesia
  - confabulation
  - immediate memory fine, recall very poor

**Prognosis**
- Progression with continued drinking, may improve with abstinence
Classification and other causes of dementia

Cortical
- Alzheimer’s Disease
- Lobar atrophy eg fronto-temporal dementia
- Spongiform Encephalopathies e.g. CJD (extremely rare, rapidly progressive, myoclonus and spasticity, cerebellar ataxia, psychotic symptoms, death 3-12 months, M=F, death within 3-12 months)

Sub-cortical
- Parkinson’s disease
- Huntington’s chorea
- Progressive Supra Nuclear Palsy
- Vascular dementia

Cortical/sub-cortical
- Lewy Body Dementia
- Vascular Dementia

Subcortical dementia
Midbrain and brainstem affected
- psychomotor slowing
- amnesia
- perseveration
- impaired manipulation of acquired knowledge
- poor planning ability
- motor abnormalities
- higher cortical functions relatively spared e.g. apraxia, agnosia etc

Investigations
FBC, ESR, B12 and Folate, TFTs, LFTs, U+E’s, Glucose
MSU
ECG
CT brain

EEG
Normal ageing: slowed alpha, inc theta, inc delta
Alzheimer’s Disease
- non-specific changes
- diffuse slowing, dec alpha and beta, inc theta and delta, paroxysmal bifrontal delta waves
Vascular
- asymmetry and localised slow waves
Frontotemporal
- more likely to be normal
CJD
- slow background rhythm with paroxysmal sharp waves
Notes by Rebecca Exley 2009

Neuropathology

Alzheimer’s Disease
- global brain atrophy, ventricular enlargement, sulcal widening, marked in frontal and temporal lobes
- neuronal loss, shrinking of dendritic branching, reactive astrocytosis
- neurofibrillary tangles
- Neuritic plaques – core of amyloid

Pick’s disease
- asymmetrical atrophy of anterior temporal and frontal lobes, knife blade gyri, ventricular enlargement
- Pick’s bodies – straight neurofilaments, paired helical filaments, endoplasmic reticulum

Lewy Body disease
- Lewy bodies – protein neurofilaments, granular material, microtubule assembly protein, ubiquitin, tau protein
- neurofibrillary tangles and neuritic plaques
- density of Lewy bodies is much higher in the cingulate gyrus, parahippocampal gyrus and temporal cortex than when compared with Parkinson’s disease

Treatment

Biological
- cholinesterase inhibitors
- antipsychotics
- antidepressants

The Cholinergic hypothesis
Antimuscarinics cause memory deficits and confusion
Loss of ACh neurones in Alzheimer’s disease
Acetylcholinesterase in the CNS and periphery
Butyrylcholinesterase in the plasma and glial cells - inhibition may cause unwanted side-effects
LBD - also has ACh impairment
Vascular - best managed by treating vascular pathology, controlling hypertension and diabetes

Psychological
Social
- Social services
- Day centres

Please Note
These notes were written by Dr Rebecca Exley as an F1 doctor in 2009. They are presented in good faith and every effort has been taken to ensure their accuracy. Nevertheless, medical practice changes over time and it is always important to check the information with your clinical teachers and with other reliable sources. Disclaimer: no responsibility can be taken by either the author or publisher for any loss, damage or injury occasioned to any person acting or refraining from action as a result of this information