Dementia

Definition: The global impairment of higher cortical functions including memory… in the absence of clouding of consciousness.
Epidemiology: There are approximately 20 million sufferers of dementia in the world.
Clinical features: Amnesia (Short term and Long term), Apraxia, Agnosia, Aphasia and Neuropsychiatric features
Differential diagnosis: Can be confused with Delirium; Depression; Normal ageing: late onset schizophrenia
Causes: Lots of causes but main causes **Alzheimer's disease, vascular dementia, Dementia with Lewy Bodies**

1. Alzheimer's Disease

Epidemiology: Alzheimer's disease (AD) is one of a number of dementing illnesses. There are approximately 11 million people in the world with AD. At present in the UK, there are approximately 1/3 million patients suffering from AD. Since AD is largely a disease of old age this figure is likely to double by the year 2025 as the number of people aged over 65 doubles. Epidemiological studies have shown that increasing age is the most robust risk factor for AD and its prevalence appears to approximately double for every five years increase in age, at least up until the age of 90 years. Incidence and prevalence studies suggested an increased incidence and prevalence of AD amongst women. Apart from increasing age the clearest associated risk factor for AD is that of a positive family history amounting to an approximately three fold higher risk in first-degree relatives of patients with AD. This familial factor is likely to be genetic since recent twin studies suggest that the heritability of AD is substantial (between 0.6 - 0.74). More direct support for a genetic component to AD comes from the recognition of a small number of patients (approximately 200 family's worldwide) who develop the disease largely before the age of 65 years in a clear autosomal dominant pattern. To date a number of mutations in three genes (Amyloid precursor protein (APP), presenilin 1 and presenilin 2) have been described which lead to this early form of AD. In AD developing after the age of 65, no clear autosomal dominant patterns have been established. However, a wide number of different candidate genes have been proposed, mutations in which have been associated with an increased risk of developing AD. Of these candidates, the most substantially corroborated evidence remains that of the presence of the common polymorphism Apolipoprotein E ε4. Prevalence studies suggest that a presence of one copy of the APOE ε4 allele is associated with a three times increased risk of developing AD whilst the presence of two copies is associated with an increased risk of approximately nine times. However, it is also clear that possession of the ApoE ε4 allele is neither a necessary or sufficient condition for the development of AD. Although AD is clearly multi-factorial, studies looking for environmental risk factors have been largely disappointing. These have included early reports suggesting that AD was associated with exposure to aluminium, alcohol, head injury and a family history of psychiatric illness, especially depressive illness. In addition other studies have suggested an inverse association with arthritis and education.
Pathogenesis: AD is characterised by the presence of cortical neuritic plaques and tangles. Plaques are relatively large extra cellular structures, which in their mature form contain a central condensed core of amyloid protein surrounded by a halo of

degenerating neurites. The amyloid of the core is composed of peptides derived from the larger transmembranous amyloid precursor protein (APP). Amyloid is formed from a small segment of the APP parent protein. The cleavage of APP at the extra cellular surface of the membrane results in cleavage within the amyloid forming moiety itself (β-amyloid). This non-amyloidogenic metabolism soluble fragments. In contrast, cleavage of the APP compound on either side of the β-amyloid peptide (by beta and gamma secretase) yields a number of fragments, some of which contain intact β-amyloid. β-amyloid peptides vary in length by a few amino acids with the larger forms aggregating more readily into neuritic plaques than others do. Patients with mutations in presenilin 1, presenilin 2 or APP are more prone to produce this relatively increased form. The second main pathological characteristic of AD, neurofibrillary tangles are composed of massive accumulations of a microtubule-associated protein, tau, an essential component of the neurocytoskeleton. The role of APOE ε4 in the pathogenesis of plaque and tangle formation is controversial and still largely unknown.

Clinical features: A wide variety of cognitive symptoms occur in AD, but memory loss is the most common. Memory loss is usually the presenting complaint with patients having difficulty in learning new information, such as names, shopping lists and details of conversations. Although later on in the disease remote memories are also affected. Other cognitive deficits include aphasia, apraxia, agnosia and executive deficits. Cognitive deficit relate more clearly to disease progression than any other symptoms leading to the widespread use of cognitive scales such as the MMSE (see table) to monitor disease progression.

Non-cognitive symptoms have received less attention than cognitive changes, this is because although they are very common, unlike cognitive deficits, they are not always present. A wide variety of non-cognitive symptoms have been described including disorders of thought, perception, affect and behaviour.

Diagnosis: AD is diagnosed once a dementing illness has been confirmed, and other dementing illnesses have been excluded. In most late onset cases it is usually sufficient to exclude other common dementing illnesses including Vascular Dementia, Dementia with Lewy Bodies and Frontal Lobe Dementia and also exclude potentially treatable but rarer causes including neurosyphilis, normal pressure hydrocephalus, hypothyroidism, vitamin B12 and folate deficiencies. CT brain scan can help differentiate AD from vascular dementia and other potentially treatable causes of dementia but the absence of cerebral atrophy is not incompatible with the correct diagnosis in even severe AD and the presence of vascular pathology cannot rule out additional AD pathology.

Management: Historically the management of patients with AD has been largely influenced by the lack of specific treatments that can affect the course of the disease. Thus, management is largely focussed on helping carers to cope with the increase in physical dependence of patients as the disease progresses or with the emergence of troublesome non-cognitive symptoms. Commonly used approaches include the use of community psychiatric nurse and domiciliary support, day care and respite care. Institutional care is usually reserved for patients with more severe physical or persistent non-cognitive symptoms. Current treatment options include the use of acetyl-cholinesterase inhibitors that increase the amount of available acetylcholine in the brains of patients with AD. These treatments are currently available for patients with mild to moderate disease and in some individuals these drugs appear to temporarily delay cognitive deterioration.

Non-cognitive symptoms may be the result of physical problems unrelated to the dementing process. Thus, adequate note should be taken of other illness that may be causing pain or an acute-on-chronic confusional state. For non-cognitive symptoms a non-pharmacological approach may be warranted particularly if the symptoms are non-severe. Indeed it may be better to wait a few weeks to see if these symptoms resolve without the use of drugs or ask carers to try simple psychological strategies such as reassuring touch in the cases of symptoms such as agitation. In AD the use of specific drugs for the pharmacological treatment of non-cognitive symptoms is still largely empirical and is based upon the treatment of psychiatric illness in a younger population and the avoidance of drugs with marked anticholinergic properties. Thus, the treatment of depressive symptoms in AD patients is with non-tricyclic antidepressants e.g. SSRI's, trazodone and MAOI's. The treatment of psychotic symptoms is with atypical antipsychotics e.g. amisulpiride. Aggressive symptoms in AD are treated with atypical antipsychotics, non-tricyclic antidepressants or anticonvulsants e.g. carbamazepine. Agitated behaviours in AD are treated with atypical antipsychotics , non-tricyclic antidepressants or in severe cases short acting benzodiazepines. Treatment responses vary markedly and in practice the choice of one class of drug over another is more limited by the emergence of treatment specific side effects than clear efficacy of one drug over another. The amount of medication needed is often difficult to determine beforehand and the best treatment advice is to start with low doses (1/4 or 1/2 adult dosage) and titrate slowly upwards until treatment response. Not all patients respond and so after trying different approaches a partial response with institutionalised care may be the only realistic alternative.
Prognosis: In late onset AD almost one half of patients are dead within three years. However, individual variation in duration of illness is large ranging from 2 to 16 years.

2. Vascular dementia.

Epidemiology: Less common than AD (about 10% of dementia). Increased risk with Age, Male gender, Diabetes, Hypercholesterolaemia, Ethnicity (e.g. African Americans, Japanese), smoking, Myocardial infarction, Hypertension.
Pathogenesis: As for stroke. Majority multiple small infarcts but some single strategic infarct.
Clinical features: Like AD but "classically" ; acute, stepwise, history of CVAs/TIAs, focal NS signs or symptoms, preservation of insight/character, mood disturbance
Management: as for AD (CHEI not yet licensed) but control risk factors.

3. Dementia with Lewy Bodies

Epidemiology: Less common than AD (less than 10% of dementia). Increased risk with Male gender, **Pathogenesis**: Lewy bodies present in brain cortex
Clinical features: Like AD but vivid visual hallucinations, parkinsonism and cognitive fluctuation
Management: as for AD (CHEI not yet licensed). Avoid standard neuroleptics.

Delirium

Epidemiology: older medical patients 15-25%; older post surgery patients 30-35% Risk increased if existing dementia and older age
Pathogenesis: Drugs, Infections, Cardiac disease, Metabolic/Endocrine, Dehydration, hypothermia, renal and hepatic failure, Intracranial lesions, epilepsy, Alcohol/drug use. No cause found (5 - 20%)
Clinical features: Rapid onset, fluctuates, Impairment of consciousness, incoherence, disorientation, poor memory, perceptual disturbance, esp. visual hallucinations, under/overactivity, Disturbed sleep/wake cycle, Fearfulness/anxiety/apathy.
Management: 1.*Find cause* and *treat.* 2. *Drugs:* Avoid if possible. Haloperidol may be best because not anticholinergic, not too sedative, low doses effective, antipsychotic. *3.Environment* Familiar faces - e.g. family. Reduce strangeness, good lighting, no XS sensory stimulation.

Depression in Old Age

Epidemiology: Major Depression (DSM-IV or ICD-10) < 3 %, Pervasive/Case Level Depression (what a psychiatrist would treat) about 12 %, One or More Depressive Symptoms short of caseness are very common, probably > 50 %.
Pathogenesis: Definite risk factors 1. *Medical illness* Over 50% , especially stroke, abdominal cancer, handicapping disease 2. *Location* Residential home > General hospital > Community 3. *Social factors* Life events e.g. bereavement, poor social networks, losses (e.g. ddeath of spouse, offspring (most severe risk factor, loss of job) Possible risk factors Genetics (less important in late life); cerebrovascular disease (infarcts in some cases).
Clinical features: Guilt, hypochondriasis, impoverishment, psychomotor retardation, nihilistic ideas, masked depression, cognitive impairment, anxiety and agitation, suicide.
Management: As for depression in younger individuals including CBT but avoid tricyclics. Use lower doses of SSRI's. ECT ok.

Very late onset Schizophrenia

Epidemiology: Two main forms of schizophrenia in Old age. Graduates and New cases. Female gender (F:M ratio up to 8:1).
Pathogenesis: As for schizophrenia covered elsewhere: poor premorbid personality adjustment, long standing deafness, family history of schizophrenia**.**
Clinical features: Graduates as chronic schizophrenia: New cases: delusions, especially persecution
Hallucinations especially auditory, insight usually absent, personality preserved, little thought interference, no thought disorder.
Management: 1. Engage the patient (the most difficult thing of all), 2. Atypical antipsychotic e.g. risperidone or olanzapine to minimize extra-pyramidal side-effects, 3. Don't contradict delusions but don't "reinforce" them, e.g. by condoning or assisting with a move to alternative accommodation "away from the voices", 4. Expect "encapsulation" of delusions rather than complete remission.