

ALZHEIMER'S DISEASE

Alzheimer's Disease

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Alzheimer's disease (AD) is a degenerative disease affecting primarily the associative cortical brain areas. It is the most common cause of degenerative dementia and gradually impairs memory, reasoning, judgement, language, and eventually the ability to carry out even the simplest of tasks. In 2009 the number of Australians with dementia was estimated to be 245,000 (over 1.0% of the population)¹. Over the age of 75, the annual incidence of AD in men and women is about 1.0% per year increasing to approximately 10% or more at age 85. In 2005 there were nearly 52,000 Australians newly diagnosed with dementia. By 2050, there are projected to be over 385,000 new cases every year, more than the total number of people with dementia in Australia in 2009². However, other studies state that senile dementia occurs within a specific age range rather than being a result of the aging process itself³. The high prevalence of AD combined with an ever rising aged world population has created a dramatic health care problem in modern day society. Therefore, there is an increasing need for accurate and easily administered screening tests to aid early diagnosis and pharmaceutical interventions to treat the disease⁴. Three phases of in the progression of AD have been identified⁵. A pre-clinical phase lasting 10 to 15 years where cerebral histological damage is constituted without any clinical symptoms, a pre-demential phase lasting 2 to 5 years in which time a pure amnesic syndrome appears coupled with a dulling of the patients emotions, and a final phase where the patient is amnesic and shows cognitive deficits. For those diagnosed with AD and their loved ones, a common important question is how the disease will affect their behaviour. If the onset of AD occurs before the age of 65 ('early-onset'), it is more commonly associated with a rapid course, with particularly marked disturbances of higher cortical functions⁶ and is more likely to have a genetic determinant. The deficits that often develop soon after onset include in the first instance, memory deficits although patients may also have an impaired ability to write (agraphia) and have difficulties in recognising words or reading (alexia). As the disease progresses patients may have an impaired ability to understand or express speech (aphasia), and problems in making intentional movements (apraxia). 'Late-onset' disease typically starts in the late 70s or after, but is defined as a disease with a clinically observable onset after the age of 65. Loss of memory is usually the main symptom and progression is usually slower than in early-onset disease. Although 'early' and 'late' onset AD differ in terms of disease progression, they both share similar clinical characteristics. Indeed, one of the most noticeable and perhaps most widely associated deficits of the disease is that of memory. This form of dementia has a deficit in memory as one of its earliest and most pronounced symptoms^{7, 8}. As with normal aging, there is a reduction in most aspects of memory in patients with AD, but in an accelerated rate of degeneration. In AD, the memory impairment first affects recent information due to anterograde amnesia, with preservation for only a few remote occurrences. However, as the disease progresses, recent information is severely impaired and past memory recall is badly affected due to transient retrograde amnesia⁹. AD patients have great difficulty in keeping up to date with current affairs as well as impairment for events pertaining to ongoing reality¹⁰. Due to such short-term memory problems, new long-term information is subsequently affected. Of all the symptoms of AD, the loss of self referent information or autobiographical memory is often the most disturbing for the individual in the early phase of the disease when they are aware of the problem. However, for family and friends, the later stages are very stressful and upsetting when the patient is no longer able to recognise them yet is unaware of this inability¹¹.

As well as the cognitive effects of AD, neuropathological characteristics have been identified that enable pathologists at post-mortem investigation to diagnose with some confidence that a patient has suffered from AD. A typical AD patient's brain has undergone gross cerebral atrophy which has been accompanied by an over-abundance of senile plaques and neurofibrillary tangles¹². Biochemical markers of AD include a reduction in the enzyme activity of choline acetyltransferase

(CAT) especially in the neocortical regions of the brain. A deficit in the ascending cholinergic system is the best established biochemical marker of AD. The cholinergic system is linked to performance on cognitive tasks including memory and attentional processes. Drug therapies offered hope for treatment of the disease. However, many have side effects and have been found to be most effective if administered in the mild stages of AD (e.g. Rivastigmine). Further to a reduction in CAT, excitotoxicity, a term given to the over-stimulation of the neurotransmitter Glutamate, could also be responsible for neuronal damage as found in patients with AD¹³. Recent advances in neuroimaging techniques are now making it possible to look for AD associated pathology in vivo (e.g. the development of β -amyloid ($A\beta$) binding ligands that allow identification of AD associated pathology using positron emission tomography (PET))¹⁴. This is particularly beneficial for relatives of AD patients who may wish to investigate if they could be at risk of developing the disease. Though there are still unanswered questions regarding the specific prognostic value of such techniques, it provides hope for the use of imaging to facilitate secondary prevention trials for AD. Ultimately, as a cure is not available, it will be of huge human and economic advantage to enable earlier diagnosis and timely intervention of AD.

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