

Alzheimer's Disease

Alzheimer's disease is the name given to a form of cortical dementia, affecting higher mental functions and is the most common cause of **dementia**. Patients experience irreversible global, progressive impairment of brain function, leading to reduced intellectual ability.

Neurodegeneration in Alzheimer's disease is estimated to start 20-30 years before clinical onset.

Epidemiology

- Alzheimer's disease is the most common form of dementia, accounting for 50%-60% of all cases.^{[1][2]}
- The prevalence of dementia is below 1% in individuals aged 60-64 years, but shows an almost exponential increase with age, so that in people aged 85 years or older the prevalence is between 24% and 33% in the Western world.
- Sporadic Alzheimer's disease is very common with more than 15 million people affected worldwide.^[1] The cause of the sporadic form of the disease is unknown, probably because the disease is heterogeneous, caused by ageing in concert with a complex interaction of both genetic and environmental risk factors.
- Familial Alzheimer's disease is a very rare autosomal dominant disease with early onset.^[3]

Risk factors

- Ageing.
- Caucasian.
- More common in women.
- Apolipoprotein E4 variant (associated with an increased risk of Alzheimer's disease presenting at an earlier age).
- **Head injury**.
- Risk factors associated with vascular disease, ie **hypercholesterolaemia**, **hypertension**, atherosclerosis, **coronary heart disease**, smoking, obesity and **diabetes**.

Sporadic Alzheimer's disease has been shown to have a significant genetic background. A large population-based twin study showed that the extent of heritability for the sporadic disease is almost 80%.

Studies have suggested that the risk of the disease is reduced in patients treated with non-steroidal anti-inflammatory drugs.

Diagnosis

The DSM-IV criteria for dementia of the Alzheimer's type are:

- The development of multiple cognitive defects manifested by both:
 - Memory impairment: impaired ability to learn new information as well as recall previously learned information.
 - One or more of the following cognitive disturbances:
 - Language disturbance.
 - Apraxia (inability to carry out motor activities despite intact motor function).
 - Agnosia (failure to recognise or identify objects despite intact sensory function).
 - Disturbance of planning, organising, sequencing, abstracting and other higher functioning.

Other features

- The cognitive deficits cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
- The course of the illness includes a gradual onset and continuing cognitive decline.
- The cognitive deficits are not due to any central nervous system conditions, systemic conditions or substance-induced conditions.
- The deficits do not occur exclusively during a period of **acute confusional state**.
- The disorder is not better accounted for by any other neuropsychiatric disorder, eg **depression**, **schizophrenia**.

Presentation

Alzheimer's disease is a slowly progressive disorder, with insidious onset and progressive impairment of episodic memory; instrumental signs include aphasia, apraxia, and agnosia, together with general cognitive symptoms, such as impaired judgement, decision-making and orientation.

Behavioural signs, such as aggression, psychomotor agitation and psychosis (hallucinations and delusions), are very common in patients with Alzheimer's disease, especially in the late stages of the disease.

Features include:

- Memory: both recall and new memory formation are affected early causing a severe amnesia.
- Aphasia occurs fairly early: difficulties with word meaning, word finding, object naming and definitions.
- Attention and visuospatial problems are quite common.
- Personality and behaviour are well preserved until later stages.
- Visuospatial, perceptual and problem-solving skills are initially preserved.
- Neurological examination is normal.
- A score of 23/30 in the **mini mental state examination** (MMSE) is generally considered to be diagnostic of dementia.

Criteria for the clinical diagnosis of PROBABLE Alzheimer's disease ^[4]

- Dementia established by clinical examination and documented by the MMSE or some similar examination and confirmed by neuropsychological tests.
- Deficits in two or more areas of cognition.
- Progressive worsening of memory and other cognitive functions.
- No disturbance of consciousness.
- Onset between ages of 40 and 90, most often after the age of 65.
- Absence of systemic disorders or other brain diseases that could account for the symptoms.

The diagnosis of PROBABLE Alzheimer's disease

- This is supported by progressive deterioration of specific cognitive functions such as language (aphasia), motor skills (apraxia), and perceptions (agnosia).
- Impaired activities of daily living and altered patterns of behaviour.
- Family history of similar disorders
- Normal lumbar puncture, normal pattern or nonspecific changes in EEG, evidence of cerebral atrophy on CT scan with progression documented by serial observation.

Other clinical features consistent with the diagnosis of PROBABLE Alzheimer's disease

- Plateaus in the course of progression of the illness.
- Associated symptoms of depression, insomnia, incontinence, delusions, illusions, hallucinations.
- Catastrophic verbal, emotional or physical outbursts, sexual disorders and weight loss.
- Other neurological abnormalities in some patients, especially with more advanced disease.

Differential diagnosis

Cognitive changes with ageing may be very difficult to distinguish in the mildly affected, early stages of Alzheimer's disease.

- Other forms of dementia - see [separate article Dementia](#).
- [Normal pressure hydrocephalus](#).
- [Parkinson's disease](#).
- [Hypothyroidism](#).
- Drug-induced cognitive impairment, eg [benzodiazepines](#).
- [Vitamin B12 deficiency](#).
- Depression, schizophrenia.
- Acute confusional state, amnesia.
- [Neurosyphilis](#), [AIDS dementia complex](#).

Investigations

There are several tools available for screening for cognitive impairment.

Other routine investigations are detailed in the separate [Dementia article](#).

Associated diseases

- About 50% of patients with neuropathological disease have significant concomitant cerebrovascular pathology.
- There is also a large overlap in pathology between Alzheimer's disease and [Lewy body dementia](#).

Management

Management must focus both on treating patients and on supporting their carers.

A co-ordinated and integrated multi-agency approach is required in the treatment and care of people with dementia and their carers. Ideally there should be locally agreed written policies and a combined care plan agreed by health and social services that takes into account the changing needs of the person with dementia and his or her carers.^[5] Such support may include respite care, day centres or longer-term residential care.

- There should be named health and/or social care staff to operate the care plan.
- The plan should be endorsed by the person with dementia and/or carers.
- Formal reviews of the care plan should occur.

Early referral is indicated in young patients with Alzheimer's disease - they often have different needs to older patients, eg driving.

Valid consent for treatment^[5]

Health and social care professionals should always seek valid consent from people with dementia:

- This should entail informing the person of options and checking that he or she understands.
- Checking also that there is no coercion and that he or she continues to consent over time.
- If the person lacks the capacity to make a decision, the provisions of the [Mental Capacity Act 2005](#) must be followed.

Drug treatment

Four drugs are available in the UK for treatment of dementia.

The National Institute for Health and Clinical Excellence (NICE) has recently reviewed its guidance on the use of these drugs in mild and moderate Alzheimer's disease,^[6] bringing it more in line with the Scottish Intercollegiate Guidelines Network (SIGN).^[4]

Previous NICE guidance concentrated on the mini-mental state examination (MMSE) score in discriminating between mild (21-26), moderate (15-19), moderately severe (10-14) and severe (<10) Alzheimer's disease when deciding to treat with AChE inhibitors.

NICE and SIGN now appear to agree that:

- The MMSE is not sensitive enough to differentiate patients who would benefit from treatment from those who would not, and was not designed for this use.
- Performance can be affected by several factors, including intelligence, ability to speak English and co-existing physical illness on the day of taking the test. Minor variations can occur from day to day in the same individual.
- The MMSE should be part of a full assessment of a patient, including quality of life changes and social interaction. Clinicians should be free to treat patients after this assessment, and should not be precluded from doing so on the basis of the MMSE score.

NICE recommendations:

- Acetylcholinesterase (AChE) inhibitor treatment (donepezil, galantamine or rivastigmine) should be considered in patients with mild or moderate Alzheimer's disease. It should only be started by dementia specialists (psychiatrists, neurologists, and physicians specialising in the care of older people), after appropriate discussion with family and carers. These drugs have cholinergic side-effects and should be started at a low dose, and then be titrated according to response.
- Memantine (a N-methyl-D-aspartate (NMDA) antagonist) is recommended by NICE as a second-line option for managing patients with *moderate* Alzheimer's disease where AChE inhibitors are not tolerated or contra-indicated, or in the treatment of *severe* Alzheimer's disease.
- Drug treatment should be continued only as long as it is having a worthwhile effect on cognitive, global, functional or behavioural symptoms.
- Patients on treatment should be reviewed regularly by an appropriate specialist team, or by shared care with GPs where such an agreement exists. This should include cognitive, global, functional and behavioural assessments and discussion with carers.

SIGN comments:^[7]

- Acetylcholinesterase inhibitors should be considered for all Alzheimer's patients, irrespective of whether the dementia is mild, moderate or severe.
- People with mild-stage Alzheimer's disease should be eligible for treatment at the earliest opportunity after diagnosis. This would enable the patient to be involved in decisions about their care, and give time for carers to be educated.
- It would be wrong to exclude a patient from treatment after he or she has been diagnosed when they would be more likely to regain higher levels of ability than would be possible later in the illness.
- Acquisition cost should be taken into account, but should not over-ride other clinical considerations.
- Concentrating on treatment in the severe stage of the illness could deter GPs from referring at an early stage.
- Not all patients have ready access to a specialist or specialist clinic, especially in remote rural areas. In these cases, GPs should be allowed to initiate treatment.^[5]

Complications

- Patients deteriorate over time in activities of daily living and in their ability to care for themselves.
- If they have the disease long enough, patients commonly develop various problems, including incontinence, sleep-wake cycle disturbance, and wandering.

- Patients can also have affective and psychotic psychiatric symptoms.
- Inability to feed independently leads to weight loss, malnutrition, and dehydration.
- Immobility, mutism, pressure ulcers, and infections are all complications of dementia. The difficulties with care can cause a great deal of difficulty for families and carers, who therefore need a great deal of support.

Prognosis

- Alzheimer's disease is a progressive condition for which there is currently no cure and no known way to slow the progression of this disease.
- Symptoms in some people in the early and middle stages of the disease may be relieved by medication. Medications may also help control behavioural symptoms.
- The course of Alzheimer's disease varies from person to person, with some people having the disease for five years, and others for up to 20 years.
- The most common cause of death is infection.^[1]

Prevention

- Fruit and vegetable juices may play an important role in delaying the onset of Alzheimer's disease, particularly among those who are at high risk for the disease.^[8]
- Some evidence suggests that dietary intake of homocysteine-related vitamins (vitamin B12 and folate), antioxidants (eg vitamin C and vitamin E), unsaturated fatty acids and also moderate alcohol intake (especially wine) may reduce the risk of Alzheimer's disease, but the evidence is currently too weak to allow any definite conclusions or recommendations.
- Statins do not reduce the risk of developing Alzheimer's disease but there is some evidence that lowering cholesterol may slow the progression of the disease.

Recommend a 'brain healthy lifestyle':^[9]

- Keep the brain active.
- Eat healthily.
- Be physically active.
- Manage blood pressure, cholesterol, sugar and weight.
- Keep active socially.
- Avoid smoking and, if you drink alcohol, do so in moderation.
- Avoid head injury.

Further reading & references

- [Services for Younger people with Alzheimer's disease and other dementias](#), Royal College of Psychiatrists (2006)
1. [Blennow K, de Leon MJ, Zetterberg H](#); Alzheimer's disease. *Lancet*. 2006 Jul 29;368(9533):387-403. [abstract]
 2. [Alzheimer's Society](#); Dementia care and research
 3. [Alzheimer Disease](#), Online Mendelian Inheritance in Man (OMIM)
 4. [Management of patients with dementia](#), Scottish Intercollegiate Guidelines Network - SIGN (Feb 2006)
 5. [Dementia: Supporting people with dementia and their carers in health and social care](#), NICE Clinical Guideline (2006 - amended March 2011)
 6. [Alzheimer's disease - donepezil, galantamine, rivastigmine and memantine](#), NICE Technology Appraisal Guideline (March 2011); Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease
 7. [Alzheimer Scotland](#); Action on Dementia
 8. [Dai Q, Borenstein AR, Wu Y, et al](#); Fruit and vegetable juices and Alzheimer's disease: the Kame Project. *Am J Med*. 2006 Sep;119(9):751-9. [abstract]
 9. [Burns A, Iliffe S](#); Alzheimer's disease. *BMJ*. 2009 Feb 5;338:b158. doi: 10.1136/bmj.b158.

Disclaimer: This article is for information only and should not be used for the diagnosis or treatment of medical conditions. EMIS has used all reasonable care in compiling the information but make no warranty as to its accuracy. Consult a doctor or other health care professional for diagnosis and treatment of medical conditions. For details see our [conditions](#).

View this article online at www.patient.co.uk/doctor/Alzheimer's-Disease.htm.

Discuss Alzheimer's Disease and find more trusted resources at www.patient.co.uk.

EMIS is a trading name of Egton Medical Information Systems Limited.