

Alzheimer's disease

Dementia is an umbrella term used to describe various conditions which damage brain cells and lead to a loss of brain function over time. Dementia causes a progressive decline in a person's mental functioning. It is a broad term, which describes a loss of memory, intellect, rationality, social skills and normal emotional reactions

The symptoms of dementia develop gradually over a period of years. The progression of these diseases is largely unpredictable for each individual. How and what symptoms develop depend on what parts of the brain are affected by which illness, and the unique characteristics of each individual.

The facts in brief

- Dementia has a life changing physical, emotional and mental impact on the affected person and their primary carer and family. There are more than 100 conditions that cause dementia.
- While the risk of dementia increases with age, it is not a natural part of ageing.
- Dementia affects approximately one in 20 of people aged over 65 years. This rises to one in five in the 80 plus age group.
- While it is comparatively rare, dementia can affect younger people. There are approximately 3,800 people under the age of 65 with Younger Onset Dementia in the Ireland.
- A person with dementia will live for an average of four to eight years, depending on their age at diagnosis. Average life span will also be affected by gender, other medical conditions and the severity of dementia at the time of diagnosis.
- Dementia ranks as the fourth leading cause of death among the population aged 65 years and over.
- Alzheimer's disease, the most common cause of dementia in Ireland, accounts for more than 50% of all cases; the second most common form is vascular dementia, which may be preventable.

Risk Factors

The risk factors for AD include

- Increasing age
- Being female
- Family history
- Head injury
- Parkinsonism
- Hypothyroidism
- Exposure to dietary aluminium
- Cardiovascular disease
- Smoking
- High alcohol intake



10 common signs of early stage Alzheimer's Disease:

- Getting stuck for words or having language difficulties
- Forgetting things – names, dates, places, faces
- Loss of interest in starting projects or doing things
- Difficulty in solving problems or doing puzzles
- Difficulty in performing everyday tasks
- Misplacing things regularly
- Poor or decreased judgment
- Changes in mood and behaviour
- Disorientation in familiar surroundings
- Changes in personality

Stages of Alzheimer's Disease

Stage 1: Mild Alzheimer's Disease

The mild stage of Alzheimer's Disease can last from 2 to 4 years or longer. Those in this phase of the disease may:

- **Say the same thing over and over**
- **Lose interest in things they once enjoyed**
- **Have trouble finding names for common items**
- **Lose things more often than normal**
- **Seem to experience personality changes**
- **Have difficulty grasping complex ideas**

People with mild Alzheimer's Disease are usually alert, sociable, and enjoy life, but their forgetfulness can interfere with daily living and may frustrate them. They may be overly emotional and temperamental, or apathetic.

Stage 2: Moderate Alzheimer's Disease

The moderate stage of Alzheimer's Disease is often the longest, lasting from 2 to 10 years.

In this stage, a person may:

- **Get lost easily, even in places they know well**
- **Become more confused about recent events**
- **Need assistance with or supervision with tasks such as dressing or washing**
- **Argue more than usual**
- **Believe things are real when they are not**
- **Experience restlessness and agitation**
- **Have difficulty sleeping and may wander**

Stage 3: Severe Alzheimer's Disease

The severe stage can last from 1 to 3 years or longer. People with severe Alzheimer's Disease cannot do things on their own anymore.

They may not be able to:

- **Use or understand words**
- **Recognize family members**
- **Care for themselves**
- **Move around independently**

Constant care, 24 hours a day, seven days a week, is usually necessary.

Diagnosis

As there is no straightforward test for Alzheimer's Disease, making a diagnosis is often difficult, particularly in the early stages. A diagnosis is usually made by excluding other causes such as infection, vitamin deficiency, thyroid problems, brain tumour, depression and the side effects of drugs which all can produce similar symptoms.

Diagnosis involves a variety of medical assessments and observations. Assessment usually includes a mini mental state examination (MMSE). Other assessments for AD include the Alzheimer's disease assessment scale (ADAS) and the Blessed test of information, memory and concentration.

Specialists can only make a probable diagnosis. An absolute diagnosis requires autopsy to confirm the presence of distinct microscopic features in the brain. However, clinicians with experience in memory loss are able to diagnose AD to within 80-90% accuracy. Neuro-imaging can support a diagnosis.

The severity of dementia in AD can be categorised as follows:

- **Mild: MMSE score 21-26**

Symptoms tend to be so slight that they are not noticed by relatives. Patients tend to be less energetic and slightly "forgetful".

- **Moderate: MMSE score 10-20**

Signs include aphasia (impairment of speech and comprehension of speech), memory loss and difficulty with language (eg) Problems with reading or writing) but patients may still manage daily activities.

- **Severe: MMSE score <10**

Patients have difficulty performing daily tasks, such as brushing their teeth or lacing shoes. Patients may fail to recognise friends and family.

Pathology

AD has both microscopic and biochemical features.

Microscopy: AD is associated with the presence of amyloid plaques (due to the accumulation of beta amyloid protein) and neurofibrillary tangles (due to hyperphosphorylation of tau proteins). These features result in neuronal death in the cortical and subcortical brain regions.

Biochemistry: acetylcholine is a neurotransmitter that affects cognition by acting on cholinergic receptors. Current AD therapy attempts to prevent the breakdown of acetylcholine by inhibiting cholinesterases.

Health maintenance and general medical treatment

As Alzheimer's disease progresses, various conditions develop that may lead to death, such as septicemia, pneumonia and upper respiratory infections, nutritional disorders, pressure sores, fractures, and wounds.

Management of these conditions is critical. In the early stages of Alzheimer's disease, the clinician should encourage health maintenance activities, including exercise, the control of hypertension and other medical conditions, annual immunization against influenza, dental hygiene, and the use of eyeglasses and hearing aids as needed for visual and auditory impairments. In later phases of the disease, it is important to address basic requirements such as nutrition, hydration, and skin care. Decisions about the use of methods of extending life, such as gastrostomy, intravenous hydration, and the administration of antibiotics, should respect advance directives by patients and incorporate guidance from surrogate decision makers

Benefits of Treatment

Treatments can offer improvement with the following:

Memory and Thinking

Memory loss and forgetfulness are early symptoms of Alzheimer's Disease and people often pass this off as a normal part of the ageing process. Everyone can forget a name or a face occasionally but memory problems become more frequent and severe for a person with Alzheimer's Disease. These treatments can help improve a person's memory and enable the person to retain new information for longer.

Everyday Activities

When a person has Alzheimer's Disease even simple mundane tasks can be difficult. Examples of this might include using the phone, doing household chores, getting dressed, preparing meals, or managing money. Medication can help some people to continue managing their activities of daily living independently for longer.

Behaviour

Symptoms of Alzheimer's disease can include hallucinations, wandering, aggression and moodiness. Medications can help with these symptoms.

Treatment

Non-drug approaches are not effective in modifying memory loss. Four drugs are approved for treatment of dementia in AD in the UK and Ireland: **donepezil (ARICEPT®)**, **DOZEPT®**, **galantamine (REMINYL®)**, **rivastigmine (EXELON®)** and **memantine (EBIXA®)**. The first three are cholinesterase inhibitors and memantine is a NMDA receptor antagonist. All of these drugs must be started under specialist care.

The most common side effects are cholinergic, namely nausea, vomiting, diarrhoea and anorexia. These can be a particular problem because many people with AD lose weight. However, tolerance to these adverse effects normally develops.

Trials have been conducted on cholinesterase inhibitors. These trials have demonstrated modest improvement in cognitive symptoms. Some studies demonstrated a beneficial effect for up to two years after starting treatment. There are no studies of longer periods of medication but most patients can expect that, in time, they will stop responding to treatment as the disease progresses. If tolerance develops some prescribers recommend a 'drug holiday', for example the drug is stopped for six weeks and then started again by retitration.

Donepezil has demonstrated in the short term (six months) a beneficial effect on mood and behaviour. Donepezil is initiated at a dose of 5 mg per day, and the dose is increased to 10 mg per day after one month. Rivastigmine is licensed to treat dementia in Parkinson's disease. The dose of rivastigmine increases from 1.5 mg twice daily to 3 mg twice daily, then to 4.5 mg twice daily, and to a maximal dose of 6 mg twice daily. The dose may be increased at intervals of one to four weeks; fewer side effects emerge with longer periods between increases. Exelon 4.6mg/24hr transdermal patch and Exelon 9.5mg/ 24hr transdermal patch have been recently launched. The initial dose is 4.6mg/24hr for a minimum of four weeks, and if tolerated, can be increased to 9.6mg/24hr which is considered the recommended effective dose. The rivastigmine patch is considered to have fewer side effects than the oral version.

Of the four drugs available memantine is the only one licensed to treat moderate severe AD. However, according to NICE (National Institute for Health and Clinical Excellence) in the UK, memantine should only be used for moderately severe to severe AD as part of a well designed clinical study, however patients already receiving memantine should continue treatment until the specialist considers it is appropriate to stop.

There are no guidelines to recommend one drug over the others but prescribing considerations include compliance issues. For example only donepezil and modified release galantamine can be taken once a day. Other treatments for AD that have been tried include selegiline, vitamin E and Ginkgo biloba. According to a recent Cochrane Review no clear benefit with selegiline (ELDEPRYL®) has been established. There is also insufficient evidence to support the use of vitamin E in AD. Further studies are required to test Ginkgo biloba.

How can behavioural and psychological difficulties be managed?

General assessment

If a person with dementia develops distressing symptoms or challenging behaviour, an assessment to identify modifiable factors that may influence behaviour (such as depression, adverse effects of drugs, individual biography, and psychosocial or physical environmental factors) is important. A physical examination may, for example, discover a source of pain that underlies challenging behaviour. There could be many external causes for challenging behaviour including overcrowding, poor communication between the person and staff, lack of privacy, lack of activities, conflicts between staff and carers, and inadequate attention from staff. The sequence of events may be important in determining causation. For example, did a change happen after an alteration in medication, moving rooms in a nursing home, or even a change in staffing?

Treatment for behavioural and psychiatric problems

Non Drug Treatment

Non-drug approaches are important first line treatments for agitation. Environmental factors play a role in the causing agitation, and non-drug approaches are important first line treatments. Non-drug approaches that have been used with benefit include aromatherapy, bright light therapy, music or dance and massage.

Antipsychotics

Antipsychotic drugs reduce agitation but are linked with an increased risk of mortality and impair cognition. The first line treatment for psychotic symptoms in Alzheimer patients is atypical antipsychotic (*olanzapine*, *risperidone*). These are associated with fewer extrapyramidal* effects than conventional antipsychotics. The NICE dementia guidelines recommend that if antipsychotic drug treatment is used, it should be at the lowest effective dose.

Dosing in the evening with once daily atypical antipsychotics can help patients who have problem sleeping. Although atypical antipsychotics are first line, *haloperidol* has been used to get initial control of behavioural disorders. It should be used at low doses for short periods (days) after which a patient should be transferred to an atypical antipsychotic. Anticonvulsants such as *Carbamazepine* (TEGRETOL®) are recommended as second line treatments when patients fail to respond to antipsychotics. Short term trials have shown that anticonvulsants are well tolerated and effective.

Antidepressants

Exercise may help reduce the symptoms of depression, and randomised controlled trials support the use of antidepressants. Newer selective serotonin reuptake inhibitors are the preferred class, rather than the older tricyclic agents, which have troublesome side effects. Small studies have demonstrated beneficial effects with *trazodone* (MOLIPAXIN[®]) and *citalopram*. Anxiolytics are also prescribed.

*extrapyramidal effects include **Parkinson symptoms** (Tremor), **dystonia** (abnormal face and body movements), **akathisia** (restlessness) and **tardive dyskinesia** (rhythmic, involuntary movements of tongue, face and jaw)

Family members

Care should be taken when discussing Alzheimer's disease or dementia—many people have seen a relative with a disease and will have their own preconception, often profoundly negative, of what the disease is.

Other causes of Dementia

Vascular Dementia

Vascular dementia occurs when there is restricted flow of blood to the brain and nerve cells are deprived of oxygen, causing them to die. Probable risk factors include high blood pressure, high cholesterol, and advanced age and it is commonly associated with post-stroke patients. The symptoms of Vascular dementia are similar to Alzheimer's disease. However, unlike Alzheimer's disease, vascular dementia affects specific parts of the brain, therefore certain abilities may be affected and some may remain unaffected. Unlike Alzheimer's disease, which is steadily progressive, symptoms of Vascular dementia may stay the same for some time and then suddenly appear to decline.

Disclaimer: Please ensure you consult with your healthcare professional before making any changes recommended

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