

A REVIEW ON ALZHEIMER'S DISEASE: ITS CAUSE, SYMPTOMS, AND TREATMENT AT WORLD WIDE

Pandey Shivanand*

*Smt. R. B. P. M. Pharmacy College, Atkot-360040, Rajkot, Gujarat. India.

Abstract: Is a progressive and fatal brain disease. As many as 5.3 million Americans are living with Alzheimer's disease. Alzheimer's destroys brain cells, causing [memory loss](#) and problems with thinking and behavior severe enough to affect work, lifelong hobbies or social life. Alzheimer's gets worse over time, and it is fatal. Today it is the seventh-leading cause of death in the United States. Learn more: [Warning Signs](#) and [Stages of Alzheimer's Disease](#). Has no current cure. But treatments for symptoms, combined with the right services and support, can make life better for the millions of Americans living with Alzheimer's. There is an accelerating worldwide effort under way to find better ways to treat the disease, delay its onset, or prevent it from developing. Learn more about recent progress in Alzheimer research funded by the Alzheimer's Association in the [Research](#) section.

Keywords: Alzheimer's disease, memory loss, fatal disease, Alzheimer's Association

Introduction: Alzheimer's disease is a brain disorder named for German physician Aloes Alzheimer, who first described it in 1906. Scientists have learned a great deal about Alzheimer's disease in the century since Dr. Alzheimer first drew attention to it. Today we know that Alzheimer's: Is the most common form of dementia, a general term for memory loss and other intellectual abilities serious enough to interfere with daily life. Alzheimer's disease accounts for 50 to 80 percent of dementia cases. Other types of dementia include vascular dementia, mixed dementia, dementia with Lewy bodies and front temporal dementia. Learn more: Related Dementias(<http://www.alz.org/alzheimers>).

Pathophysiology

Neuropathology: Alzheimer's disease is characterised by loss of neurons and synapses in the cerebral cortex and certain subcortical regions(<http://www.medicinenet.com>). This loss results in gross atrophy of the affected regions, including degeneration in the temporal lobe and parietal lobe, and parts of the frontal cortex and cingulate gyrus. Studies using MRI and positron emission tomography have documented reductions in the size of specific brain regions in patients as they progressed from mild cognitive impairment to Alzheimer's disease, and in comparison with similar images from healthy older adults. Both amyloid plaques and neurofibrillary tangles are clearly visible by microscopy in brains of those afflicted by AD. Plaques are dense (<http://topnews.net.nz>), mostly insoluble deposits of amyloid-beta peptide and cellular material outside and around neurons. Tangles (neurofibrillary tangles) are aggregates of the microtubule-associated protein tau which has become hyperphosphorylated and accumulate inside the cells themselves. Although many older individuals develop some plaques and tangles as a consequence of ageing, the brains of AD patients have a greater number of them in specific brain regions such as the temporal lobe. Lewy bodies are not rare in AD patient's brains(www.medicinenet.com, 5, Berchtold NC et al 1998). Various inflammatory processes and cytokines may also have a role in the pathology of Alzheimer's disease. Inflammation is a general marker of tissue damage in any disease, and may be either secondary to tissue damage in AD or a marker of an immunological response. Alterations in the distribution of different neurotrophic factors and in the expression of their receptors such as the brain derived neurotrophic factor (BDNF) have been described in AD(<http://www.alzheimers-research.org.uk/>).

Warning signs of Alzheimer's (Bermejo-Pareja F et al 2008, Ferri CP et al 2005)

1. Memory loss that disrupts daily life: One of the most common signs of Alzheimer's is memory loss, especially forgetting recently learned information. Others include forgetting important dates or events; asking for the same information over and over; relying on memory aides (e.g., reminder notes or electronic devices) or family members for things they used to handle on their own.

2. Challenges in planning or solving problems: Some people may experience changes in their ability to develop and follow a plan or work with numbers. They may have trouble following a familiar recipe or keeping track of monthly bills. They may have difficulty concentrating and take much longer to do things than they did before.

3. Difficulty completing familiar tasks at home, at work or at leisure: People with Alzheimer's often find it hard to complete daily tasks. Sometimes, people may have trouble driving to a familiar location, managing a budget at work or remembering the rules of a favorite game.

4. Confusion with time or place: People with Alzheimer's can lose track of dates, seasons and the passage of time. They may have trouble understanding something if it is not happening immediately. Sometimes they may forget where they are or how they got there.

5. Trouble understanding visual images and spatial relationships: For some people, having vision problems is a sign of Alzheimer's. They may have difficulty reading, judging distance and determining color or contrast. In terms of perception, they may pass a mirror and think someone else is in the room. They may not realize they are the person in the mirror.

6. New problems with words in speaking or writing: People with Alzheimer's may have trouble following or joining a conversation. They may stop in the middle of a conversation and have no idea how to continue or they may repeat themselves. They may struggle with vocabulary, have problems finding the right word or call things by the wrong name (e.g., calling a "watch" a "hand-clock").

7. Misplacing things and losing the ability to retrace steps: A person with Alzheimer's disease may put things in unusual places. They may lose things and be unable to go back over their steps to find them again. Sometimes, they may accuse others of stealing. This may occur more frequently over time.

8. Decreased or poor judgment: People with Alzheimer's may experience changes in judgment or decision-making. For example, they may use poor judgment when dealing with money, giving large amounts to telemarketers. They may pay less attention to grooming or keeping themselves clean.

9. Withdrawal from work or social activities: A person with Alzheimer's may start to remove themselves from hobbies, social activities, work projects or sports. They may have trouble keeping up with a favorite sports team or remembering how to complete a favorite hobby. They may also avoid being social because of the changes they have experienced.

10. Changes in mood and personality: The mood and personalities of people with Alzheimer's can change. They can become confused, suspicious, depressed, fearful or anxious. They may be easily upset at home, at work, with friends or in places where they are out of their comfort zone¹

The Difference between Alzheimer's and Typical Age-Related Changes

Signs of Alzheimer's	Typical age-related changes
Poor judgment and decision making	Making a bad decision once in a while
Inability to manage a budget	Missing a monthly payment
Losing track of the date or the season	Forgetting which day it is and remembering later
Difficulty having a conversation	Sometimes forgetting which word to use
Misplacing things and being unable to retrace steps to find them	Losing things from time to time

How is the diagnosis of Alzheimer's disease made?

As of June 2007, there is no specific "blood test" or imaging test that is used for the diagnosis of Alzheimer's disease. Alzheimer's disease is diagnosed when: 1) a person has sufficient cognitive decline to meet criteria for dementia; 2) the clinical course is consistent with that of Alzheimer's disease; 3) no other brain diseases or other processes are better explanations for the dementia (Immunotherapy as treatment for Alzheimer's disease, Solomon B 2007).

What other conditions should be screened for?

There are many conditions that can cause dementia, to include the following:

Neurological disorders: Parkinson's disease, cerebrovascular disease and strokes, brain tumors, blood clots, and multiple sclerosis can sometimes be associated with dementia although many patients with these conditions are cognitively normal. **Infectious diseases:** Some brain infections such as chronic syphilis, chronic HIV, or chronic fungal meningitis can cause dementia.

Side effects of medications: Many medicines can cause cognitive impairment, especially in elderly patients. Perhaps the most frequent offenders are drugs used to control bladder urgency and incontinence. "Psychiatric medications" such as anti-depressants and anti-anxiety medications and "neurological medications" such as anti-seizure medications can also be associated with cognitive impairment. If a physician evaluates a person with cognitive impairment who is on one of these medications, the medication is often gently tapered and/or discontinued to determine whether it might be the cause of the cognitive impairment. If it is clear that the cognitive impairment preceded the use of these medications, such tapering may not be necessary. On the other hand, "psychiatric," "neurological," and "incontinence" medications are often appropriately prescribed to patients with Alzheimer's disease. Such patients need to be followed carefully to determine whether these medications cause any worsening of cognition (Blumenthal M et al 1998, Eikelenboom P et al 2000).

Psychiatric disorders: In older persons, some forms of depression can cause problems with memory and concentration that initially may be indistinguishable from the early symptoms of Alzheimer's disease. Sometimes, these conditions, referred to as pseudodementia, can be reversed. Studies have shown that persons with depression and coexistent cognitive (thinking, memory) impairment are highly likely to have an underlying dementia when followed for several years.

Substance Abuse: Abuse of legal and/or illegal drugs and alcohol abuse is often associated with cognitive impairment.

Metabolic Disorders: Thyroid dysfunction, some steroid disorders, and nutritional deficiencies such as vitamin B12 deficiency or thiamine deficiency are sometimes associated with cognitive impairment.

Trauma: Significant head injuries with brain contusions may cause dementia. Blood clots around the outside of the brain (subdural hematomas) may also be associated with dementia.

Toxic Factors: Long term consequences of acute carbon monoxide poisoning can lead to an encephalopathy with dementia. In some rare cases, heavy metal poisoning can be associated with dementia.

Tumors: Many primary and metastatic brain tumors can cause dementia. However, many patients with brain tumors have no or little cognitive impairment associated with the tumor.

The Importance of Comprehensive Clinical Evaluation

Because many other disorders can be confused with Alzheimer's disease, an omprehensive clinical evaluation is essential in arriving at a correct diagnosis. Such an assessment should include at least three major components; 1) a thorough general medical workup, 2) a neurological examination including testing of memory and other functions of thinking , and 3) a psychiatric evaluation to assess mood, anxiety, and clarity of thought. Such an evaluation takes time - usually at least an hour. In the United States healthcare system, neurologists, psychiatrists, or geriatricians frequently become involved. Nonetheless, any physician may be able to perform a thorough evaluation.

The American Academy of Neurology has published guidelines that include imaging of the brain in the initial evaluation of patients with dementia. These studies are either a noncontrast CT scan or an MRI scan. Other imaging procedures that look at the function of the brain (functional neuroimaging), such as SPECT, PET, and fMRI, may be helpful in specific cases, but generally are not needed. However, in many healthcare systems outside of the United States, brain imaging as not a standard part of the assessment for possible Alzheimer's disease. Despite many attempts, identification of a blood test to diagnose Alzheimer's disease has remained elusive. As of June 2007, such testing is neither widely available nor recommended (McGeer PL et al 2000).

Evidence

On Wednesday, an expert jury concluded that fish oil, exercise and solving puzzles might all be good for the mind, but there is no strong proof that any of these can put off Alzheimer's disease. Neither can any other supplements, medicines or social communication, the independent panel conference at the outside Washington concluded.

The group of specialists observed dozens of studies, which have recommended methods to avoid Alzheimer's, a distressing and untreatable breakdown of the brain, and discovered that none were good enough to form evidence. Dr. Martha Daviglius of Northwestern, who chaired the panel, said, "We wish we could tell people that taking a pill or doing a puzzle every day would prevent this terrible disease, but current evidence doesn't support this". Daviglius said that majority of the studies that have been conducted confirm relationships, but not cause and effect. The 15 specialists assembled under the NIH's state-of-the-science conference program that aspires to direct future investigation in an essential study area. They consisted of specialists in geriatrics, long-term care, nursing, psychiatry and other spheres. Panelists might not be staff, nor may they have monetary stakes in any treatments that were considered (McGeer PL et al).

The management of Alzheimer's disease consists of medication based and non-medication based treatments. Two different classes of pharmaceuticals are approved by the FDA for treating Alzheimer's disease: cholinesterase inhibitors and partial glutamate antagonists. Neither class of drugs has been proven to slow the rate of progression of Alzheimer's disease. Nonetheless, many clinical trials suggest that these medications are superior to placebos (sugar pills) in relieving some symptoms (Yasojima K, et al Lema MJ et al).

Cholinesterase inhibitors

In patients with Alzheimer's disease there is a relative lack of a brain chemical neurotransmitter called acetylcholine. (Neurotransmitters are chemical messengers produced by nerves that the nerves use to communicate with each other in order to carry out their functions.) Substantial research has demonstrated that acetylcholine is important in the ability to form new memories. The cholinesterase inhibitors (ChEIs) block the breakdown of acetylcholine. As a result, more acetylcholine is available in the brain, and it may become easier to form new memories (Sainali SM et al).

Four ChEIs have been approved by the FDA, but only donepezil hydrochloride (Aricept), rivastigmine (Exelon), and galantamine (Razadyne - previously called Reminyl) are used by most physicians because the fourth drug, tacrine (Cognex) has more undesirable side effects than the other three. Most experts in Alzheimer's disease do not believe there is an important difference in the effectiveness of these three drugs. Several studies suggest that the progression of symptoms of patients on these drugs seems to plateau for six to 12 months, but inevitably progression then begins again (NSAIDs and adverse effects at Bandolier, <http://www.fda.gov>).

Of the three widely used AchEs, rivastigmine and galantamine are only approved by the FDA for mild to moderate Alzheimer's disease, whereas donepezil is approved for mild, moderate, and severe Alzheimer's disease. It is not known whether rivastigmine and galantamine are also effective in severe Alzheimer's disease, although there does not appear to be any good reason why they shouldn't. The principal side effects of ChEIs involve the gastrointestinal system and include nausea, vomiting, cramping, and diarrhea. Usually these side effects can be controlled with change in size or timing of the dose or administering the medications with a small amount of food. Between 75% and 90% of patients will tolerate therapeutic doses of ChEIs (<http://www.eurekalert.org>, Behl C et al, Markesbery WR et al).

Conclusion: In the early stages, the most commonly recognised symptom is memory loss, such as difficulty in remembering recently learned facts. Mental stimulation, exercise, and a balanced diet are suggested, as both a possible prevention and a sensible way of managing the disease. Because AD cannot be cured and is degenerative, management of patients is essential. The role of the main caregiver is often taken by the spouse or a close relative. Alzheimer's disease is known for placing a great burden on caregivers; the pressures can be wide-ranging, involving social, psychological, physical, and economic elements of the caregiver's life. In developed countries, AD is one of the most costly diseases to society

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