

# Alzheimer's Disease

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## FACT SHEET

**A**lzheimer's disease is an irreversible, progressive brain disease that slowly destroys memory and thinking skills, and eventually even the ability to carry out the simplest tasks. In most people with Alzheimer's, symptoms first appear after age 65. Estimates vary, but experts suggest that as many as 5 million Americans age 65 and older may have Alzheimer's disease.

Alzheimer's disease is the most common cause of dementia among older people. Dementia is the loss of cognitive functioning—thinking, remembering, and reasoning—and behavioral abilities, to such an extent that it interferes with a person's daily life and activities. Dementia ranges in severity from the mildest stage, when it is just beginning to affect a person's functioning, to the most severe stage, when the person must depend completely on others for basic activities of daily living.

Alzheimer's disease is named after Dr. Alois Alzheimer. In 1906, Dr. Alzheimer noticed changes in

the brain tissue of a woman who had died of an unusual mental illness. Her symptoms included memory loss, language problems, and unpredictable behavior. After she died, he examined her brain and found many abnormal clumps (now called amyloid plaques) and tangled bundles of fibers (now called neurofibrillary tangles). Plaques and tangles in the brain are two of the main features of Alzheimer's disease. The third is the loss of connections between nerve cells (neurons) in the brain.

### **Changes in the Brain in Alzheimer's Disease**

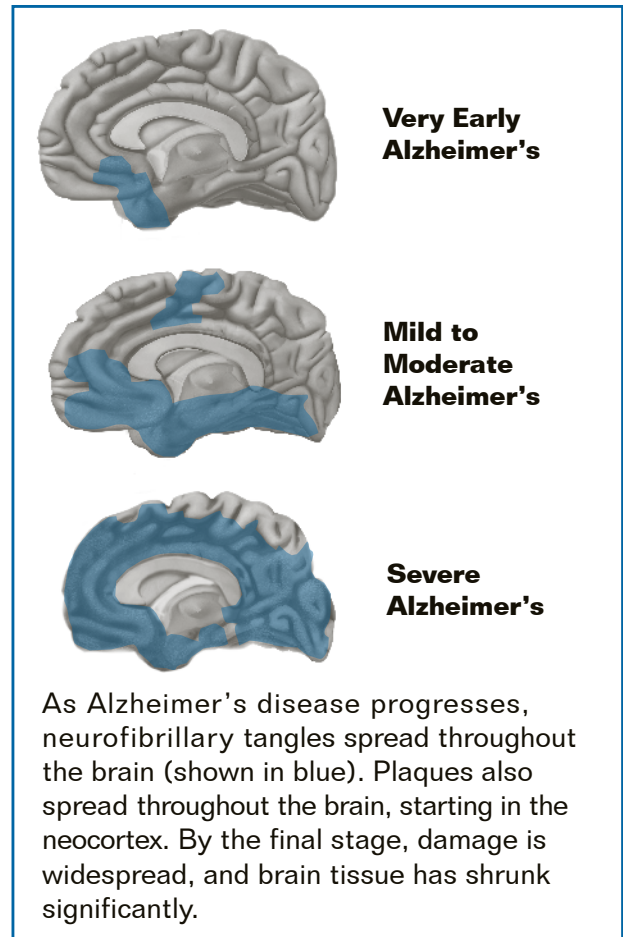
Although we still don't know how the Alzheimer's disease process begins, it seems likely that damage to the brain starts a decade or more before problems become evident. During the preclinical stage of Alzheimer's disease, people are free of symptoms but toxic changes are taking place in the brain. Abnormal deposits of proteins form amyloid plaques and tau tangles throughout the brain, and once-healthy neurons

begin to work less efficiently. Over time, neurons lose their ability to function and communicate with each other, and eventually they die.

Before long, the damage spreads to a nearby structure in the brain called the hippocampus, which is essential in forming memories. As more neurons die, affected brain regions begin to shrink. By the final stage of Alzheimer's, damage is widespread, and brain tissue has shrunk significantly.

### Very Early Signs and Symptoms

Memory problems are typically one of the first warning signs of cognitive loss, possibly due to the development of Alzheimer's disease. Some people with memory problems have a condition called amnesic mild cognitive impairment (MCI). People with this condition have more memory problems than normal for people their age, but their symptoms are not as severe as those seen in people with Alzheimer's disease. Other recent studies have found links between some movement difficulties and MCI. Researchers also have seen links between MCI and some problems with the sense of smell. The ability of people with MCI to perform normal daily activities is not significantly impaired. However, more older people with MCI, compared with those without MCI, go on to develop Alzheimer's.



A decline in other aspects of cognition, such as word-finding, vision/spatial issues, and impaired reasoning or judgment, may also signal the very early stages of Alzheimer's disease. Scientists are looking to see whether brain imaging and biomarker studies, for example, of people with MCI and those with a family history of Alzheimer's, can detect early changes in the brain like those seen in Alzheimer's. Initial studies indicate that early detection using biomarkers and imaging may be possible, but findings will need to be confirmed by other studies before these techniques can be used to

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help with diagnosis in everyday medical practice.

These and other studies offer hope that someday we may have tools that could help detect Alzheimer's early, track the course of the disease, and monitor response to treatments.

### Mild Alzheimer's Disease

As Alzheimer's disease progresses, memory loss worsens, and changes in other cognitive abilities are evident. Problems can include, for example, getting lost, trouble handling money and paying bills, repeating questions, taking longer to complete normal daily tasks, using poor judgment, and having some mood and personality changes. People often are diagnosed in this stage.

### Moderate Alzheimer's Disease

In this stage, damage occurs in areas of the brain that control language, reasoning, sensory processing, and conscious thought. Memory loss and confusion grow worse, and people begin to have problems recognizing family and friends. They may be unable to learn new things, carry out tasks that involve multiple steps (such as getting dressed), or cope with new situations. They may have hallucinations, delusions, and paranoia, and may behave impulsively.

### Severe Alzheimer's Disease

By the final stage, plaques and tangles have spread throughout the brain, and brain tissue has shrunk significantly.

People with severe Alzheimer's cannot communicate and are completely dependent on others for their care. Near the end, the person may be in bed most or all of the time as the body shuts down.

## What Causes Alzheimer's

Scientists don't yet fully understand what causes Alzheimer's disease, but it has become increasingly clear that it develops because of a complex series of events that take place in the brain over a long period of time. It is likely that the causes include some mix of genetic, environmental, and lifestyle factors. Because people differ in their genetic make-up and lifestyle, the importance of any one of these factors in increasing or decreasing the risk of developing Alzheimer's may differ from person to person.

### The Basics of Alzheimer's

Scientists are conducting studies to learn more about plaques, tangles, and other features of Alzheimer's disease. Advances in brain imaging techniques now allow researchers to visualize abnormal levels of beta-amyloid and tau proteins in the living brain. Scientists are also exploring the very earliest steps in the disease process. Findings from these studies will help them understand the causes of Alzheimer's.

One of the great mysteries of Alzheimer's disease is why it largely strikes older adults. Research on how the brain changes normally

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with age is shedding light on this question. For example, scientists are learning how age-related changes in the brain may harm neurons and contribute to Alzheimer's damage. These age-related changes include atrophy (shrinking) of certain parts of the brain, inflammation, the production of unstable molecules called free radicals, and mitochondrial dysfunction (a breakdown of energy production within a cell).

### Genetics

Early-onset Alzheimer's is a rare form of the disease. It occurs in people age 30 to 60 and represents less than 5 percent of all people who have Alzheimer's disease. Most cases of early-onset Alzheimer's are familial Alzheimer's disease, caused by changes in one of three known genes inherited from a parent.

Most people with Alzheimer's disease have "late-onset" Alzheimer's, which usually develops after age 60. Many studies have linked the apolipoprotein E (APOE) gene to late-onset Alzheimer's. This gene has several forms.

One of them, APOE  $\epsilon$ 4, seems to increase a person's risk of getting the disease. However, carrying the APOE  $\epsilon$ 4 form of the gene does not necessarily mean that a person will develop Alzheimer's disease, and people carrying no APOE  $\epsilon$ 4 can also develop the disease.

Most experts believe that additional genes may influence the development of late-onset Alzheimer's. Scientists around the world are searching for these genes, and have identified a number of common genes in addition to APOE  $\epsilon$ 4 that may increase a person's risk for late-onset Alzheimer's.

For more about this area of research, see the **Alzheimer's Disease Genetics Fact Sheet**, available at [www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers).

### Environmental/Lifestyle Factors

Research also suggests that a host of factors beyond basic genetics may play a role in the development and course of Alzheimer's disease. There is a great deal of interest, for example, in associations between cognitive decline and vascular and metabolic conditions such as heart disease, stroke, high blood pressure, diabetes, and obesity. Understanding these relationships and testing them in clinical trials will help us understand whether reducing risk factors for these conditions may help with Alzheimer's as well.

Further, a nutritious diet, physical activity, social engagement, and mentally stimulating pursuits can all help people stay healthy as they age. New research suggests the possibility that these and other factors also might help to reduce the risk of cognitive decline and Alzheimer's disease. Clinical trials

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of specific interventions are underway to test some of these possibilities.

## **Diagnosing Alzheimer's Disease**

Alzheimer's disease can be definitively diagnosed only after death, by linking clinical measures with an examination of brain tissue and pathology in an autopsy. But doctors now have several methods and tools to help them determine fairly accurately whether a person who is having memory problems has "possible Alzheimer's dementia" (dementia may be due to another cause) or "probable Alzheimer's dementia" (no other cause for dementia can be found).

To diagnose Alzheimer's, doctors may:

- Ask questions about overall health, past medical problems, ability to carry out daily activities, and changes in behavior and personality
- Conduct tests of memory, problem solving, attention, counting, and language
- Carry out standard medical tests, such as blood and urine tests, to identify other possible causes of the problem
- Perform brain scans, such as computed tomography (CT) or magnetic resonance imaging (MRI), to distinguish Alzheimer's from

other possible causes for symptoms, like stroke or tumor

These tests may be repeated to give doctors information about how the person's memory is changing over time.

Early, accurate diagnosis is beneficial for several reasons. It can tell people whether their symptoms are from Alzheimer's or another cause, such as stroke, tumor, Parkinson's disease, sleep disturbances, side effects of medications, or other conditions that may be treatable and possibly reversible.

Beginning treatment early on in the disease process can help preserve function for some time, even though the underlying disease process cannot be changed. Having an early diagnosis also helps families plan for the future, make living arrangements, take care of financial and legal matters, and develop support networks.

In addition, an early diagnosis can provide greater opportunities for people to get involved in clinical trials. In a typical clinical trial, scientists test a drug or treatment to see if that intervention is effective and for whom it would work best. (See the box for more information.)

## **Treating Alzheimer's Disease**

Alzheimer's disease is complex, and it is unlikely that any one intervention will be found to delay, prevent, or cure

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it. That's why current approaches in treatment and research focus on several different aspects, including helping people maintain mental function, managing behavioral symptoms, and slowing or delaying the symptoms of disease.

### Maintaining Mental Function

Four medications are approved by the U.S. Food and Drug Administration to treat Alzheimer's. Donepezil (Aricept®), rivastigmine (Exelon®), and galantamine (Razadyne®) are used to treat mild to moderate Alzheimer's (donepezil can be used for severe Alzheimer's as well). Memantine (Namenda®) is used to treat moderate to severe Alzheimer's. These drugs work by regulating neurotransmitters (the chemicals that transmit messages between neurons). They may help maintain thinking, memory, and speaking skills, and help with certain behavioral problems. However, these drugs don't change the underlying disease process, are effective for some but not all people, and may help only for a limited time.

### Managing Behavioral Symptoms

Common behavioral symptoms of Alzheimer's include sleeplessness, agitation, wandering, anxiety, anger, and depression. Scientists are learning why these symptoms occur and are studying new treatments—drug and non-drug—to manage them. Treating behavioral symptoms often makes people with Alzheimer's

## Participating in Clinical Trials

People with Alzheimer's disease, those with MCI, those with a family history of Alzheimer's, and healthy people with no memory problems and no family history of the disease may be able to take part in clinical trials. Participants in clinical trials for Alzheimer's disease help scientists learn about the brain in healthy aging as well as what happens in Alzheimer's. Results of clinical trials may lead to improved prevention and treatment approaches. Volunteering to participate in clinical trials is one way to help in the fight against Alzheimer's disease.

The National Institute on Aging (NIA), part of the National Institutes of Health (NIH), leads the Federal Government's research efforts on Alzheimer's. NIA-supported Alzheimer's Disease Centers located throughout the United States conduct many clinical trials and carry out a wide range of research, including studies of the causes, diagnosis, and management of Alzheimer's. NIA also sponsors the Alzheimer's Disease Cooperative Study (ADCS), a consortium of leading researchers throughout the U.S. and Canada who conduct clinical trials on promising Alzheimer's treatments.

To find out more about Alzheimer's clinical trials, talk to your health care provider or contact NIA's ADEAR Center at 1-800-438-4380. Or, visit the ADEAR Center clinical trials database at [www.nia.nih.gov/alzheimers/clinical-trials](http://www.nia.nih.gov/alzheimers/clinical-trials). You also can sign up for email alerts that let you know when new clinical trials are added to the database. More information about clinical trials is available at [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov). Also see **Participating in Alzheimer's Disease Clinical Trials and Studies** at [www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers).

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more comfortable and makes their care easier for caregivers.

### Slowing, Delaying, or Preventing Alzheimer's Disease

Alzheimer's disease research has developed to a point where scientists can look beyond treating symptoms to think about addressing underlying disease processes. In ongoing clinical trials, scientists are looking at many possible interventions, such as immunization therapy, cognitive training, physical activity, antioxidants, and the effects of cardiovascular and diabetes treatments.

### Supporting Families and Caregivers

Caring for a person with Alzheimer's disease can have high physical, emotional, and financial costs. The demands of day-to-day care, changing family roles, and difficult decisions about placement in a care facility can be hard to handle. Researchers have learned much about Alzheimer's caregiving, and studies are helping to develop new ways to support caregivers.

Becoming well-informed about the disease is one important long-term strategy. Programs that teach families about the various stages of Alzheimer's and about flexible and practical strategies for dealing with difficult caregiving situations provide vital help to those who care for people with Alzheimer's.

Developing good coping skills and a strong support network of family and

friends also are important ways that caregivers can help themselves handle the stresses of caring for a loved one with Alzheimer's disease. For example, staying physically active provides physical and emotional benefits.

Some Alzheimer's caregivers have found that participating in a support group is a critical lifeline. These support groups allow caregivers to find respite, express concerns, share experiences, get tips, and receive emotional comfort. Many organizations, such as those listed in the "For More Information" section, sponsor in-person and online support groups across the country. There are a growing number of groups for people in the early stage of Alzheimer's and their families. Support networks can be especially valuable when caregivers face the difficult decision of whether and when to place a loved one in a nursing home or assisted living facility. For more information about at-home caregiving, see **Caring for a Person with Alzheimer's Disease: Your Easy-to-Use Guide from the National Institute on Aging** at [www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers).

### Advancing Understanding

Thirty years ago, we knew very little about Alzheimer's disease. Since then, scientists have made important advances. Research supported by NIA and other organizations has expanded knowledge of brain function in healthy older people, identified ways we might lessen normal age-related declines in mental function, and deepened our understanding of the

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disease. Many scientists and physicians are now working together to untangle the genetic, biological, and

environmental factors that, over many years, ultimately result in Alzheimer's. This effort is bringing us closer to

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better managing and, ultimately, preventing this devastating disease.

disease clinical trials database; and more.

### **For More Information**

To learn about support groups, services, research centers, research studies, and publications about Alzheimer's disease, contact the following resources:

#### **Alzheimer's Disease Education and Referral (ADEAR) Center**

P.O. Box 8250  
Silver Spring, MD 20907-8250  
1-800-438-4380 (toll-free)  
[www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers)

The National Institute on Aging's ADEAR Center offers information and publications for families, caregivers, and professionals on diagnosis, treatment, patient care, caregiver needs, long-term care, education and training, and research related to Alzheimer's disease. Staff members answer telephone, email, and written requests and make referrals to local and national resources. The ADEAR website provides free, online publications in English and Spanish; email alerts; an Alzheimer's

#### **Alzheimer's Association**

225 N. Michigan Avenue, Floor 17  
Chicago, IL 60601-7633  
1-800-272-3900 (toll-free)  
1-866-403-3073 (TDD/toll-free)  
[www.alz.org](http://www.alz.org)

#### **Alzheimer's Foundation of America**

322 Eighth Avenue, 7th Floor  
New York, NY 10001  
1-866-AFA-8484  
(1-866-232-8484; toll-free)  
[www.alzfdn.org](http://www.alzfdn.org)

#### **Eldercare Locator**

1-800-677-1116 (toll-free)  
[www.eldercare.gov](http://www.eldercare.gov)

#### **Family Caregiver Alliance**

785 Market Street, Suite 750  
San Francisco, CA 94103  
1-800-445-8106 (toll-free)  
[www.caregiver.org](http://www.caregiver.org)

#### **NIH Senior Health**

[www.nihseniorhealth.gov/alzheimersdisease/toc.html](http://www.nihseniorhealth.gov/alzheimersdisease/toc.html)