

# Alzheimer's Disease

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**A**lzheimer's disease is a brain disorder that slowly destroys memory and thinking skills, and, eventually, the ability to carry out the simplest tasks. In most people with Alzheimer's, symptoms first appear later in life. Estimates vary, but experts suggest that more than 6 million Americans, most of them age 65 or older, may have dementia caused by Alzheimer's.

Alzheimer's disease is a leading cause of death in the United States, and recent estimates indicate the disorder may rank third, just behind heart disease and cancer, as a cause of death for older people.

Alzheimer's is the most common cause of dementia among older adults. 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 help with basic activities of daily living.

The causes of dementia can vary, depending on the types of brain changes that may be taking place. Other dementias include Lewy body dementia, frontotemporal disorders, and vascular dementia. It is common for people to have mixed dementia — a combination of two or more types of dementia. For example, some people have both Alzheimer's disease and vascular dementia.

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, or tau, tangles).

These plaques and tangles in the brain are still considered some of the main features of Alzheimer's disease. Another feature is the loss of connections between neurons in the brain. Neurons transmit messages between different parts of the brain, and from the brain to muscles and organs in the body.

## Alzheimer's and the Brain

Scientists continue to unravel the complex brain changes involved in Alzheimer's disease. Changes in the brain may begin a decade or more before symptoms appear. During this very early stage of Alzheimer's, toxic changes are taking place in the brain, including abnormal buildups of proteins that form amyloid plaques and tau tangles. Previously healthy neurons stop functioning, lose connections with other neurons, and die. Many other complex brain changes are thought to play a role in Alzheimer's as well.

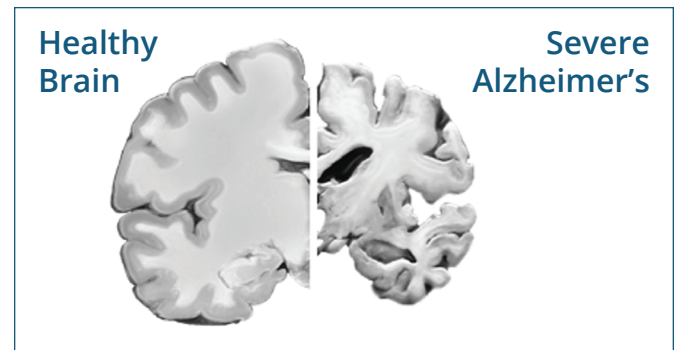
The damage initially appears to take place in the hippocampus and the entorhinal cortex, which are parts of the brain that are essential in forming memories. As more neurons die, additional parts of the brain are affected and begin to shrink. By the final stage of Alzheimer's, damage is widespread and brain tissue has shrunk significantly.

## Signs and Symptoms

Memory problems are typically one of the first signs of cognitive impairment related to Alzheimer's. Some people with memory problems have a condition called mild cognitive impairment (MCI). With MCI, people have more memory problems than normal for their age, but their symptoms do not interfere with their everyday lives. Movement difficulties and problems with the sense of smell have also been linked to MCI. Older people with MCI are at greater risk for developing Alzheimer's, but not all of them do so. Some may even revert to normal cognition.

The first symptoms of Alzheimer's vary from person to person. For many, decline in nonmemory aspects of cognition, such as word-finding, vision/spatial issues, and impaired reasoning or judgment may signal the very early stages of the disease. Researchers are studying biomarkers

(biological signs of disease found in brain images, cerebrospinal fluid, and blood) to detect early changes in the brains of people with MCI and in cognitively normal people who may be at greater risk for Alzheimer's. More research is needed before these techniques can be used broadly and routinely to diagnose Alzheimer's in a health care provider's office.



## Stages of Alzheimer's

### Mild Alzheimer's Disease

As Alzheimer's worsens, people experience greater memory loss and other cognitive difficulties. Problems can include wandering and getting lost, trouble handling money and paying bills, repeating questions, taking longer to complete normal daily tasks, and personality and behavior changes. People are often diagnosed in this stage.

### Moderate Alzheimer's Disease

In this stage, damage occurs in areas of the brain that control language, reasoning, conscious thought, and sensory processing, such as the ability to correctly detect sounds and smells. 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 multistep tasks such as getting dressed, or cope with new situations. In addition, people at this stage may have hallucinations, delusions, and paranoia and may behave impulsively.

## Severe Alzheimer's Disease

Ultimately, plaques and tangles spread throughout the brain, and brain tissue shrinks significantly. People with severe Alzheimer's cannot communicate and are completely dependent on others for their care. Near the end of life, the person may be in bed most or all of the time as the body shuts down.

## What Causes Alzheimer's?

In recent years, scientists have made tremendous progress in better understanding Alzheimer's and the momentum continues to grow. Still, scientists don't yet fully understand what causes Alzheimer's disease in most people. In people with early-onset Alzheimer's, a genetic mutation may be the cause. Late-onset Alzheimer's arises from a complex series of brain changes that may occur over decades. The causes probably include a combination of genetic, environmental, and lifestyle factors. 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 biological features of Alzheimer's disease. Advances in brain imaging techniques allow researchers to see the development and spread of abnormal amyloid and tau proteins in the living brain, as well as changes in brain structure and function. Scientists are also exploring the very earliest steps in the disease process by studying changes in the brain and body fluids that can be detected years before Alzheimer's symptoms appear. Findings from these studies will help in understanding the causes of Alzheimer's and make diagnosis easier.



Neuron cells in the brain with amyloid plaques and tau tangles

One of the great mysteries of Alzheimer's disease is why it largely affects older adults. Research on normal brain aging is exploring this question. For example, scientists are learning how age-related changes in the brain may harm neurons and affect other types of brain cells to contribute to Alzheimer's damage. These age-related changes include atrophy (shrinking) of certain parts of the brain, inflammation, blood vessel damage, production of unstable molecules called free radicals, and mitochondrial dysfunction (a breakdown of energy production within a cell).

## Alzheimer's Disease Genetics

Most people with Alzheimer's have the late-onset form of the disease in which symptoms become apparent in their mid-60s or later. Researchers have not found a specific gene that directly causes late-onset Alzheimer's, but having a form of the apolipoprotein E (*APOE*) gene increases a person's risk. This gene has several forms, and one of those, *APOE*  $\epsilon 4$ , increases a person's risk of developing Alzheimer's and is also associated with an earlier age of disease onset. However, carrying the *APOE*  $\epsilon 4$  form of the gene does not mean that a person will definitely develop the disease, and some people with no *APOE*  $\epsilon 4$  may also develop Alzheimer's.

Scientists also have identified several regions of interest in the genome (an organism's complete set of DNA) that may increase or decrease a person's risk for late-onset Alzheimer's to varying degrees.

Early-onset Alzheimer's occurs between a person's 30s and mid-60s and represents less than 10% of all people with Alzheimer's. Some cases are caused by an inherited change in one of three genes. For others, research shows that other genetic components are involved.

Most people with Down syndrome develop Alzheimer's. This may be because people with Down syndrome have an extra copy of chromosome 21, which contains the gene that generates harmful amyloid.

For more about Alzheimer's genetics research, see NIA's *Alzheimer's Disease Genetics Fact Sheet* at [www.nia.nih.gov/health/alzheimers-disease-genetics-fact-sheet](http://www.nia.nih.gov/health/alzheimers-disease-genetics-fact-sheet).

## Health, Environmental, and Lifestyle Factors

Research suggests that a host of factors beyond genetics may play a role in the development and course of Alzheimer's. There is a great deal of interest, for example, in the relationship between cognitive decline and vascular conditions such as heart disease, stroke, and high blood pressure, as well as conditions such as diabetes and obesity. Ongoing research will help us understand whether and how reducing risk factors for these conditions may also reduce the risk of Alzheimer's.

A nutritious diet, physical activity, social engagement, and mentally stimulating pursuits have all been associated with helping people stay healthy as they age.

These factors might also help reduce the risk of cognitive decline and Alzheimer's. Researchers are testing some of these possibilities in clinical trials.

## How Is Alzheimer's Disease Diagnosed?

Doctors use several methods and tools to help determine whether a person who is having memory problems has Alzheimer's disease.

To diagnose Alzheimer's, doctors may:

- Ask the person and a family member or friend questions about overall health, use of prescription and over-the-counter medicines, diet, 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), magnetic resonance imaging (MRI), or positron emission tomography (PET), to support an Alzheimer's diagnosis or to rule out other possible causes for symptoms.

These tests may be repeated to give doctors information about how the person's memory and other cognitive functions are changing over time.

People with memory and thinking concerns should talk to their doctor to find out whether their symptoms are due to Alzheimer's or another cause, such as stroke, tumor, Parkinson's disease, sleep disturbances, side effects of medication, an infection, or another type of dementia. Some of these conditions may be treatable and possibly reversible.



If the diagnosis is Alzheimer's, beginning treatment as early as possible in the disease process could help preserve daily functioning for a while. An early diagnosis also helps families plan for the future. They can take care of financial and legal matters, address potential safety issues, learn about living arrangements, and develop support networks.

In addition, an early diagnosis provides people with more opportunities to participate in clinical trials or other research studies testing possible new treatments for Alzheimer's.

## Participating in Alzheimer's Disease Clinical Trials

Everybody — those with Alzheimer's disease or MCI as well as healthy volunteers with or without a family history of Alzheimer's — may be able to take part in clinical trials and studies. Participants in Alzheimer's clinical research help scientists learn how the brain changes in healthy aging and in Alzheimer's. Currently, at least 270,000 volunteers are needed to participate in more than 250 active clinical trials and studies that are testing ways to understand, diagnose, treat, and prevent Alzheimer's disease.

Volunteering for a clinical trial is one way to help in the fight against Alzheimer's. Studies need participants of different ages, sexes, races, and ethnicities to ensure that results are meaningful for many people.

NIA leads the federal government's research efforts on Alzheimer's. NIA-supported Alzheimer's Disease Research Centers throughout the United States conduct a wide range of research, including studies of the causes, diagnosis, and management of the disease. NIA also sponsors the Alzheimer's Clinical Trials Consortium, which is designed to accelerate and expand studies and therapies in Alzheimer's and related dementias.

### **To learn more about Alzheimer's clinical trials and studies:**

- Talk to your health care provider about local studies that may be right for you.
- Contact Alzheimer's Disease Research Centers in your community at [www.nia.nih.gov/health/alzheimers-disease-research-centers](http://www.nia.nih.gov/health/alzheimers-disease-research-centers).
- Visit the Alzheimers.gov Clinical Trials Finder at [www.alzheimers.gov/clinical-trials](http://www.alzheimers.gov/clinical-trials) to learn about participating in Alzheimer's research, search for a trial near you, and watch videos of participants talking about their experiences.
- Sign up for email alerts about new trials at [www.nia.nih.gov/about/stay-connected](http://www.nia.nih.gov/about/stay-connected).
- Sign up for a registry or matching service to be invited to participate in studies at [www.nia.nih.gov/health/registries-and-matching-services-clinical-trials](http://www.nia.nih.gov/health/registries-and-matching-services-clinical-trials).

Learn more about participating in clinical trials at [www.nia.nih.gov/health/clinical-trials](http://www.nia.nih.gov/health/clinical-trials).

## How Is Alzheimer's Disease Treated?

Alzheimer's is complex, and it is therefore unlikely that any one drug or other intervention will successfully treat it in all people living with the disease.

Scientists are exploring many avenues to delay or prevent the disease as well as to treat its symptoms. In ongoing clinical trials, scientists are developing and testing several possible interventions. Under study are drug therapies aimed at a variety of disease interventions, as well as nondrug approaches such as physical activity, diet, cognitive training, and combinations of these. Just as we have many treatments for heart disease and cancer, we will likely need many options for treating Alzheimer's. Precision medicine — getting the right treatment to the right person at the right time — will likely play a major role.

Current approaches to treating Alzheimer's focus on helping people maintain mental function, treating the underlying disease process, and managing behavioral symptoms.

### Medications To Maintain Mental Function

Several medications are approved by the U.S. Food and Drug Administration (FDA) to treat symptoms of Alzheimer's. Donepezil, rivastigmine, and galantamine are used to treat the symptoms of mild to moderate Alzheimer's. Donepezil, memantine, the rivastigmine patch, and a combination medication of memantine and donepezil are used to treat moderate to severe Alzheimer's symptoms. All of these drugs work by regulating neurotransmitters, the chemicals that transmit messages between neurons. They may help reduce symptoms and help with certain behavioral problems.



However, these drugs don't change the underlying disease process. They are effective for some but not all people and may help only for a limited time.

### Medications To Treat the Underlying Disease Process

Aducanumab is the first disease-modifying therapy approved by the FDA to treat Alzheimer's disease. The medication helps to reduce amyloid deposits in the brain and may help slow the progression of Alzheimer's, although it has not yet been shown to affect clinical outcomes such as progression of cognitive decline or dementia. A doctor or specialist will likely perform tests, such as a PET scan or analysis of cerebrospinal fluid, to look for evidence of amyloid plaques and help decide if the treatment is right for the patient.

Aducanumab was approved through the FDA's Accelerated Approval Program. This process requires an additional study after approval to confirm the anticipated clinical benefit. If the follow-up trial fails to verify clinical benefit, the FDA may withdraw approval of the drug. Results of the phase 4 clinical trial for aducanumab are expected to be available by early 2030.

Several other disease-modifying medications are being tested in people with mild cognitive impairment or early Alzheimer's as potential treatments.

## Managing Behavioral Symptoms

Common behavioral symptoms of Alzheimer's include sleeplessness, wandering, agitation, anxiety, and aggression. Scientists are learning why these symptoms occur and are studying new treatments — drug and nondrug — to manage them. Research has shown that treating behavioral symptoms can make people with Alzheimer's more comfortable and makes things easier for caregivers.

## Support for Families and Caregivers

Caring for a person with Alzheimer's can have significant physical, emotional, and financial costs. The demands of day-to-day care, changes in family roles, and decisions about placement in a care facility can be difficult. NIA supports efforts to evaluate programs, strategies, approaches, and other research to

improve the quality of care and life for those living with dementia and their 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 ways to deal with difficult behaviors and other caregiving challenges can help.

Good coping skills, a strong support network, and respite care are other things that may help caregivers handle the stress of caring for a loved one with Alzheimer's. For example, staying physically active provides physical and emotional benefits.

Some caregivers have found that joining a support group is a critical lifeline. These support groups enable caregivers to find respite, express concerns, share experiences, get tips, and receive emotional comfort. Many organizations sponsor in-person and online support groups, including groups for people with early-stage Alzheimer's and their families.

For more information, see *Alzheimer's Caregiving* at [www.nia.nih.gov/health/alzheimers/caregiving](http://www.nia.nih.gov/health/alzheimers/caregiving).



## For More Information About Alzheimer's Disease

### NIA Alzheimer's and related Dementias Education and Referral (ADEAR) Center

800-438-4380 (toll-free)

[adear@nia.nih.gov](mailto:adear@nia.nih.gov)

[www.nia.nih.gov/alzheimers](http://www.nia.nih.gov/alzheimers)

The NIA ADEAR Center offers information and publications for families, caregivers, and health professionals on Alzheimer's disease and related dementias, including information on caregiving, clinical trials, and research. Staff members answer inquiries by phone, email, and in writing and make referrals to local and national resources. Visit the ADEAR website to learn more about Alzheimer's and related dementias, find clinical trials, and sign up for email updates.

### Alzheimers.gov

[www.alzheimers.gov](http://www.alzheimers.gov)

Explore the Alzheimers.gov portal for information and resources on Alzheimer's and related dementias from across the federal government.

### Alzheimer's Association

800-272-3900 (toll-free)

866-403-3073 (TTY/toll-free)

[info@alz.org](mailto:info@alz.org)

[www.alz.org](http://www.alz.org)

### Alzheimer's Foundation of America

866-232-8484 (toll-free)

[info@alzfdn.org](mailto:info@alzfdn.org)

<https://alzfdn.org>

### Eldercare Locator

800-677-1116 (toll-free)

[eldercarelocator@n4a.org](mailto:eldercarelocator@n4a.org)

<https://eldercare.acl.gov>

### Family Caregiver Alliance

800-445-8106 (toll-free)

[www.caregiver.org/contact](http://www.caregiver.org/contact)

[www.caregiver.org](http://www.caregiver.org)

### MedlinePlus

National Library of Medicine

[www.medlineplus.gov](http://www.medlineplus.gov)



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