

THE DEMENTIAS

Hope Through Research

LEARN ABOUT:

- Types of dementia
- Risk factors
- Diagnosis and treatment
- Current research



National Institutes of Health

National Institute of Neurological Disorders and Stroke
National Institute on Aging

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA) are part of the National Institutes of Health, the nation's medical research agency—supporting scientific studies that turn discovery into health.

NINDS is the nation's leading funder of research on the brain and nervous system. The NINDS mission is to seek fundamental knowledge of the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. For more information and resources, visit www.ninds.nih.gov or call **1-800-352-9424**.

NIA leads the federal government effort conducting and supporting research on aging and the health and well-being of older people. NIA's Alzheimer's and related Dementias Education and Referral (ADEAR) Center offers information and publications on dementia and caregiving for families, caregivers, and professionals. For more information, visit www.alzheimers.gov or call **1-800-438-4380**.

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Introduction

A diagnosis of dementia can be frightening for those affected by the syndrome, their family members, and caretakers. Unfortunately, there is a stigma associated with this term. Learning more about this medical condition can help. This booklet provides a general overview of various types of dementia, describes how the disorders are diagnosed and treated, and offers highlights of research supported by the National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA), both part of the National Institutes of Health (NIH).



Alzheimer's disease and related dementias have a high impact on public health and are a priority for NIH-supported research.

A glossary of terms can be found on pages 31-32.

The Basics of Dementia and Cognitive Impairment

Dementia is the loss of cognitive functioning—the ability to think, remember, or reason—to such an extent that it interferes with a person's daily life and activities. These functions include memory, language skills, visual perception, problem solving, self-management, and the ability to focus and pay attention. Some people with dementia cannot control their emotions, and their personalities may change. 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.

Age is the primary risk factor for developing dementia. For that reason, the number of people living with dementia could double in the next 40 years as the number of Americans age 65 and older increases from 48 million today to more than 88 million in 2050. Regardless of the form of dementia, the personal, economic, and societal demands can be devastating.

Dementia is not the same as age-related cognitive decline—when certain areas of thinking, memory, and information processing slow with age, but intelligence remains unchanged. Unlike dementia, age-related memory loss isn't disabling. Occasional lapses of forgetfulness are normal in elderly adults. While dementia is more common with advanced age (as many as half of all people age 85 or older may have some form of dementia), it is not an inevitable part of aging. Many people live into their 90s and beyond without any signs of dementia.

Dementia is also not the same as delirium, which is usually a short-term complication of a medical condition and most often can be treated successfully. Signs and symptoms of dementia result when once-healthy neurons (nerve cells) in the brain stop working, lose connections with

other brain cells, and die. While everyone loses some neurons as they age, people with dementia experience far greater loss.

Mild cognitive impairment (MCI) is a stage between normal cognitive changes that may occur with age and more serious symptoms that indicate dementia. Symptoms of MCI can include problems with thinking, judgment, memory, and language, but the loss doesn't significantly interfere with the ability to handle everyday activities. Symptoms of MCI include mild memory loss; difficulty with planning or organization; trouble finding words; frequently losing or misplacing things; and forgetting names, conversations, and events. Someone who has MCI may be at greater risk of eventually developing Alzheimer's or another type of dementia, particularly if the degree of memory impairment is significant, but MCI does not always progress to dementia. Symptoms may remain stable for several years, and even improve over time in some people.

It is common to have more than one cause of dementia. Many people with dementia have both Alzheimer's disease and one or more closely related disorders that share brain scanning or clinical features (and sometimes both) with Alzheimer's disease. When a person is affected by more than one dementia disorder, the dementia can be referred to as a mixed dementia.

Autopsy studies of the brains of people who had dementia suggest that a majority of those age 80 and older probably had mixed dementia caused by Alzheimer's-related neurodegenerative processes, vascular disease-related processes, or another neurodegenerative condition. In fact, some studies indicate that mixed vascular-degenerative dementia is the most common cause of dementia in the elderly.

Researchers are still trying to understand the underlying disease processes involved in dementia. Scientists have some theories about mechanisms that may lead to different forms of dementia, but more research is needed to better understand if and how these mechanisms are involved.

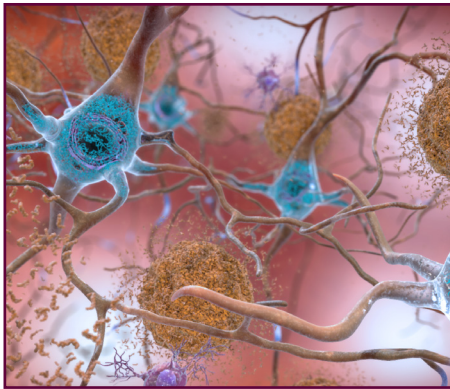
Dementias Associated with Aging and Neurodegeneration

Various disorders and factors contribute to dementia, resulting in a progressive and irreversible loss of neurons and brain functions. Currently, there are no cures for these neurodegenerative disorders.

Some specific causes of dementia disorders are explained below.

Alzheimer's Disease

Alzheimer's disease is the most common cause of dementia in older adults. As many as 5 million Americans age 65 and older may have the disease. In most neurodegenerative diseases, certain proteins abnormally clump together and are thought to damage healthy neurons, causing them to stop functioning and die. In Alzheimer's, fragments of a protein called amyloid form abnormal clusters called plaques between brain cells, and a protein called tau forms tangles inside nerve cells.



It seems likely that damage to the brain starts a decade or more before memory and other cognitive problems appear. The damage often initially appears in the hippocampus, the part of the brain essential in forming memories. Ultimately, the abnormal plaques and tangles spread throughout the brain, and brain tissue significantly shrinks.

As Alzheimer's disease progresses, 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. Memory loss and confusion worsen, and people begin to have problems recognizing family and friends. They may be unable to learn new things, carry out multi-step 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.

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 body functions shut down. Certain drugs can temporarily slow some symptoms of Alzheimer's from getting worse, but currently there are no treatments that stop the progression of the disease. For more information on Alzheimer's disease, visit the Alzheimer's and related Dementias Education and Referral (ADEAR) Center at www.alzheimers.gov.

Researchers have not found a single gene solely responsible for Alzheimer's disease; rather, multiple genes are likely involved. One genetic risk factor—having one form of the apolipoprotein E (APOE) gene on chromosome 19—does increase a person's risk for developing Alzheimer's. People who inherit one copy of this APOE $\epsilon 4$ allele have an increased chance of developing the disease; those who inherit two copies of the allele are at even greater risk. (An allele is a variant form of a pair of genes that are located on a particular chromosome and control the same trait.) The APOE $\epsilon 4$ allele may also be associated with an earlier onset of memory loss and other symptoms. Researchers have found that this allele is associated with an increased number of amyloid plaques in the brain tissue of affected people.

Frontotemporal Disorders

Frontotemporal disorders are forms of dementia caused by a family of neurodegenerative brain diseases collectively called frontotemporal lobar degeneration. They primarily affect the frontal and temporal lobes of the brain, rather than the widespread shrinking and wasting away (atrophy) of brain tissue seen in Alzheimer's disease. In these disorders, changes to nerve



cells in the brain's frontal lobes affect the ability to reason and make decisions, prioritize and multitask, act appropriately, and control movement. Changes to the temporal lobes affect memory and how people understand words, recognize objects, and recognize and respond to emotions. Some people decline rapidly

over 2 to 3 years, while others show only minimal changes for many years. People can live with frontotemporal disorders for 2 to 10 years, sometimes longer, but it is difficult to predict the time course for an affected individual. The signs and symptoms may vary greatly among individuals as different parts of the brain are affected. No treatment that can cure or reverse frontotemporal disorders is currently available.

Clinically, frontotemporal disorders are classified into two main types of syndromes:

- **Behavioral variant frontotemporal dementia (bvFTD)** involves changes in behavior, judgment, and personality. People with this disorder may have problems with cognition, but their memory may stay relatively intact. They may do impulsive things that are out of character or may engage in repetitive, unusual behaviors. People with bvFTD also may say or do inappropriate things or become uncaring. Over time, language and/or movement problems may occur.
- **Primary progressive aphasia (PPA)** involves changes in the ability to speak, understand, and express thoughts and/or words and to write and read. Many people with PPA, though not all, develop symptoms of dementia. Problems with memory, reasoning, and judgment are not apparent at first but can develop and progress over time. Sometimes a person with PPA cannot recognize the faces of familiar people and common objects (called semantic PPA). Other individuals have

increasing trouble producing speech and may eventually be unable to speak at all (called agrammatic PPA). PPA is a language disorder that is not the same as the problems with speech and ability to read and write (called aphasia) that can result from a stroke.

Other types of frontotemporal disorders include:

- **Corticobasal degeneration (CBD)** involves progressive nerve-cell loss and atrophy of specific areas of the brain, which can affect memory, behavior, thinking, language, and movement. The disease is named after parts of the brain that are affected—the cerebral cortex (the outer part of the brain) and the basal ganglia (structures deep in the brain involved with movement). Not everyone who has CBD has problems with memory, cognition, language, or behavior. The disease tends to progress gradually, with early symptoms beginning around age 60. Some of the movement symptoms of CBD are similar to those seen in Parkinson's disease.
- **Frontotemporal dementia with motor neuron disease (FTD/MND, also called FTD-ALS)** is a combination of behavioral variant frontotemporal dementia and the progressive neuromuscular weakness typically seen in amyotrophic lateral sclerosis (ALS). ALS is a neurodegenerative disease that attacks nerve cells responsible for controlling voluntary muscles (muscle action that can be controlled, such as that in the arms, legs, and face). Symptoms of either disease may appear first, with other symptoms developing over time.
- **Pick's disease** is characterized by Pick bodies—masses comprised of the protein tau that accumulate inside nerve cells, causing them to appear enlarged or balloon-like. It is usually seen with bvFTD but sometimes with PPA. Some symptoms are similar to those of Alzheimer's disease, including loss of speech, changes in behavior, and trouble with thinking. However, while inappropriate behavior characterizes the early stages of Pick's disease, memory loss is often

the first symptom of Alzheimer's. Antidepressants and antipsychotics can control some of the behavioral symptoms of Pick's disease, but no treatment is available to stop the disease from progressing.

- **Progressive supranuclear palsy (PSP)** is a brain disease that can cause problems with thinking, memory, behavior, problem solving, and judgment. It also affects the control of eye movements, mood, speech, swallowing, vision, concentration, and language. Because certain parts of the brain that control movement are damaged, this disease shares some of the problems with movement seen in people with corticobasal degeneration and Parkinson's disease.

Lewy Body Dementia

Lewy body dementia (LBD) is one of the most common causes of dementia after Alzheimer's disease and vascular disease. It typically begins after age 50, but can occur earlier. It involves abnormal protein deposits called Lewy bodies, which are balloon-like structures that form inside nerve cells. The abnormal buildup of the protein alpha-synuclein and other proteins causes neurons to work less effectively and die. Initial symptoms may vary, but over time, people with these disorders develop similar cognitive, behavioral, physical, and sleep-related symptoms.

Lewy body dementia includes two related conditions—dementia with Lewy bodies and Parkinson's disease dementia. In dementia with Lewy bodies, the cognitive symptoms are seen within a year of movement symptoms called parkinsonism (including tremor, difficulty with walking and posture, and rigid muscles). In Parkinson's disease dementia, the cognitive symptoms develop more than a year after movement problems begin.

- **Dementia with Lewy bodies (DLB)** is one of the more common forms of progressive dementia. Neurons in the outer layer of the brain (cortex) and in the substantia nigra (a region involved with the production of dopamine) degenerate. Many neurons that remain contain Lewy bodies.

Symptoms such as difficulty sleeping, loss of smell, and visual hallucinations often precede movement and other problems by as many as 10 years. Later in the course of DLB, some signs and symptoms are similar to Alzheimer's disease and may include memory loss, poor judgment, and confusion. Other signs and symptoms of DLB are similar to those of Parkinson's disease, including difficulty with movement and posture, a shuffling walk, and changes in alertness and attention. There is no cure for DLB, but there are drugs that control some symptoms.



- **Parkinson's disease dementia (PDD)** can occur in people with Parkinson's disease, but not all people with Parkinson's disease will develop dementia. PDD may affect memory, social judgment, language, or reasoning. Autopsy studies show that people with PDD often have Lewy bodies in the cortex and other brain areas, and many have amyloid plaques and tau tangles like those found in people with Alzheimer's disease, though it is not understood what these similarities mean. The time from the onset of movement symptoms to the onset of dementia symptoms varies greatly from person to person. Risk factors for developing PDD include the onset of Parkinson's-related movement symptoms followed by mild cognitive impairment and REM sleep behavior disorder, which involves having frequent nightmares and hallucinations.

Vascular Contributions to Cognitive Impairment and Dementia

Vascular contributions to cognitive impairment and dementia (VCID) cause significant changes to memory, thinking, and behavior. Cognition and brain function can be significantly affected by the size, location, and number of brain injuries. Vascular dementia and vascular cognitive impairment arise

as a result of risk factors that similarly increase the risk for cerebrovascular disease (stroke), including atrial fibrillation, hypertension, diabetes, and high cholesterol. Symptoms of VCID can begin suddenly and progress or subside during one's lifetime. VCID can occur along with Alzheimer's disease. Persons with VCID almost always have abnormalities in the brain on magnetic resonance imaging scans. These include evidence of prior strokes, often small and asymptomatic, as well as diffuse changes in the brain's "white matter"—the connecting "wires" of the brain that are critical for relaying messages between brain regions. Microscopic brain examination shows thickening of blood vessel walls called arteriosclerosis and thinning or loss of components of the white matter.

Forms of VCID include:

- **Vascular dementia** refers to progressive loss of memory and other cognitive functions caused by vascular injury or disease within the brain. Symptoms of vascular dementia may sometimes be difficult to distinguish from Alzheimer's disease. Problems with organization, attention, slowed thinking, and problem solving are all more prominent in VCID, while memory loss is more prominent in Alzheimer's.
- **Vascular cognitive impairment** involves changes with language, attention, and the ability to think, reason, and remember that are noticeable but are not significant enough to greatly impact daily life. These changes, caused by vascular injury or disease within the brain, progress slowly over time.
- **Post-stroke dementia** can develop months after a major stroke. Not everyone who has had a major stroke will develop vascular dementia, but the risk for dementia is significantly higher in someone who has had a stroke.
- **Multi-infarct dementia** is the result of many small strokes (infarcts) and mini-strokes. Language or other functions may be impaired, depending on the region of the brain that is affected. The risk for dementia is

significantly higher in someone who has had a stroke. Dementia is more likely when strokes affect both sides of the brain. Even strokes that don't show any noticeable symptoms can increase the risk of dementia.

- **Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy**

(CADASIL) is an extremely rare inherited disorder caused by a thickening of the walls of small- and medium-sized blood vessels, which reduces the flow of blood to the brain. CADASIL is associated with multi-infarct dementia, stroke, and other disorders. The first symptoms can appear in people between ages 20 and 40. CADASIL may have symptoms that can be confused with multiple sclerosis. Many people with CADASIL are undiagnosed.

- **Subcortical vascular dementia**, previously called Binswanger's disease, involves extensive microscopic damage to the small blood vessels and nerve fibers that make up white matter. Some consider it an aggressive form of multi-infarct dementia. Cognitive changes include problems with short-term memory, organization, attention, decision making, and behavior. Symptoms tend to begin after age 60, and they progress in a stepwise manner. People with subcortical vascular disease often have high blood pressure, a history of stroke, or evidence of disease of the large blood vessels in the neck or heart valves.
- **Cerebral amyloid angiopathy** is a buildup of amyloid plaques in the walls of blood vessels in the brain. It is generally diagnosed when multiple tiny bleeds in the brain are discovered using magnetic resonance imaging.



Neuropathology of Neurodegenerative Disorders

The different forms of age-related dementia, as well as many age-related neurodegenerative diseases, are thought to be caused by changes in various proteins. These diseases are called proteinopathies because they involve the abnormal buildup of specific proteins in the brain. Mutations in genes that provide instructions for making these proteins have been found to cause dementia in families. However, in the vast majority of affected individuals, dementia is not inherited, and the cause is unknown. Alzheimer's disease, frontotemporal disorders, and Lewy body dementia are proteinopathies.

In some dementias, changes in the protein tau cause it to form clumps inside nerve cells in the brain, which is believed to make the cells stop functioning properly and die. Disorders that are associated with the abnormal buildup of tau are called tauopathies.

In Alzheimer's disease, the tau protein aggregates (accumulates into abnormal clumps) and becomes twisted and tangled, forming fibers—called neurofibrillary or tau tangles—inside neurons. Abnormal clumps (plaques) of another protein, called beta-amyloid, are prominent in spaces between brain cells. Both plaques and tangles are thought to contribute to reduced function and nerve-cell death in Alzheimer's and are the hallmarks of the disease.

Beta-amyloid plaques are also seen in some forms of LBD, cerebral amyloid angiopathy, and Parkinson's disease dementia. They are also common in elderly individuals who do not have dementia.

Some, but not all, forms of frontotemporal disorders are tauopathies. Other forms of these disorders are associated with the buildup of the protein TDP-43. A mutation in a gene called progranulin, and another in a gene called C9orf72, can cause frontotemporal disorders with accumulation of TDP-43 in nerve cells.

In other dementias and some brain disorders, the protein synuclein becomes misshapen and forms harmful clumps inside neurons in different brain regions. Disorders in which synuclein builds up inside neurons are called synucleinopathies. Changes in synuclein and/or its function are the basis of LBD and other disorders such as multiple system atrophy. Multiple system atrophy is a progressive neurodegenerative disorder characterized by a combination of symptoms that affect both the autonomic nervous system (the part of the nervous system that controls involuntary action such as blood pressure or digestion) and movement. These changes cause parkinsonism, a condition resembling Parkinson's disease.



Reversible Dementia-like Disorders and Conditions

Many conditions that cause dementia-like symptoms can be halted or even reversed with the appropriate treatment.

- **Normal pressure hydrocephalus** is an abnormal buildup of cerebrospinal fluid in the brain. Elderly individuals with the condition usually have trouble with walking and bladder control before the onset of dementia. Normal pressure hydrocephalus can be treated or even reversed by implanting a shunt system to divert fluid from the brain.
- **Nutritional deficiencies** of vitamin B1 (thiamine), caused by chronic alcoholism, and of vitamin B12 can be reversed with treatment. People who have abused substances such as alcohol and recreational drugs sometimes display signs of dementia even after the substance abuse has stopped.
- **Side effects of medications** or drug combinations may cause cognitive impairment that looks like a degenerative or vascular dementia but that could reverse upon stopping these medications.
- **Vasculitis**, an inflammation of brain blood vessels, can cause dementia after multiple strokes and may be treated with immunosuppressive medications.
- **Subdural hematoma**, or bleeding between the brain's surface and its outer covering (the dura), is common after a fall. Subdural hematomas can cause dementia-like symptoms and changes in mental function. With treatment, some symptoms can be reversed.
- Some **non-malignant brain tumors** can cause symptoms resembling dementia. Recovery occurs following their removal by neurosurgery.
- Some **chronic infections** around the brain, so-called chronic meningitis, can cause dementia and may be treatable by drugs that kill the infectious agent.

Other Neurodegenerative Diseases and Conditions with Dementia or Dementia-like Symptoms

Doctors have identified many other conditions that can cause dementia or dementia-like symptoms. The diseases have different symptoms that involve body and brain functions, and they affect mental health and cognition.

- **Argyrophilic grain disease** is a common, late-onset degenerative disease that affects brain regions involved in memory and emotion. It causes cognitive decline and changes in memory and behavior, with difficulty finding words. The disease's signs and symptoms are indistinguishable from late-onset Alzheimer's disease. Confirmation of the diagnosis can be made only at autopsy.
- **Creutzfeldt-Jakob disease** is a rare brain disorder that is characterized by rapidly progressing dementia. Infectious proteins called prions become misfolded and tend to clump together, causing the brain damage. Initial symptoms include impaired memory, judgment, and thinking, along with loss of muscle coordination and impaired vision. Some symptoms of this brain disorder are similar to symptoms of other progressive neurological disorders such as Alzheimer's disease.
- **Chronic traumatic encephalopathy (CTE)** is caused by repeated traumatic brain injury (TBI) in some people who suffered multiple concussions. People with CTE may develop dementia, poor coordination, slurred speech, and other symptoms similar to those seen in Parkinson's disease 20 years or more after the injury. Late-stage CTE is also characterized by brain atrophy and widespread deposits of tau in nerve



cells. In some people, even just 5 to 10 years beyond the TBI, behavioral and mood changes may occur. Dementia may not yet be present and the brain may not have started to shrink, but small deposits of tau are seen in specific brain regions at autopsy.

- **Huntington's disease** is an inherited, progressive brain disease that affects a person's judgment, memory, ability to plan and organize, and other cognitive functions. Symptoms typically begin around age 30 or 40 and include abnormal and uncontrollable movements called chorea, as well as problems with walking and lack of coordination. Cognitive problems worsen as the disease progresses, and problems controlling movement lead to complete loss of ability for self-care.
- **HIV-associated dementia (HAD)** can occur in people who have human immunodeficiency virus (HIV), the virus that causes AIDS. HAD damages the brain's white matter and leads to a type of dementia associated with memory problems, social withdrawal, and trouble concentrating. People with HAD may develop movement problems as well. The incidence of HAD has dropped dramatically with the availability of effective antiretroviral therapies for managing the underlying virus.
- **Secondary dementias** occur in people with disorders that damage brain tissue. Such disorders may include multiple sclerosis, meningitis, and encephalitis, as well as Wilson's disease (in which excessive amounts of copper build up to cause brain damage). People with malignant brain tumors may develop dementia or dementia-like symptoms because of damage to their brain circuits or a buildup of pressure inside the skull.

Risk Factors for Dementia and Cognitive Impairment

The following risk factors may increase a person's chance of developing one or more kinds of dementia. Some of these factors can be modified, while others cannot.

- **Age.** Advancing age is the best-known risk factor for developing dementia.
- **Hypertension.** High blood pressure has been linked to cognitive decline, stroke, and types of dementia that damage the white matter regions of the brain. High blood pressure causes "wear and tear" to brain blood vessel walls called arteriosclerosis.
- **Stroke.** A single major stroke or a series of smaller strokes increases a person's risk of developing vascular dementia. A person who has had a stroke is at an increased risk of having additional strokes, which further increases the risk of developing dementia.
- **Alcohol use.** Most studies suggest that regularly drinking large amounts of alcohol increases the risk of dementia. Specific dementias, such as Wernicke-Korsakoff syndrome, are associated with alcohol abuse.
- **Atherosclerosis.** The accumulation of fats and cholesterol in the lining of arteries, coupled with an inflammatory process that leads to a thickening of the blood vessel walls (known as atherosclerosis), can lead to stroke, which raises the risk for vascular dementia.
- **Diabetes.** Poorly controlled diabetes is a risk factor for stroke and cardiovascular disease, which in turn increase the risk for vascular dementia.
- **Down syndrome.** Many people with Down syndrome develop symptoms of Alzheimer's disease by the time they reach middle age.



- **Genetics.** The chance of developing a genetically linked form of dementia increases when more than one family member has the disorder. In many dementias, there can be a family history of a similar disease. In some cases, such as with frontotemporal disorders, having just one parent who carries a mutation increases the risk of inheriting the condition. A very small proportion of dementia is inherited.
- **Head injury.** An impact to the head can cause a TBI. Certain types of TBI or repeated TBIs can cause dementia and other severe cognitive problems.
- **Parkinson's disease.** The degeneration and death of nerve cells in the brain of people with Parkinson's disease can cause dementia and significant memory loss.
- **Smoking.** Smoking increases the risk of developing cardiovascular diseases that slow or stop blood from getting to the brain.

The National Academies of Sciences, Engineering, and Medicine recently released a report of the evidence on preventing dementia:

www.ncbi.nlm.nih.gov/books/NBK436397.



Diagnosis

To diagnose dementia, doctors first assess whether an individual has an underlying treatable condition such as abnormal thyroid function, vitamin deficiency, or normal pressure hydrocephalus that may relate to cognitive difficulties. Early detection of symptoms is important, as some causes can be treated. In many cases, the specific type of dementia may not be confirmed until after the person has died and the brain is examined.

An assessment generally includes:

- **Medical history and physical exam.** Assessing a person's medical and family history, current symptoms and medication, and vital signs can help the doctor detect conditions that might cause or occur with dementia. Some conditions may be treatable.
- **Neurological evaluations.** Assessing balance, sensory response, reflexes, and other functions helps the doctor identify signs of conditions that may affect the diagnosis or are treatable with drugs. Doctors also might use an electroencephalogram to check for abnormal electrical brain activity.
- **Brain scans.** Computed tomography and magnetic resonance imaging can detect structural abnormalities and rule out other causes of dementia. Positron emission tomography can look for patterns of altered brain activity that are common in dementia. Recent advances in positron emission tomography can detect amyloid plaques and tau tangles in Alzheimer's disease.
- **Cognitive and neuropsychological tests.** These tests are used to assess memory, language skills, math skills, problem solving, and other abilities related to mental functioning.



- **Laboratory tests.** Testing a person's blood and other fluids, as well as checking levels of various chemicals, hormones, and vitamin levels, can identify or rule out conditions that may contribute to dementia.
- **Presymptomatic tests.** Genetic testing can help some people who have a strong family history of dementia identify risk for a dementia with a known gene defect.
- **Psychiatric evaluation.** This evaluation will help determine if depression or another mental health condition is causing or contributing to a person's symptoms.

Guidelines prepared by NIA and the Alzheimer's Association focus on three stages of Alzheimer's disease: dementia due to Alzheimer's, mild cognitive impairment (MCI) due to Alzheimer's, and preclinical (presymptomatic) Alzheimer's. (Presymptomatic identification is exclusively used as a research diagnosis at this point and is not relevant to routine clinical practice.) The guidelines also include biomarker tests used in research studies to measure biological changes in the brain associated with Alzheimer's disease and criteria for documenting and reporting Alzheimer's-related changes observed during an autopsy.



Treatment and Management

There are currently no treatments to stop or slow dementia caused by neurodegenerative diseases. Some diseases that occur at the same time as dementia, such as diabetes and depression, can be treated. Other symptoms that may occur in dementia-like conditions can also be treated, although some symptoms may only respond to treatment for a period of time. A team of specialists—doctors, nurses, and speech, physical, and other therapists—familiar with these disorders can help guide patient care.

Medications are available to treat certain behavioral symptoms, delusions, depression, muscle stiffness, and risk factors for vascular cognitive impairment such as high blood pressure. Always consult with a doctor as some medications may make symptoms worse.



Neurodegenerative diseases can be treated and managed as follows:

- **Alzheimer's disease.** Most drugs are used to treat symptoms in Alzheimer's. One class of drugs, called cholinesterase inhibitors, can temporarily improve or stabilize memory and thinking skills in some people by increasing activity of the cholinergic brain network—a subsystem in the brain that is highly involved with memory and learning. These drugs include donepezil, rivastigmine, and galantamine. The drug memantine is in another class of medications called NMDA receptor antagonists, which prevent declines in learning and memory. Memantine may be combined with a cholinesterase inhibitor for added benefits. These drugs are sometimes used to treat other dementias in which Alzheimer's disease is believed to co-occur.

- **Frontotemporal disorders.** There are no medications approved to treat or prevent these disorders and most other types of progressive dementia. Sedatives, antidepressants, and other drugs used to treat Parkinson's and Alzheimer's symptoms may help manage certain symptoms and behavioral problems associated with the disorders.
- **Dementia with Lewy bodies.** Medicines for managing DLB are aimed at relieving symptoms such as gait and balance disturbances, stiffness, hallucinations, and delusions. Studies suggest that cholinesterase inhibitor drugs used to treat people with Alzheimer's disease may offer some benefit to people with DLB.
- **Parkinson's disease dementia.** Some studies suggest that the cholinesterase inhibitors used to treat people with Alzheimer's might improve cognitive, behavioral, and psychotic symptoms in people with PDD. Unfortunately, many of the medications used to treat the motor symptoms of Parkinson's disease worsen the cognitive problems. The U.S. Food and Drug Administration has approved rivastigmine, an Alzheimer's drug, to treat cognitive symptoms in PDD.
- **Vascular contributions to cognitive impairment and dementia.** This type of dementia is often managed with drugs to prevent strokes or reduce the risk of additional brain damage. Some studies suggest that drugs that improve memory in Alzheimer's might benefit people with early vascular dementia. Treating the modifiable risk factors can help prevent additional stroke.

A team of therapists can help with maintaining physical movement, addressing speech and swallowing issues, and learning new ways to handle loss of skills with everyday tasks such as feeding oneself.

It is important to educate family, friends, and caregivers about a loved one's medical issues. Also, in-person and online support groups offered by many disease awareness and caregiver advocacy organizations can give families and other caregivers additional resources, as well as opportunities to share experiences and express concerns. (See the **Resources** section at the end of this booklet).



Research

The National Institute of Neurological Disorders and Stroke (NINDS), a component of the National Institutes of Health (NIH), is the leading federal funder of research on nervous system disorders, including dementia. Another NIH Institute, the National Institute on Aging (NIA), is the leading federal



funder of research on Alzheimer's disease and related dementias. Together, these Institutes are world leaders in supporting research on the dementias, including Lewy body dementia, frontotemporal disorders, and vascular contributions to cognitive impairment and dementia.

Although scientists have some understanding of the dementias and the mechanisms involved, ongoing research may lead to new ways to understand the causes of these diseases and to diagnose, treat, or perhaps prevent or block disease development.

Research partnerships on dementia involving NIA and NINDS include:

The **National Alzheimer's Project Act (NAPA)** authorized a coordinated national plan to attack Alzheimer's disease and improve care and services. NAPA calls for increased collaboration between scientists, the federal government, and public organizations while improving patient care. The resulting **National Plan to Address Alzheimer's Disease** is designed to expand research on Alzheimer's and related dementias prevention and treatment and to move the most promising drugs from discovery into clinical trials. The National Plan also calls for increased federal funding for Alzheimer's research, as well as support for those affected by the disease and their families, increased public awareness about Alzheimer's, and improved data collection and analysis. These goals also apply to Lewy body, frontotemporal, mixed, and vascular dementias. The Plan's overarching

research goal is to "prevent or effectively treat Alzheimer's disease by 2025." For more information, see <http://aspe.hhs.gov/national-alzheimers-project-act>.

Accelerating Medicine Partnership–Alzheimer's Disease (AMP-AD) is a multi-sector partnership among NIH, 10 biopharmaceutical companies, and several nonprofit organizations to develop new, clinically relevant therapeutics and biomarkers to confirm existing therapies. The goal is to speed up the process of bringing new medicines to people either with or at risk of Alzheimer's disease. For more information, see www.nia.nih.gov/research/amp-ad.

M²OVE-AD (Molecular Mechanisms of the Vascular Etiology of Alzheimer's Disease) allows scientists from diverse fields to work collaboratively to understand the complex molecular mechanisms by which vascular risk factors influence Alzheimer's. The work also will identify new targets for treatment and prevention. M²OVE-AD builds on the open-science approach and the big-data infrastructure established by AMD-AP. For more information, see www.nih.gov/file/27681.

The **Tau Center Without Walls** program is designed to increase collaboration and sharing of data and resources among researchers to better understand the protein tau and its involvement in disorders such as frontotemporal degeneration. These efforts may lead to advances in prevention, diagnosis, or treatment of tau toxicity associated with frontotemporal disorders and contribute to tool development that can be applied in clinical trials for frontotemporal and other tau-related disorders.

The **Dementia with Lewy Bodies Consortium** is designed to expand the collection of clinical data and biological specimens in the NINDS Parkinson's Disease Biomarkers Program to include data from people with Lewy body dementias. Standardized research and data collection and reporting systems will make it easier for researchers to share and confirm their research. For more information, see https://pdbp.ninds.nih.gov/dementia_with_lewy_bodies_consortium_U01.

Researchers in the **Small Vessel Vascular Contributions to Cognitive Impairment and Dementia (VCID) Biomarkers Program** hope to develop biomarkers of key vascular processes related to VCID in Alzheimer's disease. Identifying biomarkers may improve the efficiency and outcome of trials designed to test drug effectiveness and safety in humans and speed the development of therapies for the dementias.

Additional NIA/NINDS research on age-related and other dementias includes:

Clinical studies. Clinical studies offer an opportunity to help researchers find better ways to safely detect, treat, or prevent the dementias. Various NIH Institutes support clinical studies on Alzheimer's disease and related dementias at the NIH research campus in Bethesda, MD, and at medical research centers throughout the United States. For information about participating in clinical studies for Alzheimer's, related dementias, and other disorders, visit "NIH Clinical Research Trials and You" at www.nih.gov/health/clinicaltrials. For a list of Alzheimer's and related dementias clinical trials and studies, see www.nia.nih.gov/alzheimers/clinical-trials. For a comprehensive list of all trials, go to www.clinicaltrials.gov and type in the name of the dementia, such as "Lewy body dementia" or "vascular dementia."

Biomarkers. Several research projects hope to identify dementia biomarkers (measurable biological signs that may indicate disease risk and progression or confirm diagnosis). Such biomarkers could be detected through brain imaging or even blood tests. Research projects include the study of possible biomarkers to predict cognitive decline in people with Parkinson's disease, the Alzheimer's Biomarkers Consortium of Down Syndrome (many people with Down syndrome have Alzheimer's-related brain changes in their 30s that can lead to dementia in their 50s and 60s), and genetic and biomarker studies that may lead to promising treatments for frontotemporal disorders. The Alzheimer's Disease Neuroimaging Initiative (ADNI) is a longitudinal study to validate the use of biomarkers for Alzheimer's disease clinical trials and diagnosis (see www.adni-info.org).

Drugs and compounds. A number of drugs and compounds that might slow the progression of Alzheimer's disease and other dementias are in various stages of testing. A NINDS-NIA study found that tau antisense oligonucleotides—compounds that are genetically engineered to block a cell's assembly line production of the toxic form of the protein tau—could prevent and reverse some brain injury caused by tau in animal models. NIH-supported prevention trials are testing promising drugs that target amyloid proteins that form plaques in the brain. Other NIH studies include the use of drugs being developed to treat autism spectrum disorders to see if they can improve cognitive function in people with age-related cognitive decline.

Exercise. Physical activity can benefit mental well-being and improve daily functioning and quality of life in people with dementia. Researchers are assessing the combined approach of aerobic and cognitive exercise to see if it can delay or slow the progression of Alzheimer's disease in at-risk older adults. Other research is assessing the benefit of exercise to delay MCI in older individuals and to improve brain function in older adults who may be at risk for developing Alzheimer's.



Genetics. NIH scientists continue to look for new genes that may be responsible for the development of Alzheimer's disease and other forms of dementia. One approach is using genome-wide association studies, which can rapidly scan the complete sets of DNA, or genomes, of many people to find genetic variations associated with a particular disease. Identifying new genetic associations for neurodegenerative diseases may lead to better strategies to detect, treat, and prevent the dementias.

Imaging. Clinical imaging may help researchers better understand changes in the brains of people with dementia, as well as help diagnose these disorders. For example, research hopes to enhance brain imaging techniques to make it possible to detect and try to stop the earliest changes in the protective blood-brain barrier that may contribute to VCID. ADNI

has identified and developed imaging techniques and biomarker measures in blood and cerebrospinal fluid that are being used in research to track changes in the living brains of older people who are cognitively normal, have MCI, or have mild Alzheimer's disease.



International efforts. The International Alzheimer's Disease Research Portfolio (IADRP) helps individuals learn about research related to both Alzheimer's and related dementias at public and private organizations worldwide. It also helps organizations leverage resources and avoid duplication of effort. The Common Alzheimer's Disease Research Ontology—a classification system that allows organizations to integrate and compare research portfolios—was developed by NIA, NIH, and the Alzheimer's Association. For more information, see <http://iadrp.nia.nih.gov>.

Natural history studies. Studying groups of people over time may lead to ways to identify those at risk of developing dementia or cognitive impairment. Three NIH-funded research teams, for example, are conducting longitudinal studies of individuals in which frontotemporal disorders run in families or appear on their own to understand the progression of frontotemporal disorders both before and after symptom onset; identify genes; discover biomarkers for diagnosis, progression, and prognosis; and establish a clinical research consortium to support therapy development.

Proteins. A number of proteins—including tau, alpha-synuclein, TDP-43, and beta-amyloid—are involved with various cellular processes. When there is a change in the genes that direct the production or rate of clearance of these proteins, the proteins can build into abnormal amounts and form abnormal clumps that damage nerve cells in the brain, causing dementia, movement, and other symptoms. NIH-funded research projects seek to better understand the toxic effects of protein buildup and how it is related to the development of dementia. For example, a number of studies target the buildup of amyloid, which forms plaques that are characteristic in Alzheimer's disease. Other researchers hope to better understand how proteins misfold and become harmful in frontotemporal disorders and LBD.

Stem cells. Stem cells are unique in that they have the potential to develop into many different cell types in the body, including brain cells. Scientists are exploring various types of cells, including stem cells, to discover nerve-cell mechanisms that lead to the onset and progression of Alzheimer's disease and other forms of dementia. For example, scientists converted human skin cells into a model of human neurons. Such neurons, when created from individuals with familial forms of Alzheimer's, show biochemical changes that are typical of the disease. Researchers are also investigating the mechanism by which human Alzheimer's neurons develop cellular and molecular defects in protein production and degradation.

Additional NIH research projects. More information about dementias research supported by NIA, NINDS, and other NIH Institutes and Centers can be found using NIH RePORTER, a searchable database of current and past research projects supported by NIH and other federal agencies. RePORTER also includes links to publications and resources from these projects. See <https://projectreporter.nih.gov>.

Conclusion

Currently, there are no cures for the common dementias caused by progressive neurodegeneration, including Alzheimer's disease, frontotemporal disorders, and Lewy body dementia. Some evidence suggests that controlling vascular risk factors, such as high blood pressure, may reduce the risk of developing dementia decades later. Some symptoms of dementia and conditions that cause dementia or have dementia-like symptoms are treatable. A better understanding of dementia disorders, as well as their diagnosis and treatment, will make it possible for affected individuals and their caretakers to live their lives more fully and meet daily challenges. NIH, primarily through research activities funded by NIA and NINDS, continues to improve diagnosis, design therapeutic approaches to dementias, and create tools and resources to help speed the development of treatments that can be used in practice. These discoveries may eventually lead to ways to slow disease progression or even cure and prevent the dementias.



Glossary

Alpha-synuclein—the major protein present in abnormal clumps called Lewy bodies, which are seen in the brains of people with Parkinson's disease and some dementias. Disorders in which alpha-synuclein accumulates inside nerve cells are called synucleinopathies.

Alzheimer's disease—the most common cause of dementia in older adults. Nearly all brain functions, including memory, movement, language, judgment, and behavior, are eventually affected. Alzheimer's disease is defined by high levels of amyloid plaques and tau tangles in the brain.

Amyloid—a protein that aggregates to form plaques that appear in the brains of people with Alzheimer's disease.

Biomarkers—measurable biological signs in the living body that may indicate risk or progression of a disease and improve diagnosis.

Corticobasal degeneration—a progressive disorder characterized by abnormal buildup of the protein tau, nerve-cell loss, and atrophy in multiple areas of the brain.

Dementia—a condition in which impaired thinking and memory significantly interfere with daily life.

Dementia with Lewy bodies—a type of Lewy body dementia.

Frontotemporal disorders—a group of dementias characterized by degeneration of nerve cells, especially those in the frontal and temporal lobes of the brain.

Lewy body dementia—a progressive dementia characterized by the presence of abnormal structures called Lewy bodies in the brain.

Mild cognitive impairment—a stage between normal cognitive changes that may occur with age and the more serious symptoms that indicate dementia.

Mixed dementia—dementia in which one form of dementia and another condition or dementia cause damage to the brain; for example, Alzheimer's disease and small vessel disease or vascular dementia.

Multi-infarct dementia—a type of vascular cognitive impairment and dementia caused by numerous small strokes in the brain.

Neurodegeneration—the progressive loss of nerve cell structure or function.

Neurofibrillary tangles—bundles of twisted filaments largely made up of a protein called tau, found in nerve cells in the brains of people with Alzheimer's disease and other types of dementia such as frontotemporal dementia.

Parkinson's disease dementia—a secondary dementia that sometimes occurs in people with advanced Parkinson's disease. Many people with Parkinson's have the amyloid plaques and neurofibrillary tangles found in Alzheimer's disease, but it is not clear if the diseases are linked.

Plaques—abnormal clumps of amyloid protein that are found in large numbers in the brains of people with Alzheimer's disease.

Tau—a protein that helps the functioning of microtubules, which are part of the cell's structural support and help deliver substances throughout the cell. In several dementia disorders, tau twists into filaments that become tangles. Disorders associated with an accumulation of tau, such as frontotemporal dementia, are called tauopathies.

Vascular contributions to cognitive impairment and dementia—conditions arising from stroke and other vascular brain injuries that cause significant changes to memory, thinking, and behavior.

Vascular dementia—a type of dementia caused by brain damage from cerebrovascular or cardiovascular problems, usually strokes.

Resources

For more information on disorders or research programs funded by the National Institute of Neurological Disorders and Stroke or the National Institute on Aging, please contact:



National Institute of Neurological Disorders and Stroke BRAIN

1-800-352-9424 (toll-free)

braininfo@ninds.nih.gov

www.ninds.nih.gov



National Institute on Aging Alzheimer's and related Dementias Education and Referral (ADEAR) Center

1-800-438-4380 (toll-free)

adear@nia.nih.gov

www.alzheimers.gov

Information on dementia also is available from the following organizations:



Alzheimer's Association

1-800-272-3900 (toll-free)

1-866-403-3073 (TTY/toll-free)

info@alz.org

www.alz.org



Alzheimer's Drug Discovery Foundation

1-212-901-8000

info@alzdiscovery.org

www.alzdiscovery.org



Alzheimer's Foundation of America

1-866-232-8484 (toll-free)

info@alzfdn.org

www.alzfdn.org



Association for Frontotemporal Degeneration

1-866-507-7222 (toll-free)

info@theaftd.org

www.theaftd.org



The Bluefield Project to Cure Frontotemporal Dementia

rodney.pearlman@bluefieldproject.org

www.bluefieldproject.org



BrightFocus Foundation

1-800-437-2423 (toll-free)

info@brightfocus.org

www.brightfocus.org/alzheimers



Lewy Body Dementia Association

1-404-975-2322

1-844-311-0587 (toll-free LBD Caregiver Link)

lbda@lbda.org

www.lbda.org



National Institute of Mental Health

1-866-615-6464 (toll-free)

1-866-415-8051 (TTY/toll-free)

nimhinfo@nih.gov

www.nimh.nih.gov



National Organization for Rare Disorders

1-800-999-6673 (toll-free Patient Services)

orphan@rarediseases.org

www.rarediseases.org

The Dementias: Hope Through Research was jointly produced by the National Institute of Neurological Disorders and Stroke and the National Institute on Aging, both part of the National Institutes of Health.

Also available are publications and information about Alzheimer's disease as well as the booklets *Frontotemporal Disorders: Information for Patients, Families, and Caregivers* and *Lewy Body Dementia: Information for Patients, Families, and Professionals*.

For additional copies of this publication or further information, contact:

National Institute of Neurological Disorders and Stroke

www.ninds.nih.gov

1-800-352-9424

National Institute on Aging

Alzheimer's and related Dementias Education and Referral Center

www.alzheimers.gov

1-800-438-4380



National Institutes of Health

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Alzheimer's Disease Fact Sheet

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- [How Is Alzheimer's Disease Treated?](#)
- [Support for Families and Alzheimer's Disease Caregivers](#)

Alzheimer's disease is an irreversible, progressive 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 in their mid-60s. 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 currently ranked as the sixth leading cause of death in the United States, but [recent estimates](#) indicate that 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 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.

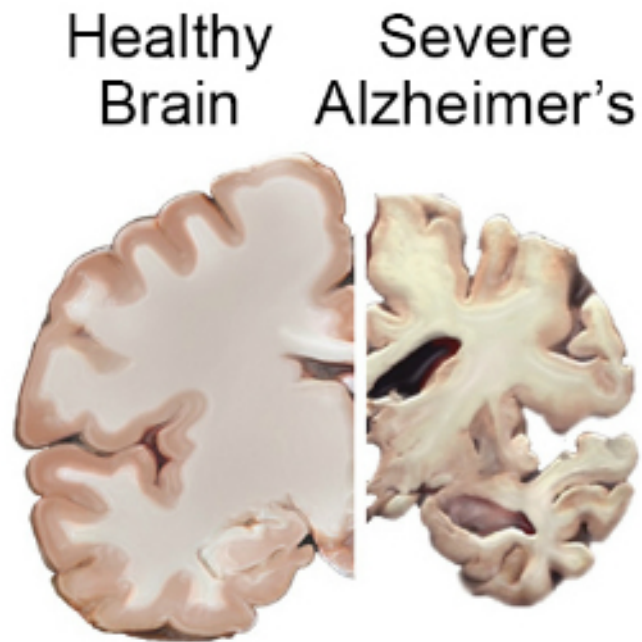
Alzheimer's disease is named after Dr. Alois Alzheimer. In 1906, Dr. Alzheimer noticed changes in the brain tissue of a woman who had died of an unusual mental illness. Her symptoms included memory loss, language problems, and unpredictable behavior. After she died, he examined her brain and found many 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 nerve cells (neurons) in the brain. Neurons transmit messages between different parts of the brain, and from the brain to muscles and organs in the body.

How Does Alzheimer's Disease Affect the Brain?

Scientists continue to unravel the complex brain changes involved in the onset and progression of Alzheimer's disease. It seems likely that changes in the brain may begin a decade or more before memory and other cognitive problems appear. During this preclinical stage of Alzheimer's disease, people seem to be symptom-free, but toxic changes are taking place in the brain. Abnormal deposits of proteins form amyloid plaques and tau tangles throughout the brain. Once-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, too.

The damage initially appears to take place in the hippocampus and the entorhinal cortex, parts of the brain 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 of Alzheimer's Disease

[Memory problems](#) are typically one of the first signs of cognitive impairment related to Alzheimer's disease. Some people with memory problems have a condition called [mild cognitive impairment](#) (MCI). In 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. Some may even go back to normal cognition.

The first symptoms of Alzheimer's vary from person to person. For many, decline in non-memory aspects of cognition, such as word-finding, vision/spatial issues, and impaired reasoning or judgment, may signal the very early stages of Alzheimer's 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. Studies indicate that such early detection is possible, but more research is needed before these techniques can be used routinely to diagnose Alzheimer's disease in everyday medical practice.

Stages of Alzheimer's Disease

Mild Alzheimer's Disease

As Alzheimer's disease progresses, 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, 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 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](#), the person may be in bed most or all of the time as the body shuts down.

What Causes Alzheimer's Disease?

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 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 Disease

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.

One of the great mysteries of Alzheimer's disease is why it largely strikes 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, vascular 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. Researchers have not found a specific gene that directly causes late-onset Alzheimer's. However, having one form of the apolipoprotein E (APOE) gene does increase a person's risk. This gene has several forms. One of them, APOE ϵ 4, increases a person's risk of developing the disease and is also associated with an earlier age of disease onset. However, carrying the APOE ϵ 4 form of the gene does not mean that a person will definitely develop Alzheimer's disease, and some people with no APOE ϵ 4 may also develop the disease.

Also, scientists have identified a number of 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 disease occurs between a person's 30s and mid-60s and represents less than 10 percent 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](#).

Health, Environmental, and Lifestyle Factors that May Contribute to Alzheimer's Disease

Research suggests that a host of factors beyond genetics may play a role in the development and course of Alzheimer's disease. 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 metabolic 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 disease. Clinical trials are testing some of these possibilities.

How Is Alzheimer's Disease Diagnosed?

Doctors use several methods and tools to help determine 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 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 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.

Alzheimer's disease can be *definitely* diagnosed only after death, by linking clinical measures with an examination of brain tissue in an autopsy.

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 a [non-Alzheimer's dementia](#). Some of these conditions may be treatable and possibly reversible.

[If the diagnosis is Alzheimer's](#), beginning treatment early in the disease process may help preserve daily functioning for some time, even though the underlying disease process cannot be stopped or reversed. 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 gives people greater opportunities to participate in clinical trials that are testing possible new treatments for Alzheimer's disease or other research studies.

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 about 200 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 disease. Studies need participants of different ages, sexes, races, and ethnicities to ensure that results are meaningful for many people.

The National Institute on Aging (NIA) at the National Institutes of Health (NIH) 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 Alzheimer's. 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 find out more about Alzheimer's clinical trials and studies:

- Talk to your healthcare provider about local studies that may be right for you.
- Contact [Alzheimer's disease research centers](#) or memory or neurology clinics in your community.
- Search the [Alzheimers.gov Clinical Trials Finder](#) for a trial near you or to [sign up for email alerts](#) about new trials.
- Sign up for a registry (such as the [Alzheimer's Prevention Registry](#)) or matching service (such as [TrialMatch](#)) to be invited to participate in studies.

Learn more about [participating in clinical trials](#).

[Watch videos](#) of participants in Alzheimer's disease clinical trials talking about their

experiences.

How Is Alzheimer's Disease Treated?

Alzheimer's disease is complex, and it is unlikely that any one drug or other intervention can successfully [treat](#) it. Current approaches focus on helping people maintain mental function, manage behavioral symptoms, and slow down certain problems, such as memory loss. Researchers hope to develop therapies targeting specific genetic, molecular, and cellular mechanisms so that the actual underlying cause of the disease can be stopped or prevented.

Medications to Maintain Mental Function in Alzheimer's Disease

[Several medications](#) are approved by the U.S. Food and Drug Administration (FDA) to treat symptoms of 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®), the Exelon® patch, and Namzaric® (a combination of memantine and donepezil) are used to treat moderate to severe Alzheimer's. 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 Manage Behavior in Alzheimer's Disease

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 non-drug—to manage them. Research has shown that treating [behavioral symptoms](#) can make people with Alzheimer's more comfortable and makes things easier for caregivers.

Looking for New Treatments for Alzheimer's Disease

Alzheimer's research has developed to a point where scientists are exploring ways to delay or prevent the disease as well as treat its symptoms. In ongoing clinical trials supported by NIA, scientists are developing and testing several possible interventions. Under study are drug therapies aimed at a variety of targets, including the beta-amyloid protein, cerebrovascular function, loss of synapses, and specific neurotransmitters, as well as nondrug interventions, such as physical activity, diet, cognitive training, and combinations of these approaches.

Support for Families and Alzheimer's Disease Caregivers

Caring for a person with Alzheimer's disease can have high 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. There are several evidence-based approaches and programs that can help, and researchers are continuing to look for new and better 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 ways to deal with difficult behaviors and other caregiving challenges can help.

Good coping skills, a strong support network, and respite care are other ways that help caregivers handle the stress of caring for a loved one with Alzheimer's disease. 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 allow 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](#).

Read about this [topic in Spanish](#). Lea sobre este [tema en español](#).

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

www.nia.nih.gov/alzheimers

The National Institute on Aging's ADEAR Center offers information and free print publications about Alzheimer's disease and related dementias for families, caregivers, and health professionals. ADEAR Center staff answer telephone, email, and written requests and make referrals to local and national resources.

Alzheimers.gov

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

www.alz.org

Eldercare Locator

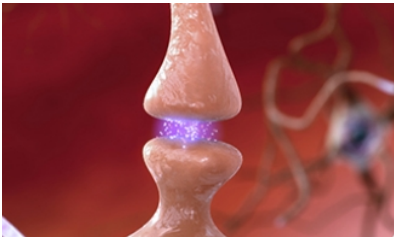
800-677-1116 (toll-free)

eldercarelocator@n4a.org

This content is provided by the NIH National Institute on Aging (NIA). NIA scientists and other experts review this content to ensure it is accurate and up to date.

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