# Alzheimer's disease

## Introduction

Alzheimer's disease is the most common cause of dementia, which is the loss of intellectual and social abilities severe enough to interfere with daily functioning. Dementia occurs in people with Alzheimer's disease because healthy brain tissue degenerates, causing a steady decline in memory and mental abilities.

About 4 million older Americans have Alzheimer's, a disease that usually develops in people age 65 or older. This number is expected to triple by the year 2050 as the population ages.

Although there's no cure for Alzheimer's disease, researchers have made progress. Treatments are available that improve the quality of life for some people with Alzheimer's. Also, more drugs are being studied, and scientists have discovered several genes associated with Alzheimer's, which may lead to new treatments to block progression of this complex disease.

In the meantime, caring for someone with Alzheimer's takes patience and a focus on the things a person can still do and enjoy. Those with Alzheimer's — as well as those who care for them — need support and affection from friends and family to cope.

## Signs and symptoms

Everyone has occasional lapses in memory. It's normal to forget the names of people whom you rarely see. But it's not a normal part of aging to forget the names of familiar people and objects.

Alzheimer's disease — a progressive, degenerative brain disease — causes more than simple forgetfulness. It may start with slight memory loss and confusion, but it eventually leads to irreversible mental impairment that destroys a person's ability to remember, reason, learn and imagine.

Most people with Alzheimer's share certain signs and symptoms of the disease. These may include:

- **Increasing and persistent forgetfulness.** At its onset, Alzheimer's disease is marked by periods of forgetfulness, especially of recent events or simple directions. But what begins as mild forgetfulness persists and worsens. People with Alzheimer's may repeat things and forget conversations or appointments. They routinely misplace things, often putting them in illogical locations. They frequently forget names, and eventually, they may forget the names of family members and everyday objects.
- **Difficulties with abstract thinking.** People with Alzheimer's may initially have trouble balancing their checkbook, a problem that progresses to trouble recognizing and dealing with numbers.
- **Difficulty finding the right word.** It may be a challenge for those with Alzheimer's to find the right words to express thoughts or even follow conversations. Eventually, reading and writing also are affected.
- **Disorientation.** People with Alzheimer's often lose their sense of time and dates, and may find themselves lost in familiar surroundings.
- **Loss of judgment.** Solving everyday problems, such as knowing what to do if food on the stove is burning, becomes increasingly difficult, eventually impossible. Alzheimer's is characterized by greater difficulty in doing things that require planning, decision making and judgment.

- **Difficulty performing familiar tasks.** Once-routine tasks that require sequential steps, such as cooking, become a struggle as the disease progresses. Eventually, people with advanced Alzheimer's may forget how to do even the most basic things.

- **Personality changes.** People with Alzheimer's may exhibit mood swings. They may express distrust in others, show increased stubbornness and withdraw socially. Early on, this may be a response to the frustration they feel as they notice uncontrollable changes in their memory. Depression often coexists with Alzheimer's disease. Restlessness also is a common sign. As the disease progresses, people with Alzheimer's may become anxious or aggressive and behave inappropriately.

Because early Alzheimer's symptoms progress slowly, diagnosis is often delayed. People developing the condition may be frighteningly aware of their problems — but careful to keep them hidden, refusing to see a doctor. As a result, even their families may fail to see what's going on. When the signs and symptoms are too obvious to miss, those closest to the person often realize that similar — but less severe — difficulties have been present for years.

The disease's course varies from person to person. Eight years is the average length of time from diagnosis of Alzheimer's to death. Survival begins to decline three years after diagnosis, but some people live more than a decade with the disease.

## Causes

The causes of Alzheimer's are poorly understood, but its effect on brain tissue has been demonstrated clearly. Alzheimer's damages and kills brain cells.

A healthy brain has billions of nerve cells called neurons. Neurons generate electrical and chemical signals that are relayed from neuron to neuron to help you think, remember and feel. Chemicals called neurotransmitters help these signals flow seamlessly between neurons.

Initially in people with Alzheimer's, neurons in certain locations of the brain begin to die. When they die, lower levels of neurotransmitters are produced, creating signaling problems in the brain.

**Plaques and tangles**
Alzheimer's disease is named after Dr. Alois Alzheimer, a German neurologist. In 1906, he examined the brain of a woman who had died after years of progressive dementia. Her brain tissue showed abnormal clumps and irregular knots of brain cells. Today, these clumps (now called plaques) and knots (now called tangles) are considered hallmarks of Alzheimer's disease.

Studies of plaques and tangles from the brains of people who have died of Alzheimer's suggest several possible roles these structures might play in the disease. Some of the theories:

- **Possible role of plaques.** Plaques are made up of a normally harmless protein called beta-amyloid. Although the ultimate cause of neuron death in Alzheimer's isn't known, mounting evidence suggests that a form of beta-amyloid protein may be the culprit. Three genetic mutations — in amyloid precursor protein and presenilin 1 (PS1) and presenilin 2 (PS2) proteins — are known to cause a small number of early-onset forms of Alzheimer's disease. These mutations result in the production of amyloid plaques. Together, these three genetic mutations account for less than 10 percent of all Alzheimer's cases.

- **Possible role of tangles.** The internal support structure for brain neurons depends on the normal functioning of a protein called tau. In people with Alzheimer's, threads of tau protein undergo alterations that cause them to become twisted. Many researchers believe this may seriously damage neurons, causing them to die.

**Inflammatory response as the common path.** Researchers have observed inflammation in the brains of some people with Alzheimer's disease. Inflammation is your body's response to injury or infection and a natural part of the healing process. Even as beta-amyloid plaques develop in the spaces between neurons, immune cells are at work getting rid of dead cells and other waste products in the brain. Although researchers believe the inflammation occurs before plaques have fully formed, they aren't sure how this development relates to the disease process. There's also debate about whether inflammation has a damaging effect on neurons or whether it is beneficial in clearing away plaques.

Alzheimer's is a complex disease likely caused by a combination of factors — such as infection or reduced circulation — and genetic susceptibility. Although all the contributing factors may never be known, scientists have identified several common threads. They include:

## Risk factors

- **Age.** Alzheimer's usually affects people older than 65, but can, rarely, affect those younger than 40. Less than 5 percent of people between 65 and 74 have Alzheimer's. For people 85 and older, that number jumps to nearly 50 percent.
- **Heredity.** Your risk of developing Alzheimer's appears to be slightly higher if a first-degree relative — parent, sister or brother — has the disease. Although the genetic mechanisms of Alzheimer's among families remain largely unexplained, researchers have identified a few genetic mutations that greatly increase risk in some families. Three genetic mutations are known to cause early-onset Alzheimer's. In addition, one form of the apolipoprotein E (APOE) gene increases your chance of developing late-onset Alzheimer's.
- **Sex.** Women are more likely than men are to develop the disease, in part because they live longer.
- **Lifestyle.** The same factors that put you at risk of heart disease, such as high blood pressure and high cholesterol, may also increase the likelihood that you'll develop Alzheimer's disease. Poorly controlled diabetes is another risk factor. And keeping your body fit isn't your only concern — you've got to exercise your mind as well. Some studies have suggested that remaining mentally active throughout your life, especially in your later years, reduces the risk of Alzheimer's disease.
- **Education levels.** Studies have found an association between less education and the risk of Alzheimer's. Some researchers theorize that the more you use your brain, the more synapses you create, which provides a greater reserve as you age. It remains unclear, however, whether less education and less mental activity create a risk of Alzheimer's or if it's simply harder to detect Alzheimer's in people who exercise their minds frequently or who have more education.
- **Toxicity.** One long-standing theory is that overexposure to certain trace metals or chemicals may cause Alzheimer's. For a time, aluminum seemed a likely candidate, because some people with Alzheimer's have deposits of aluminum in their brains. After many years of studies, however, no one has been able to link aluminum exposure directly to Alzheimer's. At this point, there's no evidence that any particular substance increases a person's risk of Alzheimer's.
- **Head injury.** The observation that some ex-boxers eventually develop dementia suggests that serious traumatic injury to the head (for example, a concussion with a prolonged loss of consciousness) may be a risk factor for Alzheimer's. Several studies indicate a definite link between the two, but others show no link.
- **Hormone replacement therapy.** The exact role hormone replacement therapy may play in the development of dementia isn't yet clear. Throughout the 1980s and '90s, evidence seemed to show that estrogen supplements given after menopause could reduce the risk of dementia. But results from the large-scale Women's Health Initiative Memory Study indicated an increased risk of dementia for women taking estrogen after age 65. The verdict is not yet in on whether estrogen affects the risk of dementia if given at an earlier age.

## Screening and diagnosis

There's no one test to diagnose Alzheimer's disease. Typically, doctors start the diagnostic process by ruling out other diseases and conditions that also can cause memory loss.

Small, undetected strokes, for example, can cause dementia by temporarily interrupting blood flow to the brain. People with Parkinson's disease, a degenerative nerve disorder, also can develop dementia. Depression, too, can cause lapses in memory. In addition, many older adults are on multiple medications that may impair their ability to think clearly.

To help distinguish Alzheimer's disease from other causes of memory loss, doctors typically rely on the following:

- **Medical history.** Doctors may ask about a person's general health

## Complications

In advanced Alzheimer's disease, people may lose all ability to care for themselves. This can make them more prone to additional health problems such as:

- **Pneumonia.** Difficulty swallowing food and liquids may cause people with Alzheimer's to inhale (aspirate) some of what they eat and drink into their airways and lungs, which can lead to pneumonia.
- **Infections.** Urinary incontinence may require the placement of a urinary catheter, which increases the risk of urinary tract infections. Untreated urinary tract infections can lead to more serious, life-threatening infections.
- **Falls and their complications.** People with Alzheimer's may become disoriented, increasing their risk of falls. Falls can lead to fractures. In addition, falls are a common cause of serious head injuries, such as bleeding in the brain. Surgery to repair injury from a fall carries risks as well. For instance, prolonged immobilization — which may be necessary to recover from injuries related to a fall — increases the risk of a blood clot in the lungs (pulmonary embolism), which can be life-threatening.

## Treatment

Currently, there's no cure for Alzheimer's disease. Doctors sometimes prescribe drugs to improve symptoms that often accompany Alzheimer's, including sleeplessness, wandering, anxiety, agitation and depression. But only two varieties of medications have been proved to slow the cognitive decline associated with Alzheimer's.

**Cholinesterase inhibitors**
This group of medications — which includes donepezil (Aricept), rivastigmine (Exelon) and galantamine (Reminyl) — works by improving the levels of neurotransmitters in the brain. Donepezil has been approved by the Food and Drug Administration for the treatment of mild, moderate and severe Alzheimer's disease.

Donepezil also appears to delay the onset of Alzheimer's for about a year in people who have mild cognitive impairment (MCI). People who have MCI have more memory problems than other people their age, but they are not demented.

Cholinesterase inhibitors don't work for everyone. As many as half the people who take these drugs show no improvement. Other people may choose to stop taking the drugs because of the side effects, which include diarrhea, nausea and vomiting.

**Memantine (Namenda)**
The first drug approved to treat moderate to severe stages of Alzheimer's, memantine (Namenda), protects brain cells from damage caused by the chemical messenger glutamate. It sometimes is used in combination with a cholinesterase inhibitor. Memantine's most common side effect is dizziness, although it also appears to increase agitation and delusional behavior in some people.