alzheimer's $\ref{eq:second}$ association[®]

BASICS OF ALZHEIMER'S DISEASE

WHAT IT IS AND WHAT YOU CAN DO

Geri T., living with Alzheimer's, and her spouse and care partner, Jim T.

WHAT IS ALZHEIMER'S DISEASE?

Alzheimer's (AHLZ-high-merz) is a disease of the brain that causes problems with memory, thinking and behavior. It is not a normal part of aging.

Alzheimer's gets worse over time. Although symptoms can vary widely, the first problem many people notice is forgetfulness severe enough to affect their ability to function at home or at work, or to enjoy hobbies.

The disease may cause a person to become confused, get lost in familiar places, misplace things or have trouble with language.

It can be easy to explain away unusual behavior as part of normal aging, especially for someone who seems physically healthy. Any concerns about memory loss should be discussed with a doctor.





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1. ALZHEIMER'S DISEASE AND OTHER TYPES OF DEMENTIA

Alzheimer's disease

More than 5 million Americans have Alzheimer's disease, the most common form of dementia. Alzheimer's accounts for 60 to 80 percent of all dementia cases. That includes 11 percent of those age 65 and older and one-third of those 85 and older. The disease also impacts more than 15 million family members, friends and caregivers.

Dementia

Dementia is a general term for the loss of memory and other cognitive abilities serious enough to interfere with daily life.

Other types of dementia

- » Vascular dementia is a decline in thinking skills caused by conditions that block or reduce blood flow to the brain, depriving brain cells of vital oxygen and nutrients. These changes sometimes occur suddenly following strokes that block major brain blood vessels. It is widely considered the second most common cause of dementia after Alzheimer's disease.
- » Mixed dementia is a condition in which abnormalities characteristic of more than one type of dementia occur simultaneously. Symptoms may vary, depending on the types of brain changes involved and the brain regions affected, and may be similar to or even indistinguishable from those of Alzheimer's or another dementia.
- » Parkinson's disease dementia is an impairment in thinking and reasoning that many people with Parkinson's disease eventually develop. As brain changes gradually spread, they often begin to affect

mental functions, including memory and the ability to pay attention, make sound judgments and plan the steps needed to complete a task.

- » Dementia with Lewy bodies is a type of progressive dementia that leads to a decline in thinking, reasoning and independent function due to abnormal microscopic deposits that damage brain cells.
- » Huntington's disease dementia is a progressive brain disorder caused by a defective gene. It causes changes in the central area of the brain, which affect movement, mood and thinking skills.
- » Creutzfeldt-Jakob disease is the most common human form of a group of rare, fatal brain disorders known as prion diseases. Misfolded prion protein destroys brain cells, resulting in damage that leads to rapid decline in thinking and reasoning as well as involuntary muscle movements, confusion, difficulty walking and mood changes.
- » Frontotemporal dementia (FTD) is a group of disorders caused by progressive cell degeneration in the brain's frontal lobes (the areas behind the forehead) or its temporal lobes (the regions behind the ears).
- » Normal pressure hydrocephalus is a brain disorder in which excess cerebrospinal fluid accumulates in the brain's ventricles, causing thinking and reasoning problems, difficulty walking and loss of bladder control.
- » Down syndrome dementia develops in people born with extra genetic material from chromosome 21, one of the 23 human chromosomes. As individuals with Down syndrome age, they have a greatly increased risk of developing a type of dementia that's either the same as or very similar to Alzheimer's disease.

- » Korsakoff syndrome is a chronic memory disorder caused by severe deficiency of thiamine (vitamin B-1). It is most commonly caused by alcohol misuse, but certain other conditions can also cause the syndrome.
- » Posterior cortical atrophy (PCA) is the gradual and progressive degeneration of the outer layer of the brain (the cortex) located in the back of the head (posterior). It is not known whether PCA is a unique disease or a possible variant form of Alzheimer's disease.

2. HOW ALZHEIMER'S AFFECTS THE BRAIN

The changes that take place in the brain begin at the microscopic level long before the first signs of memory loss.

What goes wrong in the brain

The brain has 100 billion nerve cells (neurons). Each nerve cell connects to many others to form communication networks. In addition to nerve cells, the brain includes cells specialized to support and nourish other cells.

Groups of nerve cells have special jobs. Some are involved in thinking, learning and memory. Others help us see, hear, smell and tell our muscles when to move.

Brain cells operate like tiny factories. They receive supplies, generate energy, construct equipment and get rid of waste. Cells also process and store information and communicate with other cells. Keeping everything running requires coordination as well as large amounts of fuel and oxygen.

Scientists believe Alzheimer's disease prevents parts of a cell's factory from running well. They are not sure where the trouble starts. But just like a real factory, backups and breakdowns in

TAKE A CLOSER LOOK



Take our Inside the Brain: An Interactive Tour at **alz.org/brain** to learn how Alzheimer's affects the brain and its functions.

one system cause problems in other areas. As damage spreads, cells lose their ability to do their jobs and, eventually, die.

The role of plaques and tangles

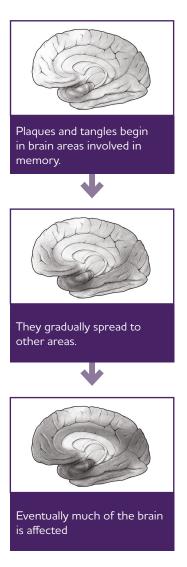
The brains of individuals with Alzheimer's have an abundance of plaques and tangles. Plaques are deposits of a protein fragment called beta-amyloid that build up in the spaces between nerve cells. Tangles are twisted fibers of another protein called tau that build up inside cells.

Though autopsy studies show that most people develop some plaques and tangles as they age, those with Alzheimer's tend to develop far more and in a predictable pattern, beginning in the areas important for memory before spreading to other regions.

Scientists do not know exactly what role plaques and tangles play in Alzheimer's disease. Most experts believe that they disable or block communication among nerve cells and disrupt processes the cells need to survive.

The destruction and death of nerve cells causes memory failure, personality changes, problems in carrying out daily activities and other symptoms of Alzheimer's disease.

How Alzheimer's spreads in the brain



Illustrations:

Alzheimer's Disease Education and Referral Center, a service of the National Institute on Aging

3. CAUSES AND RISK FACTORS

While scientists know that Alzheimer's disease involves the failure of nerve cells, it's still unknown why this happens. However, they have identified certain risk factors that increase the likelihood of developing Alzheimer's.

Age

The greatest known risk factor for Alzheimer's is increasing age. Most individuals with the disease are 65 and older. One in nine people in this age group and nearly one-third of people age 85 and older have Alzheimer's.

Family history

Another risk factor is family history. Research has shown that those who have a parent, brother or sister with Alzheimer's are more likely to develop the disease than individuals who do not. The risk increases if more than one family member has the illness.

Familial Alzheimer's and genetics

Two categories of genes influence whether a person develops a disease: risk genes and deterministic genes. Risk genes increase the likelihood of developing a disease but do not guarantee it will happen. Deterministic genes directly cause a disease, guaranteeing that anyone who inherits one will develop a disorder.

Researchers have found several genes that increase the risk of Alzheimer's. APOE-e4 is the first risk gene identified and remains the one with strongest impact. Other common forms of the APOE gene are APOE-e2 and APOE-e3. Everyone inherits a copy of some form of APOE from each parent. Those who inherit one copy of APOE-e4 have an increased risk of developing Alzheimer's; those who inherit two copies have an even higher risk, but not a certainty. Rare deterministic genes cause Alzheimer's in a few hundred extended families worldwide. These genes are estimated to account for less than 1 percent of cases. Individuals with these genes usually develop symptoms in their 40s or 50s.

LATINOS AND AFRICAN-AMERICANS

Research shows that older Latinos are about one-and-a-half times as likely as older whites to have Alzheimer's and other dementias, while older African-Americans are about twice as likely to have the disease as older whites. The reason for these differences is not well understood, but researchers believe that higher rates of vascular disease in these groups may also put them at greater risk for developing Alzheimer's.

Other risk factors

Age, family history and genetics are all risk factors we can't change. However, research is beginning to reveal clues about other risk factors that we may be able to influence. There appears to be a strong link between serious head injury and future risk of Alzheimer's. It's important to protect your head by buckling your seat belt, wearing a helmet when participating in sports and proofing your home to avoid falls.

One promising line of research suggests that strategies for overall healthy aging may help keep the brain healthy and may even reduce the risk of developing Alzheimer's. These measures include eating a healthy diet, staying socially active, avoiding tobacco and excess alcohol, and exercising both the body and mind. Some of the strongest evidence links brain health to heart health. The risk of developing Alzheimer's or vascular dementia appears to be increased by many conditions that damage the heart and blood vessels. These include heart disease, diabetes, stroke, high blood pressure and high cholesterol. Work with your doctor to monitor your heart health and treat any problems that arise.

Studies of donated brain tissue provide additional evidence for the heart-head connection. These studies suggest that plaques and tangles are more likely to cause Alzheimer's symptoms if strokes or damage to the brain's blood vessels are also present.

4. HOW TO FIND OUT IF IT'S ALZHEIMER'S DISEASE

Not everyone experiencing memory loss or other possible Alzheimer's warning signs recognizes that they have a problem. Signs of dementia are sometimes more obvious to family members or friends.

The first step in following up on symptoms is finding a doctor with whom a person feels comfortable. There is no single type of doctor that specializes in diagnosing and treating memory symptoms or Alzheimer's disease. Many people contact their regular primary care physician about their concerns. Primary care doctors often oversee the diagnostic process themselves.

In some cases, the doctor may refer the individual to a specialist, such as a:

- » Neurologist, who specializes in diseases of the brain and nervous system.
- » Psychiatrist, who specializes in disorders that affect mood or the way the mind works.

» Psychologist with special training in testing memory and other mental functions.

There is no single test that proves a person has Alzheimer's. The workup is designed to evaluate overall health and identify any conditions that could affect how well the mind is working. When other conditions are ruled out, the doctor can then determine if it is Alzheimer's or another dementia.

Experts estimate that a skilled physician can diagnose Alzheimer's with more than 90 percent accuracy. Physicians can almost always determine that a person has dementia, but it may sometimes be difficult to determine the exact cause.

STEPS TO DIAGNOSIS INCLUDE:

Understanding the problem

Be prepared for the doctor to ask:

- » What kind of symptoms have occurred.
- » When they began.
- » How often they happen.
- » If they have gotten worse.



Reviewing medical history

The doctor will interview the person being tested and others close to him or her to gather information about current and past mental and physical illnesses. It is helpful to bring a list of all the medications the person is taking.

The doctor will also obtain a history of key medical conditions affecting other family members, especially whether they may have or had Alzheimer's disease or other dementias.

Evaluating mood and mental status

Mental status testing evaluates memory, the ability to solve simple problems and other thinking skills.

This testing gives an overall sense of whether a person:

- » Is aware of symptoms.
- » Knows the date, time and where he or she is.
- » Can remember a short list of words, follow instructions and do simple calculations.

The doctor may ask the person his or her address, what year it is or who is serving as president. The individual may also be asked to spell a word backward, draw a clock or copy a design. The doctor will also assess mood and sense of well-being to detect depression or other illnesses that can cause memory loss and confusion.

Physical exam and diagnostic tests

A physician will:

- » Evaluate diet and nutrition.
- » Check blood pressure, temperature and pulse.
- » Listen to the heart and lungs.
- » Perform other procedures to assess overall health.

The physician will collect blood and urine samples and may order other laboratory tests. Information from these tests can help identify disorders such as anemia, infection, diabetes, kidney or liver disease, certain vitamin deficiencies, thyroid abnormalities, and problems with the heart, blood vessels or lungs. All of these conditions may cause confused thinking, trouble focusing attention, memory problems or other symptoms similar to dementia.

Neurological exam

A doctor will closely evaluate the person for problems that may signal brain disorders other than Alzheimer's.

The physician will also test:

- » Reflexes
- » Coordination
- » Muscle tone and strength
- » Eye movement
- » Speech
- » Sensation

The doctor is looking for signs of small or large strokes, Parkinson's disease, brain tumors, fluid accumulation on the brain, and other illnesses that may impair memory or thinking.

The neurological exam may also include a brain imaging study. The most common types are magnetic resonance imaging (MRI) or computed tomography (CT). MRIs and CTs can reveal tumors, evidence of small or large strokes, damage from severe head trauma or a buildup of fluid. Researchers are studying other imaging techniques so they can better diagnose and track the progress of Alzheimer's.

5. WHEN THE DIAGNOSIS IS ALZHEIMER'S

Once testing is complete, the doctor will make an appointment to review results and share his or her conclusions. A diagnosis of Alzheimer's reflects a doctor's best judgment about the cause of a person's symptoms, based on the testing performed.

You may want to ask the doctor:

- » Why the diagnosis is Alzheimer's.
- » Where the person may be in the course of the disease.
- » What to expect in the future.

Find out if the doctor will manage care going forward and, if not, who will be the primary doctor. The doctor can then schedule the next appointment or provide a referral.

Alzheimer's disease is life-changing for both the diagnosed individual and those close to him or her. While there is currently no cure, treatments are available that may help relieve some symptoms. Research has shown that taking full advantage of available treatment, care and support options can improve quality of life.



Consider:

- » How to provide increasing levels of care as the disease progresses.
- » How the individual and family members will cope with changes in the person's ability to drive, cook and perform other daily activities.
- » How to ensure a safe environment.

It is also important to begin making legal and financial plans. A timely diagnosis often allows the person with dementia to participate in this planning. The person can also decide who will make medical and financial decisions on his or her behalf in later stages of the disease.

CREATE AN ACTION PLAN

Alzheimer's Navigator® helps guide individuals facing dementia when planning for the future. This interactive tool evaluates needs, outlines action steps and links the user to local services and Association programs. Visit alz.org/alzheimersnavigator to start planning.

6. THE DISEASE

Alzheimer's disease typically progresses slowly in three general stages: early, middle and late (sometimes referred to as mild, moderate and severe in a medical context). Since Alzheimer's affects people in different ways, each person may experience symptoms — or progress through the stages — differently.

Overview of disease progression

The symptoms of Alzheimer's worsen over time, but because the disease affects people in different ways, the rate of progression varies. On average, a person with Alzheimer's lives four to eight years after diagnosis, but can live as long as 20 years, depending on other factors.

Changes in the brain related to Alzheimer's begin years before any signs of the disease. This period is referred to as preclinical Alzheimer's disease.

The following stages provide an overall idea of how abilities change once symptoms appear and should be used as a general guide. Stages may overlap, making it difficult to place a person with Alzheimer's in a specific stage.

Early-stage Alzheimer's

In the early stage of Alzheimer's, a person may function independently. He or she may still drive, work and be part of social activities. Despite this, the person may feel as if he or she is having memory lapses, such as forgetting familiar words or the location of everyday objects.

Friends, family or others close to the individual begin to notice difficulties. During a detailed medical interview, doctors may be able to detect problems in memory or concentration. Common difficulties include:

- » Problems coming up with the right word or name.
- » Trouble remembering names when introduced to new people.
- » Challenges performing tasks in social or work settings.
- » Forgetting material that was just read.
- » Losing or misplacing a valuable object.
- » Increasing trouble with planning or organizing.

Middle-stage Alzheimer's

Middle-stage Alzheimer's is typically the longest stage and can last for many years. As the disease progresses, the person with Alzheimer's will require a greater level of care.

You may notice the person with Alzheimer's confusing words, getting frustrated or angry, or acting in unexpected ways, such as refusing to bathe. Damage to nerve cells in the brain can make it difficult to express thoughts and perform routine tasks.

At this point, symptoms will be noticeable to others and may include:

- » Forgetfulness of events or about one's own personal history.
- » Feeling moody or withdrawn, especially in socially or mentally challenging situations.
- » Being unable to recall their address or telephone number or the high school or college from which they graduated.
- » Confusion about where they are or what day it is.
- » The need for help choosing proper clothing for the season or the occasion.
- » Trouble controlling bladder and bowels in some individuals.
- » Changes in sleep patterns, such as sleeping during the day and becoming restless at night.
- » An increased risk of wandering and becoming lost.
- » Personality and behavioral changes, including suspiciousness and delusions or compulsive, repetitive behavior like hand wringing or tissue shredding.

WANDERING

Six out of 10 people with Alzheimer's will wander and become lost. People can wander or become confused about their location at any stage of the disease. If not found within 24 hours, up to half of those who get lost risk serious injury or death.

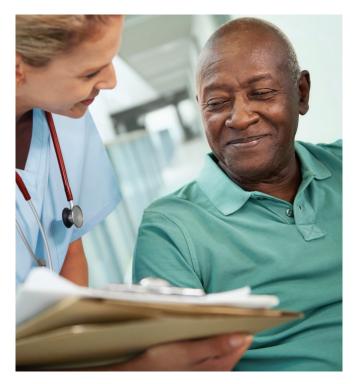
Visit **alz.org/safety** to learn about **MedicAlert® + Alzheimer's Association Safe Return®**, a 24-hour emergency response service that provides assistance when a person with dementia becomes lost or has a medical emergency.

Late-stage Alzheimer's

In the final stage of the disease, individuals lose the ability to respond to their environment, carry on a conversation and, eventually, control movement. They may still say words or phrases, but communicating pain becomes difficult. As memory and cognitive skills worsen, significant personality changes may occur and extensive help with daily activities may be required.

At this stage, individuals may:

- » Need round-the-clock assistance with daily activities and personal care.
- » Lose awareness of recent experiences as well as of their surroundings.
- » Experience changes in physical abilities, including the ability to walk, sit and, eventually, swallow.
- » Have greater difficulty communicating.
- » Become increasingly vulnerable to infections, especially pneumonia.



7. TREATING THE SYMPTOMS

Currently, there is no cure for Alzheimer's and no way to stop the underlying death of brain cells. But drugs and non-drug treatments may help with both cognitive and behavioral symptoms.

A comprehensive care plan for Alzheimer's disease:

- » Considers appropriate treatment options.
- » Monitors treatment effectiveness as the disease progresses.
- » Changes course and explores alternatives as necessary.
- » Respects individual and family goals for treatment and tolerance for risk.

Cognitive symptoms

Three types of drugs are currently approved by the FDA to treat cognitive symptoms of Alzheimer's disease. The first, cholinesterase (KOH-luh-NES-ter-ays) inhibitors, prevents the breakdown of acetylcholine (a-SEA-til-KOH-lean), a chemical messenger important for memory and learning. By keeping levels of acetylcholine high, these drugs support communication among nerve cells.

Three cholinesterase inhibitors are commonly prescribed:

- » Donepezil (Aricept[®]), approved in 1996 to treat mild-to-moderate Alzheimer's and in 2006 for the severe stage.
- » Rivastigmine (Exelon®), approved in 2000 for mild-to-moderate Alzheimer's.
- » Galantamine (Razadyne[®]), approved in 2001 for mild-to-moderate stages.

The second type of drug works by regulating the activity of glutamate, a different messenger chemical involved in information processing:

» Memantine (Namenda[®]), approved in 2003 for moderate-to-severe stages, is the only drug in this class currently available.

The third type is a combination of cholinesterase inhibitor and a glutamate regulator:

» Donepezil and memantine (Namzaric[®]), approved in 2014 for moderate-to-severe stages.

The effectiveness of these treatments varies from person to person. While they may temporarily help symptoms, they do not slow or stop the brain changes that cause Alzheimer's to become more severe over time.

Behavioral symptoms

Many find behavioral changes, like anxiety, agitation, aggression and sleep disturbances, to be the most challenging and distressing effect of Alzheimer's disease. These changes can greatly impact the quality of life for individuals. As with cognitive symptoms of Alzheimer's, the chief underlying cause of behavioral and psychiatric symptoms is the progressive damage to brain cells. Other possible causes of behavioral symptoms include:

» Drug side effects

Side effects from prescription medications may be at work. Drug interactions may occur when taking multiple medications for several conditions.

» Medical conditions

Symptoms of infection or illness, which may be treatable, can affect behavior. Pneumonia or urinary tract infections can bring discomfort. Untreated ear or sinus infections can cause dizziness and pain.

» Environmental influences

Situations affecting behavior include moving to a new private residence or residential care facility; misperceived threats; or fear and fatigue from trying to make sense of a confusing world.

There are two types of treatments for behavioral symptoms: non-drug treatments and prescription medications.

Non-drug treatments

Steps to developing non-drug treatments include:

- » Identifying the symptom.
- » Understanding its cause.
- » Changing the caregiving environment to remove challenges or obstacles.

Pinpointing what has triggered behaviors can often help guide the best approach. Often the trigger is a change in the person's environment, such as:

- » New caregivers.
- » Different living arrangements.

- » Travel.
- » Admission to a hospital.
- » Presence of houseguests.
- » Being asked to bathe or change clothes.

Because people with Alzheimer's gradually lose the ability to communicate, it is important to regularly monitor their comfort and anticipate their needs.

Prescription medications

Medications can be effective in managing some behavioral symptoms, but they must be used carefully and are most effective when combined with non-drug treatments. Medications should target specific symptoms so that response to treatment can be monitored.

Prescribing any drug for a person with Alzheimer's is medically challenging. Use of drugs for behavioral and psychiatric symptoms should be closely supervised.

Some medications, called psychotropic medications (antipsychotics, antidepressants, anti-convulsants and others), are associated with an increased risk of serious side effects. These drugs should only be considered when non-pharmacological approaches are unsuccessful in reducing dementia-related behaviors that are causing physical harm to the person with dementia or his or her caregivers.



KEY TERMS

SYMPTOMS

Cognitive: Symptoms that affect memory, awareness, language, judgment, and an individual's ability to plan, organize and carry out other thought processes.

Behavioral: A group of additional symptoms that occur — at least to some degree — in many individuals with Alzheimer's. Early on, people may experience personality changes such as irritability, anxiety or depression. In later stages, individuals may develop sleep disturbances; agitation (physical or verbal aggression, general emotional distress, restlessness, pacing, shredding paper or tissues, yelling); delusions (firmly held belief in things that are not real); or hallucinations (seeing, hearing or feeling things that are not there). Individuals with the disease may develop wandering impulses at any stage.

TREATMENTS

FDA-approved: Medication approved by the U.S. Food and Drug Administration (FDA) that treats symptoms of Alzheimer's disease.

Non-drug: A treatment other than medication that helps relieve symptoms of Alzheimer's disease.

8. FUTURE

The Alzheimer's Association is the world's largest nonprofit funder of Alzheimer's research. Since 1982, we have awarded over \$350 million to more than 2,300 research investigations worldwide.

When Dr. Alois Alzheimer first described the disease in 1906, a person in the United States lived an average of about 50 years. Few people reached the age of greatest risk. As a result, the disease was considered rare and attracted little scientific interest. That attitude changed as the average life span increased and scientists began to realize how often Alzheimer's strikes people in their 70s and 80s. The Centers for Disease Control and Prevention recently estimated the average life expectancy to be 78.8 years.

Today, Alzheimer's is at the forefront of biomedical research, with 90 percent of what we know discovered in the last 20 years. Some of the most remarkable progress has shed light on how Alzheimer's affects the brain. Better understanding of the disease's impact may lead to better treatments.

Clinical studies drive progress

Scientists are constantly working to advance our understanding of Alzheimer's. But without clinical research and the help of human volunteers, we cannot treat, prevent or cure Alzheimer's. Clinical trials test new interventions or drugs to prevent, detect or treat disease for safety and effectiveness. Clinical studies are any type of clinical research involving people and those that look at other aspects of care, such as improving quality of life. Every clinical trial or study contributes valuable knowledge, regardless if favorable results are achieved.



Visit **alz.org/TrialMatch** to learn more about **Alzheimer's Association TrialMatch**[®], a clinical studies matching service that connects individuals living with Alzheimer's, caregivers, healthy volunteers and physicians with current Alzheimer's-related clinical studies.

New directions in treatment and prevention

One promising target is beta-amyloid. This protein fragment builds up into the plaques considered to be one hallmark of Alzheimer's disease. Researchers have developed several ways to clear beta-amyloid from the brain or prevent it from clumping together into plaques. Experimental drugs that zero in on beta-amyloid are now being tested.

Many other new approaches to treatment are also under investigation worldwide. We don't yet know which of these strategies may work, but scientists say that with the necessary funding, the outlook is good for developing treatments that slow or stop Alzheimer's.



While there is no known way to prevent Alzheimer's disease, emerging research suggests that the steps people take to maintain heart health may also reduce the risk of cognitive decline.

This connection makes sense, because the brain is nourished by one of the body's richest networks of blood vessels, and the heart is responsible for pumping blood through these blood vessels to the brain. It's especially important for people to do everything they can to keep weight, blood pressure, cholesterol and blood sugar within recommended ranges to reduce the risk of heart disease, stroke and diabetes. Eating a diet low in saturated fats and rich in fruits and vegetables, exercising regularly, and staying mentally and socially active may all help protect the brain.



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The Alzheimer's Association is the leading voluntary health organization in Alzheimer's care, support and research. Our mission is to eliminate Alzheimer's disease through the advancement of research; to provide and enhance care and support for all affected; and to reduce the risk of dementia through the promotion of brain health.

Our vision is a world without Alzheimer's disease[®].

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