

# Section

2



# ALZHEIMER'S DISEASE

*Unraveling the Mystery*



National Institute on Aging  
National Institutes of Health



# **ALZHEIMER'S** DISEASE

*Unraveling the Mystery*



# Preface

Over the past few decades, Alzheimer's disease (AD) has emerged from obscurity. Once considered a rare disorder, it is now seen as a major public health problem that has a severe impact on millions of older Americans and their families. The National Institute on Aging (NIA) is the

lead agency for AD research at the National Institutes of Health (NIH). NIA launched its AD program in 1978, and since then, the study of this disease has become one of NIA's top priorities. Several other NIH institutes also conduct and sponsor studies on AD.

Thanks to the work of NIH institutes, other research orga-

nizations around the world, and many private-sector research, education, and advocacy groups, the study of AD is moving ahead rapidly. This book explains what AD is, describes the main areas in which researchers are working, and highlights new approaches for helping families and friends care for people with AD.

## TO GET THE MOST OUT OF THIS BOOK

### Learn the Basics of the Healthy Brain

- The parts of the brain (pages 10-13)
- How neurons work (pages 14-16)
- The changing brain in healthy aging (pages 17-19)

### Discover What Happens to the Brain in AD

- The hallmarks of AD (pages 21-26)
- The changing brain in AD (pages 27-33)

### Explore Cutting-Edge AD Research

- Looking for causes (pages 36-47)
- Diagnosing AD (pages 48-53)
- Searching for treatments (pages 54-61)

### Learn about Caregiver Support

- Who are AD caregivers? (page 63)
- Reducing the personal costs of caregiving (pages 64-67)
- Taking care of mom or dad from a distance (page 68)

## TO LEARN EVEN MORE

Visit NIA's Alzheimer's Disease Education and Referral Center website at [www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers). There, you will find resources to accompany this book, such as downloadable versions of the illustrations and an animation that shows what happens to the changing brain in AD. And while you are there, explore the ADEAR Center's many other offerings. These include free publications about AD and AD caregiving, clinical trials information, a list of NIA-funded Alzheimer's Disease Centers, and NIA's searchable AD Library database of thousands of materials about AD.

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# Introduction

*“Never have I loved my husband of 41 years more than I do today....Though he may not know I’m his wife, he does know that my presence means his favorite foods and drinks are near at hand....I wonder why I can sit daily by his side as I play tapes, relate bits and pieces of news, hold his hand, tell him I love him. Yet I am content when I am with him, though I grieve for the loss of his smile, the sound of my name on his lips.”*

This excerpt from *Lessons Learned: Shared Experiences in Coping*, by participants of the Duke University Alzheimer Support Groups, gives a glimpse into what a person with Alzheimer’s disease (AD) and a family caregiver might experience as the disease progresses. The gradual slipping away of mind and memory is frightening and frustrating, both for the person with the disease and for family and friends, and can elicit strong feelings of love, grief, anger, and exhaustion.

AD is an irreversible, progressive brain disease that slowly destroys memory and thinking skills, eventually even the ability to carry out the simplest tasks. In most people with AD, symptoms first appear after age 60. AD is caused by a disease that affects the brain. In the absence of disease, the human brain often can function well into the 10th decade of life.

Not so long ago, we were not able to do much for people with AD. Today, that situation is changing. Thousands of scientists, voluntary organizations, and health care professionals are

studying AD so that they can find ways to manage, treat, and one day prevent this terrible disease.

## AD: A GROWING NATIONAL PROBLEM

For many older adults and their families, AD stands in the way of the “Golden Years.” It also presents a major problem for our health care system and society as a whole. AD is the most common cause of **dementia** among older people. Recent estimates of how many people in the United States currently have AD differ, with numbers ranging from 2.4 million to 4.5 million, depending on how AD is measured. But scientists agree that unless the disease can be effectively treated or prevented, the numbers will increase significantly if current population trends continue.

Our aging society makes AD an especially critical issue. A 2005 Census Bureau report on aging in the United States notes that the population age 65 and older is expected to double in size to about 72 million people within the next 25 years. Moreover, the 85 and older age group is now the fastest growing segment of the population. This is all the more important for a **neurodegenerative**

**disease** like AD because the number of people with the disease doubles for every 5-year age interval beyond age 65.

AD not only affects the people with the disease, of course. The number of AD caregivers—and their needs—can be expected to rise rapidly as the population ages and as the number of people with AD grows. During their years of AD caregiving, spouses, relatives, and friends experience great emotional, physical, and financial challenges. As the disease runs its course and the abilities of people with AD steadily decline, family members face difficult, and often costly, decisions about the long-term care of their loved ones.

The growing number of people with AD and the costs associated with the disease also put a heavy economic burden on society. The national direct and indirect costs of caring for people with AD are estimated to be more than \$100 billion a year. A 2004 study provided an equally sobering picture of the impact of AD. It is estimated that if current AD trends continue, total Federal Medicare spending to treat beneficiaries with the disease will increase from \$62 billion in 2000 to \$189 billion in 2015.

For these reasons, AD is an urgent research priority. We need to find ways to manage and treat AD because of its broad-reaching and devastating impact. We now know that the disease process

begins many years, perhaps even decades, before symptoms emerge. Discovering ways to identify AD in the earliest stages and halt or slow its progress will benefit individuals, families, and the Nation as a whole.

## ABOUT THIS BOOK

Thinking about AD leads to questions such as: What causes it? What can be done to cure it or prevent it? Will I get it? Scientists ask the same types of questions, and this book describes their search for answers. It is written for people with AD, their family members and friends, caregivers, and others interested in AD.

This book has four sections:

- **Part 1** gives readers some basics about the healthy brain. Illustrations and text show what a healthy brain looks like and how it works.
- **Part 2** focuses on what happens in the brain during AD.

Visit the National Institute on Aging (NIA) Alzheimer’s Disease Education and Referral (ADEAR) Center website at [www.nia.nih.gov/Alzheimers/ADvideo](http://www.nia.nih.gov/Alzheimers/ADvideo) to view an animation that helps this part of the book come alive.

See the glossary on page 70 for definitions of **boldfaced** terms.

- **Part 3** talks about current research and the advances that are bringing us closer to ways of managing and eventually defeating AD.
- **Part 4** focuses on issues important to AD caregivers and families, including current research that is finding ways to improve caregiver support.

The end of the book includes a list of publications and resources that people with AD, family members, and caregivers may find useful as they live day to day with the disease.

A book like this is possible only because of the major progress that scientists throughout the world have made. Not long ago, we knew very little about AD other than some facts about its major characteristics. Today, we are beginning to understand more about what AD is and who gets it, how and why it develops, and what course it follows. We are learning about the complex interface between AD and normal age-related changes in the brain. We also are getting much

better at diagnosing it early and accurately. Most important, we now have some promising leads on possible treatments. Studies also are beginning to focus on preventive strategies by examining lifestyle factors that might influence a person's risk of developing AD.

Since the 1970s, research supported by NIA and other organizations has deepened our understanding of this devastating disease. It also has expanded our knowledge of brain

function in healthy older people and identified ways we might lessen normal age-related declines in mental function. Most importantly, this accumulated research has increased our appreciation for just how complex AD is. It is now clear that many scientific and clinical disciplines need to work together to untangle the genetic, biological, and environmental factors that, over many years, set a person on a course that ultimately results in AD.

## Then and Now: The Fast Pace of Developments in AD Research

As shown in this timeline, we have learned a lot since Dr. Alzheimer presented the case of his patient, Auguste D. The pace of research continues to accelerate as new findings open more and more doors to discovery.

### 1906

- Dr. Alois Alzheimer, a German neurologist and psychiatrist, describes the case of a 51-year-old woman, Auguste D., who had been admitted to a hospital 5 years earlier with a cluster of unusual symptoms, including problems with comprehension and memory, an inability to speak, disorientation, behavioral problems, and hallucinations. After her death, Dr. Alzheimer examined her brain tissue and described two of the hallmarks of AD—numerous globs of sticky proteins in the spaces between neurons (beta-amyloid plaques) and a tangled bundle of fibrils within neurons (neurofibrillary tangles).

### 1910s – 1940s

- Belief persists that “senile dementia” is a normal part of aging.

### 1950s

- Scientists study the biological structure of plaques and tangles.

### 1960s

- Scientists discover a link between dementia and the number of plaques present in the brain. AD is recognized as a distinct disease, not a normal part of aging.

### 1970s

- Scientists find that levels of **acetylcholine**, a **neurotransmitter** important in memory formation, falls sharply in people with AD. This discovery is one of the first to link AD with biochemical changes in the brain.
- “Alzheimer’s disease” becomes a common term as recognition of AD as a major public health problem grows.
- NIA is established.

### 1980s

- Diagnostic criteria for AD are established.
- Genetic links to early-onset AD begin to surface.
- Congress mandates NIA as lead Federal agency for AD research.

- Scientists start to unravel the biological pathways that lead to the development of beta-amyloid plaques in the brain.
- Abnormal **tau** protein in tangles is identified.

### 1990s

- The U.S. Food and Drug Administration (FDA) approves tacrine (Cognex®), the first drug used to treat AD. This drug has since been replaced by other medications.
- Genetic mutations linked to early-onset and late-onset AD are discovered.
- The first **transgenic** mouse model of AD is created.
- Additional diagnostic criteria are developed for AD.
- Characteristics of **mild cognitive impairment** are described and defined.
- NIA launches the Alzheimer’s Disease Education and Referral Center, AD Cooperative Study, and other initiatives to conduct and support AD treatment and prevention **clinical trials**.

### 2000s

- The FDA approves other AD drugs, including rivastigmine (Exelon®), galantamine (Razadyne®), donepezil (Aricept®), and memantine (Namenda®) to treat symptoms of AD.
- Early work on an AD vaccine begins.
- Many new AD clinical trials, initiatives, and studies are launched, looking at a broad array of translational, treatment, and prevention issues.
- New transgenic mouse models, including one that develops both plaques and tangles, are developed.
- Pittsburgh Compound B (PiB) is developed, allowing researchers to “see” beta-amyloid plaques in the brains of living people.
- The growing sophistication of neuroimaging techniques, genetics, memory and cognitive tests, structured interviews, and other technologies improve our ability to identify people at high risk of AD. ●



PART

1

# The Basics of the Healthy Brain

To understand AD, it is important to know a bit about the brain. This part of *Unraveling the Mystery* gives an inside view of the normal brain, how it works, and what happens during aging.

The brain is a remarkable organ. Seemingly without effort, it allows us to carry out every element of our daily lives. It manages many body functions, such as breathing, blood circulation, and digestion, without our knowledge or direction. It also directs all the functions we carry out consciously. We can speak, hear, see, move, remember, feel emotions, and make decisions because of the complicated mix of chemical and electrical processes that take place in our brains.

The brain is made of nerve cells and several other cell types. Nerve cells also are called **neurons**. The neurons of all animals function in basically the same way, even though animals can be very different from each other. Neurons survive and function with the help and support of **glial cells**, the other main type of cell in the brain. Glial cells hold neurons in place, provide them with nutrients, rid the brain of damaged cells and other cellular debris, and provide insulation to neurons in the brain and spinal cord. In fact, the brain has many more glial cells than neurons—some scientists estimate even 10 times as many.

Another essential feature of the brain is its enormous network of blood vessels. Even though

## The Brain's Vital Statistics

**ADULT WEIGHT**  
about 3 pounds

**ADULT SIZE**  
a medium cauliflower

**NUMBER OF NEURONS**  
about 100,000,000,000 (100 billion)

**NUMBER OF SYNAPSES**  
(the gaps between neurons)  
about 100,000,000,000,000 (100 trillion)

**NUMBER OF CAPILLARIES**  
(tiny blood vessels)  
about 400,000,000,000 (400 billion)



the brain is only about 2 percent of the body's weight, it receives 20 percent of the body's blood supply. Billions of tiny blood vessels, or **capillaries**, carry oxygen, glucose (the brain's principal source of energy), nutrients, and hormones to brain cells so they can do their work. Capillaries also carry away waste products.

# Inside *the* Human Brain

The brain has many parts, each of which is responsible for particular functions. The following section describes a few key structures and what they do.

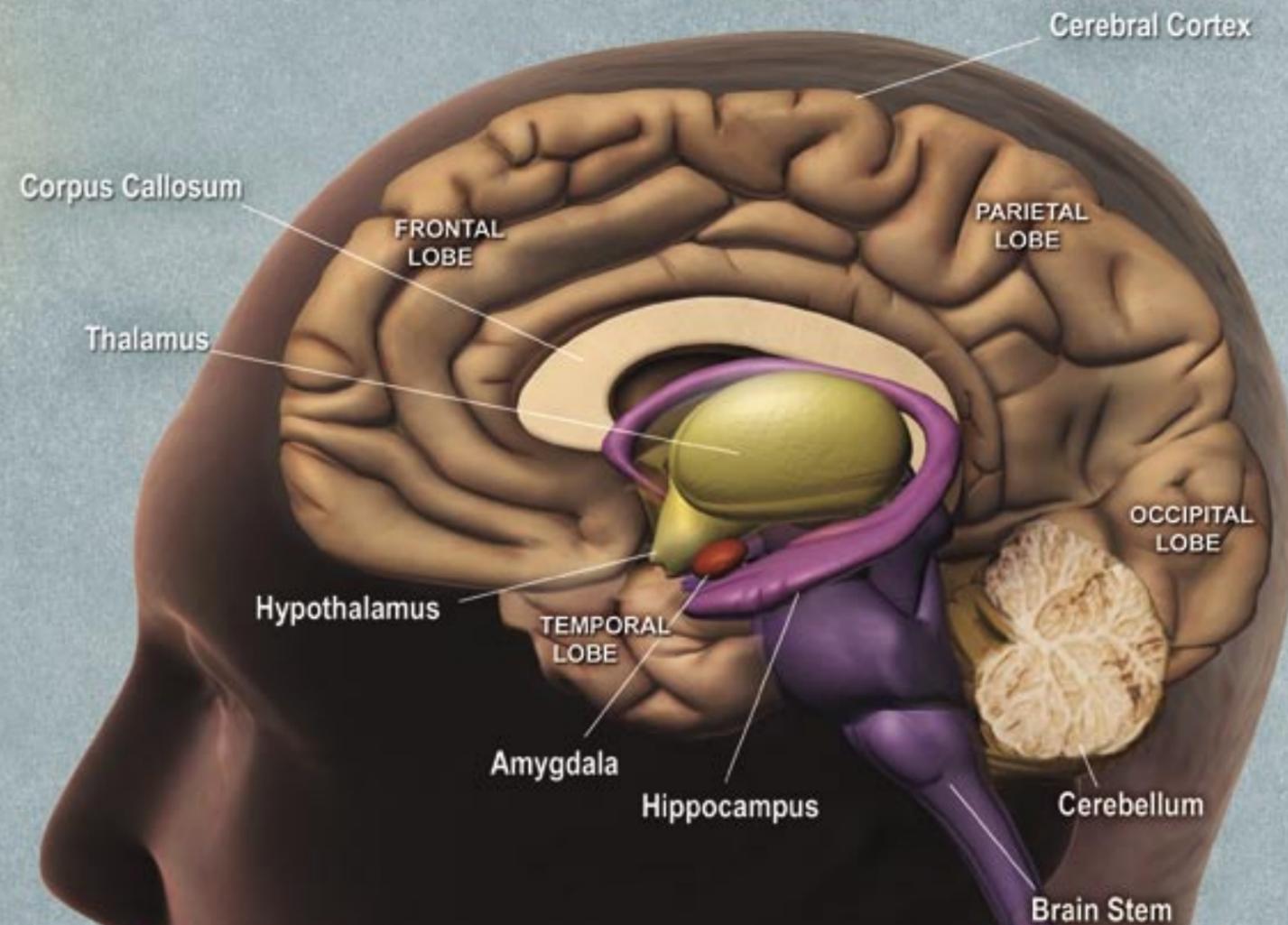
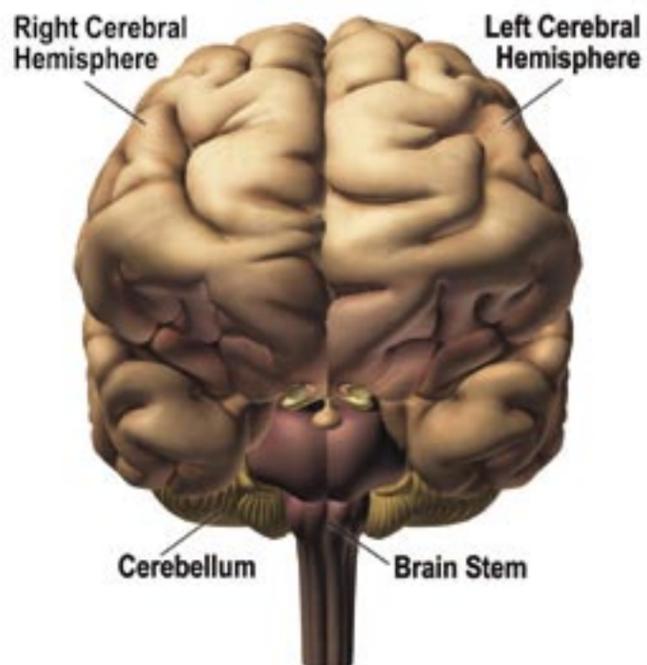
## THE MAIN PLAYERS

Two **cerebral hemispheres** account for 85 percent of the brain's weight. The billions of neurons in the two hemispheres are connected by thick bundles of nerve cell fibers called the **corpus callosum**. Scientists now think that the two hemispheres differ not so much in *what* they do (the "logical versus artistic" notion), but in *how* they process information. The left hemisphere appears to focus on details (such as recognizing a particular face in a crowd). The right hemisphere focuses on broad background (such as understanding the relative position of objects in a space). The cerebral hemispheres have an outer layer called the **cerebral cortex**. This is where the brain processes sensory information received from the outside world, controls voluntary movement, and regulates **cognitive functions**, such as thinking, learning, speaking, remembering, and making decisions. The hemispheres have four lobes, each of which has different roles:

- The frontal lobe, which is in the front of the brain, controls "executive function" activities like thinking, organizing, planning, and problem solving, as well as memory, attention, and movement.
- The parietal lobe, which sits behind the frontal lobe, deals with the perception and integration of stimuli from the senses.

- The occipital lobe, which is at the back of the brain, is concerned with vision.
- The temporal lobe, which runs along the side of the brain under the frontal and parietal lobes, deals with the senses of smell, taste, and sound, and the formation and storage of memories.
- The **cerebellum** sits above the brain stem and beneath the occipital lobe. It takes up a little more than 10 percent of the brain. This part of the brain plays roles in balance and coordination. The cerebellum has two hemispheres, which receive information from the eyes, ears, and muscles and

## Front View of the Brain



## Side View of the Brain

This illustration shows a three-dimensional side view of one of two cerebral hemispheres of the brain. To help visualize this, imagine looking at the cut side of an avocado sliced long ways in half, with the pit still in the fruit. In this illustration, the "pit" is several key structures that lie deep within the brain (the hypothalamus, amygdala, and hippocampus) and the brain stem.

joints about the body's movements and position. Once the cerebellum processes that information, it sends instructions to the body through the rest of the brain and spinal cord. The cerebellum's work allows us to move smoothly, maintain our balance, and turn around without even thinking about it. It also is involved with motor learning and remembering how to do things like drive a car or write your name.

■ The **brain stem** sits at the base of the brain. It connects the spinal cord with the rest of the brain. Even though it is the smallest of the three main players, its functions are crucial to survival. The brain stem controls the functions that happen automatically to keep us alive—our heart rate, blood pressure, and breathing. It also relays information between the brain and the spinal cord, which then sends out messages to the muscles, skin, and other organs. Sleep and dreaming are also controlled by the brain stem.

#### OTHER CRUCIAL PARTS

Several other essential parts of the brain lie deep inside the cerebral hemispheres in a network of structures called the **limbic system**. The limbic system links the brain stem with the higher reasoning elements of the cerebral cortex. It plays a key role in developing and carrying out instinctive behaviors and emotions and also is important in perceiving smells and linking them with memory, emotion, and instinctive behaviors. The limbic system includes:

■ The **amygdala**, an almond-shaped structure involved in processing and remembering strong emotions such as fear. It is located in the temporal lobe just in front of the hippocampus.

■ The **hippocampus**, which is buried in the temporal lobe, is important for learning and short-term memory. This part of the brain is thought to be the site where short-term memories are converted into long-term memories for storage in other brain areas.

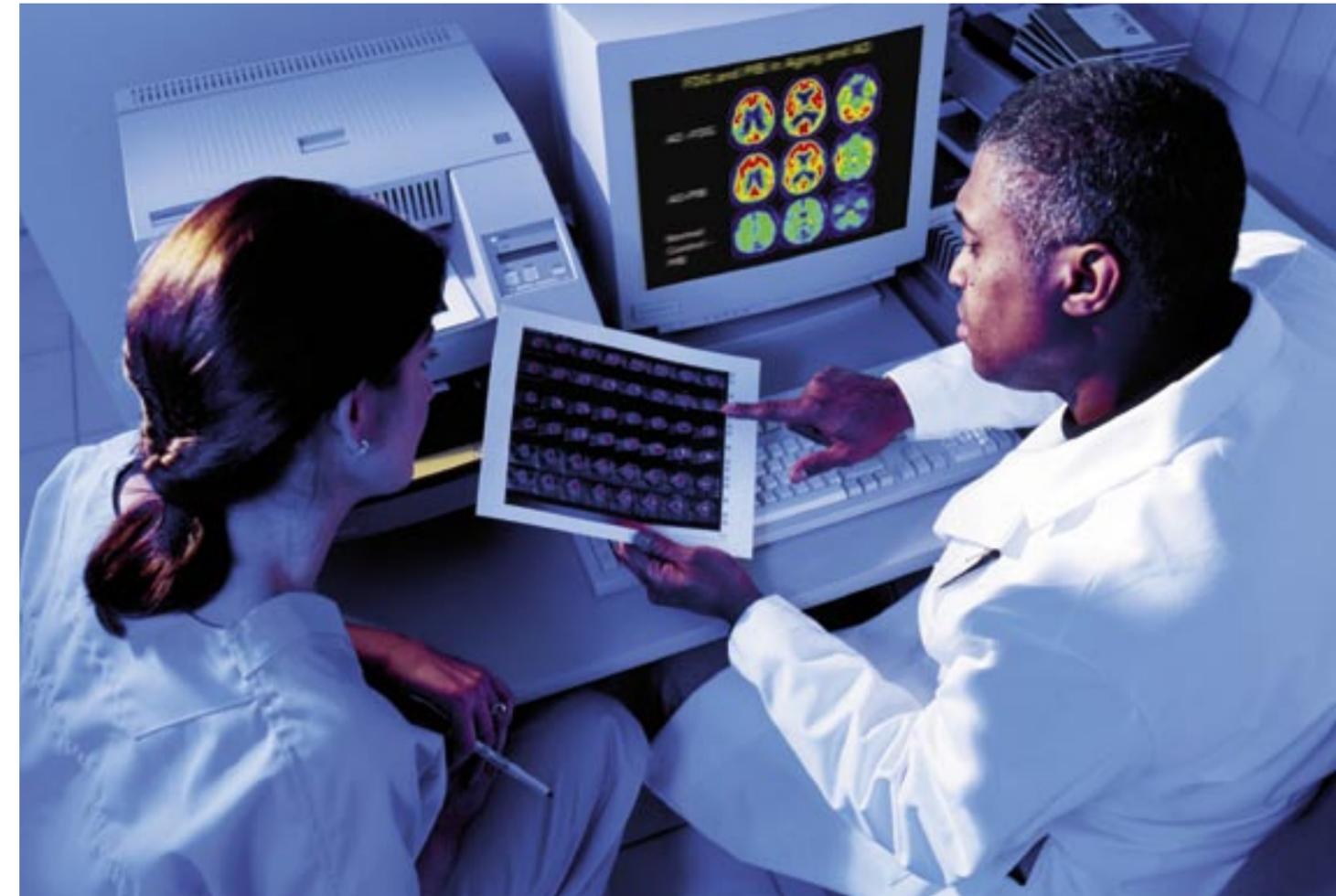
■ The **thalamus**, located at the top of the brain stem, receives sensory and limbic information, processes it, and then sends it to the cerebral cortex.

■ The **hypothalamus**, a structure under the thalamus, monitors activities such as body temperature and food intake. It issues instructions to correct any imbalances. The hypothalamus also controls the body's internal clock.

#### THE BRAIN IN ACTION

Sophisticated brain-imaging techniques allow scientists to monitor brain function in living people and to see how various parts of the brain are used for different kinds of tasks. This is opening up worlds of knowledge about brain function and how it changes with age or disease.

One of these imaging techniques is called **positron emission tomography**, or PET scanning. Some PET scans measure blood flow and glucose **metabolism** throughout the brain. (For more on metabolism, see page 16.) During a PET scan, a small amount of a radioactive substance is attached to a compound, such as glucose, and injected into the bloodstream. This tracer substance eventually goes to the brain. When nerve cells in a region of the brain become active, blood flow and glucose metabolism in that region increase. When colored to reflect metabolic activity, increases usually look red and yellow. Shades of blue and black indicate decreased or no activity within a brain region.



In essence, a PET scan produces a “map” of the active brain.

Scientists can use PET scans to see what happens in the brain when a person is engaged in a physical or mental activity, at rest, or even while sleeping or dreaming. Certain tracers can track the activity of brain chemicals, for example neurotransmitters such as dopamine and

serotonin. (To learn about exciting developments using one new tracer, see **PiB and PET** on page 28.) Some of these neurotransmitters are changed with age, disease, and drug therapies.

# Neurons and Their Jobs

The human brain is made up of billions of neurons. Each has a cell body, an **axon**, and many **dendrites**. The cell body contains a **nucleus**, which controls much of the cell's activities. The cell body also contains other structures, called organelles, that perform specific tasks.

The axon, which is much narrower than the width of a human hair, extends out from the cell body. Axons transmit messages from neuron to neuron. Sometimes, signal transmissions—like those from head to toe—have to travel over very long distances. Axons are covered with an insulating layer called **myelin** (also called white matter because of its whitish color). Myelin, which is made by a particular kind of glial cell, increases the speed of nerve signal transmissions through the brain.

Dendrites also branch out from the cell body. They receive messages from the axons of other neurons. Each neuron is connected to thousands of other nerve cells through its axon and dendrites.

Groups of neurons in the brain have special jobs. For example, some are involved with thinking, learning, and memory. Others are responsible for receiving information from the sensory organs (such as the eyes and ears) or the skin. Still others communicate with muscles, stimulating them into action.

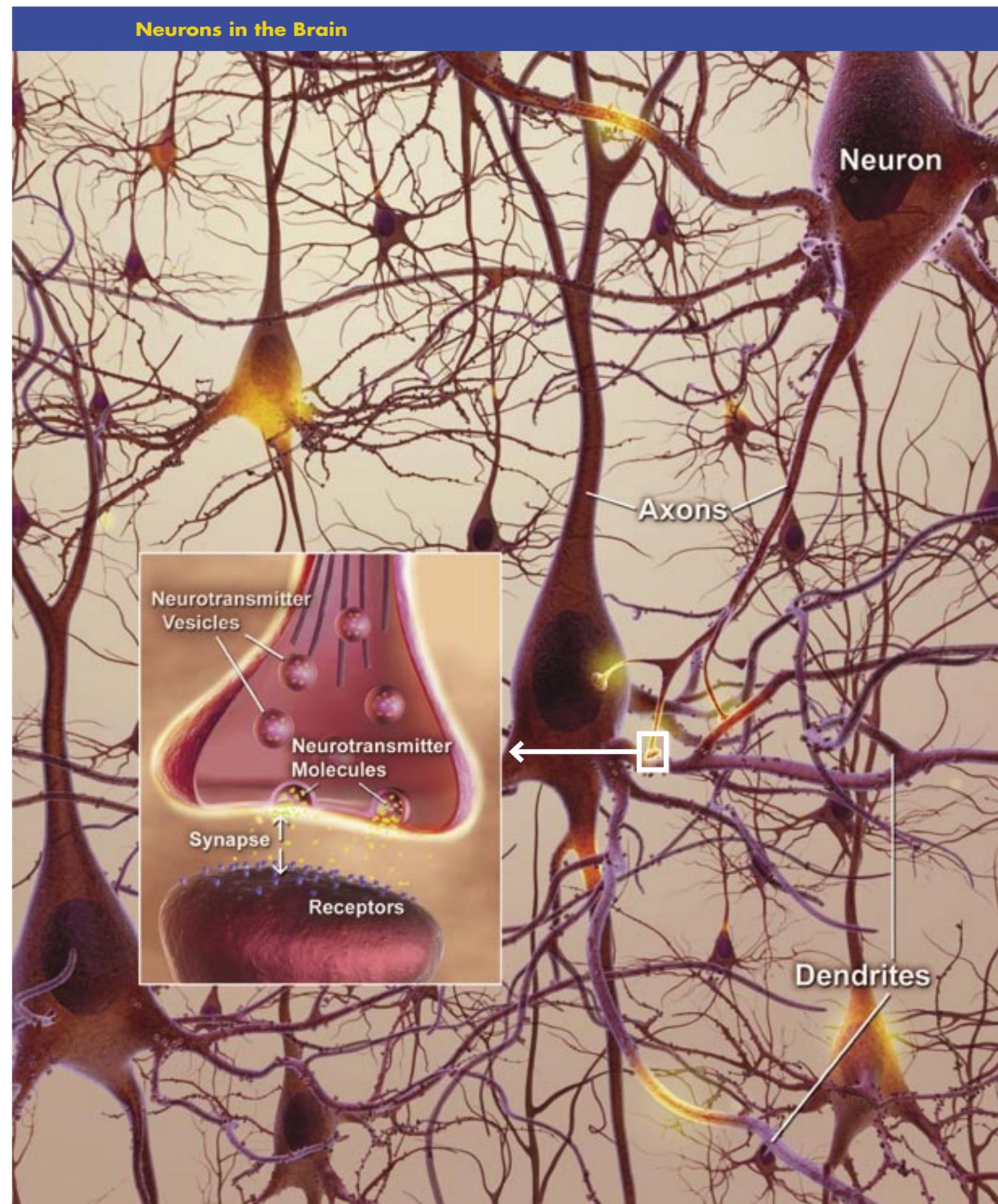
Several processes all have to work smoothly together for neurons, and the whole organism,

to survive and stay healthy. These processes are communication, metabolism, and repair.

## COMMUNICATION

Imagine the many miles of fiber-optic cables that run under our streets. Day and night, millions of televised and telephonic messages flash at incredible speeds, letting people strike deals, give instructions, share a laugh, or learn some news. Miniaturize it, multiply it many-fold, make it much more complex, and you have the brain. Neurons are the great communicators, always in touch with their neighbors.

Neurons communicate with each other through their axons and dendrites. When a dendrite receives an incoming signal (electrical or chemical), an “action potential,” or nerve impulse, can be generated in the cell body. The action potential travels to the end of the axon and once there, the passage of either electrical current or, more typically, the release of chemical messengers, called neurotransmitters, can be triggered. The neurotransmitters are released from the axon terminal and move across a tiny gap, or **synapse**, to specific receptor sites on the receiving, or post-synaptic, end of dendrites of nearby neurons. A typical neuron has thousands of synaptic connections, mostly on its many dendrites, with other neurons. Cell bodies also have receptor sites for neurotransmitters.



Once the post-synaptic receptors are activated, they open channels through the cell membrane into the receiving nerve cell's interior or start other processes that determine what the receiving nerve cell will do. Some neurotransmitters inhibit nerve cell function (that is, they make it less likely that the nerve cell will send an electrical signal down its axon). Other neurotransmitters stimulate nerve cells, priming the receiving cell to become active or send an electrical signal down the axon to more neurons in the pathway. A neuron receives signals from many other neurons simultaneously, and the sum of a neuron's neurotransmitter inputs at any one instant will determine whether it sends a signal down its axon to activate or inhibit the action of other neighboring neurons.

During any one moment, millions of these signals are speeding through pathways in the brain, allowing the brain to receive and process information, make adjustments, and send out instructions to various parts of the body.

### METABOLISM

All cells break down chemicals and nutrients to generate energy and form building blocks that make new cellular molecules such as proteins. This process is called metabolism. To maintain metabolism, the brain needs plenty of blood constantly circulating through its billions of capillaries to supply neurons and other brain cells with oxygen and glucose. Without oxygen and glucose, neurons will quickly die.

### REPAIR

Nerve cells are formed during fetal life and for a short time after birth. Unlike most cells, which have a fairly short lifespan, neurons in the brain live a long time. These cells can live for up to 100 years or longer. To stay healthy, living neurons must constantly maintain and repair themselves. In an adult, when neurons die because of disease or injury, they are not usually replaced. Research, however, shows that in a few brain regions, new neurons can be generated, even in the old brain.

# The Changing Brain in Healthy Aging

In the past several decades, investigators have learned much about what happens in the brain when people have a neurodegenerative disease such as Parkinson's disease, AD, or other dementias. Their findings also have revealed much about what happens during healthy aging. Researchers are investigating a number of changes related to healthy aging in hopes of learning more about this process so they can fill gaps in our knowledge about the early stages of AD.

As a person gets older, changes occur in all parts of the body, including the brain:

- Certain parts of the brain shrink, especially the prefrontal cortex (an area at the front of the frontal lobe) and the hippocampus. Both areas are important to learning, memory, planning, and other complex mental activities.
- Changes in neurons and neurotransmitters affect communication between neurons. In certain brain regions, communication between neurons can be reduced because white matter (myelin-covered axons) is degraded or lost.
- Changes in the brain's blood vessels occur. Blood flow can be reduced because arteries narrow and less growth of new capillaries occurs.

- In some people, structures called plaques and tangles develop outside of and inside neurons, respectively, although in much smaller amounts than in AD (see [The Hallmarks of AD](#) on page 21 for more information on plaques and tangles).

- Damage by **free radicals** increases (free radicals are a kind of molecule that reacts easily with other molecules; see [The Aging Process](#) on page 42 for more on these molecules).

- Inflammation increases (inflammation is the complex process that occurs when the body responds to an injury, disease, or abnormal situation).

What effects does aging have on mental function in healthy older people? Some people may notice a modest decline in their ability to learn new things and retrieve information, such as remembering names. They may perform worse on complex tasks of attention, learning, and memory than would a younger person. However, if given enough time to perform the task, the scores of healthy people in their 70s and 80s are often similar to those of young adults. In fact, as they age, adults often improve in other cognitive areas, such as vocabulary and other forms of verbal knowledge.

It also appears that additional brain regions can be activated in older adults during cognitive tasks,



such as taking a memory test. Researchers do not fully understand why this happens, but one idea is that the brain engages mechanisms to compensate for difficulties that certain regions may be having. For example, the brain may recruit alternate brain networks in order to perform a task. These findings have led many scientists to believe that major declines in mental abilities are not inevitable as people age. Growing evidence of the adaptive (what scientists call “plastic”) capabilities of the older brain provide hope that people may be able to do things to sustain good brain function as they age. A variety of interacting factors, such as lifestyle, overall health, environment, and genetics also may play a role.

Another question that scientists are asking is why some people remain cognitively healthy as they get older while others develop cognitive impairment or dementia. The concept of “cognitive reserve” may provide some insights. Cognitive reserve refers to the brain’s ability to operate effectively even when some function is disrupted. It also refers to the amount of damage that the brain can sustain before changes in cognition are evident. People vary in the cognitive reserve they have, and this variability may be because of differences in genetics, education, occupation, lifestyle, leisure activities, or other life experiences. These factors could provide a certain amount of tolerance and ability to adapt to change and damage that occurs during aging. At some point, depending on a person’s cognitive reserve

and unique mix of genetics, environment, and life experiences, the balance may tip in favor of a disease process that will ultimately lead to dementia. For another person, with a different reserve and a different mix of genetics, environment, and life experiences, the balance may result in no apparent decline in cognitive function with age.

Scientists are increasingly interested in the influence of all these factors on brain health, and studies are revealing some clues about actions people can take that may help preserve healthy brain aging. Fortunately, these actions also benefit a person’s overall health. They include:

- Controlling risk factors for chronic disease, such as heart disease and diabetes (for example, keeping blood cholesterol and blood pressure at healthy levels and maintaining a healthy weight)
- Enjoying regular exercise and physical activity
- Eating a healthy diet that includes plenty of vegetables and fruits
- Engaging in intellectually stimulating activities and maintaining close social ties with family, friends, and community

**Vascular Disease** on page 43 and **Lifestyle Factors** on page 45 provide more information about these issues and how they may influence the risk of developing AD.

## ACTIVE Study May Provide Clues to Help Older Adults Stay Mentally Sharp

The phrase “use it or lose it” may make you think of your muscles, but scientists who study brain health in older people have found that it may apply to cognitive skills as well. In 2006, scientists funded by NIA and the National Institute of Nursing Research completed a study of cognitive training in older adults. This study, the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study, was the first randomized controlled trial to demonstrate long-lasting, positive effects of brief cognitive training in older adults.

The ACTIVE study included 2,802 healthy adults age 65 and older who were living independently. Participants were randomly assigned to four groups. Three groups took part in up to 10 computer-based training sessions that targeted a specific cognitive ability—memory, reasoning, and speed of processing (in other words, how fast participants could respond to prompts on a computer screen). The fourth group (the control group) received no cognitive training. Sixty percent of those who completed the initial training also took part in 75-minute “booster” sessions 11 months later. These sessions were designed to maintain improvements gained from the initial training.

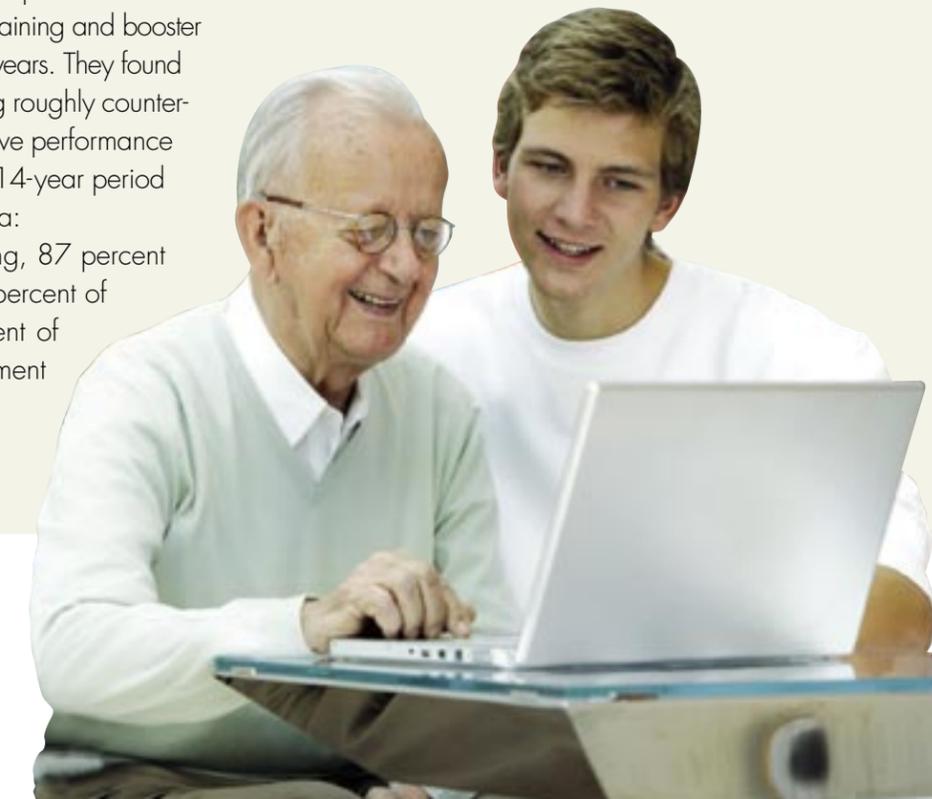
The investigators tested the participants at the beginning of the study, after the initial training and booster sessions, and once a year for 5 more years. They found that the improvements from the training roughly counteracted the degree of decline in cognitive performance that would be expected over a 7- to 14-year period among older people without dementia:

- Immediately after the initial training, 87 percent of the processing-speed group, 74 percent of the reasoning group, and 26 percent of the memory group showed improvement in the skills taught.

- After 5 years, people in each group performed better on tests in their respective areas of training than did people in the control group. The reasoning and processing-speed groups who received booster training had the greatest benefit.

The researchers also looked at the training’s effects on participants’ everyday lives. After 5 years, all three groups who received training reported less difficulty than the control group in tasks such as preparing meals, managing money, and doing housework. However, these results were statistically significant for only the group that had the reasoning training.

As they get older, many people worry about their mental skills getting “rusty.” The ACTIVE study offers hope that cognitive training may be useful because it showed that relatively brief and targeted cognitive exercises can produce lasting improvements in the skills taught. Next steps for researchers are to determine ways to generalize the training benefits beyond the specific skills taught in ACTIVE and to find out whether cognitive training programs could prevent, delay, or diminish the effects of AD. ●





PART **2**

*What Happens  
to the*  
**Brain**  
*in*  
**AD**

## *The* **Hallmarks** of AD

**A**lzheimer's disease disrupts critical metabolic processes that keep neurons healthy. These disruptions cause nerve cells in the brain to stop working, lose connections with other nerve cells, and finally die. The destruction and death of nerve cells causes the memory failure, personality changes, problems in carrying out daily activities, and other features of the disease.

The brains of people with AD have an abundance of two abnormal structures—**amyloid plaques** and **neurofibrillary tangles**—that are made of misfolded proteins (see **Protein Misfolding** on page 41 for more information). This is especially true in certain regions of the brain that are important in memory.

The third main feature of AD is the loss of connections between cells. This leads to diminished cell function and cell death.

### **AMYLOID PLAQUES**

Amyloid plaques are found in the spaces between the brain's nerve cells. They were first described by Dr. Alois Alzheimer in 1906. Plaques consist of largely insoluble deposits of an apparently toxic protein peptide, or fragment, called **beta-amyloid**.

We now know that some people develop some plaques in their brain tissue as they age. However, the AD brain has many more plaques in particular brain regions. We still do not know whether amyloid plaques themselves cause AD or whether they are a by-product of the AD process. We do know that genetic mutations can increase production of beta-amyloid and can cause rare, inherited forms of AD (see **Genes and Early-Onset Alzheimer's Disease** on page 38 for more on inherited AD).



To view a video showing what happens to the brain in AD, go to [www.nia.nih.gov/Alzheimers/ADvideo](http://www.nia.nih.gov/Alzheimers/ADvideo).

## From APP to Beta-Amyloid Plaques

**A**myloid precursor protein (APP), the starting point for amyloid plaques, is one of many proteins associated with the cell membrane, the barrier that encloses the cell. As it is being made inside the cell, APP becomes embedded in the membrane, like a toothpick stuck through the skin of an orange (Figure 1).

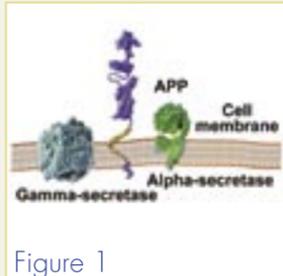


Figure 1

In a number of cell compartments, including the outermost cell membrane, specific **enzymes** snip, or cleave, APP into discrete fragments. In 1999 and 2000, scientists identified the enzymes responsible

for cleaving APP. These enzymes are called alpha-secretase, beta-secretase, and gamma-secretase. In a major breakthrough, scientists then discovered that, depending on which enzyme is involved and the segment of APP where the cleaving occurs, APP processing can follow one of two pathways that have very different consequences for the cell.

In the benign pathway, alpha-secretase cleaves the APP molecule within the portion that has the potential to become beta-amyloid. This eliminates the production of the beta-amyloid peptide and the potential for plaque buildup. The cleavage releases from the neuron a fragment called sAPP $\alpha$ , which has beneficial properties, such as promoting neuronal growth and survival. The remaining APP fragment, still tethered in the neuron's membrane, is then cleaved by gamma-secretase at the end of the beta-amyloid segment. The smaller of the resulting fragments also is released into the space

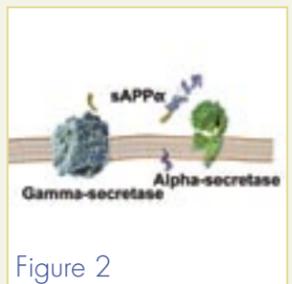


Figure 2

outside the neuron, while the larger fragment remains within the neuron and interacts with factors in the nucleus (Figure 2).

In the harmful pathway, beta-secretase first cleaves

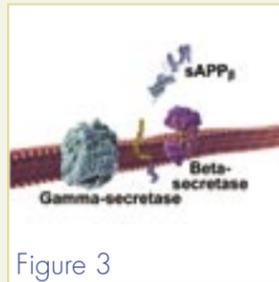


Figure 3

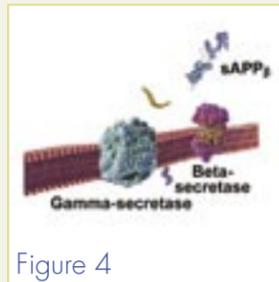
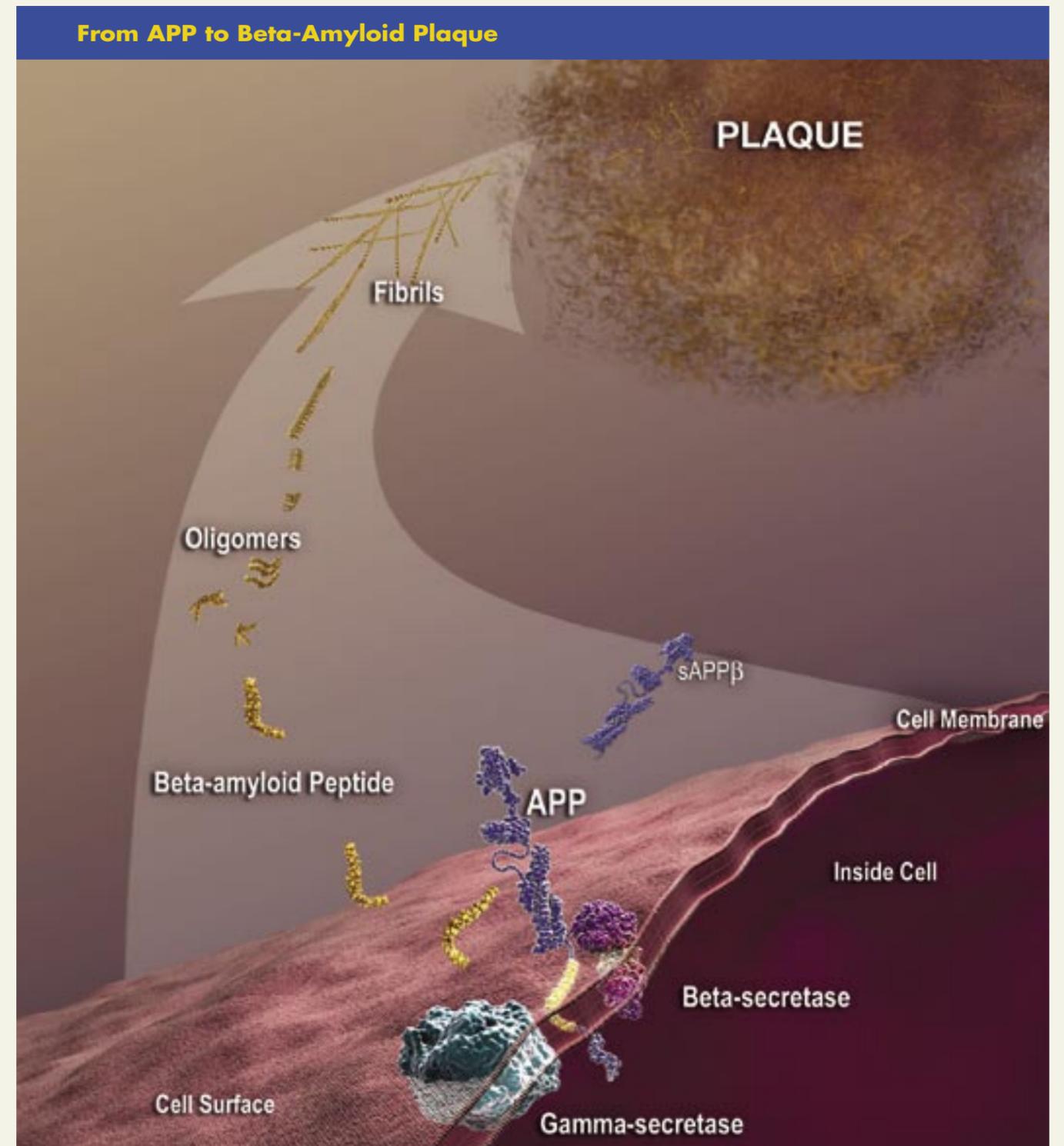


Figure 4

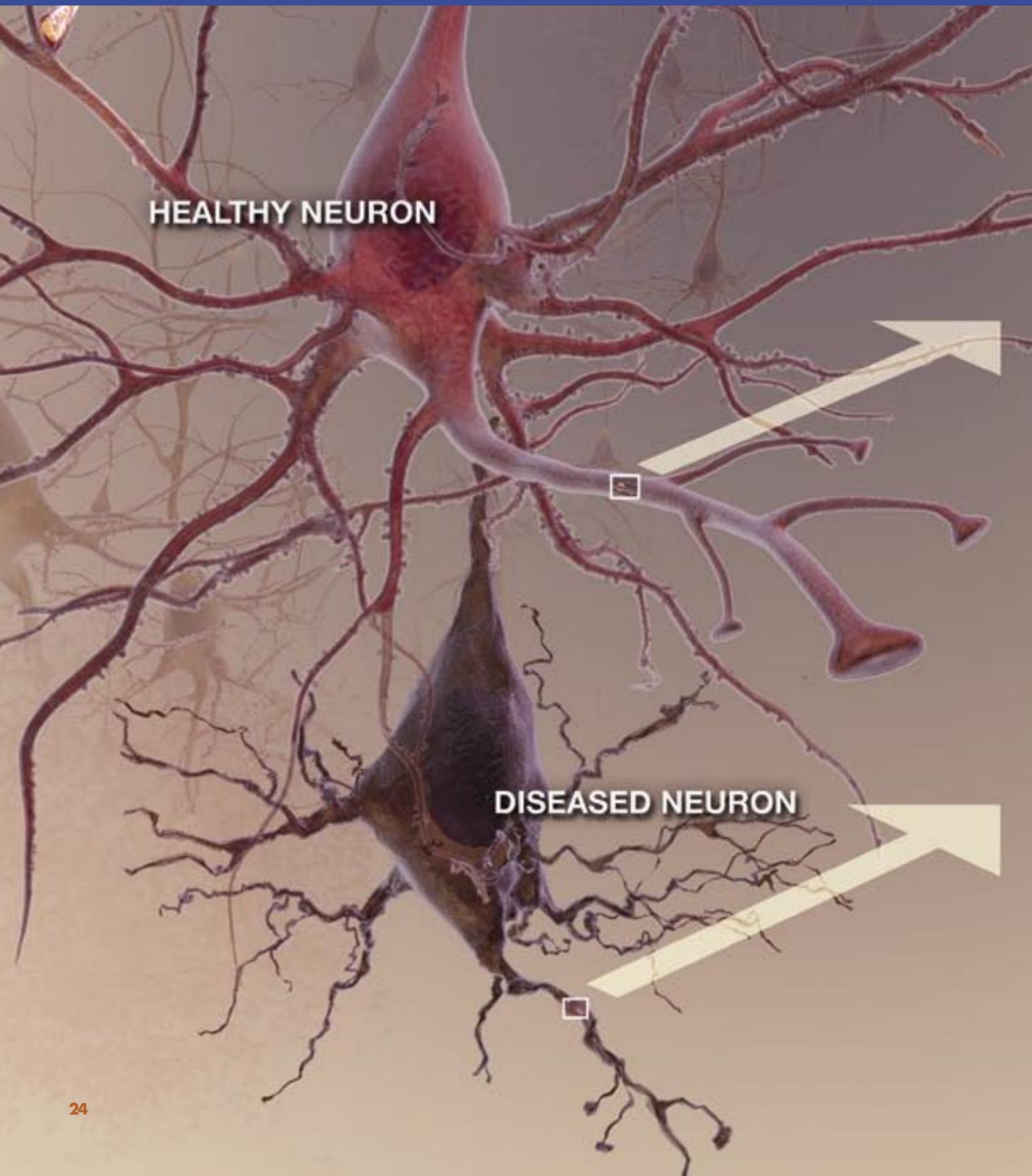
the APP molecule at one end of the beta-amyloid peptide, releasing sAPP $\beta$  from the cell (Figure 3). Gamma-secretase then cuts the resulting APP fragment, still tethered in the neuron's membrane, at the other end of the beta-amyloid peptide. Following the cleavages at each end, the beta-amyloid peptide is released into the space outside the neuron and begins to stick to other beta-amyloid peptides (Figure 4). These small, soluble aggregates of two, three, four, or even up to a dozen beta-amyloid peptides are called oligomers. Specific sizes of oligomers may be responsible for reacting with receptors on neighboring cells and synapses, affecting their ability to function.

It is likely that some oligomers are cleared from the brain. Those that cannot be cleared clump together with more beta-amyloid peptides. As the process continues, oligomers grow larger, becoming entities called protofibrils and fibrils. Eventually, other proteins and cellular material are added, and these increasingly insoluble entities combine to become the well-known plaques that are characteristic of AD.

For many years, scientists thought that plaques might cause all of the damage to neurons that is seen in AD. However, that concept has evolved greatly in the past few years. Many scientists now think that oligomers may be a major culprit. Many scientists also think that plaques actually may be a late-stage attempt by the brain to get this harmful beta-amyloid away from neurons. ●



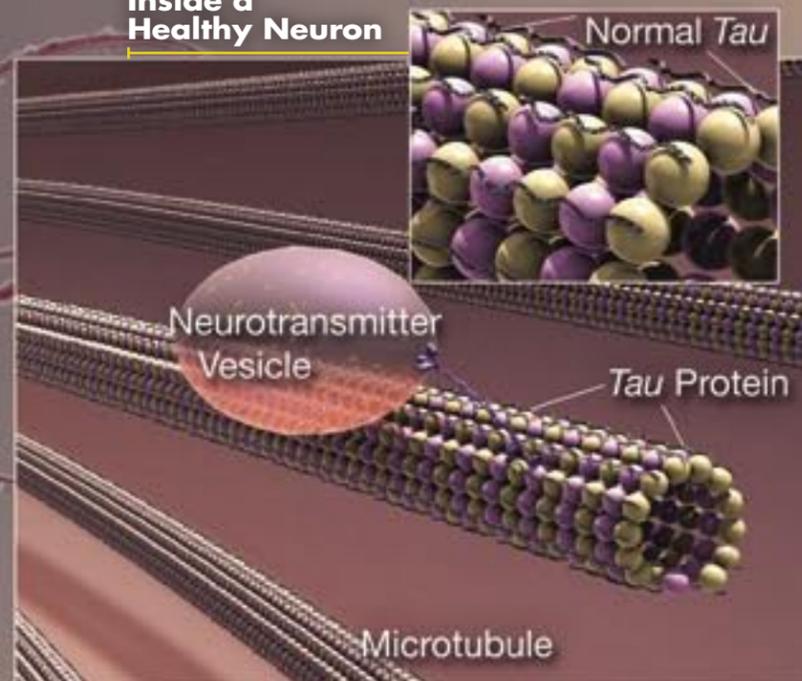
Healthy and Diseased Neurons



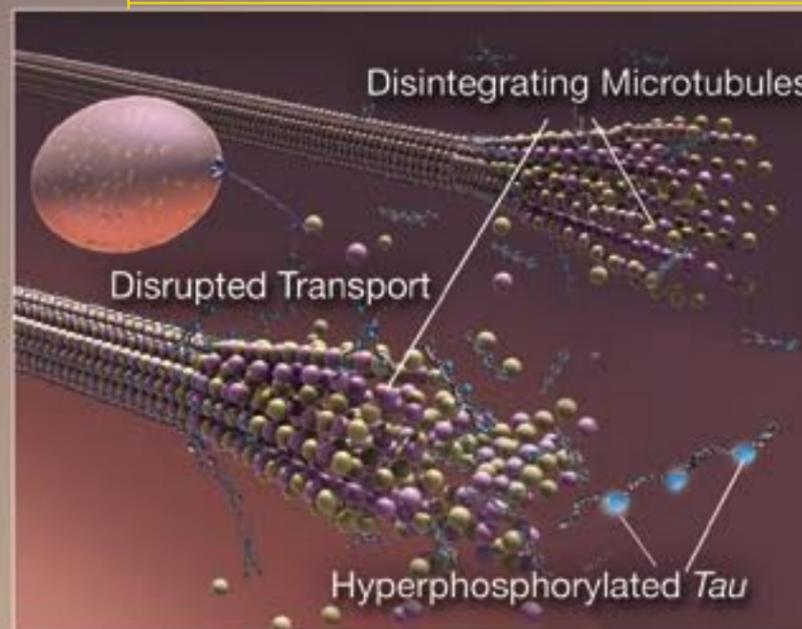
HEALTHY NEURON

DISEASED NEURON

Inside a Healthy Neuron



Inside a Diseased Neuron



Formation of Tau Tangles



NEUROFIBRILLARY TANGLES

The second hallmark of AD, also described by Dr. Alzheimer, is neurofibrillary tangles. Tangles are abnormal collections of twisted protein threads found inside nerve cells. The chief component of tangles is a protein called *tau*.

Healthy neurons are internally supported in part by structures called **microtubules**, which help transport nutrients and other cellular components, such as neurotransmitter-containing **vesicles**, from the cell body down the axon.

*Tau*, which usually has a certain number of phosphate molecules attached to it, binds to microtubules and appears to stabilize them. In AD, an abnormally large number of additional phosphate molecules attach to *tau*. As a result of this “hyperphosphorylation,” *tau* disengages from the microtubules and begins to come together with other *tau* threads. These *tau* threads form structures called paired helical filaments, which can become enmeshed with one another, forming tangles within the cell. The microtubules can disintegrate in the process, collapsing the neuron’s internal transport network. This collapse damages the ability of neurons to communicate with each other.

DYING NEURON

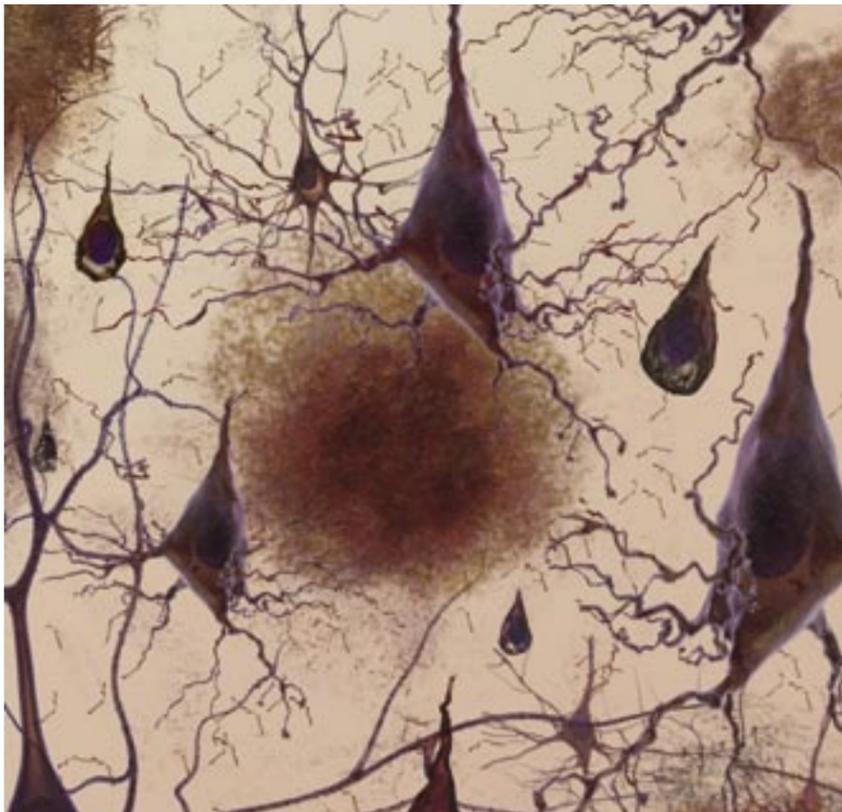
Tangles



### LOSS OF CONNECTION BETWEEN CELLS AND CELL DEATH

The third major feature of AD is the gradual loss of connections between neurons. Neurons live to communicate with each other, and this vital function takes place at the synapse. Since the 1980s, new knowledge about plaques and tangles has provided important insights into their possible damage to synapses and on the development of AD.

The AD process not only inhibits communication between neurons but can also damage neurons to the point that they cannot function properly and eventually die. As neurons die throughout the brain, affected regions begin to shrink in a process called brain atrophy. By the final stage of AD, damage is widespread, and brain tissue has shrunk significantly.



#### Loss of Connection Between Cells

This illustration shows the damage caused by AD: plaques, tangles, and the loss of connection between neurons.

# The Changing Brain in AD

No one knows exactly what starts the AD process or why some of the normal changes associated with aging become so much more extreme and destructive in people with the disease. We know a lot, however, about what happens in the brain once AD takes hold and about the physical and mental changes that occur over time. The time from diagnosis to death varies—as little as 3 or 4 years if the person is older than 80 when diagnosed to as long as 10 or more years if the person is younger. Several other factors besides age also affect how long a person will live with AD. These factors include the person’s sex, the presence of other health problems, and the

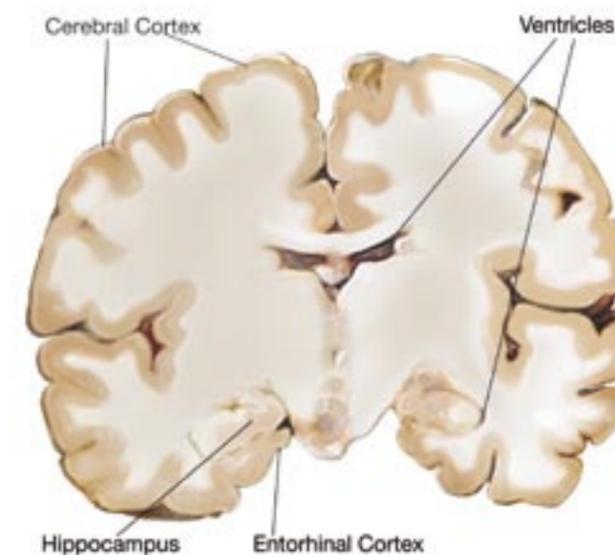
severity of cognitive problems at diagnosis. Although the course of the disease is not the same in every person with AD, symptoms seem to develop over the same general stages.

#### PRECLINICAL AD

AD begins deep in the brain, in the **entorhinal cortex**, a brain region that is near the hippocampus and has direct connections to it. Healthy neurons in this region begin to work less efficiently, lose their ability to communicate, and ultimately die. This process gradually spreads to the hippocampus, the brain region that plays a major role in learning and is involved in converting short-term memories to long-term memories. Affected regions begin to atrophy. **Ventricles**, the fluid-filled spaces inside the brain, begin to enlarge as the process continues.

Scientists believe that these brain changes begin 10 to 20 years before any clinically detectable signs or symptoms of forgetfulness appear. That’s why they are increasingly interested in the very early stages of the disease process. They hope to learn more about what happens in the brain that sets a person on the path to developing AD. By knowing more about the early stages, they also hope to be able to

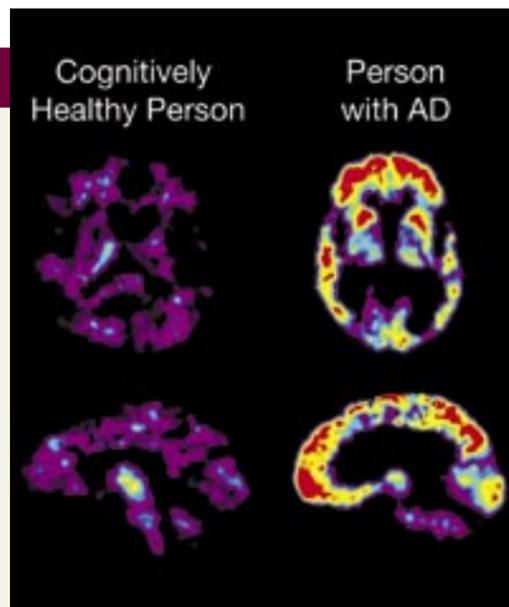
#### Preclinical AD



## PiB and PET

Imagine being able to see deep inside the brain tissue of a living person. If you could do that, you could find out whether the AD process was happening many years before symptoms were evident. This knowledge could have a profound impact on improving early diagnosis, monitoring disease progression, and tracking response to treatment.

Scientists have stepped closer to this possibility with the development of a radiolabeled compound called Pittsburgh Compound B (PiB). PiB binds to beta-amyloid plaques in the brain and it can be imaged using PET scans. Initial studies showed that people with AD take up more PiB in their brains than do cognitively healthy older people. Since then, scientists have found high levels of PiB in some cognitively healthy people, suggesting that the damage from beta-amyloid may already be underway. The next step will be to follow these cognitively healthy people who have high PiB levels to see whether they do, in fact, develop AD over time. ●



In this PET scan, the red and yellow colors indicate that PiB uptake is higher in the brain of the person with AD than in the cognitively healthy person.

develop drugs or other treatments that will slow or stop the disease process before significant impairment occurs (see [The Search for New Treatments](#) on page 54 for more information).

### VERY EARLY SIGNS AND SYMPTOMS

At some point, the damage occurring in the brain begins to show itself in very early clinical signs and symptoms. Much research is being done to identify these early changes, which may be useful in predicting dementia or AD. An important part of this research effort is the development of increasingly sophisticated neuroimaging techniques (see [Exciting New Developments in AD Diagnosis](#) on page 50 for more on neuroimaging) and the use of biomarkers. Biomarkers are indicators, such as changes in sensory abilities, or substances that appear in body fluids, such as blood, **cerebrospinal fluid**, or urine. Biomarkers can indicate exposure

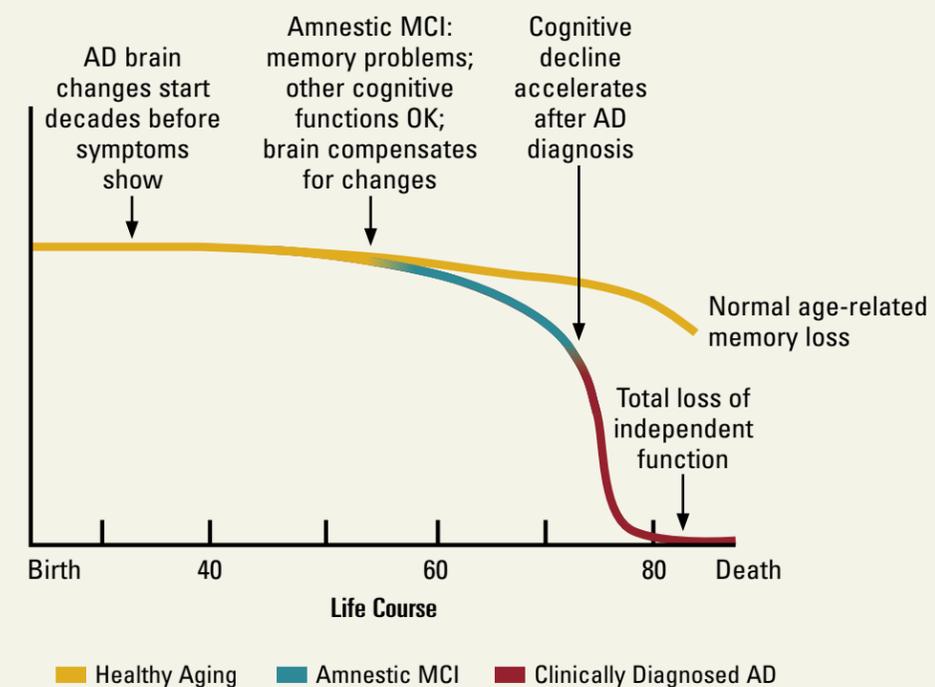
to a substance, the presence of a disease, or the progression over time of a disease. For example, high blood cholesterol is a biomarker for risk of heart disease. Such tools are critical to helping scientists detect and understand the very early signs and symptoms of AD.

### Mild Cognitive Impairment

As some people grow older, they develop memory problems greater than those expected for their age. But they do not experience the personality changes or other problems that are characteristic of AD. These people may have a condition called **mild cognitive impairment** (MCI). MCI has several subtypes. The type most associated with memory loss is called amnesic MCI. People with MCI are a critically important group for research because

## Charting the Course from Healthy Aging to AD

This chart shows current thinking about the evolution from healthy aging to AD. Researchers view it as a series of events that occur in the brain over many years. This gradual process, which results from the combination of biological, genetic, environmental, and lifestyle factors, eventually sets some people on a course to MCI and possibly AD. Other people, whose genetic makeup may be the same or different and who experience a different combination of factors over a lifetime, continue on a course of healthy cognitive aging. ●



a much higher percentage of them go on to develop AD than do people without these memory problems. About 8 of every 10 people who fit the definition of amnesic MCI go on to develop AD within 7 years. In contrast, 1 to 3 percent of people older than 65 who have normal cognition will develop AD in any one year.

However, researchers are not yet able to say definitively why some people with amnesic MCI do not progress to AD, nor can they say who will or will not go on to develop AD. This raises pressing questions, such as: In cases when MCI progresses to AD, what was happening in the brain that made that transition possible? Can MCI be prevented or its progress to AD delayed?

Scientists also have found that genetic factors may play a role in MCI, as they do in

AD (see [Genetic Factors at Work in AD](#) on page 36 for more information). And, they have found that different brain regions appear to be activated during certain mental activities in cognitively healthy people and those with MCI. These changes appear to be related to the early stages of cognitive impairment.

### Other Signs of Early AD Development

As scientists have sharpened their focus on the early stages of AD, they have begun to see hints of other changes that may signal a developing disease process. For example, in the Religious Orders Study, a large AD research effort that involves older nuns, priests, and religious brothers, investigators have

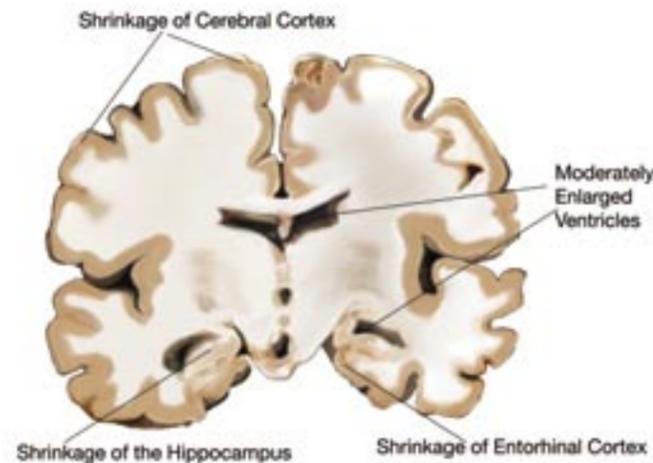
explored whether changes in older adults' ability to move about and use their bodies might be a sign of early AD. The researchers found that participants with MCI had more movement difficulties than the cognitively healthy participants but less than those with AD. Moreover, those with MCI who had lots of trouble moving their legs and feet were more than twice as likely to develop AD as those with good lower body function.

It is not yet clear why people with MCI might have these motor function problems, but the scientists who conducted the study speculate that they may be a sign that damage to blood vessels in the brain or damage from AD is accumulating in areas of the brain responsible for motor function. If further research shows that some people with MCI do have motor function problems in addition to memory problems, the degree of difficulty, especially with walking, may help identify those at risk of progressing to AD.

Other scientists have focused on changes in sensory abilities as possible indicators of early cognitive problems. For example, in one study they found associations between a decline in the ability to detect odors and cognitive problems or dementia.

These findings are tentative, but they are promising because they suggest that, some day, it may be possible to develop ways to improve early detection of MCI or AD. These tools also will help scientists answer questions about causes and very early development of AD, track changes in brain and cognitive function over time, and ultimately track a person's response to treatment for AD.

### Mild to Moderate AD



#### MILD AD

As AD spreads through the brain, the number of plaques and tangles grows, shrinkage progresses, and more and more of the cerebral cortex is affected. Memory loss continues and changes in other cognitive abilities begin to emerge. The clinical diagnosis of AD is usually made during this stage. Signs of mild AD can include:

- Memory loss
- Confusion about the location of familiar places (getting lost begins to occur)
- Taking longer than before to accomplish normal daily tasks
- Trouble handling money and paying bills
- Poor judgment leading to bad decisions
- Loss of spontaneity and sense of initiative
- Mood and personality changes, increased anxiety and/or aggression

In mild AD, a person may seem to be healthy but is actually having more and more trouble making sense of the world around him or her. The realization that something is wrong often comes gradually to the person and his or her family.

Accepting these signs as something other than normal and deciding to go for diagnostic tests can be a big hurdle for people and families. Once this hurdle is overcome, many families are relieved to know what is causing the problems. They also can take comfort in the fact that despite a diagnosis of MCI or early AD, a person can still make meaningful contributions to his or her family and to society for a time.

#### MODERATE AD

By this stage, AD damage has spread to the areas of the cerebral cortex that control language, reasoning, sensory processing, and conscious thought. Affected regions continue to shrink, ventricles enlarge, and signs and symptoms of the disease become more pronounced and widespread. Behavioral problems, such as wandering and agitation, can occur. More intensive supervision and care become necessary, which can be difficult for many spouses and families. The symptoms of this stage can include:

- Increasing memory loss and confusion
- Shortened attention span
- Inappropriate outbursts of anger
- Problems recognizing friends and family members
- Difficulty with language and problems with reading, writing, and working with numbers
- Difficulty organizing thoughts and thinking logically
- Inability to learn new things or to cope with new or unexpected situations
- Restlessness, agitation, anxiety, tearfulness, wandering—especially in the late afternoon or at night
- Repetitive statements or movement, occasional muscle twitches

- Hallucinations, delusions, suspiciousness or paranoia, irritability
- Loss of impulse control (shown through undressing at inappropriate times or places or vulgar language)
- An inability to carry out activities that involve multiple steps in sequence, such as dressing, making a pot of coffee, or setting the table

Behavior is the result of complex brain processes, all of which take place in a fraction of a second in the healthy brain. In AD, many of those processes are disturbed, and these disrupted communications between neurons are the basis for many distressing or inappropriate behaviors. For example, a person may angrily refuse to take a bath or get dressed because he does not understand what his caregiver has asked him to do. If he does understand, he may not remember how to do it. The anger can be a mask for his confusion and anxiety. Or, a person with AD may constantly follow her husband or caregiver and fret when the person is out of sight. To a person who cannot remember the past or anticipate the future, the world can be strange and frightening. Sticking close to a trusted and familiar caregiver may be the only thing that makes sense and provides security.

#### SEVERE AD

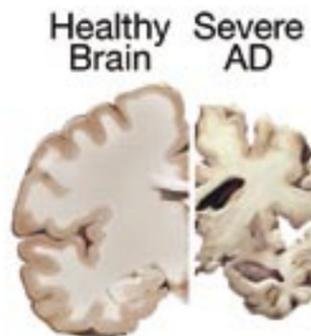
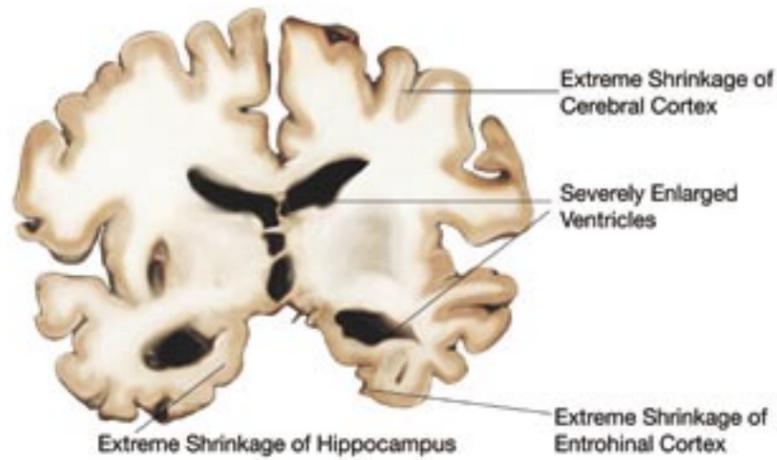
In the last stage of AD, plaques and tangles are widespread throughout the brain, most areas of the brain have shrunk further, and ventricles have enlarged even more. People with AD cannot recognize family and loved ones or communicate in any way. They are completely dependent on others for care. Other symptoms can include:

- Weight loss
- Seizures
- Skin infections
- Difficulty swallowing

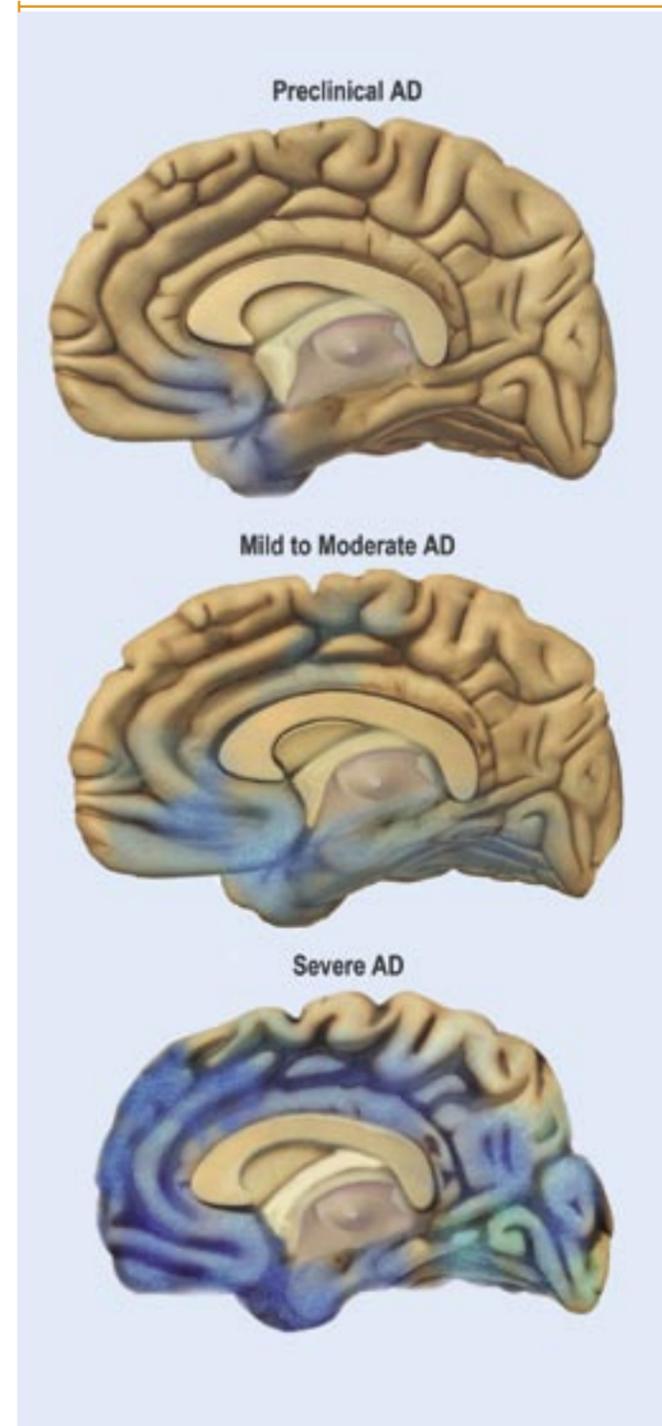
- Groaning, moaning, or grunting
- Increased sleeping
- Lack of bladder and bowel control

Near the end, the person may be in bed much or all of the time. The most frequent cause of death for people with AD is aspiration pneumonia. This type of pneumonia develops when a person is not able to swallow properly and takes food or liquids into the lungs instead of air.

### Severe AD



### AD Spreads Through the Brain



### The Buddy Program at Northwestern University

The medical school curriculum demands that students spend enormous amounts of time in the classroom and clinic learning the information and skills necessary for a career in medicine. However, little or no time is set aside for students to be with patients outside the hospital or clinic setting. As a result, it is hard for medical students to get to know the human side of the diseases they are learning about.



The Buddy Program pairs medical students and people with AD to spend time with—and learn from—each other.

A program at Northwestern University's Cognitive Neurology and Alzheimer's Disease Center is adding just that element to its medical education. The Buddy Program, begun in 1998, matches first-year medical students with people diagnosed with AD or another form of dementia. About 10 to 15 medical students participate every year. They first take a 3-hour orientation course on AD, family issues, and communication skills. Then, for the next year, they spend at least 4 hours a month with a person with dementia in addition to monthly meetings with the program coordinators. Together with the person's caregiver and the program's professional staff, students and their "buddies" choose activities for their visits together. Activities can include shopping, visiting

museums, exercising together, or even just sharing a coffee or a meal. The students also are able to observe their buddies' clinical evaluations at the Center. Other medical schools have started similar programs.

The people with AD and their families are selected from Northwestern's Alzheimer's Disease Center and other related programs at the university. Families are contacted about participating, and the people with AD are selected based on their ability to understand the nature of the program and their willingness to spend time every month with the student buddy.

The program has clear benefits for both the medical student and the person with AD. For the medical student, it provides a

hands-on way to learn about AD and related dementias, and it helps him or her understand the daily realities and issues involved in caring for and supporting people with AD and their families. It also introduces them to the career path of research and clinical practice in AD and related dementias. For the person with AD, participation in the program provides an opportunity for friendship and socializing and an outlet for sharing their experiences with a sympathetic listener.

For many of the students, the program is a transformative experience. They become very close to their buddies and family caregivers during their year together, and continue the friendship even after the year is over. ●



**PART**

**3**

**AD RESEARCH:**

# Better Questions, New Answers

Scientists have studied AD from many angles. They have looked at populations to see how many cases of AD occur every year and whether there might be links between the disease and lifestyles or genetic backgrounds. They also have conducted clinical studies with healthy older people and those at various stages of AD. They have done many studies with laboratory animals. They have begun to look at neuronal circuits and networks of cells to learn how AD pathology develops and spreads. They even have examined individual nerve cells to see how beta-amyloid, *tau*, and other molecules affect the ability of cells to function normally.

These studies have led to a fuller understanding of many aspects of the disease, improved diagnostic tests, new ways to manage behavioral aspects of AD, and a growing number of possible

drug treatments. Findings from current research are pointing scientists in promising directions for the future. They are also helping researchers to ask better questions about the issues that are still unclear.

Part 3 of *Unraveling the Mystery* describes what scientists are learning from their search for:

- The causes of AD
- New techniques to help in diagnosis
- New treatments

Results from this research will bring us closer to the day when we will be able to delay the onset of, prevent, or cure the devastating disease that robs our older relatives and friends of their most precious possession—their minds.

# Looking for the **Causes** of AD

One of the most important parts of unraveling the AD mystery is finding out what causes the disease. What makes the disease process begin in the first place? What makes it worse over time? Why does the number of people with the disease increase with age? Why does one person develop AD while another remains healthy?

Some diseases, such as measles or pneumonia, have clear-cut causes. They can be prevented with vaccines or cured with antibiotics. Others, such as diabetes or arthritis, develop when genetic, lifestyle, and environmental factors work together to start a disease process. The role that any or all of these factors play may be different for each individual.

AD fits into the second group of diseases. We do not yet fully understand what causes AD, but we believe it develops because of a complex series of events that take place in the brain over a long period of time. Many studies are exploring the factors involved in the cause and development of AD.

## GENETIC FACTORS AT WORK IN AD

Genetic studies of complex neurodegenerative diseases such as AD focus on two main issues—whether a gene might influence a person’s overall risk of developing a disease and whether a gene might influence some particular aspect of a

person’s risk, such as the age at which the disease begins. Slow and careful detective work by scientists has paid off in discoveries of genetic links to the two main types of AD.

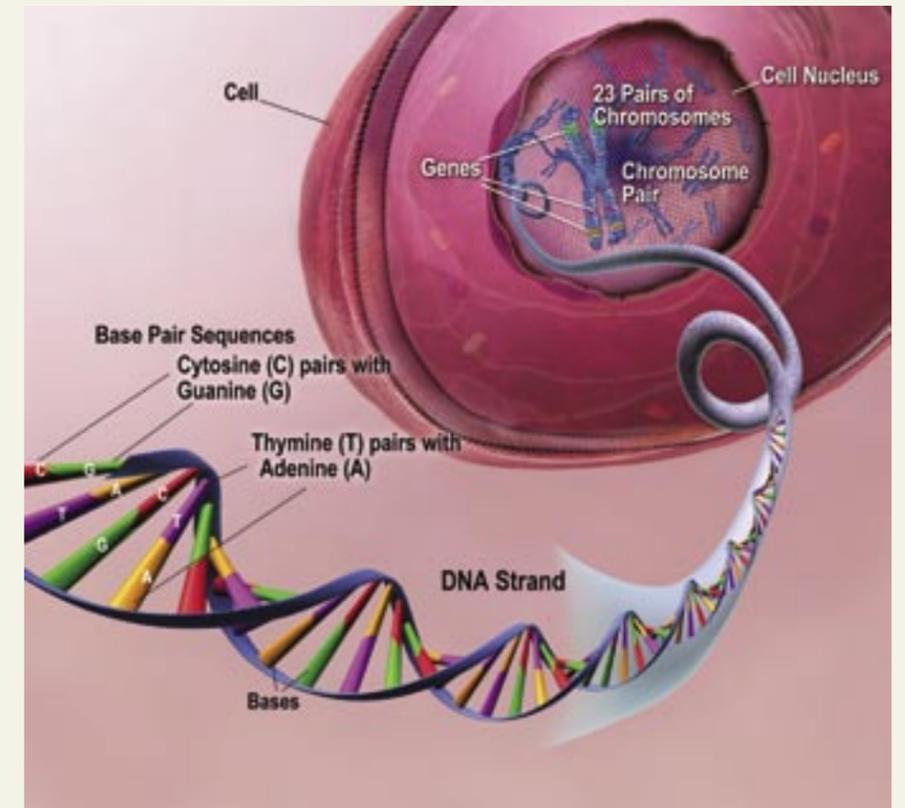
One type is the rare, **early-onset Alzheimer’s disease**. It usually affects people aged 30 to 60. Some cases of early-onset disease are inherited and are called familial AD (FAD). The other is **late-onset Alzheimer’s disease**. It is by far the more common form and occurs in those 60 and older. Gaining insight into the genetic factors associated with both forms of AD is important because identifying genes that either cause the disease or influence a person’s risk of developing it improves our ability to understand how and why the disease starts and progresses.



## DNA, Chromosomes, and Genes: The Body’s Amazing Control Center

The nucleus of almost every human cell contains an encrypted “blueprint,” along with the means to decipher it. This blueprint, accumulated over eons of genetic trial and error, carries all the instructions a cell needs to do its job. The blueprint is made up of **DNA**, which exists as two long, intertwined, thread-like strands called **chromosomes**. Each cell has 46 chromosomes in 23 pairs. The DNA in chromosomes is made up of four chemicals, or bases, strung together in various sequence patterns. The DNA in nearly all cells of an individual is identical.

Each chromosome contains many thousands of segments, called **genes**. People inherit two copies of each gene from their parents, except for genes on the X and Y chromosomes, which are chromosomes that, among other functions, determine a person’s sex. Each person normally has one pair of sex chromosomes (females are XX and males are XY). The sequence of bases in a gene tells the cell how to make specific proteins. Proteins in large part determine the different kinds of cells that make up an organism and direct almost every aspect of the cell’s



construction, operation, and repair. Even though all genes are present in most cells, the pattern in which they are activated varies from cell to cell, and gives each cell type its distinctive character. Even slight alterations in a gene can produce an abnormal protein, which, in turn, may lead to cell malfunction and, eventually, to disease.

Any permanent change in the sequence of bases in a gene’s

DNA that causes a disease is called a **mutation**. Mutations also can change the activation of a particular gene. Other more common (or frequent) changes in a gene’s sequence of bases do not automatically cause disease, but they can increase the chances that a person will develop a particular disease. When this happens, the changed gene is called a **genetic risk factor**. ●

## Genes and Early-Onset Alzheimer's Disease

In the early days of AD genetics research, scientists realized that some cases, particularly of the rare early-onset AD, ran in families. This led them to examine DNA samples from these families to see whether they had some genetic trait in common. Chromosomes 21, 14, and 1 became the focus of attention. The scientists found that some families have a mutation in selected genes on these chromosomes. On chromosome 21, the mutation causes an abnormal amyloid precursor protein to be produced (see page 22 for more on APP). On chromosome 14, the mutation causes an abnormal protein called presenilin 1 to be produced. On chromosome 1, the mutation causes another abnormal protein to be produced. This protein, called presenilin 2, is very similar to presenilin 1. Even if only one of these genes that are inherited from a parent contains a mutation, the person will almost inevitably develop early-onset AD. This means that in these families, children have about a 50-50 chance of developing the disease if one of their parents has it.

Early-onset AD is very rare, and mutations in these three genes do not play a role in the more common late-onset AD. However, these findings were crucial because they showed that genetics was indeed a factor in AD, and they helped to identify some key cell pathways involved in the AD disease process. They showed that mutations in APP can cause AD, highlighting the presumed key role of beta-amyloid in the disease. Mutations in presenilin 1 and 2 also cause an increased amount of the damaging beta-amyloid to be made in the brain.

## A Different Genetic Story in Late-Onset Alzheimer's Disease

While some scientists were studying the role of chromosomes 21, 14, and 1 in early-onset AD, others were looking elsewhere to see if they could find genetic clues for the late-onset form. By 1992, investigators had narrowed their search to a region of chromosome 19. They found a gene on chromosome 19 that they were able to link to late-onset AD.

This gene, called APOE, produces a protein called **apolipoprotein E**. APOE comes in several forms, or alleles— $\epsilon$ 2,  $\epsilon$ 3, and  $\epsilon$ 4:

- The APOE  $\epsilon$ 2 allele is relatively rare and may provide some protection against the disease. If AD does occur in a person with this allele, it develops later in life than in those with an APOE  $\epsilon$ 4 allele.
- APOE  $\epsilon$ 3 is the most common allele. Researchers think it plays a neutral role in AD.
- APOE  $\epsilon$ 4 occurs in about 40 percent of all people who develop late-onset AD and is present in about 25 to 30 percent of the population. People with AD are more likely to have an APOE  $\epsilon$ 4 allele than people who do not have AD. However, at least one-third of people with AD do not have an APOE  $\epsilon$ 4 allele. Dozens of studies have confirmed that the APOE  $\epsilon$ 4 allele increases the risk of developing AD, but how that happens is not yet understood. These studies also have helped to explain some of the variation in the age at which AD develops, as people who inherit one or two APOE  $\epsilon$ 4 alleles tend to develop AD at an earlier age than those who do not. However, inheriting an APOE  $\epsilon$ 4 allele does not mean that a person will definitely develop AD. Some people with one or two APOE  $\epsilon$ 4 alleles never get the disease, and others who do develop AD do not have any APOE  $\epsilon$ 4 alleles.

## The Hunt for New AD Genes

For some time, scientists have suspected that, in addition to APOE  $\epsilon$ 4, as many as half a dozen other risk-factor genes exist for late-onset AD, but they have been unable to find them. In 2007, scientists unveiled their discovery of one new AD risk-factor gene.

This AD risk-factor gene is called SORL1. It is involved in recycling APP from the surface of cells, and its association with AD was identified and confirmed in three separate studies. Researchers found that when SORL1 is expressed at low levels or in a variant form, harmful beta-amyloid levels increase, perhaps by deflecting APP away from its normal pathways and forcing it into cellular compartments that generate beta-amyloid.

As AD genetics research has intensified, it has become increasingly clear that scientists need many different samples of genetic material if they are to continue making progress in identifying new risk-factor genes. Genetic material is also essential for identifying associated environmental factors and understanding the interactions of genes and the environment. These advances ultimately will allow investigators to identify people at high risk of developing AD and help them focus on new pathways for prevention or treatment.

In 2003, NIA launched the **Alzheimer's Disease Genetics Study** to identify at least 1,000 families with members who have late-onset AD as well as members who do not have the disease. All of these family members provide blood samples and other clinical data for the initiative. The material collected allows investigators to create and maintain "immortalized" cell lines—cells that are continuously regenerated in the laboratory. These cell lines are crucial for the exhaustive DNA analysis studies needed to identify risk-factor genes, each of which may have relatively small effects on AD development. More than 4,000 new cell lines are now available for researchers to study risk-factor genes for late-onset AD.

A new initiative, the **Alzheimer's Disease Genetics Consortium**, was launched in 2007 to accelerate the application of genetics technologies to late-onset AD through collaborations among most of the leading researchers in AD genetics. The ultimate goal of this effort is to obtain genetic material from 10,000 people with AD and 10,000 cognitively healthy people to comprehensively scan the whole genome for the remaining AD risk-factor genes, as well as those for age-related cognitive decline. Some of the genetic material will



be drawn from existing samples of blood and tissue; other genetic material will be collected from new participants.

New AD genetics discoveries are possible largely because of close collaboration among scientists, participation of volunteer families, new genetics technologies, statistical and analytic advances, and rapid data sharing. For example, the SORL1 studies involved 14 scientific institutions in North America, Europe, and Asia and the participation of more than 6,000 people who donated blood and tissue for genetic typing. An important part of NIA's efforts to promote and accelerate AD genetics research is to make biological samples and data publicly available to approved researchers. ●

### OTHER FACTORS AT WORK IN AD

Genetics explains some of what might cause AD, but it does not explain everything. So, researchers continue to investigate other possibilities that may explain how the AD process starts and develops.

#### Beta-Amyloid

We now know a great deal about how beta-amyloid is formed and the steps by which beta-amyloid fragments stick together in small aggregates (oligomers), and then gradually form into plaques (see page 22 in **The Hallmarks of AD** for more on this process). Armed with this knowledge, investigators are intensely interested in the toxic effects that beta-amyloid, oligomers, and plaques have on neurons. This research is possible in part because scientists have been able to develop transgenic animal models of AD. Transgenics are animals that have been specially bred to develop AD-like features, such as beta-amyloid plaques.

Beta-amyloid studies have moved forward to the point that scientists are now carrying out preliminary tests in humans of potential therapies aimed at removing beta-amyloid, halting its formation, or breaking down early forms before they can become harmful.

For example, one line of research by a pharmaceutical company started with the observation that injecting beta-amyloid into AD transgenic mice caused them to form antibodies to the beta-amyloid and reduced the number of amyloid plaques in the brain. This exciting finding led to other studies and ultimately to clinical trials in which human participants were immunized with beta-amyloid. These studies had to be stopped because some of the participants developed harmful side effects, but the investigators did not give up hope. Rather, they went back to the drawing board to rethink their strategy. More

refined antibody approaches are now being tested in clinical trials, and additional research on new ways of harnessing the antibody response continues in the lab.

Another important area of research is how beta-amyloid may disrupt cellular communication well before plaques form. One recent study described how beta-amyloid oligomers target specific synaptic connections between neurons, causing them to deteriorate. Other scientists are studying other potentially toxic effects that plaques have on neurons and in cellular communication. Understanding more about these processes may allow scientists to develop specific therapies to block the toxic effects.

#### Tau

*Tau*, the chief component of neurofibrillary tangles (see page 25 in **The Hallmarks of AD** for more on *tau*), is generating new excitement as an area of study. The recent focus on *tau* has been spurred by the finding that a mutant form of the protein is responsible for one form of frontotemporal dementia, the third most common cause of late-life dementia, after AD and vascular dementia. This form is known as frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17). Finding this mutant protein was important because it suggested that abnormalities in the *tau* protein itself can cause dementia.

New transgenic mouse models of AD have helped *tau* research make rapid progress. For example, a recent model, the “triple transgenic” mouse, forms plaques and tangles over time in brain regions similar to those in human AD. Another recent transgenic mouse model, which contains only human *tau*, forms clumps of damaging *tau* filaments also in a region-specific fashion similar to AD in humans.

These studies of *tau* also have suggested a mechanism for *tau* damage that is different from that previously suspected. With these new insights,

scientists now speculate that one reason *tau* may damage and kill neurons is because it upsets the normal activity of the cell, in addition to forming neurofibrillary tangles.

Other studies of mutant *tau* in mice suggest that the accumulation of *tau* in tangles may not even be the culprit in memory loss. Rather, as with beta-amyloid, it may be that an earlier and more soluble abnormal form of the protein causes the damage to neurons.

#### Protein Misfolding

Researchers have found that a number of devastating neurodegenerative diseases (for example, AD, Parkinson’s disease, dementia with Lewy bodies, frontotemporal lobar degeneration, Huntington’s disease, and prion diseases) share a key characteristic—protein misfolding.

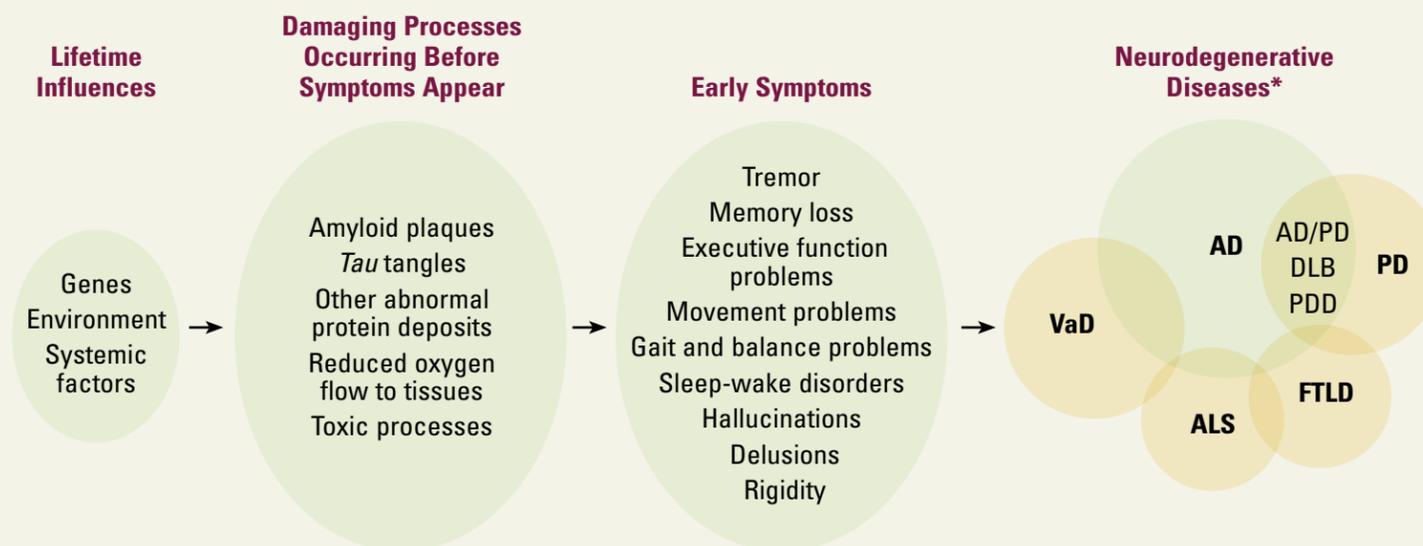
When a protein is formed, it “folds” into a unique three-dimensional shape that helps it

### Researchers Explore Neurodegenerative “Cousins”

Neurodegenerative diseases like AD, Parkinson’s disease, amyotrophic lateral sclerosis (ALS), and dementia with Lewy bodies share more than the basic characteristic of misfolded proteins. They also share clinical characteristics. For example, people with AD have trouble moving, a characteristic of Parkinson’s disease. Sleep-wake disorders, delusions, psychiatric disturbances, and memory loss occur in all of these diseases. These diseases also result from

a combination of genetic, lifestyle, and environmental causes and they develop over many years.

This graphic shows one way of thinking about how these diseases may be linked as well as what makes them unique. By investigating the unique characteristics of these diseases as well as the characteristics they share, scientists hope to learn even more than they would if they focused on each disease by itself.



\*AD = Alzheimer’s disease, AD/PD = AD with parkinsonism, ALS = amyotrophic lateral sclerosis, DLB = dementia with Lewy bodies, FTLD = frontotemporal lobar degeneration, VaD = vascular dementia (includes multi-infarct dementia), PD = Parkinson’s disease, PDD = Parkinson’s disease with dementia

Adapted from an Emory University illustration

perform its specific function. This crucial process can go wrong for various reasons, and more commonly does go wrong in aging cells. As a result, the protein folds into an abnormal shape—it is misfolded. In AD, the misfolded proteins are beta-amyloid (the cleaved product of APP; see **From APP to Beta-Amyloid Plaques** on page 22 for more on the formation of beta-amyloid) and a cleaved product of *tau*.

Normally, cells repair or degrade misfolded proteins, but if many of them are formed as part of age-related changes, the body's repair and clearance process can be overwhelmed. Misfolded proteins can begin to stick together with other misfolded proteins to form insoluble aggregates. As a result, these aggregates can build up, leading to disruption of cellular communication, and metabolism, and even to cell death. These effects may predispose a person to AD or other neurodegenerative diseases.

Scientists do not know exactly why or how these processes occur, but research into the unique characteristics and actions of various misfolded proteins is helping investigators learn more about the similarities and differences across age-related neurodegenerative diseases. This knowledge may someday lead to therapies.

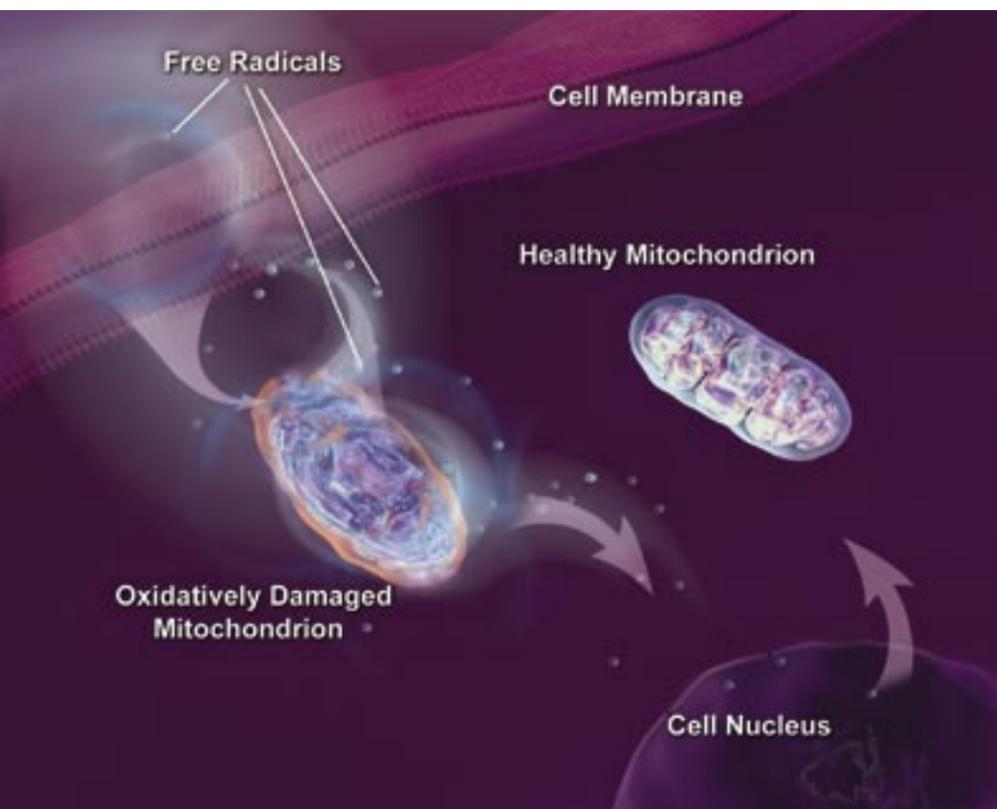
### The Aging Process

Another set of insights about the cause of AD comes from the most basic of all risk factors—aging itself. Age-related changes, such as inflammation, may make AD damage in the brain worse. Because cells and compounds that are known to be involved in inflammation are found in AD plaques, some researchers think that components of the inflammatory process may play a role in AD.

Other players in the aging process that may be important in AD are free radicals, which are oxygen or nitrogen molecules that combine easily with other molecules (scientists call them “highly reactive”). Free radicals are generated in mitochondria, which are structures found in all cells, including neurons. Mitochondria are the cell's power plant, providing the energy a cell needs to maintain its structure, divide, and carry

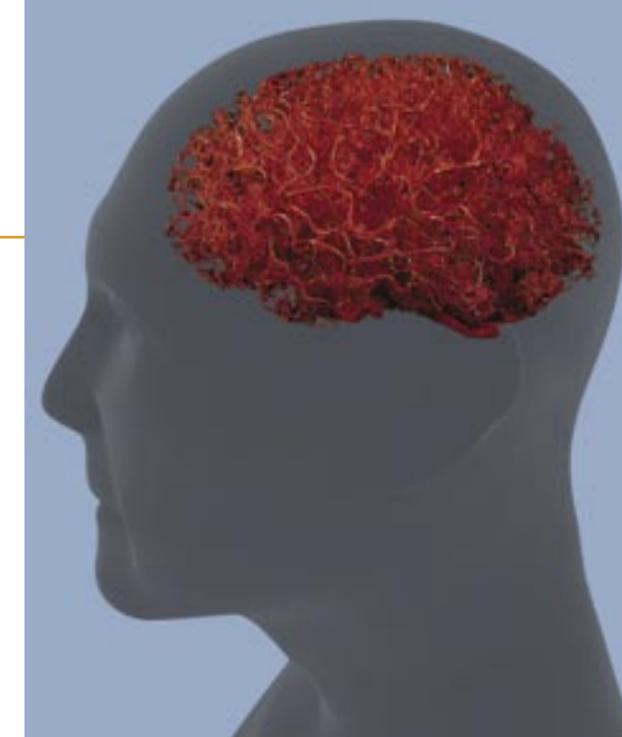
### Mitochondria and Free Radicals

Any given cell has hundreds of mitochondria. This illustration shows two—a healthy mitochondrion and an oxidatively stressed and damaged one. The arrows indicate the movement of free radicals, which can spread easily from damaged mitochondria to other parts of the cell.



### The Brain's Vascular System

This image shows the complexity of the human brain's vascular system, particularly large and small arteries that carry oxygen from the lungs to the brain. Although many blood vessels are visible here, this image shows fewer than half of the total number in the brain.



out its functions. Energy for the cell is produced in an efficient metabolic process. In this process, free radicals are produced. Free radicals can help cells in certain ways, such as fighting infection. However, because they are very active and combine easily with other molecules, free radicals also can damage the neuron's cell membrane or its DNA. The production of free radicals can set off a chain reaction, releasing even more free radicals that can further damage neurons (see illustration on page 42). This kind of damage is called **oxidative damage**. The brain's unique characteristics, including its high rate of metabolism and its long-lived cells, may make it especially vulnerable to oxidative damage over the lifespan. The discovery that beta-amyloid generates free radicals in some AD plaques is a potentially significant finding in the quest for better understanding of AD as well as for other neurodegenerative disorders and unhealthy brain aging.

Researchers also are studying age-related changes in the working ability of synapses in certain areas of the brain. These changes may reduce the ability of neurons to communicate with each other, leading to increased neuronal vulnerability in regions of the brain important in AD. Age-related reductions in levels of particular growth factors, such as **nerve growth factor** and **brain-derived neurotrophic factor**, also may cause important cell populations to be compromised. Many studies are underway to tease out the possible effects of the aging process on the development of AD.

### Vascular Disease

For some time now, hints have been emerging that the body's vast network of small and large blood vessels—the vascular system—may make an important contribution in the development of dementia and the clinical symptoms of AD. Some scientists are focusing on what happens with the brain's blood vessels in aging and AD. Others are looking at the relationship between AD and vascular problems in other parts of the body.

### AD and Vascular Problems in the Brain

The brain requires a constant and dependable flow of oxygen and glucose to survive and flourish. The brain's blood vessels provide the highways to deliver these vital elements to neurons and glial cells.

Aging brings changes in the brain's blood vessels—arteries can narrow and growth of new capillaries slows down. In AD, whole areas of nervous tissue, including the capillaries that supply

and drain it, also are lost. Blood flow to and from various parts of the brain can be affected, and the brain may be less able to compensate for damage that accumulates as the disease progresses.

For some time now, study of the brain's blood vessel system in AD has been a productive line of inquiry. One important finding has been that the brain's ability to rid itself of toxic beta-amyloid by sending it out into the body's blood circulation is lessened. Some scientists now think that poor clearance of beta-amyloid from the brain, combined with a diminished ability to develop new capillaries and abnormal aging of the brain's blood vessel system, can lead to chemical imbalances in the brain and damage neurons' ability to function and communicate with each other. These findings are exciting because they may help to explain part of what happens in the brain during the development of AD. These findings also suggest several new targets for potential AD therapies.

### ***AD and Vascular Problems in Other Parts of the Body***

Research also has begun to tease out some relationships between AD and other vascular diseases, such as heart disease, stroke, and type 2 diabetes. It is important to sort out the various effects on the brain of these diseases because they are major causes of illness and death in the United States today.

Much of this evidence comes from epidemiologic studies, which compare the lifestyles, behaviors, and characteristics of groups of people (see **Describing Scientific Findings: The Type of Study Makes an Important Difference** on page 47 for more information about epidemiologic

studies). These studies have found, for example, that heart disease and stroke may contribute to the development of AD, the severity of AD, or the development of other types of dementia. Studies also show that high blood pressure that develops during middle age is correlated with cognitive decline and dementia in later life.

Another focus of AD vascular research is the metabolic syndrome, a constellation of factors that increases the risk of heart disease, stroke, and type 2 diabetes. Metabolic syndrome includes obesity (especially around the waist), high triglyceride levels, low HDL ("good cholesterol") levels, high blood pressure, and insulin resistance (a condition in which insulin does not regulate blood sugar levels very well). Evidence from epidemiologic studies now suggests that people with the metabolic syndrome have increased risk of cognitive impairment and accelerated cognitive decline.

Nearly one in five Americans older than age 60 has type 2 diabetes, and epidemiologic studies suggest that people with this disease may be at increased risk of cognitive problems, including MCI and AD, as they age. The higher risk associated with diabetes may be the result of high levels of blood sugar, or it may be due to other conditions associated with diabetes (obesity, high blood pressure, abnormal blood cholesterol levels, progressive atherosclerosis, or too much insulin in the blood). These findings about diabetes have spurred research on a number of fronts—epidemiologic studies, test tube and animal studies, and clinical trials. The objective of these studies is to learn more about the relationship between diabetes and cognitive problems and to find out in clinical trials whether treating the disease rigorously can positively affect cognitive health and possibly slow or prevent the development of AD.

### **Lifestyle Factors**

We know that physical activity and a nutritious diet can help people stay healthy as they grow older. A healthy diet and exercise can reduce obesity, lower blood cholesterol and high blood pressure, and improve insulin action. In addition, association studies suggest that pursuing intellectually stimulating activities and maintaining active contacts with friends and family may contribute to healthy aging. A growing body of evidence now suggests that these lifestyle factors may be related to cognitive decline and AD. Researchers who are interested in discovering the causes of AD are intensively studying these issues, too.

### ***Physical Activity and Exercise***

Exercise has many benefits. It strengthens muscles, improves heart and lung function, helps prevent osteoporosis, and improves mood and overall well-being. So it is not surprising that AD investigators began to think that if exercise helps every part of the body from the neck down, then it might help the brain as well.

Epidemiologic studies, animal studies, and human clinical trials are assessing the influence of exercise on cognitive function. Here are a few things these studies have found:

- Animal studies have shown that exercise increases the number of capillaries that supply blood to the brain and improves learning and memory in older animals.

If you want to know more about the benefits of exercise and physical activity and learn ways to be active every day, NIA has free information just for you!

Call 1-800-222-2225 or visit [www.nia.nih.gov/Exercise](http://www.nia.nih.gov/Exercise).



- Epidemiologic studies show that higher levels of physical activity or exercise in older people are associated with reduced risk of cognitive decline and reduced risk of dementia. Even moderate exercise, such as brisk walking, is associated with reduced risk.

- Clinical trials show some evidence of short-term positive effects of exercise on cognitive function, especially executive function (cognitive abilities involved in planning, organizing, and decision making). One trial showed that older adults who participated in a 6-month program of brisk walking showed increased activity of neurons in key parts of the brain.

More clinical trials are underway to expand our knowledge about the relationship of exercise to healthy brain aging, reduced risk of cognitive decline, and development of AD. (See **Participating in a Clinical Trial** on page 59 for more information).

### ***Diet***

Researchers have explored whether diet may help preserve cognitive function or reduce AD risk, with some intriguing findings. For example, studies have examined specific foods that are rich in antioxidants and anti-inflammatory properties to find out whether those foods affect age-related

changes in brain tissue. One laboratory study found that curcumin, the main ingredient of turmeric (a bright yellow spice used in curry), can bind to beta-amyloid and prevent oligomer formation. Another study in mice found that diets high in DHA (docosahexaenoic acid), a type of healthy omega-3 fatty acid found in fish, reduced beta-amyloid and plaques in brain tissue.

Other studies have shown that old dogs perform better on learning tasks when they eat diets rich in antioxidants, such as vitamin E and other healthful compounds, while living in an “enriched” environment (one in which the dogs have many opportunities to play and interact with people and other dogs).

Scientists also have examined the effects of diet on cognitive function in people. A very large epidemiologic study of nurses found an association between participants who ate the most vegetables (especially green leafy and cruciferous vegetables) and a slower rate of cognitive decline compared with nurses who ate the least amount of these foods. An epidemiologic study of older adults living in Chicago found the same association. The researchers do not know the exact reason behind this association, but speculate that the beneficial effects may result from the high antioxidant and folate content of the vegetables.

Dietary studies, such as the curcumin study in mice or the vegetables study in nurses, generally examine individual dietary components so that scientists can pinpoint their specific effects on an issue of interest. This approach has obvious limitations because people do not eat just single foods or nutrients. Several recent epidemiologic studies have taken a different approach and looked at an entire dietary pattern.



In one of these studies, researchers worked with older adults living in New York who ate the “Mediterranean diet”—a diet with lots of fruits, vegetables, and bread; low to moderate amounts of dairy foods, fish, and poultry; small amounts of red meat; low to moderate amounts of wine; and frequent use of olive oil. The researchers found that sticking to this type of diet was associated with a reduced risk of AD and that the association seemed to be driven by the whole approach, rather than by its individual dietary components. A follow-up study found that this pattern also was associated with longer survival in people with AD.

All of these results are exciting and suggestive, but they are not definitive. To confirm the results, scientists are conducting clinical trials to examine the relationship of various specific dietary components and their effect on cognitive decline and AD.

### *Intellectually Stimulating Activities and Social Engagement*

Many older people love to read, do puzzles, play games, and spend time with family and friends. All these activities are fun and help people feel alert and engaged in life. Researchers are beginning to find other possible benefits as well, for some studies have shown that keeping the brain active is associated with reduced AD risk. For example, over a 4-year period, one group of researchers tracked how often a large group of older people did activities that involved significant information processing, such as listening to the radio, reading newspapers, playing puzzle games, and going to museums. The researchers then looked at how many of the participants developed AD. The researchers found that

the risk of developing AD was 47 percent lower in the people who did them the most frequently compared with the people who did the activities least frequently. Another study supported the value of lifelong learning and mentally stimulating activity by finding that, compared with older study participants who may have had AD or who had AD, healthy older participants had engaged in more mentally stimulating activities and spent more time at them during their early and middle adulthood.

Studies of animals, nursing home residents, and people living in the community also have suggested a link between social engagement and cognitive performance. Older adults who have a full social network and participate in many social activities tend to have less cognitive decline and a decreased risk of dementia than those who are not socially engaged.

The reasons for these findings are not entirely clear, but a number of explanations are possible. Among them:

- Intellectually stimulating activities and social engagement may protect the brain in some way, perhaps by establishing a cognitive reserve.
- These activities may help the brain become more adaptable and flexible in some areas of mental function so that it can compensate for declines in other areas.
- Less engagement with other people or in intellectually stimulating activities could be the result of very early effects of the disease rather than its cause.
- People who engage in stimulating activities may have other lifestyle qualities that may protect them against developing AD.

## Describing Scientific Findings: The Type of Study Makes an Important Difference

These days, the media are full of stories about scientific studies. It can be hard to know what to conclude about their findings. Knowing how the study was conducted can help put the results into the right perspective.

One main type of research is the epidemiologic study. These studies are observational—they gather information about people who are going about their daily lives. Study participants follow many behaviors and practices. It is difficult, therefore, to determine the exact benefits or risks of one particular behavior from among all the healthy or harmful behaviors

followed by the participants. That is why, in epidemiologic studies of AD, scientists only say that a finding is “associated with” AD, or not. The epidemiologic evidence linking a behavior and AD is, at best, suggestive, but we do not know that the behavior by itself actually helps to cause or prevent AD.

Other types of research—test tube studies and studies in animals—add to the findings from epidemiologic studies. Scientists use them to examine the same issue but in ways in which the various factors that might influence a result are controlled to a greater degree. This element

of control allows scientists to be more certain about why they get the results they do. It also allows them to be more definitive in the words they use to describe their results. Of course, showing a cause-and-effect relationship in tissue samples or even in animal studies still does not mean that the relationship will be the same in humans. Clinical trials in humans are the gold standard for deciding whether a behavior or a specific therapeutic agent actually prevents or delays AD (see [Participating in a Clinical Trial](#) on page 59 for more on this kind of research). ●

# New Techniques Help in Diagnosing AD

*A man in his mid-60s begins to notice that his memory isn't as good as it used to be. More and more often, a word will be on the tip of his tongue but he just can't remember it. He forgets appointments, makes mistakes when paying his bills, and finds that he's often confused or anxious about the normal hustle and bustle of life around him. One evening, he suddenly finds himself walking in a neighborhood he doesn't recognize. He has no idea how he got there or how to get home.*

Not so long ago, this man's condition would have been swept into a broad catch-all category called "senile dementia" or "senility." Although we now know that AD and other causes of dementia are distinct diseases, in the early stages it is difficult to differentiate between the onset of AD and other types of age-related cognitive decline. We have improved our ability to diagnose AD correctly, and doctors experienced in AD can diagnose the disease with up to 90 percent accuracy. A definitive diagnosis of AD, however, is still only possible after death, during an autopsy, and we are still far from the ultimate goal—a reliable, valid, inexpensive, and early diagnostic marker that can be used in any doctor's office.

Early diagnosis has several advantages. For example, many conditions cause symptoms that

mimic those of AD. Finding out early that the observed changes in cognitive abilities are not AD but something else is almost always a relief and may be just the prod needed to seek appropriate medical treatment (see **Causes of Dementia** on page 50 for more information). For the small percentage of dementias that are treatable or even reversible, early diagnosis increases the chances of successful treatment. Increasing early diagnosis and improving treatment are among NIA's most important goals.

Even when the cause of a loved one's dementia turns out to be AD, it is best to find out sooner rather than later. One benefit of knowing is medical. The drugs now available to treat AD can help some people maintain their mental abilities for months to years, although they do not change the underlying course of the disease (see **Helping People with AD Maintain their Mental Functioning** on page 55 for more about these drugs).

Other benefits are practical. The sooner the person with AD and the family have a firm diagnosis, the more time they have to make future living arrangements, handle financial matters, establish a durable power of attorney and advance directives, deal with other legal issues, create a support

## Current Tools for Diagnosing AD

With the tools now available, experienced physicians can be reasonably confident about making an accurate diagnosis of AD in a living person. Here is how they do it.

### They take a detailed patient history, including:

- A description of how and when symptoms developed.
- A description of the person's and his or her family's overall medical condition and history.
- An assessment of the person's emotional state and living environment.

### They get information from family members or close friends:

- People close to the person can provide valuable insights into

how behavior and personality have changed; many times, family and friends know something is wrong even before changes are evident on tests.

### They conduct physical and neurological examinations and laboratory tests:

- Blood and other medical tests help determine neurological functioning and identify possible non-AD causes of dementia.

### They conduct neuropsychological testing:

- Question-and-answer tests or other tasks that measure memory, language skills, ability to do arithmetic, and other abilities related to brain functioning help show what kind of cognitive changes are occurring.

### They may do a computed tomography (CT) scan or a magnetic resonance imaging (MRI) test:

- CT and MRI scans can detect strokes or tumors or can reveal changes in the brain's structure that indicate early AD.

Exams and tests may be repeated every so often to give physicians information about how the person's memory and other symptoms are changing over time.

Based on findings from these exams and tests, experienced physicians can diagnose or rule out other causes of dementia, or determine whether the person has MCI, "possible AD" (the symptoms may be due to another cause), or "probable AD" (no other cause for the symptoms can be found). ●

network, and even consider joining a clinical trial or other research study. Being able to participate for as long as possible in making personal decisions is important to many people with AD.

Early diagnosis also gives families time to recognize that life does not stop with a diagnosis of AD. The person is still able to participate in many of the daily activities he or she has always enjoyed, and families can encourage the person to continue

with them for as long as possible. Finally, early diagnosis gives family caregivers the opportunity to learn how to recognize and cope with changes over time in their loved one as well as to develop strategies that support their own physical, emotional, and financial health.

## Causes of Dementia

Dementia is the loss of cognitive functioning—thinking, remembering, and reasoning—to such an extent that it interferes with a person’s daily life and activities. It is not a disease itself, but a group of symptoms that often accompanies a disease or condition. Some dementias are caused by neurodegenerative diseases. Dementia also has other causes, some of which are treatable.

### Neurodegenerative Diseases that Cause Dementia

- Alzheimer’s disease
- Vascular dementia
- Parkinson’s disease with dementia
- Frontotemporal lobar degeneration, including:
  - frontotemporal dementia
  - frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17)
  - Pick’s disease
  - supranuclear palsy
  - corticobasal degeneration

### Other Causes of Dementia

- Medication side effects
- Depression
- Vitamin B<sub>12</sub> deficiency
- Chronic alcoholism
- Certain tumors or infections of the brain
- Blood clots pressing on the brain
- Metabolic imbalances, including thyroid, kidney, or liver disorders

Scientists also see advantages to early diagnosis. Developing tests that can reveal what is happening in the brain in the early stages of AD will help them understand more about the cause and development of the disease. It also will help scientists learn when and how to prescribe the use of drugs and other treatments so they can be most effective.

### EXCITING NEW DEVELOPMENTS IN AD DIAGNOSIS

Scientists are now exploring ways to help physicians diagnose AD earlier and more accurately. For example, some studies are focusing on changes in mental functioning. These changes can be

measured through memory and recall tests. Tests that measure a person’s abilities in areas such as abstract thinking, planning, and language can help pinpoint changes in these areas of cognitive function. Researchers are working to improve standardized tests that might be used to point to early AD or predict which individuals are at higher risk of developing AD in the future.

Other studies are examining the relationship between early damage to brain tissue and outward clinical signs. Still others are looking for changes in biomarkers in the blood or cerebrospinal fluid that may indicate the progression of AD (see [Very Early Signs and Symptoms](#) on page 28 for more on this work).

One of the most exciting areas of ongoing research in this area is neuroimaging. Over the past decade, scientists have developed several

highly sophisticated imaging systems that have been used in many areas of medicine, including AD. PET scans, **single photon emission computed tomography** (SPECT), and MRI are all examples. These “windows” on the living brain may help scientists measure the earliest changes in brain function or structure in order to identify people who are at the very first stages of the disease—well before they develop clinically apparent signs and symptoms.

To help advance this area of research, NIA launched the multi-year AD Neuroimaging Initiative (ADNI) in 2004. This project is following about 200 cognitively healthy individuals and 400 people with MCI for 3 years and 200 people with early AD for 2 years. Over the course of this study, participants undergo multiple MRI and PET scans so that study staff can assess how the brain changes in the course of normal aging and MCI, and with the progression of AD. By using MRI and PET scans at regularly scheduled intervals, study investigators hope to learn when and where in the brain degeneration occurs as memory problems develop.

Another innovative aspect of ADNI is that scientists are correlating the participants’ imaging information with information from clinical, memory, and other cognitive function tests, and with information from blood, cerebrospinal fluid, and urine samples. Results from these samples may provide valuable biomarkers of disease progress, such as changing levels of beta-amyloid and *tau*, indicators of inflammation, measures of oxidative stress, and changing cognitive abilities.

An important ADNI achievement is the creation of a publicly accessible database of images, biomarker data, and clinical information available to qualified researchers worldwide.



Biological samples also are available for approved biomarker projects. NIA hopes that this initiative will help create rigorous imaging and biomarker standards that will provide measures for the success of potential treatments. This would substantially increase the pace and decrease the cost of developing new treatments. The ADNI study is being replicated in similar studies by researchers in Europe, Japan, and Australia.

These types of neuroimaging scans are still primarily research tools, but one day they may be used more commonly to help physicians diagnose AD at very early stages. It is conceivable that these tools also may someday be used to monitor the progress of the disease and to assess responses to drug treatment.

## New Technologies Help People Participate in AD Research at Home

Traditionally, AD scientists have collected data by asking people to come to a clinic once or twice a year over a period of years. They give the participants a physical exam and ask them to take a series of memory, language, and other cognitive function tests.

These studies collect much useful information, but they have their limitations. For one thing, participants are seen only once or twice during the year, so the data collected represent only a “snapshot” in time. The studies cannot effectively capture day-to-day fluctuations in behaviors and cognitive abilities. Another limitation is that participants are seen in a research setting, not in their natural community environment. For many, coming to the clinic can be inconvenient, difficult, or both.

Advances in technology, as shown in the two research projects described here, offer some hope for dealing with these challenges by bringing research to people right in their own homes.

### MOTION DETECTORS TELL AN INTERESTING STORY

Scientists who are trying to develop methods for diagnosing AD as early as possible continually grapple with two challenges in conducting their research. First, they need to find easy and accurate ways to collect data from older people, who often have physical, emotional, or cognitive problems. Second, they need to find ways to assess accurately the very early changes in physical or cognitive abilities that could indicate that AD is progressing.

Under an NIA grant, the Oregon Center for Aging and Technology (ORCATECH) at Oregon Health &

Science University is exploring the use of unobtrusive, simple technology and intelligent systems to detect and monitor subtle changes in movement that may indicate age-related cognitive changes. This project is building on research that has suggested that motor-function changes may arise before memory changes become apparent (see **Very Early Signs and Symptoms** on page 28 for more on this research).

All of the 300 study participants are 80 years or older or have a spouse of a similar age, and live independently in Portland-area retirement communities. Wireless, infrared motion sensors, like those used to automatically open grocery store doors, have been placed strategically throughout the participants’ homes to gather data about changes in their walking or dressing speed over time. Special software also has been installed on each participant’s home computer to measure motor skills and speed in typing or using a mouse. The sensors and computer software collect data about motion, not what the volunteer is actually doing. Privacy is largely not a concern therefore, because the volunteers are not directly observed and no video or photographs are taken.

The 3-year study began in early 2007, so results are not yet available. However, a small pilot study using the same type of sensors showed a clear difference in the walking speeds of people age 65 and older who had MCI, compared with cognitively healthy people of the same age, over time periods of nearly a year. These data suggest that a remote sensing system like this is a feasible technology and is potentially sensitive enough to distinguish accurately between affected and unaffected people.



This photo shows ORCATECH study participants at home. The small device between the photographs on the wall is an infrared motion sensor.

### USING TECHNOLOGY TO COLLECT DATA AT HOME

Researchers at nearly 30 sites nationwide are comparing various ways of collecting data, including the use of an in-home “kiosk” that combines a touch-screen computer monitor with a telephone handset, an interactive voice-response system, and traditional mail and telephone. All three methods gather the same data about several areas known to be important in early detection of cognitive decline: memory; language skills; attention and concentration; activities of daily living; quality of life; health care and resource use; and changes in “global” well-being as measured by self-rating of health, cognition, and

mood. This study is looking at questions such as how likely people are to complete the questions using each method, which method is the most efficient, and how sensitive each method is.

Having a data collection system that is easy to use and that collects data accurately and completely may encourage wider participation in AD clinical trials. It also may reduce the expense and burden of conducting AD research. Early results from this study show that the older participants were skeptical at first about using the kiosk, but once they learned how to use it, they became enthusiastic and excited about participating. ●

# The Search for New Treatments

More and more, scientists are able to think about ways to treat, slow, or perhaps even prevent AD at a number of possible points during the years-long continuum of disease progression. This continuum begins with the very earliest disease stage, even before symptoms are evident, moves to the first signs of memory and cognitive problems, then continues through the mild and moderate stages, and ends with the very late stages and the person's death.

As a result, researchers who focus on developing AD treatments think a lot about the importance of timing: When would it be best to intervene and what interventions are most appropriate at which time? These questions are similar to those asked with other conditions, such as heart disease. For example, a physician would prescribe different treatments for a patient who is seemingly healthy but who is at risk of having future heart disease than for a patient who is actually having a heart attack or whose heart disease is well established. The same decision process now can be applied to AD.

It has become clear that there probably is no single “magic bullet” that will, by itself, prevent or cure AD. Therefore, investigators are working to develop an array of options from which physicians can choose. For people who already have AD, the

most immediate need is for treatments to control cognitive loss as well as problem behaviors, such as aggression, agitation, wandering, depression, sleep disturbances, hallucinations, and delusions. Safe medications that remain effective over time are needed to ease a broad range of symptoms and to improve a person's cognitive function and ability to carry out activities of daily living. Scientists also are investigating treatments that combine medications with lifestyle strategies to lessen the risk of developing cognitive decline or AD. Eventually, scientists hope to develop treatments that attack the earliest manifestations and underlying causes of AD, thereby slowing, delaying, or preventing the disease from progressing and damaging cognitive function and quality of life. Scientists use **clinical trials** to pursue all these goals.

Today, NIA, other NIH institutes, and private industry are conducting many clinical trials of AD interventions (see page 59 for more about clinical trials). These studies focus on several key areas:

- Helping people with AD maintain their mental functioning
- Managing symptoms
- Slowing, delaying, or preventing AD

## HELPING PEOPLE WITH AD MAINTAIN THEIR MENTAL FUNCTIONING

In the mid-1970s, scientists discovered that levels of a neurotransmitter (a chemical that carries messages between neurons) called acetylcholine fell sharply in people with AD. This discovery was one of the first that linked AD with biochemical changes in the brain. Scientists found that acetylcholine is a critical player in the process of forming memories. It is used by neurons in the hippocampus and cerebral cortex, which are areas of the brain important to memory function. This discovery was an important initial breakthrough in the search for drugs to treat AD.

Four medications, tested in clinical trials, have been approved by the FDA for use in treating AD symptoms. Donepezil (Aricept®), rivastigmine (Exelon®), and galantamine (Razadyne®) are prescribed to treat mild to moderate AD symptoms. Donepezil was recently approved to treat severe AD as well. These drugs, known as cholinesterase inhibitors, act by stopping or slowing the action of acetylcholinesterase, an enzyme that breaks down acetylcholine. They help to maintain higher levels of acetylcholine in the brain. In some people, the drugs maintain abilities to carry out activities of daily living. They also may maintain some thinking, memory, or speaking skills, and can help with certain behavioral symptoms. However, they will not stop or reverse the underlying progression of AD and appear to help people only for months to a few years. The newest approved AD medication is memantine (Namenda®), which is prescribed to treat moderate to severe AD symptoms. This drug appears to work by regulating levels of glutamate, another neurotransmitter involved in memory function. Like the cholinesterase inhibitors, memantine will not stop or reverse AD.



## MANAGING SYMPTOMS

*“My father is often agitated. He paces up and down, wringing his hands and crying. I know he’s sad or anxious about something but he can’t tell me what’s bothering him. Asking him about it just makes him more upset.”*

*“Last week, I visited Mom in the nursing home. We had a great time. Then yesterday, I went to see her again. When I walked into her room, she didn’t know me. She thought I was her sister.”*

*“My husband used to be such an easy going, calm person. Now, he suddenly lashes out at me and uses awful language. Last week, he got angry when our daughter and her family came over and we sat down to eat. I never know when it’s going to happen. He’s changed so much—it scares me sometimes.”*

*“Gran hums all the time. She used to be a singer. Is she trying to relive her past?”*

As AD begins to affect memory and mental abilities, it also begins to change a person’s emotions and behaviors. Between 70 and 90 percent of people with AD eventually develop one or more behavioral symptoms. These symptoms include sleeplessness, wandering and pacing, aggression, agitation, anger, depression, and hallucinations and delusions. Some of these symptoms may become worse in the evening (a phenomenon called “sundowning”) or during daily routines, especially bathing.

The damage of AD affects many different parts of the brain. This presents a problem because even small tasks require the brain to process signals that often involve more than one region of the brain. If this processing is disrupted because of AD, the person may not be able to do the task or may act in a strange or inappropriate way.

In light of our growing understanding about the effects of AD on the brain, behaviors like the ones highlighted above suddenly make sense or even provide a loving opportunity for caregivers:

*For a man who can no longer distinguish between past and present, the anguish caused by the death of a parent may be as real today as it was many years before.*

*Sitting down to a family meal may produce intense anxiety when a person has no idea what to do with the knife and fork in front of him and all the conversation and activity feel overwhelming.*

*Memories of favorite songs from long ago resurface and provide a compelling link to a happy time in the past.*

Behavioral symptoms, often emotional and upsetting, are one of the hardest aspects of the disease for families and other caregivers to deal with. They are also a visible sign of the terrible change that has taken place in the person with AD. Researchers are slowly learning more about why behavioral symptoms occur and are conducting clinical trials on new treatments—both drug and non-drug—to deal with difficult behaviors.

### Coping with Behavioral Symptoms

For more information on how to deal with behavioral issues and symptoms, visit the caregiving section of NIA’s Alzheimer’s Disease Education and Referral (ADEAR) Center website at: [www.nia.nih.gov/Alzheimers/Caregiving/HomeAndFamily](http://www.nia.nih.gov/Alzheimers/Caregiving/HomeAndFamily).

## SLOWING, DELAYING, OR PREVENTING AD

AD research has developed to the point where scientists are looking beyond treating symptoms to addressing the underlying disease process. Slowing the progress of AD could do much to maintain the functioning of people with AD and reduce physical and emotional stress on caregivers. Delaying AD’s effects also could help to postpone or prevent placement in an assisted living facility or nursing home, and reduce the financial costs of the disease. Preventing AD altogether is, of course, the ultimate long-term goal.

NIA and pharmaceutical companies support treatment clinical trials that are aimed at slowing, delaying, or preventing AD. The advances in our knowledge about the mechanisms and risk factors associated with AD have expanded the types of interventions under study. These trials are examining a host of possible interventions, including cardiovascular treatments, hormones, type 2 diabetes treatments, antioxidants, omega-3 fatty acids, immunization, cognitive training, and exercise, among others.

For example, NIA funds pilot trials to learn whether treating one or another aspect of type 2 diabetes will affect cognitive health and AD progression. A pilot trial is a relatively small clinical trial that collects initial data on the safety, effectiveness, and best dosage of a potential treatment. This information helps investigators decide which treatments should be tested in larger, full-scale trials. One 4-month pilot trial has examined the effects on AD of administering a nasal-spray form of insulin. This trial is founded on evidence that AD is associated with reduced levels of insulin in cerebrospinal fluid and that treatment with insulin improves



memory performance. The trial will provide useful data on the safety, feasibility, and potential effectiveness of this innovative treatment approach. Investigators may be able to use the results to plan future full-scale clinical trials.

Beyond pilot studies, investigators also are conducting full-scale AD clinical trials of various interventions. One of these trials, the Alzheimer’s Disease Cooperative Study (ADCS), is testing whether one omega-3 fatty acid (DHA), found in the oil of certain fish, can slow the progression of cognitive and functional decline in people with mild to moderate AD. During the 18-month clinical trial, investigators will measure the progress of the disease using standard tests for functional and cognitive change. Researchers also will evaluate whether taking DHA supplements has a positive effect on possible physical and biological markers of AD, such as brain atrophy



and proteins in blood and spinal fluid. The ADCS is a federally established consortium conducting clinical trials on AD, with sites across the United States and Canada.

Full-scale AD prevention trials are underway as well. One such trial, Prevention of Alzheimer’s Disease with Vitamin E and Selenium (PREADVISE), is being conducted in conjunction with a National Cancer Institute-funded trial called the Selenium and Vitamin E

Cancer Prevention Trial (SELECT). SELECT is evaluating whether taking selenium and/or vitamin E supplements can prevent prostate cancer in healthy men older than 60 years. PREADVISE is evaluating whether these supplements can help prevent memory loss and dementia by protecting brain cells from oxidative damage (see [The Aging Process](#) on page 42 for more on oxidative damage). About 6,000 of the more than 30,000 men enrolled in SELECT are participating in PREADVISE.

## Participating in a Clinical Trial

Rapid advances in our knowledge about AD have led to the development of many promising new drugs and treatment strategies. However, before these new strategies can be used in clinical practice, they must be shown to work in people. This means that clinical trials—and volunteer participants—are an essential part of AD research. Advances in prevention and treatment are possible thanks to volunteers who participate in clinical trials.

Clinical trials are the primary way that researchers find out if a promising treatment is safe. Clinical trials tell researchers which treatments are the most effective and for which people they may work best. Trials can take place in various settings, such as private research facilities, teaching hospitals, specialized AD research centers, and doctors’ offices. FDA approval is necessary before scientists can begin a clinical trial.

Participating in a clinical trial is a big step for anyone, including people with AD and their caregivers. That is why physicians and clinical trials staff spend time talking with participants about what it is like to be in a trial and the pros and cons of participating. It is also why they get a signed informed consent form before a person enrolls in

a trial. Here are some facts that potential participants might want to know about clinical trials.

### WHAT KIND OF TRIALS ARE THERE?

Treatment trials with existing drugs or behavioral strategies assess whether an intervention already approved for other purposes may be useful in treating age-related cognitive decline or AD. For example, trials have tested whether drugs used to lower cholesterol help slow progression of AD.

Treatment trials with experimental drugs or strategies show whether a new drug or treatment approach can help improve cognitive function or lessen symptoms in people with AD, slow the progression to AD, or prevent it. Interventions tested in these trials are developed from knowledge about the mechanisms involved in the AD process. Experimental drugs, for example, are first tested in tissue culture and in animals to determine their actions in the body. Safety and effectiveness studies are also conducted in animals before the compounds are tested in humans.

### WHAT ARE THE PHASES OF CLINICAL TRIALS?

During Phase I trials, a research team gives the treatment to a

small number of participants and examines its action in the body and its safety. The main goals of Phase I trials are to establish the highest dose of a new drug that people can tolerate and to define the dose at which people may begin to experience harmful side effects. These trials generally last only a few months.

If results show that the treatment appears to be safe, it will go on to Phase II and Phase III clinical trials. Phase II trials involve larger numbers of people studied over longer periods of time than Phase I trials. In these trials, the study team wants to know whether the treatment is safe and effective at changing the course of the disease. Phase II trials occasionally also involve the use of a placebo (an inactive substance that looks like the study drug). Results from Phase II trials give study staff an indication of the effective dose to take into Phase III trials. Phase III trials are large studies that compare an experimental treatment with a placebo or standard treatment to determine safety and efficacy (whether the treatment has the power to produce an effect).

After these phases are complete

*Continued on next page*

## Participating in a Clinical Trial *(Continued)*

and investigators are satisfied that the treatment is safe and effective, the study team may submit its data to the FDA for approval. FDA experts review the data and decide whether to approve the drug or treatment for use in patients with the disease under study.

### WHAT HAPPENS WHEN A PERSON SIGNS UP FOR A CLINICAL TRIAL?

First, it is important to learn about the trial. Staff at the clinical research center explain the trial in detail to potential participants and describe possible risks and benefits. Staff also talk about the participants' rights as research volunteers, including their right to leave the trial at any time. Participants and their family members are entitled to have this information repeated and explained until they feel they understand the nature of the trial and any potential risks.

After all questions have been answered, participants who are still interested in joining the trial are asked to sign an informed consent form. In some cases, a participant may no longer be able to provide informed consent because of problems with memory and thinking. In such cases, it is still possible for an authorized

representative (usually a family member) to give permission for the person to participate. Laws and regulations regarding informed consent differ across States and research institutions, but all are intended to ensure that participants are protected and well cared for.

Next, people go through a screening process to see if they qualify to participate in the trial. If they qualify and can safely participate, then they are enrolled in the trial.

### WHAT HAPPENS DURING A TRIAL?

If participants agree to join the trial and an evaluation process shows they meet all the criteria for participation, then a "baseline" visit is scheduled with the trial staff. This visit generally involves cognitive and physical tests. This gives the team information against which to measure future mental and physical changes.

In most clinical trials, participants are randomly assigned to different study groups so that each study group has people in it of about the same average characteristics (such as age, sex, educational level, or cognitive ability). One group, the test group, receives the experimental drug or intervention. Other

groups may receive a different drug, a placebo, or a different intervention. Comparing results for different groups gives researchers confidence that changes in the test group are the result of the experimental treatment and not some other factor, such as the placebo effect (this is when people feel an effect because they think they are getting the test medication even though they are really getting a placebo). In many trials, no one—not even the research team—knows who is getting the treatment and who is getting the placebo or other intervention. This means that the participant, family member, and the staff are "blind" to the treatment being received. This kind of trial is called a double-blind, placebo-controlled trial.

As the trial progresses, participants and family members usually must follow strict medication or treatment instructions and keep detailed records of symptoms. Every so often, participants visit the clinic or research center to have physical and cognitive exams, give blood and urine samples, and talk with trial staff. These visits allow the investigators to collect information on the effects of the test drug or treatment, see how the disease is progressing, and see how the participant and the caregiver are doing.

### WHAT SHOULD PEOPLE CONSIDER BEFORE PARTICIPATING IN A CLINICAL TRIAL?

People who have participated in AD clinical trials say that it's a good idea to consider the following issues before deciding to join a trial.

■ **Expectations and motivations.** The test drug or treatment may relieve a symptom, change a clinical measurement, or reduce the risk of death, but clinical trials generally do not have miraculous results and participants may not receive any direct benefit. With a complex disease like AD, it is unlikely that one treatment will cure or prevent the disease. Some people choose not to participate or decide to drop out of a study because this reality does not meet their expectations. Others choose to stay in a trial because they realize that even if they get no or only a slight benefit, they are making a valuable contribution to knowledge that will help people in the future.

■ **Uncertainty.** Some families have a hard time with the uncertainties of participation—for example, not knowing whether the person is taking the test treatment, a placebo, or a control treatment, not being able to

choose which study group to be in, or not knowing for a long time whether the study was successful. Ongoing and open communication with study staff can help to reduce this frustration.

■ **Finding the right clinical trial.** Some clinical trials involve participants who are cognitively healthy or have only mild symptoms because they are testing a drug that might delay a decline in cognitive function. Other trials involve participants who have more advanced AD because they are testing a treatment that might lessen behavioral symptoms. Or, a trial may be testing new strategies to help caregivers. Even if a participant is not eligible for one trial, another trial may be just right.

■ **The biggest benefit of all.** Many families find that the biggest benefit of participating in a clinical trial is the regular contact with the study team. These visits provide an opportunity to get state-of-the-art AD care and to talk regularly with AD experts who have lots of practical experience and a broad perspective on the disease. The study team understands and can provide advice about the emotional and physical aspects of the person with AD and the caregivers' experience. Team members can suggest ways to cope with the present and



give insights into what to expect in the future. They also can share information about support groups and other helpful resources.

### FOR MORE INFORMATION

To learn more about AD clinical trials, visit the Alzheimer's Disease Education and Referral (ADEAR) Center's Clinical Trials Database website ([www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials](http://www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials)). This NIA website includes a list of AD and dementia clinical trials currently in progress at research centers throughout the United States. It also provides information about the phases of clinical trials and how to participate, explains the drug development process, and provides links to other useful websites. Also, visit the clinical trials websites of the National Institutes of Health ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) or the Alzheimer's Association ([www.alz.org](http://www.alz.org)). ●



PART

4

# Improving Support for Families and Other Caregivers

One of the greatest costs of AD can be the physical and emotional toll on family members, caregivers, and friends of people with the disease. The changes in a loved one's personality and mental abilities; the need to provide constant, loving attention for years on end; and the demands of bathing, dressing, and other caregiving duties in the later stages of the disease can be hard to bear. Many caregivers must assume new and unfamiliar roles in the family, and these changes can be both difficult and sad. Not surprisingly, caregivers of people with dementia spend significantly more time on caregiving tasks than do caregivers of people with other types of illnesses.

One of the hardest decisions that many families face is whether and when to place a loved one with AD in a nursing home or other type of care facility. Once this decision is made, families must decide what type of care is best for the person and the family. Many investigators are working to identify strategies that can lead to improved quality of care in various facilities, including adult day care centers, assisted living facilities, continuing care retirement communities, nursing homes, and special care units (separate areas within nursing homes or assisted living facilities designed especially for people with dementia).

## Who Are AD Family Caregivers?

Many primary caregivers are family members, and NIA-funded research has shown that the value of informal family caregiving of people with cognitive impairment adds up to billions of dollars every year. Who are these family caregivers?

**Spouses:** This is the largest group of caregivers. Most are older, too, and many have their own health problems.

**Daughters:** The second largest group of primary caregivers is daughters. Many are married and

raising children of their own. Juggling two sets of responsibilities is often tough for these members of the "sandwich generation."

**Daughters-in-law:** Many women in this group help take care of an older person with AD. They are the third largest group of family caregivers.

**Sons:** Although many are involved in the daily care of a parent with AD, sons often focus on the financial, legal, and business aspects of caregiving.

**Brothers and sisters:** Siblings may assume primary responsibility for care if they live close by. Many of these caregivers also are older and may be coping with their own frailties or health problems.

**Grandchildren:** Older children may become major helpers in caring for a grandparent with AD. Grandchildren may need extra support if their parents' attention is heavily focused on the ill grandparent or if the grandparent with AD lives in the family's home. ●

# Research Findings *Benefit* Caregivers

Although research on family caregiver support is still in its early days, we have already learned much about the unique aspects of caregivers' personalities and situations. For example, it is well established that AD caregivers often experience stress, anxiety, depression, and other mental health problems as a result of the continuing and demanding nature of AD care. This chronic stress can have detrimental effects on the physical health of caregivers. The physical and emotional effects of AD caregiving can last a long time, even after the death of the person with AD.

On the other hand, research also has shown that caregiving can have important positive effects, including:

- A new sense of purpose or meaning in life
- Fulfillment of a lifelong commitment to a spouse
- An opportunity to give back to a parent some of what the parent has given to them
- Renewal of religious faith
- Closer ties with people through new relationships or stronger existing relationships



AD caregivers do not all have the same psychological and physical response to caregiving. For example, caregivers who have strong support systems and well-developed coping skills may be able to weather the stresses of caring for a loved one with AD. Others who have few breaks from caregiving responsibilities and/or have preexisting illnesses may be more vulnerable to the physical and emotional stresses associated with dementia care. Caregiver research is beginning to discover effective ways to ease the burden of caregiving. Researchers have learned that:

- **The information and problem-solving needs of caregivers evolve over time as AD progresses.** Therefore, support programs should be tailored to the needs of the caregiver at various stages of caregiving. Programs can respond by offering

services and information geared to different stages of the disease.

- **Traditions and attitudes about caregiving vary across cultural groups.** For example, some researchers have found that African-American caregivers use fewer formal in-home services than do white caretakers. Some populations may find it difficult to publicly admit that a family member has AD and may be reluctant to seek help with caregiving issues. Therefore, programs and services for caregivers must be culturally appropriate and sensitive to factors that positively and negatively influence caregivers' attitudes and ability to carry out their responsibilities.

- **Use of multiple types of support over an extended period of time helps caregivers.** For example, the Resources for Enhancing Alzheimer's Caregiver Health (REACH) clinical trial showed that caregivers who received 6 months of intensive help with caregiving strategies had significant improvements in overall quality of life. They also had lower rates of clinical depression compared to caregivers who did not participate in the program. The caregiving strategies included information sharing, instruction, role plays, problem-solving, skills training, stress-management techniques, and telephone support groups. Caregivers reported that taking part in REACH helped them feel more confident in working with their loved

## Where Are People with Alzheimer's Disease Cared For?

- Home
- Assisted living facilities (those in the early stages)
- Adult day care centers
- Nursing homes
- Special care units

ones, made life easier for them, improved their caregiving ability, improved the care recipient's life, and helped them keep their loved one at home.

- **Developing ways to help caregivers become educated about AD, improve flexibility in responding to caregiving demands, and learn a variety of practical strategies can help.** Studies are teaching caregivers how to read the emotional and physical cues of the person with AD and to understand the sequence of events that often leads to inappropriate behaviors. They are also helping caregivers respond to the needs of the person with AD in a variety of creative ways, such as maintaining flexibility in the face of many demands, becoming educated about the disease, learning practical strategies, using available

### For Information About AD Support Groups

To find out whether an AD support group is operating in your area, contact:

- NIA's Alzheimer's Disease Education and Referral (ADEAR) Center at 800-438-4380 or visit [www.nia.nih.gov/Alzheimers/ResearchInformation/ResearchCenters](http://www.nia.nih.gov/Alzheimers/ResearchInformation/ResearchCenters)
- Alzheimer's Association at 800-272-3900 or visit [www.alz.org](http://www.alz.org)

resources, involving other family members and friends, and balancing the needs of the person with their own needs.

■ **Helping caregivers deal with the complicated issue of whether and when to place a loved one in a nursing home is an important aspect of caregiver support.** People with dementia are at much greater risk of nursing home placement than are other older people of the same age. Placing a loved one in a nursing home may relieve some of the burden of caregiving, but it does not necessarily reduce caregiver stress or emotional distress. Moreover, nursing home costs now average more than \$70,000 per year.

One clinical trial tested the effects of an enhanced counseling and support program on nursing home placement and caregiver health. This program for caregivers consisted of six sessions of individual and family counseling, support group participation, and on-demand telephone counseling. Participants in the program were able to delay placement of their loved ones in nursing homes by about 18 months. Researchers attributed the effects of the program to greater tolerance for memory and behavior problems in the person with AD, improved satisfaction with the support provided by family and friends, and fewer symptoms of depression. Moreover, it appears that the extra time at home did not come at the expense of the caregivers' sense of well-being.



■ **Helping caregivers stay physically active has big benefits.** Researchers have found that regular moderate exercise is an important stress reliever for caregivers. Exercise helps to reduce blood pressure increases due to stress, improves sleep quality, and reduces psychological distress and depression.

#### EARLY-STAGE AD SUPPORT GROUPS: A VITAL SOURCE OF HELP

For families and friends who care for a person with AD, talking with others who are going through the same experience can be a vital lifeline. AD support groups provide a place where caregivers can seek respite, express concerns, share experiences, get tips, and receive emotional comfort. NIA-funded Alzheimer's Disease Centers, the Alzheimer's Association, and many other organizations sponsor in-person and online AD support groups all around the country.

Improved diagnostic tests and increasing awareness of AD mean that more and more people are now being diagnosed at early stages of AD. People

in the early stages often still have good coping skills and are intensely aware of themselves and their symptoms. They also may feel considerable distress, embarrassment, and isolation because of a perceived stigma associated with the disease. As a result, a growing number of people with early-stage AD and their family members are looking for coping strategies, meaningful activities, and mental stimulation. They are eager to educate themselves about AD, share common experiences, and break the potential barriers and isolation caused by their diagnosis. This has led to the formation of early-stage support groups specifically designed to meet their needs.

Some early-stage support groups follow a structured model, with 1- to 2-hour sessions scheduled over 6 to 8 weeks. The sessions are led by a facilitator and discussion topics are determined in advance. Guest speakers provide information and help on specific topics such as legal and financial planning. In some programs, the person with AD and the caregiver meet in

separate groups; in others, people with AD and their caregivers are together for part of the session and apart for the remainder.

Other types of early-stage support groups are less structured. Members discuss topics of their own choosing, and the groups meet regularly over an extended time. Members with AD may stay in the group as long as they are able to meaningfully take part in the discussion and activities.

Early-stage support groups are not for everyone. Some people with early AD and their families may not benefit because of family conflict, denial, cognitive impairment, or discomfort with the intimacy of a group experience. However, most participants report positive outcomes, such as a greater sense of control over their lives and feelings that they are not alone. Many participants find early-stage support groups helpful because they instill a spirit of camaraderie, build coping skills, and forge relationships and emotional support that continue to help the person with AD and the caregiver even after the sessions end.



#### What Happens Next?

It is a question many people and their families ask when AD is first diagnosed. Members of an early-stage support group at the Northwestern University Alzheimer's Disease Center in Chicago wrote *What Happens Next?* to help people with early-stage dementia cope with their feelings and the practical aspects of everyday life.

For a free copy, call the Alzheimer's Disease Education and Referral (ADEAR) Center at 800-438-4380 or visit [www.nia.nih.gov/Alzheimers/Publications/WhatHappensNext.htm](http://www.nia.nih.gov/Alzheimers/Publications/WhatHappensNext.htm).

## Taking Care of Mom or Dad at a Distance

Taking care of a parent with AD who lives hundreds of miles away is a real worry facing many adults. “How can we make sure Mom gets the best care possible if we’re not there all the time?” “What can I do to help Dad live at home for as long as possible?”

That was the dilemma facing Ken Nixon and his two brothers in 2001. Their mother lived in an Arkansas farming community and wanted to stay there. Ken and his brothers lived 3 to 5 hours away—close, but not close enough.

With funding from NIA, Ken and his brothers created a multi-purpose, Internet-based system called AttentiveCare that is currently available to others faced with the same long-distance caregiving challenges. Back in 2001, broadband Internet service had just become available in their mother’s community, so the

brothers decided to see whether videoconferencing could be a way to keep in touch with her. They installed a computer with a video camera in her home so they could check on her daily, helping fulfill her wish to continue living independently on the family farm while assuring themselves that she was faring well.

“We had a need, and we patched the system together at first,” says Ken. “It exceeded our expectations in being able to keep our mother independent and connected to the family. We could call and have coffee with her every morning, and it got her day started off right. She had something to look forward to every day—one or two of her boys was going to visit.”

After 6 months of using the home-grown system, Nixon decided to develop it to help other caregivers. In 2003, he applied for and received a grant from NIA to refine the AttentiveCare prototype and test its feasibility in providing informal, long-distance care to people with AD.

He later received another grant to evaluate the software, services, and caregiver usage and benefits of the system in a variety of caregiving situations. The participants in this study are distance caregivers of persons with early- to moderate-stage AD who had the AttentiveCare system installed in their own homes and the homes of their family members with AD.

AttentiveCare now features videoconferencing, multimedia reminders to help care recipients function independently, and slide shows to keep care recipients connected with family. The system’s journal and data logging capability also allows family caregivers to maintain and share information about the care recipient’s health and well-being, whether they are across the street or thousands of miles away. ●

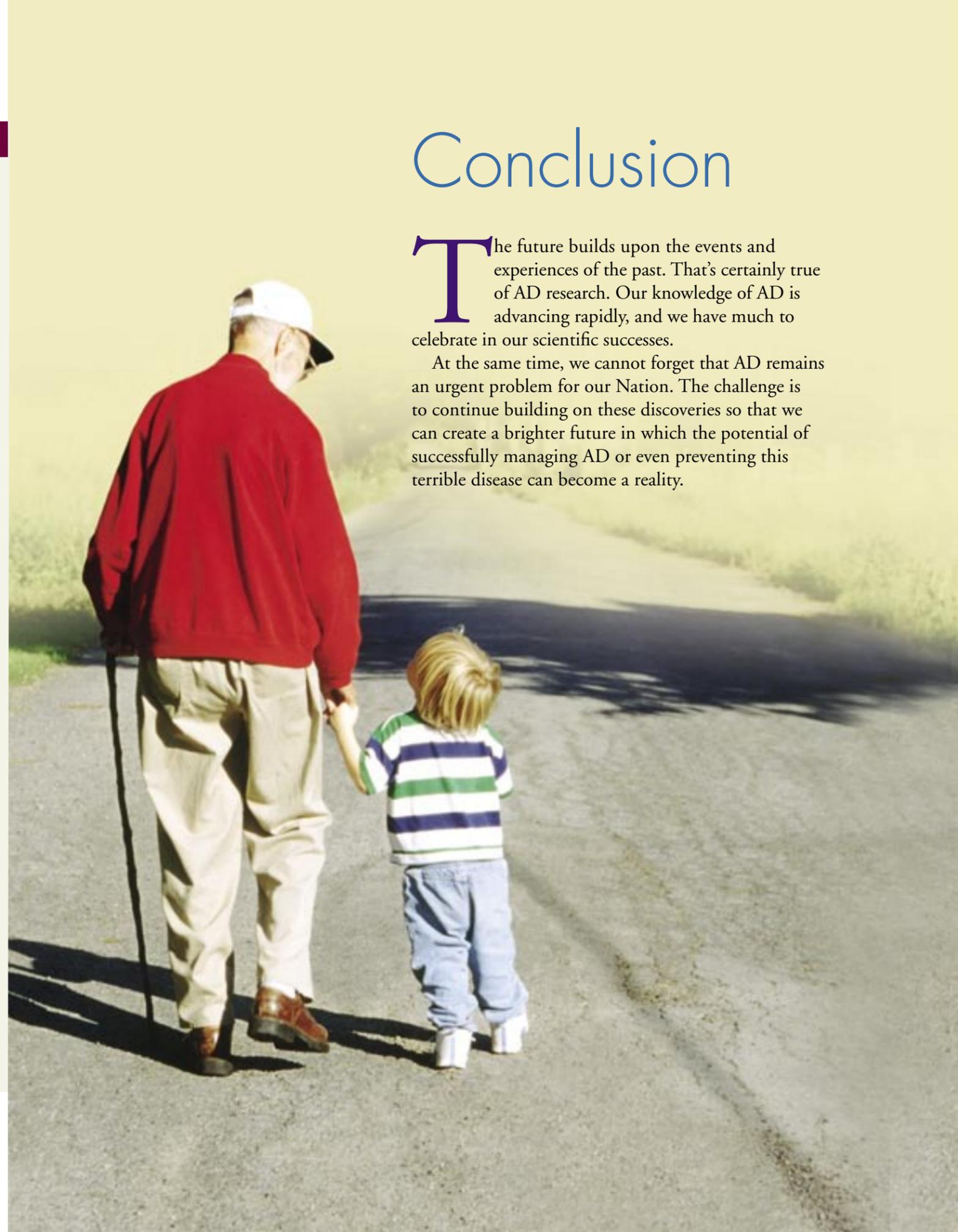


Ken Nixon and his grandson use AttentiveCare to check in with Ken’s mother.

## Conclusion

The future builds upon the events and experiences of the past. That’s certainly true of AD research. Our knowledge of AD is advancing rapidly, and we have much to celebrate in our scientific successes.

At the same time, we cannot forget that AD remains an urgent problem for our Nation. The challenge is to continue building on these discoveries so that we can create a brighter future in which the potential of successfully managing AD or even preventing this terrible disease can become a reality.



# Glossary

**Acetylcholine**—a neurotransmitter that plays an important role in many neurological functions, including learning and memory.

**Amygdala**—an almond-shaped structure involved in processing and remembering strong emotions such as fear. It is part of the limbic system and located deep inside the brain.

**Amyloid plaque**—a largely insoluble deposit found in the space between nerve cells in the brain. Plaques are made of beta-amyloid, other molecules, and different kinds of nerve and non-nerve cells.

**Amyloid precursor protein (APP)**—the larger protein from which beta-amyloid is formed.

**Apolipoprotein E**—a protein that carries cholesterol in blood and that appears to play some role in brain function. The gene that produces this protein comes in several forms, or alleles: ε2, ε3, and ε4. The APOE ε2 allele is relatively rare and may provide some protection against AD (but it may increase risk of early heart disease). APOE ε3 is the most common allele and appears to play a neutral role in AD. APOE ε4 occurs in about 40 percent of all people with AD who develop the disease in later life; it increases the risk of developing AD.

**Axon**—the long extension from a neuron that transmits outgoing signals to other cells.

**Beta-amyloid**—a part of the amyloid precursor protein found in plaques, the insoluble deposits outside neurons.

**Brain-derived neurotrophic factor (BDNF)**—a growth factor that stimulates survival, growth, and adaptability of some neurons.

**Brain stem**—the portion of the brain that connects to the spinal cord and controls automatic body functions, such as breathing, heart rate, and blood pressure.

**Capillary**—a tiny blood vessel. The brain has billions of capillaries that carry oxygen, glucose (the brain's principal source of energy), nutrients, and hormones to brain cells so they can do their work. Capillaries also carry away carbon dioxide and cell waste products.

**Cerebellum**—the part of the brain responsible for maintaining the body's balance and coordination.

**Cerebral cortex**—the outer layer of nerve cells surrounding the cerebral hemispheres.

**Cerebral hemispheres**—the largest portion of the brain, composed of billions of nerve cells in two structures connected by the corpus callosum. The cerebral hemispheres control conscious thought, language, decision making, emotions, movement, and sensory functions.

**Cerebrospinal fluid**—the fluid found in and around the brain and spinal cord. It protects these organs by acting like a liquid cushion and by providing nutrients.

**Chromosome**—a threadlike structure in the nucleus of a cell that contains DNA. DNA sequences make up genes. Most human cells have 23 pairs of chromosomes containing approximately 30,000 genes.

**Clinical trial**—a research study involving humans that rigorously tests safety, side effects, and how well a medication or behavioral treatment works.

**Cognitive functions**—all aspects of conscious thought and mental activity, including learning, perceiving, making decisions, and remembering.

**Computed tomography (CT) scan**—a diagnostic procedure that uses special x-ray equipment and computers to create cross-sectional pictures of the body.

**Corpus callosum**—thick bundles of nerve cell fibers that connect the two cerebral hemispheres.

**Dementia**—a broad term referring to a decline in cognitive function to the extent that it interferes with daily life and activities.

**Dendrite**—a branch-like extension of a neuron that receives messages from other neurons.

**DNA (deoxyribonucleic acid)**—a long, double-stranded molecule within the nucleus of the cell that forms chromosomes and genes.

**Early-onset Alzheimer's disease**—a rare form of AD that usually affects people between ages 30 and 60. It is called familial AD (FAD) if it runs in the family.

**Entorhinal cortex**—an area deep within the brain where damage from AD often begins.

**Enzyme**—a protein that causes or speeds up a biochemical reaction.

**Free radical**—a highly reactive molecule (typically oxygen or nitrogen) that combines easily with other molecules because it contains an unpaired electron. The combination with other molecules sometimes damages cells.

**Gene**—the biologic unit of heredity passed from parent to child. Genes are segments of DNA and contain instructions that tell a cell how to make specific proteins.

**Genetic risk factor**—a variant in a cell's DNA that does not cause a disease by itself but may increase the chance that a person will develop a disease.

**Glial cell**—a specialized cell that supports, protects, or nourishes nerve cells.

**Hippocampus**—a structure in the brain that plays a major role in learning and memory and is involved in converting short-term to long-term memory.

**Hypothalamus**—a structure in the brain under the thalamus that monitors activities such as body temperature and food intake.

**Late-onset Alzheimer’s disease**—the most common form of AD. It occurs in people aged 60 and older.

**Limbic system**—a brain region that links the brain stem with the higher reasoning elements of the cerebral cortex. It controls emotions, instinctive behavior, and the sense of smell.

**Magnetic resonance imaging (MRI)**—a diagnostic and research technique that uses magnetic fields to generate a computer image of internal structures in the body. MRIs are very clear and are particularly good for imaging the brain and soft tissues.

**Metabolism**—all of the chemical processes that take place inside the body. In some metabolic reactions, complex molecules are broken down to

release energy. In others, the cells use energy to make complex compounds out of simpler ones (like making proteins from amino acids).

**Microtubule**—an internal support structure for a neuron that guides nutrients and molecules from the body of the cell to the end of the axon.

**Mild cognitive impairment (MCI)**—a condition in which a person has memory problems greater than those expected for his or her age, but not the personality or cognitive problems that characterize AD.

**Mutation**—a permanent change in a cell’s DNA that can cause a disease.

**Myelin**—a whitish, fatty layer surrounding an axon that helps the axon rapidly transmit electrical messages from the cell body to the synapse.

**Nerve growth factor (NGF)**—a substance that maintains the health of nerve cells. NGF also promotes the growth of axons and dendrites, the parts of the nerve cell that are essential to its ability to communicate with other nerve cells.

**Neurodegenerative disease**—a disease characterized by a progressive decline in the structure, activity, and function of brain tissue. These diseases include AD, Parkinson’s disease, frontotemporal lobar degeneration, and dementia with Lewy bodies. They are usually more common in older people.

**Neurofibrillary tangle**—a filamentous collection of twisted and hyperphosphorylated *tau* found in the cell body of a neuron in AD.

**Neuron**—a nerve cell.

**Neurotransmitter**—a chemical messenger between neurons. These substances are released by the axon on one neuron and excite or inhibit activity in a neighboring neuron.

**Nucleus**—the structure within a cell that contains the chromosomes and controls many of its activities.

**Oxidative damage**—damage that can occur to cells when they are exposed to too many free radicals.

**Positron emission tomography (PET)**—an imaging technique using radioisotopes that allows researchers to observe and measure activity in different parts of the brain by monitoring blood flow and concentrations of substances such as oxygen and glucose, as well as other specific constituents of brain tissues.

**Single photon emission computed tomography (SPECT)**—an imaging technique that allows researchers to monitor blood flow to different parts of the brain.

**Synapse**—the tiny gap between nerve cells across which neurotransmitters pass.

**Tau**—a protein that helps to maintain the structure of microtubules in normal nerve cells. Abnormal *tau* is a principal component of the paired helical filaments in neurofibrillary tangles.

**Thalamus**—a small structure in the front of the cerebral hemispheres that serves as a way station that receives sensory information of all kinds and relays it to the cortex; it also receives information from the cortex.

**Transgenic**—an animal that has had a gene (like human APP) inserted into its chromosomes. Mice carrying the mutated human APP gene often develop plaques in their brains as they age.

**Ventricle**—a cavity within the brain that is filled with cerebrospinal fluid.

**Vesicle**—a small container for transporting neurotransmitters and other molecules from one part of the neuron to another.

# For *More* Information

## **INFORMATION AND SUPPORT RESOURCES**

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

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

This service of the National Institute on Aging (NIA) offers information and publications on diagnosis, treatment, patient care, caregiver needs, long-term care, education and training, and research related to Alzheimer's disease. Staff members answer telephone, email, and written requests and make referrals to local and national resources. The ADEAR website offers free, online publications in English and Spanish; email alerts and online *Connections* newsletter registration; an AD clinical trials database; the AD Library database; and more.

### **Alzheimer's Association**

225 North Michigan Avenue, Suite 1700  
Chicago, IL 60601-7633  
800-272-3900 (toll-free)  
[www.alz.org](http://www.alz.org)

The Alzheimer's Association is a national, non-profit organization with a network of local chapters that provide education and support for people diagnosed with AD, their families, and caregivers. Chapters offer

referrals to local resources and services and sponsor support groups and educational programs. Online and print publications are also available. The Association also funds AD research.

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

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

The Alzheimer's Foundation of America provides care and services to individuals confronting dementia and to their caregivers and families, through member organizations dedicated to improving quality of life. Services include a toll-free hotline, consumer publications and other educational materials, and conferences and workshops.

### **Dana Alliance for Brain Initiatives**

745 Fifth Avenue, Suite 900  
New York, NY 10151  
212-223-4040  
[www.dana.org/danaalliances](http://www.dana.org/danaalliances)

The Dana Alliance for Brain Initiatives, a non-profit organization of more than 265 leading neuroscientists, helps advance public awareness about the progress and promise of brain research and disseminates information about the brain.

## **CAREGIVING SUPPORT AND SERVICES**

### **Children of Aging Parents**

P.O. Box 167  
Richboro, PA 18954-0167  
800-227-7294 (toll-free)  
[www.caps4caregivers.org](http://www.caps4caregivers.org)

This nonprofit organization provides information and referrals for nursing homes, retirement communities, elder-law attorneys, adult day-care centers, insurance providers, respite care, assisted living centers, support groups, and State and county agencies. It also offers fact sheets, a newsletter, and conferences and workshops.

### **Eldercare Locator**

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

Eldercare Locator is a nationwide, directory-assistance service helping older people and their caregivers locate local support and resources. It is funded by the U.S. Administration on Aging, whose website at [www.aoa.gov](http://www.aoa.gov) also features AD information for families, caregivers, and health professionals.

### **Family Caregiver Alliance**

180 Montgomery Street, Suite 1100  
San Francisco, CA 94104  
800-445-8106 (toll-free)  
[www.caregiver.org](http://www.caregiver.org)

The Family Caregiver Alliance is a nonprofit organization that offers support services and information for people caring for adults with AD, stroke, traumatic brain injuries, and other cognitive disorders.

### **National Family Caregivers Association**

10400 Connecticut Avenue, Suite 500  
Kensington, MD 20895-3944  
800-896-3650 (toll-free)  
301-942-6430  
[www.thefamilycaregiver.org](http://www.thefamilycaregiver.org)

The National Family Caregivers Association helps educate and support people who care for loved ones with chronic illness, disability, or the frailties of old age. The Association offers an online library of information and educational materials, workshops, and other resources.

### **National Hospice and Palliative Care Organization**

1700 Diagonal Road, Suite 625  
Alexandria, VA 22314  
800-658-8898 (toll-free)  
[www.nhpco.org](http://www.nhpco.org)

This nonprofit organization works to enhance the quality of life for people who are terminally ill. It provides information, resources, and referrals to local hospice services, and offers publications and online resources.

### **Well Spouse Association**

63 West Main Street, Suite H  
Freehold, NJ 07728  
800-838-0879 (toll-free)  
[www.wellspouse.org](http://www.wellspouse.org)

The nonprofit Well Spouse Association gives support to spouses and partners of people who are chronically ill and/or disabled. It offers support groups and a newsletter.

## RESEARCH AND CLINICAL TRIALS

### Alzheimer's Disease Cooperative Study

University of California, San Diego  
9500 Gilman Drive  
La Jolla, CA 92093-0949  
858-622-5880  
[www.adcs.org](http://www.adcs.org)

The Alzheimer's Disease Cooperative Study (ADCS) is a cooperative agreement between NIA and the University of California, San Diego, to advance research in the development of drugs to treat AD. The ADCS is a consortium of medical research centers and clinics working to develop clinical trials of medicines to treat behavioral symptoms of AD, improve cognition, slow the rate of decline caused by AD, delay the onset of AD, or prevent the disease altogether. The ADCS also develops new and more reliable ways to evaluate patients enrolled in clinical trials.

### Alzheimer Research Forum

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

The Alzheimer Research Forum, an online community and resource center, offers professionals and the general public access to an annotated index of scientific papers, research news, moderated discussions on scientific topics, libraries of animal models and antibodies, and directories of clinical trials, conferences, jobs, and research-funding sources.

### ClinicalTrials.gov

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

ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world. Users can search for clinical trials and find information about each trial's purpose, who may participate, locations, and phone numbers for more details.

## RECOMMENDED READING

The ADEAR Center offers fact sheets; easy-to-read materials; booklets about topics such as being diagnosed with early-stage AD, caregiving, home safety, and comfort and care at the end of life; and more. See the ADEAR Center listing under "Information and Support Resources" above for contact information.

*Consumers and professionals interested in AD also may wish to refer to the following materials:*

Ballard, E.L., & Poer, C.M. ***Lessons Learned: Shared Experiences in Coping.*** Durham, NC: The Duke Family Support Program, 1999. Available for \$7 from the ADEAR Center, P.O. Box 8250, Silver Spring, MD 20907-8250; 800-438-4380; [www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers). This book documents the experiences of people caring for loved ones with AD. Filled with short stories and advice, it is intended for caregivers who wish to take comfort and learn from the experiences of others. Caregivers discuss the caregiving process, such as getting a diagnosis, finding support services, making decisions about treatment and living arrangements, and coping with stress and caregiver burden.

Dash, P., & Villemarette-Pittman, N. ***Alzheimer's Disease.*** New York: American Academy of Neurology, 2005.

This concise volume provides an overview of recent findings regarding the causes, diagnosis, and treatment of AD. It is designed to help caregivers and family members gain a better understanding

of AD and the available options for coping with and managing this illness. Sixteen chapters answer questions about topics such as the definition of AD and dementia, AD versus other causes of dementia, treatments for behavioral symptoms and other complications of AD, and practical issues for the patient and family. Illustrations, a glossary, and a list of resources are also included.

Doraiswamy, P.M., & Gwyther, L., with Adler, T. ***The Alzheimer's Action Plan: The Experts' Guide to the Best Diagnosis and Treatment for Memory Problems.*** New York: St. Martin's Press, 2008.

This book, by a physician and social worker at Duke University, offers information about how to get an early and accurate AD diagnosis and why it matters, life after the diagnosis, state-of-the-art treatments, coping with behavioral and emotional changes through the early and middle stages of AD, accessing the latest clinical trials, and understanding the future of AD.

Kuhn, D., & Bennett, D.A. ***Alzheimer's Early Stages: First Steps for Family, Friends and Caregivers,*** 2nd ed. Alameda, CA: Hunter House Publishers, 2003.

With increased awareness of the symptoms of AD and improved diagnostic techniques, more people are learning that they or a family member have a memory disorder. This book, written by experts at Rush University Alzheimer's Disease Center in Chicago, helps readers understand and find ways to cope with the early stages of the disease. It also includes an extensive resource list of websites, organizations, and references to consumer and professional literature.

Mace, N.L., & Rabins, P.V. ***The 36-Hour Day: A Family Guide to Caring for People With Alzheimer's Disease, Other Dementias, and Memory Loss in Later Life,*** 4th ed. Baltimore: Johns Hopkins University Press, 2006.

This book offers guidance and comfort for families caring for loved ones with AD, other dementias, and memory loss in later life. The fourth edition includes chapters on topics such as getting medical help for the person with dementia, behavioral symptoms of dementia, nursing homes and other living arrangements, and research in dementia. New information discusses diagnostic evaluation, caregiver resources, legal and financial information, nursing homes and other communal living arrangements, and the latest updates on research, medications, and the biological causes and effects of dementia. Available in a large-print version.

Messer, M. ***Pressure Points: Alzheimer's and Anger.*** Durham, NC: Duke Family Support Program, 2000. Available for \$12.50 from the ADEAR Center, P.O. Box 8250, Silver Spring, MD 20907-8250; 800-438-4380; [www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers).

In simple, easy-to-read language, this book addresses issues such as setting boundaries, managing anger positively, and risk factors for anger in AD care. It offers tangible action steps for responding appropriately, rather than abusively,

when feeling angry. Participants in Alzheimer's support groups share helpful techniques and coping mechanisms, as well as enlightening anecdotes about caring for a loved one with AD. Caregivers, family members of AD patients, clergy, and health professionals all may benefit from this publication. Two companion booklets are also available from the ADEAR Center: *"Hit Pause": Helping Dementia Families Deal with Anger* (for health professionals; \$3.00) and *Wait a Minute! When Anger Gets Too Much* (for families and caregivers; \$2.00).

Perry, G., ed., *Alzheimer's Disease: A Century of Scientific and Clinical Research*. *Journal of Alzheimer's Disease*, book edition, Fairfax, VA: IOS Press, Inc., 2006.

This volume brings together the important discoveries in the AD field since the disease's original description by Dr. Alois Alzheimer a century ago. It traces how the importance of AD as the major cause of late-life dementia came to light and narrates the evolution of the concepts related to AD throughout the years. Fifty papers are organized into sections on historical perspective, neuropathology, synaptic changes, amyloid, *tau*, disease mechanisms, genetics, and diagnosis and treatment.

Petersen, R., ed. *Mayo Clinic Guide to Alzheimer's Disease: The Essential Resource for Treatment, Coping and Caregiving*. Rochester, MN: Mayo Clinic Health Solutions, 2006.

This guide is designed to help nonprofessionals understand dementia and its effects on the mind, the differences between dementia and changes associated with normal aging, and how to improve memory and maintain good mental function. It includes information about changes that occur in normal aging; the process of diagnosing dementia; non-AD forms of dementia; how AD develops, and AD stages, diagnosis, and treatment. New information about mild cognitive impairment, ways to stay mentally sharp, and research trends, along with an action guide for caregivers, are also included.



Restak, R. *The Secret Life of the Brain*. Washington, DC: Joseph Henry Press, 2001.

This companion to the PBS documentary takes the reader on a fascinating journey through the developing brain, from infancy and childhood through adulthood and old age. The author examines brain disorders and mechanisms of brain repair and healing.

Shenk, D. *The Forgetting. Alzheimer's: Portrait of an Epidemic*. New York: Random House, Inc., 2003.

An eloquent and moving description of AD, *The Forgetting* is an exploration of, and meditation on, the nature of memory and perceptions of self. It is a readable, accessible description of the history of AD, research, and the human impact of the disease. Calling AD a "death by a thousand subtractions," the author describes the science of AD in clear and easy-to-understand terms.

Snowdon, D. *Aging With Grace: What the Nun Study Teaches Us About Leading Longer, Healthier, and More Meaningful Lives*. New York: Random House, Inc., 2002.

This book describes the participants and findings from the Nun Study, a long-term project examining aging and AD in a unique population of 678 Catholic sisters. The nuns gave Dr. Snowdon access to their medical and personal records and agreed to donate their brains upon death. The book discusses the relationship of early linguistic ability to risk of AD, the association of stroke and depression with AD, and the role of heredity and lifestyle in healthy aging.

Tanzi, R.E., & Sisodia, S.S. *Alzheimer's Disease: Advances in Genetics*, Molecular and Cellular Biology. New York: Springer Publishing Company, 2006.

This book examines every major aspect of AD—clinical, epidemiologic, structural, chemical, genetic, molecular, and therapeutic. This edition includes expanded coverage of related dementing disorders, including prion diseases, Pick's disease, frontotemporal disorders, an in-depth discussion of transgenic models, and the biochemistry of presenilins. It also discusses treatment of symptoms with therapeutic drugs and AD clinical trials. The broad coverage of AD in this book will be of special interest to clinicians, educators, investigators, and health administrators.

Uetz, D., & Lindsay, A. *Into the Mist: When Someone You Love Has Alzheimer's*. Philadelphia: Xlibris Corporation, 2005.

This book combines information from researchers, experts, and families in a comprehensive guide for AD caregivers. It offers personal accounts of three families caring for a loved one from the earliest stages to the last stages, illustrating the commonalities and differences among AD patients and the ways their families handle the most difficult challenges. It also provides information to help families cope with the psychological aspects of AD, behavior problems, and communication difficulties. The book covers such topics as the stages of AD, Medicare, Medicaid, long-term care insurance, geriatric care management, the diagnosis of AD, causes and prevention, and drug treatments.

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For additional copies of this report or further information about Alzheimer's disease, please contact:

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

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# Can Alzheimer's Disease Be Prevented?



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## **Introduction**

Newspapers, magazines, the Internet, and TV seem to be full of stories about ways to stay healthy, eat right, and keep fit. Many people are concerned about staying healthy as they get older. Along with keeping their bodies healthy, they want to keep their minds sharp. They also want to avoid brain diseases, such as Alzheimer's disease (AD), that occur more often in older people than in younger people.

Currently, AD has no known cure, but the results of recent research are raising hopes that someday it might be possible to delay the onset of AD, slow its progress, or even prevent it altogether. Delaying by even 5 years the time when AD symptoms begin could greatly reduce the number of people who have this devastating disease. The National Institute on Aging (NIA), part of the National Institutes of Health at the U.S. Department of Health and Human Services; other Government agencies; and private-sector groups support research that takes many different approaches to studying how to prevent or delay the disease.

## **Can We Prevent Complex Diseases Like AD?**

Many diseases, such as diabetes, heart disease, and arthritis, are complex. They develop when genetic, environmental, and lifestyle factors interact to cause disease and/or make it worse. The importance of these factors may be different for different people.

AD is one of these complex diseases. It develops over many years and appears to be affected by a number of factors that may increase or decrease a person's chances of developing the disease. These factors include genetic makeup, environment, life history, and current lifestyle. We can't control some of these risk factors, but we can control others.



# AD Risk Factors We Can't Control

## Age

Age is the most important known risk factor for AD. The risk of developing the disease doubles every 5 years after age 65. Several studies estimate that up to half of all people older than 85 have AD. These facts are significant because of the growing number of people 65 and older. A 2005 Census report estimates that the number of Americans 65 and older will more than double to about 72 million by 2030. Even more significant, the group with the highest risk of AD—those older than 85—is the fastest growing age group in the United States.

## Genetics

Genetic risk is another factor that a person can't control. Scientists have found genetic links to the two forms of AD—early-onset and late-onset.

Early-onset AD is a rare form of the disease, affecting only about 5 percent of all people who have AD. It develops in people ages 30 to 60. In the 1980s and early 1990s, researchers found that mutations (permanent abnormal changes) in certain genes cause most cases of early-onset AD. If a parent has any of these genetic mutations, his or her child has a 50-50 chance of inheriting the mutated gene and developing early-onset AD.

Late-onset AD, the much more common form of the disease, develops after age 60. In 1992, researchers found that three forms, or alleles ( $\epsilon$ ), of a gene called apolipoprotein E (APOE) can influence the risk of late-onset AD:

- APOE  $\epsilon$ 2, a rarely occurring form, may provide some protection against AD.
- APOE  $\epsilon$ 3, the most common form, plays a neutral role, neither increasing nor decreasing risk.

- APOE  $\epsilon$ 4, which occurs in about 40 percent of all people who develop late-onset AD and is present in about 25 to 30 percent of the population, increases risk by lowering the age of onset. Having this allele does not mean that a person will definitely develop AD; it only increases risk. Many people who develop AD do not have an APOE  $\epsilon$ 4 allele.

Researchers think that at least half a dozen other risk-factor genes exist for late-onset AD and are intensively searching for them. In 2007, they found another likely risk-factor gene called SORL1. When this gene is active at low levels or in an abnormal form, levels of harmful beta-amyloid increase in the brain. Beta-amyloid is a component of amyloid plaques, one of the hallmarks of AD. Interestingly, the SORL1 gene also was identified as a risk-factor gene for certain aspects of cognitive decline, suggesting that cognitive decline and AD may share at least one predisposing genetic factor.

### To Learn More

For more information about AD and AD genetics, visit the Alzheimer's Disease Education and Referral (ADEAR) Center website at [www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers). The ADEAR Center offers free publications, such as the *Alzheimer's Disease Fact Sheet*, the *Alzheimer's Disease Genetics Fact Sheet*, and *Alzheimer's Disease: Unraveling the Mystery*.

Finding AD risk-factor genes is essential for understanding the very early biological steps that lead to the vast majority of AD cases and for developing drugs and other prevention and treatment strategies. Finding these genes also will help scientists develop better ways to identify people at risk of AD and determine how the genes may interact with other genes or with lifestyle or environmental factors to affect an individual's AD risk.

# The Search for AD Prevention Strategies

We can't do much about our age or genetic profile, but scientists are working hard to understand a variety of other factors that may be involved in the disease. Some scientists are examining the biological bases for AD. This research might lead to the development of drugs that could protect against or block biological processes leading to cognitive decline and AD.

Other scientists are studying health, lifestyle, and environmental factors—such as exercise and diet or the control of chronic diseases like diabetes—that may play a role in preventing or slowing AD or cognitive decline. Recent research suggests that maintaining good overall health habits may help lower our chances of developing several serious diseases, including brain diseases such as AD. This area is of particular interest because it appears that there may be things that individuals can do themselves to hold off AD.

Several of these potential factors have been identified in animal studies and in epidemiologic studies (studies that compare the lifestyles, behaviors, and characteristics of groups of people). At present, these factors are only *associated* with changes in AD risk. Further research, especially clinical trials, will be needed to determine cause-and-effect—whether these factors really do help prevent cognitive decline or AD directly.

## Understanding Scientific Findings in the News

It can be hard to know what to conclude about scientific study findings. Knowing how the study was conducted can help put the results into the right perspective.

One main type of research is the *epidemiologic study*. These studies are observational—they gather information about people who are going about their daily lives. Study participants follow many behaviors and practices. It is difficult, therefore, to determine the exact benefits or risks of one particular behavior from among all the healthy or harmful things that may happen to participants or that they do. That is why, in epidemiologic studies of AD, scientists will say that a finding is “associated with” AD, or not. The epidemiologic evidence linking a behavior and AD is, at best, suggestive, but we do not know that the behavior by itself actually helps to cause or prevent AD.

Other types of research—test-tube studies and studies in animals—add to the findings from epidemiologic studies. Scientists sometimes use these studies to control factors that might otherwise influence a research result. Controlling specific factors allows scientists to be more certain about why they get the results they do. It also allows them to describe their results more precisely. Of course, showing a cause-and-effect relationship in tissue samples or even in animal studies does not mean that the relationship will be the same in humans.

*Clinical trials*—research studies in humans that rigorously test safety, side effects, and how well a medication or behavioral treatment works—are the gold standard for research. Clinical trials are used to determine whether a specific medication, device, or treatment actually prevents or delays AD.

## Assessing Physical Activity

Accumulating evidence suggests that physical activity may be good for our brains as well as our hearts, waistlines, and ability to carry out activities of daily living. Epidemiologic studies have found associations between physical activity and improved cognitive skills or reduced AD risk. For example, investigators looked at the relationship of physical activity and AD risk in about 1,700 adults aged 65 years and older over a 6-year period. They found that the risk of AD was 35 to 40 percent lower in those who exercised for at least 15 minutes 3 or more times a week than in those who exercised fewer than 3 times a week.

Scientists have sought to confirm these associations in animal studies, hoping to clarify why physical activity might be related to reduced risk of cognitive decline and AD. For example, studies in older rats and mice have found that exercise increases the number of small blood vessels that supply blood to the brain and increases the number of connections between nerve cells. Other research has shown exercise to raise the level of specific brain-growth factors in an area of the brain that is particularly important to memory and learning.

Both epidemiologic and animal studies point to associations and help to explain them. However, epidemiologic studies can't tell us whether a true cause-and-effect relationship exists between a particular factor and AD risk. For example, people who exercise tend to be healthier in other ways, such as having decreased rates of heart disease or diabetes. They may also have healthier lifestyles, such as eating a nutritious diet. This means that even if people who exercise are less likely to develop AD, we don't know whether this is due to the exercise or the more healthful eating or other lifestyle differences that distinguish them from inactive people.



Likewise, animal studies can't tell us whether an intervention will definitely work in humans. That's why investigators conduct clinical trials—controlled studies involving humans. Clinical trials are the most reliable method for showing whether intervention strategies really can work to prevent or treat AD in people. This is because clinical trial participants are randomly assigned to receive or not receive a treatment (for example, exercise). Therefore, any differences between the groups should be due to the exercise program rather than other differences between the groups.

NIA supports clinical trials related to exercise and cognitive function. One completed trial used functional magnetic resonance imaging (MRI) tests to measure changes in brain activity in older adults before and after a 6-month program of brisk walking. Results showed that brain activity increased in specific brain regions as the participants' cardiovascular fitness increased. A similar study showed that brain volume increased as a result of a walking program.

These findings strongly suggest a biological basis for the role of aerobic fitness in helping to maintain the health and cognitive functioning of adults as they age, at least in the short term. Currently, a trial is underway to look at the effects of a 1-year aerobic fitness training program on cognition and brain activity and structure in older adults. Other NIA-supported research is examining whether exercise can delay the development of AD in people with mild cognitive impairment (MCI).



## Exploring Dietary Factors

A number of studies suggest that how we eat may be linked to our risk of developing—or not developing—AD. This is another important area of current AD research. A nutritious diet—a diet that includes lots of fruits, vegetables, and whole grains and is low in fat and added sugar—can reduce the risk of many chronic diseases, including heart disease, type 2 diabetes, and obesity. Animal studies, epidemiologic studies, and clinical trials are looking at whether a healthy diet also can help preserve cognitive function or even reduce AD risk.

Studies have examined foods that are rich in antioxidants and anti-inflammatory components to find out whether those foods affect age-related changes in the brain. One study found that curcumin, the main ingredient of turmeric (a spice used in curry), can suppress the build-up of harmful beta-amyloid in the brains of rodents. Another study, in AD transgenic mice (those that are specially bred to have features of AD), found that DHA (docosahexaenoic acid, a type of omega-3 fatty acid found in some fish) reduced the presence of beta-amyloid and plaques. Other research has shown that older dogs perform better on learning tasks when they eat a diet rich in antioxidants and live in an “enriched” environment with many opportunities to play and interact with others.

In addition, studies in rats and mice have shown that dietary supplementation with blueberries, strawberries, and cranberries can improve cognitive function, both during normal aging and in animals that have been bred to develop AD. Scientists are beginning to identify some of the chemicals responsible for these berries’ beneficial effects and think that the chemicals may act by neutralizing free radicals. This may reduce inflammation or stimulate neurons to protect themselves better against some of the adversities of aging and AD.

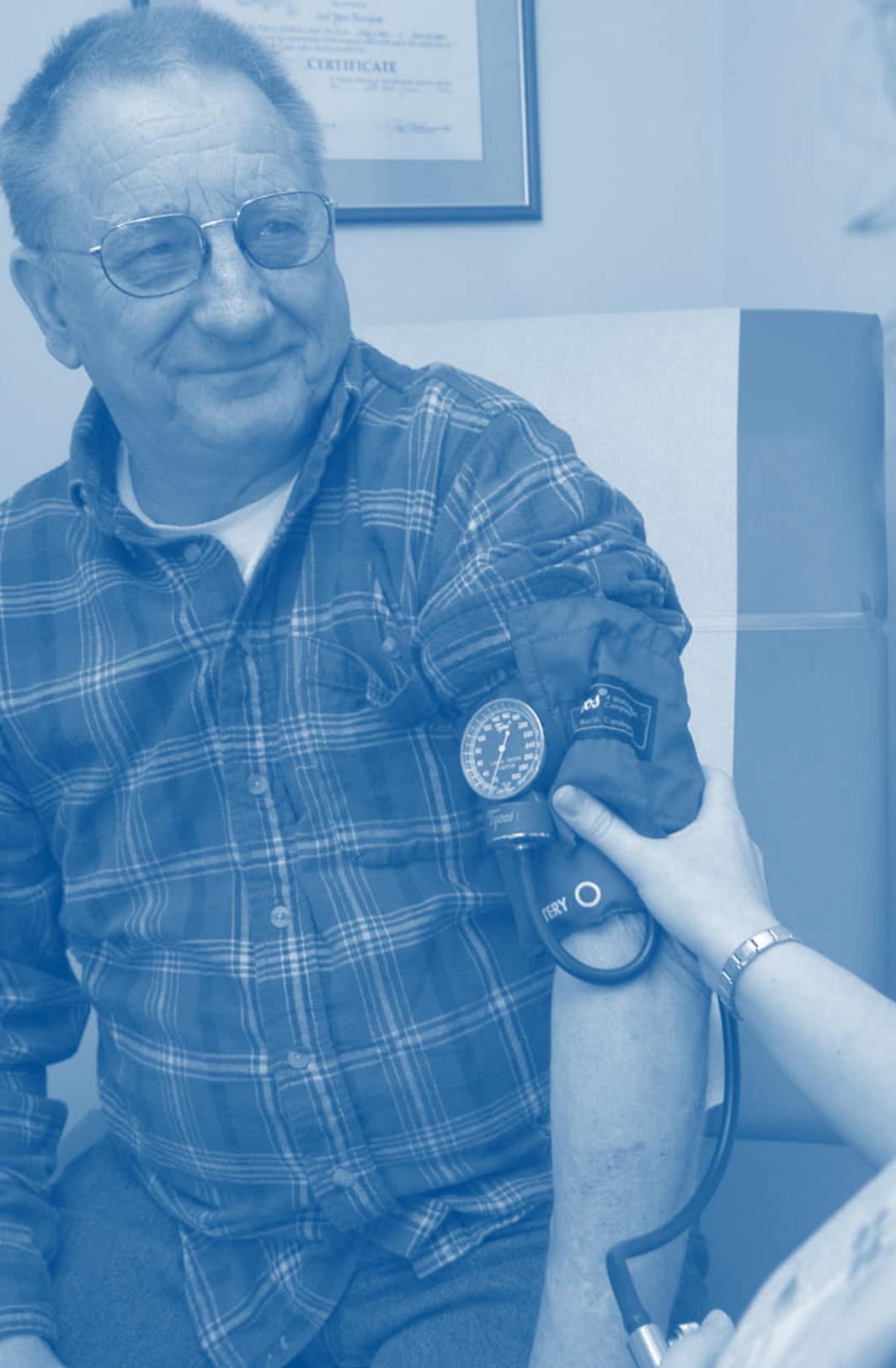
Several epidemiologic studies have shown an association between eating a diet rich in vegetables (especially green leafy vegetables and cruciferous vegetables like broccoli) and a reduced rate of cognitive decline. Researchers speculate that the beneficial effect may come from the antioxidant and folate content of the vegetables.

These results are interesting, but in their normal daily lives, people typically consume many different foods and nutrients. With this in mind, some investigators have conducted epidemiologic studies to examine a group's entire dietary pattern. One of these studies showed a reduced risk of AD in those who ate the "Mediterranean diet"—a diet that includes many fruits, vegetables, and beans; moderate amounts of fish; low-to-moderate amounts of dairy foods; small amounts of meat and poultry; regular but moderate amounts of wine; and olive oil.

These kinds of findings are exciting and suggestive, but they are not definitive. To confirm them, NIA is supporting several clinical trials to examine the relationship between specific dietary components and cognitive decline and AD.

### **Investigating Chronic Diseases**

For some years now, scientists have been finding clues that damage to the vascular system (the body's vast system of large and small blood vessels) may contribute to the development of AD or affect its severity. Several common chronic diseases that affect older people, including heart disease, stroke, and type 2 diabetes, also affect the body's vascular system and have been tied to declines in cognitive function or increased AD risk. In addition, heart disease, high blood pressure, and diabetes to a large extent can be modified by diet, exercise, and other lifestyle changes. Therefore, scientists are keenly interested in learning whether reducing the risks of or controlling these conditions through lifestyle changes also may reduce the risks of cognitive decline or AD.





Much of the evidence so far about possible relationships between vascular diseases and cognitive decline or AD risk comes from epidemiologic studies. To clarify and build on these findings, scientists have conducted a variety of studies, including test tube, animal, and additional epidemiologic studies. NIA is supporting several clinical trials, including a trial to test the effect of lowering blood pressure and blood cholesterol levels on cognition in people with diabetes. Several other trials are examining whether intensive diabetes treatment can reduce cognitive decline. Researchers are also looking at increased stiffness of blood vessels with age as another potential treatment target.

### **Examining Social Engagement and Intellectually Stimulating Activities**

Observations of nursing home residents and older people living in the community have suggested a link between social engagement and cognitive abilities. Having many friends and acquaintances and participating in many social activities also is associated with reduced cognitive decline and decreased risk of dementia in older adults. For example, the NIA-funded Chicago Health and Aging Project showed that more social networks and a higher level of social engagement were associated with a higher level of cognitive function at the beginning of the study. These factors also were related to a reduced rate of cognitive decline over time.

Studies have also shown that keeping the brain active is associated with reduced AD risk. In the Religious Orders Study, for example, investigators periodically asked more than 700 participants—older nuns, priests, and religious brothers—to describe the amount of time they spent in seven information-processing activities. These activities included listening to the radio, reading newspapers, playing puzzle games, and going to museums. After following the participants for 4 years, the investigators

found that the risk of developing AD was 47 percent lower, on average, for those who did the activities most often than for those who did them least frequently.

Other studies have shown similar results. In addition, a growing body of research suggests that, even in the presence of AD plaques, the more formal education a person has, the better his or her memory and learning abilities.

Another NIA-funded study supports the value of lifelong learning and mentally stimulating activity. It showed that during early and middle adulthood, cognitively healthy older people had engaged in more mentally stimulating activities and spent more hours doing them than did those who ultimately developed AD. Other studies have shown that people who are bilingual or multilingual seem to develop AD at a later age than do people who only speak one language.

The reasons for this apparent link between social engagement or intellectual stimulation and AD risk aren't entirely clear, but scientists suggest four possibilities:

- Such activities may protect the brain in some way, perhaps by establishing “cognitive reserve.” (Cognitive reserve is the brain’s ability to operate effectively even when some function is disrupted or the amount of damage that the brain can sustain before changes in cognition are evident.)
- These activities may help the brain become more adaptable and flexible in some areas of mental function so that it can compensate for declines in other areas.
- People who engage in these activities may have other lifestyle factors that protect them against developing AD.
- Less engagement with other people or in intellectually stimulating activities could be the result of very early effects of the disease rather than its cause.





The only way to really evaluate some of these possibilities is to test them in a controlled way in clinical trials. Several clinical trials have examined whether memory training and similar types of mental skills training can actually improve the cognitive abilities of healthy older adults and people with mild AD. In the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trial, for example, certified trainers provided 10 sessions of memory training, reasoning training, or processing-speed training to healthy adults 65 years old and older. The sessions improved participants' mental skills in the area in which they were trained. Even better, these improvements persisted for up to 5 years after the training was completed.

### **The Cognitive and Emotional Health Project**

The National Institute on Aging (NIA) has primary responsibility for research on AD and age-related declines in mental skills (also called cognitive skills), such as remembering, learning, thinking, decision making, and language. This responsibility is part of a larger mission to understand the nature of aging and find ways to help people stay physically, emotionally, and cognitively healthy for as long as possible.

Several years ago, NIA, the National Institute of Mental Health, and the National Institute of Neurological Disorders and Stroke launched the Cognitive and Emotional Health Project (<http://trans.nih.gov/CEHP>). This project has begun to identify and describe what we know about the diverse factors that may affect the emotional health and cognitive abilities of adults. Research on the most promising factors is being carried out to determine whether any of them will result in strategies that can help people remain mentally and emotionally vibrant as they age. The hope is that successful strategies will also add to our knowledge about what can be done to reduce the likelihood of developing neurodegenerative diseases such as AD.

## **Other Clues to AD Prevention**

NIA's program of AD research continues to add to what we know about AD and yield clues about possible ways to prevent the disease. The following sections briefly describe a few other areas that scientists are exploring.

### **Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)**

Inflammation in the brain is a common feature of AD, but it is unclear whether this is a cause or an effect of the disease. Some epidemiologic studies suggest an association between a reduced risk of AD and commonly used nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, naproxen, and indomethacin. So far, clinical trials have not demonstrated a benefit for AD from these drugs or from the newer cyclooxygenase-2 (COX-2) inhibitors, such as rofecoxib and celecoxib. However, scientists continue to look for ways to test how other anti-inflammatory drugs might affect the development or progression of AD.

### **Antioxidants**

Damage during aging from highly active molecules called free radicals can build up in nerve cells and result in a loss of cell function, which could contribute to AD. Some population and laboratory studies suggest that antioxidants from dietary supplements or food may provide some protection against this damage (called oxidative damage), but other studies show no effect.

Clinical trials may provide some answers. Several current trials are investigating whether antioxidants, such as vitamins E and C, alpha-lipoic acid, and coenzyme Q, can slow cognitive decline and development of AD.

NIA-sponsored sub-studies to ongoing trials have looked at whether two treatments provide any protection against cognitive decline in women. One sub-study tested low-dose aspirin and antioxidant supplementation in healthy women, and the other tested antioxidant and folate supplements in women who already had heart disease. Initial results indicate that aspirin may provide some benefits for maintaining executive function but has no impact on other cognitive domains. For vitamin E, there was no overall benefit. Analysis of these studies is ongoing.

Another study added to a prostate cancer prevention trial is examining whether taking vitamin E and/or selenium supplements over a period of 7 to 12 years can help prevent memory loss and dementia. Although the primary trial was stopped because the supplements were shown not to prevent prostate cancer, researchers are continuing to follow participants to analyze longer term effects of the supplements.

The Memory Impairment Study compared the use of donepezil (Aricept®), vitamin E supplements, or placebo (an inactive substance) in participants with mild cognitive impairment (MCI) to see whether the drugs might delay or prevent progression to AD. People with MCI have more memory problems than normal for people their age, but their symptoms are not as severe as those with AD. More people with MCI, compared with those without MCI, go on to develop AD. The study found that taking vitamin E had no effect on progression to AD. It may be that this antioxidant did not help after memory declines had already started. Donepezil seemed to delay progression to AD during the first year of treatment; however, by the end of the 3-year study there was no benefit from the drug. The U.S. Food and Drug Administration (FDA) has not approved donepezil for treatment of MCI.



## Estrogen

The hormone estrogen is produced by a woman's ovaries during her childbearing years, and its production declines dramatically after menopause. Over the past 25 years, some laboratory and animal research, as well as observational studies in women, have suggested that estrogen may protect the brain. Experts have wondered whether taking estrogen supplements could reduce the risk of AD or slow disease progression.

A number of clinical trials have shown that estrogen does not slow the progression of already-diagnosed AD and is not effective in treating or preventing AD if treatment is begun in later life. For example, a large trial found that women older than 65 who took estrogen (Premarin®) alone or estrogen with a synthetic progestin (PremPro®) were actually at increased risk of developing dementia, including AD. However, some questions, such as whether other forms of estrogen or starting treatment nearer menopause might be more effective, remain unanswered. These questions are now being investigated in clinical trials.

Researchers also are probing estrogen's possible beneficial effects on the brain. For example, scientists have developed estrogen-like molecules called SERMs (selective estrogen-receptor modulators) that protect against bone loss and other consequences of estrogen loss after menopause. These molecules may retain estrogen's neuron-protecting ability but may not have some of its other harmful effects on the body, such as increasing the risk of uterine cancer. One large clinical trial showed that raloxifene, a SERM used to prevent and treat osteoporosis and to reduce the incidence of breast cancer in women at high risk for the disease, lowered the risk of MCI in a group of postmenopausal women with osteoporosis. Another clinical trial is testing whether raloxifene can slow the rate of AD progression.

## Immunization

Could a vaccine someday prevent AD? Early vaccine studies in mice were so successful in reducing deposits of beta-amyloid and improving brain performance on memory tests that investigators conducted preliminary clinical trials in humans with AD. These studies had to be stopped because life-threatening brain inflammation occurred in some participants. However, scientists are continuing to refine this strategy in animal models of AD, hoping to find ways of maintaining the vaccine's beneficial effects while reducing the unwanted side effects. Several pharmaceutical companies have obtained permission from the FDA to test several of these new vaccine strategies for safety in early-stage clinical trials.





## Other Areas of Research

The previous sections have described areas of research focused on finding ways to preserve cognitive function or prevent cognitive decline and AD. Other areas of research may seem to be less directly related to prevention, but their findings, too, may someday lead to successful prevention interventions. For example, studies at the cellular and molecular levels are revealing the wide range of processes that interfere with, or enhance, the function and survival of nerve cells in the brain. Scientists hope this knowledge will ultimately help them identify targets for AD prevention interventions.

Another area, AD translational research, is receiving much attention. This area of research allows knowledge from the laboratory to be applied as quickly as possible to potential new tests or interventions in clinical settings. NIA is pursuing a variety of translational studies to expand possible avenues for AD prevention and treatment strategies, and eventually, the number of clinical trials to test them in humans.

Testing AD prevention strategies involves recruiting healthy older adults into clinical trials, and NIA is studying various ways to make it easier for people to participate in this research. In one study, the Healthy Aging and Memory Study, investigators are examining whether new questionnaires and survey instruments that a person can complete at home are as effective as a traditional clinic evaluation at identifying cognitive change over time and determining when people develop MCI or AD. Another study is testing three home-based technologies that assess cognition, daily functioning, mood, and other factors over time. Findings from both studies will provide valuable information on how these techniques can be used in AD prevention trials and could significantly reduce the cost of conducting such trials and increase the number of people who participate.

## Technologies Help Scientists Develop Diagnostic Procedures

One important goal of AD research is to develop better diagnostic strategies for identifying individuals who are at high risk of developing the disease or who are at very early stages of the disease. For example, scientists are trying to discover whether changes in certain biological compounds present in blood, urine, or cerebrospinal fluid could indicate early AD changes in the brain. Understanding more about these biological markers, how they work, and what causes their levels to change is important in helping scientists answer questions about what initiates AD and how it develops. Learning more about these markers also may help scientists track whether certain medications are having their intended effects early in the course of the disease and may some day lead to new prevention strategies.

The use of imaging techniques, such as magnetic resonance imaging (MRI) and positron emission tomography (PET), to measure brain structure and function, is also showing promise in AD research. An NIA public-private partnership—the AD Neuroimaging Initiative—is a large nationwide study to determine whether MRI and PET scans or other imaging or biological markers can be used to measure changes in older participants who have MCI or AD or who are cognitively normal. The measurements may one day identify people early in the disease process and also help physicians assess the response to treatment much more rapidly and less expensively than is possible today.

## So, What Can You Do?

Our knowledge about AD is growing rapidly as scientists expand their understanding of the many factors involved in this devastating disease. Although no treatments or drugs have yet been proven to prevent or delay AD, people can take some actions that are beneficial for healthy aging and that also *might* reduce the effect of possible risk factors for AD. For example, you can:

- exercise regularly
- eat a healthy diet that is rich in fruits and vegetables
- engage in social and intellectually stimulating activities
- control type 2 diabetes
- lower high blood pressure levels
- lower high blood cholesterol levels
- maintain a healthy weight

These actions lower the risk of other diseases and help maintain and improve overall health and well-being. However, it is important to remember that they will not necessarily prevent or delay AD in any one person. Even if these actions were eventually proven effective, they might not offset a person's individual genetic and other risk factors enough to prevent the development of AD.

Whether you have memory problems or not, you can take one more important action—volunteer to participate in research. Participating in clinical trials is an effective way to help in the fight against AD. People who participate in these studies say that the biggest benefit is having regular contact with experts on AD who have lots of practical experience and a broad perspective on the disease. They also feel they are making a valuable contribution to future knowledge that will help scientists, people with AD, and their families.

People who are interested in joining an AD clinical trial can visit the website of the Alzheimer's Disease Education and Referral (ADEAR) Center, a service of the NIA, at [www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers) or call the ADEAR Center toll-free at 800-438-4380 for a referral to the nearest participating study site. Visit [www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials](http://www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials) for more about AD clinical trials.

Families interested in participating in the AD Genetics Study can call the National Cell Repository for Alzheimer's Disease (NCRAD) toll-free at 800-526-2839. Information is also available on the NCRAD website at [www.ncrad.org](http://www.ncrad.org).

## **A Final Word of Caution**

Because AD is such a devastating disease, caregivers and patients may be tempted by untried, unproven, and unscientific cures, supplements, or prevention strategies. Check with your doctor before trying pills or any other prescription or non-prescription treatment that promises to prevent AD. These purchases might be unsafe or a waste of money. They might even interfere with other medical treatments that have been prescribed.

## For More Information

Becoming well informed is another important step you can take to protect your health. Thousands of websites provide health-related information, including information on AD. Some of the information on these websites is reliable, but some is not. Health websites sponsored by the Federal Government are good sources of information, as are websites of large professional organizations and well-known medical schools. Some excellent Internet sources of AD and other health-related information for consumers are:

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

P.O. Box 8250  
Silver Spring, MD 20907-8250  
800-438-4380 (toll-free)  
*www.nia.nih.gov/Alzheimers*

A service of the National Institute on Aging (NIA), the ADEAR Center offers information and publications for families, caregivers, and professionals on diagnosis, treatment, patient care, caregiver needs, long-term care, education and training, and research related to AD. Staff members answer telephone, email, and written requests and make referrals to local and national resources.

The ADEAR website offers free, online publications in English and Spanish; email alert and online *Connections* newsletter subscriptions; an AD clinical trials database; the AD Library database; and more.

### **Alzheimer Research Forum**

*www.alzforum.org*

The Alzheimer Research Forum, an online community and resource center, offers professionals and the general public access to an annotated index of scientific papers, research news, moderated discussions on scientific topics, libraries of animal models and antibodies, and directories of clinical trials, conferences, jobs, and research-funding sources.

### **Alzheimer's Association**

225 North Michigan Avenue, Floor 17  
Chicago, IL 60601-7633  
800-272-3900 (toll-free)  
866-403-3073 (TDD/toll-free)  
*www.alz.org*

The Alzheimer's Association is a national, nonprofit organization with a network of local chapters that provide education and support for people diagnosed with AD, their families, and caregivers. The Association also funds research on AD.

### **Alzheimer's Disease Cooperative Study**

University of California, San Diego  
9500 Gilman Drive  
La Jolla, CA 92093-0949  
858-622-5880  
*www.adcs.org*

The Alzheimer's Disease Cooperative Study (ADCS) is a cooperative agreement between NIA and the University of California, San Diego, to advance research in the development of drugs to treat AD. The ADCS is a consortium of medical research centers and clinics working to develop clinical trials of medicines to treat behavioral symptoms of AD, improve cognition, slow the rate of decline caused by AD, delay the onset of AD, or prevent the disease altogether. The ADCS also develops new and more reliable ways to evaluate patients enrolled in clinical trials.

### **ClinicalTrials.gov**

*www.ClinicalTrials.gov*

ClinicalTrials.gov is a registry of federally and privately supported clinical trials conducted in the United States and around the world. Users can search for clinical trials and find information about each trial's purpose, who may participate, locations, and phone numbers for more details.

For additional copies of this publication or further information on Alzheimer's disease, please contact:

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

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

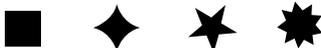
800-438-4380

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National Institutes of Health  
National Institute on Aging





U.S. DEPARTMENT OF HEALTH  
AND HUMAN SERVICES  
National Institutes of Health  
National Institute on Aging

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April 2009

# Caregiver Guide

Tips for Caregivers of People with  
Alzheimer's Disease

...from the National Institute on Aging



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## *Tips for Caregivers*

Caring for a person with Alzheimer's disease at home is a difficult task and can become overwhelming at times. Each day brings new challenges as the caregiver copes with changing levels of ability and new patterns of behavior. Research has shown that caregivers themselves often are at increased risk for depression and illness, especially if they do not receive adequate support from family, friends, and the community.

One of the biggest struggles caregivers face is dealing with the difficult behaviors of the person they are caring for. Dressing, bathing, eating—basic activities of daily living—often become difficult to manage for both the person with Alzheimer's and the caregiver. Having a plan for getting through the day can help caregivers cope. Many caregivers have found it helpful to use strategies for dealing with difficult behaviors and stressful situations. Through trial and error you will find that some of the following tips work, while others do not. Each person with Alzheimer's is unique and will respond differently, and each person changes over the course of the disease. Do the best you can, and remind yourself to take breaks.

## *Dealing with the Diagnosis*

Finding out that a loved one has Alzheimer's disease can be stressful, frightening, and overwhelming. As you begin to take stock of the situation, here are some tips that may help:

- Ask the doctor any questions you have about Alzheimer's disease. Find out what treatments might work best to alleviate symptoms or address behavior problems.
- Contact organizations such as the Alzheimer's Association and the Alzheimer's Disease Education and Referral (ADEAR) Center for more information about the disease, treatment options, and caregiving resources. Some community groups may offer classes to teach caregiving, problem-solving, and management skills. See page 20 for information on contacting the ADEAR Center and a variety of other helpful organizations.
- Find a support group where you can share your feelings and concerns. Members of support groups often have helpful ideas or know of useful resources based on their own experiences. Online support groups make it possible for caregivers to receive support without having to leave home. The Alzheimer's Association and other organizations sponsor support groups.
- Study your day to see if you can develop a routine that makes things go more smoothly. If there are times of day when the person with Alzheimer's is less confused or more cooperative, plan your routine to make the most of those moments. Keep in mind that the way the person functions may change from day to day, so try to be flexible and adapt your routine as needed.
- Consider using adult day care or respite services to ease the day-to-day demands of caregiving. These services allow you to have a break while knowing that the person with Alzheimer's is being well cared for.

- Begin to plan for the future. This may include getting financial and legal documents in order, investigating long-term care options, and determining what services are covered by health insurance and Medicare.

## *Communication*

Trying to communicate with a person who has Alzheimer's disease can be a challenge. Both understanding and being understood may be difficult.

- Choose simple words and short sentences and use a gentle, calm tone of voice.
- Avoid talking to the person with Alzheimer's like a baby or talking about the person as if he or she weren't there.
- Minimize distractions and noise—such as the television or radio—to help the person focus on what you are saying.
- Make eye contact and call the person by name, making sure you have his or her attention before speaking.
- Allow enough time for a response. Be careful not to interrupt.
- If the person with Alzheimer's is struggling to find a word or communicate a thought, gently try to provide the word he or she is looking for.
- Try to frame questions and instructions in a positive way.
- Be open to the person's concerns, even if he or she is hard to understand.

## **Bathing**

While some people with Alzheimer's disease don't mind bathing, for others it is a frightening, confusing experience. Advance planning can help make bath time better for both of you.

- Plan the bath or shower for the time of day when the person is most calm and agreeable. Be consistent. Try to develop a routine.
- Respect the fact that bathing is scary and uncomfortable for some people with Alzheimer's. Be gentle and respectful. Be patient and calm.
- Tell the person what you are going to do, step by step, and allow him or her to do as much as possible.
- Prepare in advance. Make sure you have everything you need ready and in the bathroom before beginning. Draw the bath ahead of time.
- Be sensitive to the temperature. Warm up the room beforehand if necessary and keep extra towels and a robe nearby. Test the water temperature before beginning the bath or shower.
- Minimize safety risks by using a handheld showerhead, shower bench, grab bars, and nonskid bath mats. Never leave the person alone in the bath or shower.
- Try a sponge bath. Bathing may not be necessary every day. A sponge bath can be effective between showers or baths.

## *Dressing*

For someone who has Alzheimer's, getting dressed presents a series of challenges: choosing what to wear, getting some clothes off and other clothes on, and struggling with buttons and zippers. Minimizing the challenges may make a difference.

- Try to have the person get dressed at the same time each day so he or she will come to expect it as part of the daily routine.
- Encourage the person to dress himself or herself to whatever degree possible. Plan to allow extra time so there is no pressure or rush.
- Allow the person to choose from a limited selection of outfits. If he or she has a favorite outfit, consider buying several identical sets.
- Store some clothes in another room to reduce the number of choices. Keep only one or two outfits in the closet or dresser.
- Arrange the clothes in the order they are to be put on to help the person move through the process.
- Hand the person one item at a time or give clear, step-by-step instructions if the person needs prompting.
- Choose clothing that is comfortable, easy to get on and off, and easy to care for. Elastic waists and Velcro<sup>®</sup> enclosures minimize struggles with buttons and zippers.

## *Eating*

Eating can be a challenge. Some people with Alzheimer's disease want to eat all the time, while others have to be encouraged to maintain a good diet.

- View mealtimes as opportunities for social interaction and success for the person with Alzheimer's. Try to be patient and avoid rushing, and be sensitive to confusion and anxiety.
- Aim for a quiet, calm, reassuring mealtime atmosphere by limiting noise and other distractions.
- Maintain familiar mealtime routines, but adapt to the person's changing needs.
- Give the person food choices, but limit the number of choices. Try to offer appealing foods that have familiar flavors, varied textures, and different colors.
- Serve small portions or several small meals throughout the day. Make healthy snacks, finger foods, and shakes available. In the earlier stages of dementia, be aware of the possibility of overeating.
- Choose dishes and eating tools that promote independence. If the person has trouble using utensils, use a bowl instead of a plate, or offer utensils with large or built-up handles. Use straws or cups with lids to make drinking easier.
- Encourage the person to drink plenty of fluids throughout the day to avoid dehydration.

- As the disease progresses, be aware of the increased risk of choking because of chewing and swallowing problems.
- Maintain routine dental checkups and daily oral health care to keep the mouth and teeth healthy.

## *Activities*

What to do all day? Finding activities that the person with Alzheimer's disease can do and is interested in can be a challenge. Building on current skills generally works better than trying to teach something new.

- Don't expect too much. Simple activities often are best, especially when they use current abilities.
- Help the person get started on an activity. Break the activity down into small steps and praise the person for each step he or she completes.
- Watch for signs of agitation or frustration with an activity. Gently help or distract the person to something else.
- Incorporate activities the person seems to enjoy into your daily routine and try to do them at a similar time each day.
- Try to include the person with Alzheimer's in the entire activity process. For instance, at mealtimes, encourage the person to help prepare the food, set the table, pull out the chairs, or put away the dishes. This can help maintain functional skills, enhance feelings of personal control, and make good use of time.

- Take advantage of adult day services, which provide various activities for the person with Alzheimer's, as well as an opportunity for caregivers to gain temporary relief from tasks associated with caregiving. Transportation and meals often are provided.

## *Exercise*

Incorporating exercise into the daily routine has benefits for both the person with Alzheimer's disease and the caregiver. Not only can it improve health, but it also can provide a meaningful activity for both of you to share.

- Think about what kind of physical activities you both enjoy, perhaps walking, swimming, tennis, dancing, or gardening. Determine the time of day and place where this type of activity would work best.
- Be realistic in your expectations. Build slowly, perhaps just starting with a short walk around the yard, for example, before progressing to a walk around the block.
- Be aware of any discomfort or signs of overexertion. Talk to the person's doctor if this happens.
- Allow as much independence as possible, even if it means a less-than-perfect garden or a scoreless tennis match.
- See what kinds of exercise programs are available in your area. Senior centers may have group programs for people who enjoy exercising with others. Local malls often have walking clubs and provide a place to exercise when the weather is bad.

- Encourage physical activities. Spend time outside when the weather permits. Exercise often helps everyone sleep better.

## *Incontinence*

As the disease progresses, many people with Alzheimer's begin to experience incontinence, or the inability to control their bladder and/or bowels. Incontinence can be upsetting to the person and difficult for the caregiver. Sometimes incontinence is due to physical illness, so be sure to discuss it with the person's doctor.

- Have a routine for taking the person to the bathroom and stick to it as closely as possible. For example, take the person to the bathroom every 3 hours or so during the day. Don't wait for the person to ask.
- Watch for signs that the person may have to go to the bathroom, such as restlessness or pulling at clothes. Respond quickly.
- Be understanding when accidents occur. Stay calm and reassure the person if he or she is upset. Try to keep track of when accidents happen to help plan ways to avoid them.
- To help prevent nighttime accidents, limit certain types of fluids—such as those with caffeine—in the evening.
- If you are going to be out with the person, plan ahead. Know where restrooms are located, and have the person wear simple, easy-to-remove clothing. Take an extra set of clothing along in case of an accident.

## *Sleep Problems*

For the exhausted caregiver, sleep can't come too soon. For many people with Alzheimer's disease, however, the approach of nighttime may be a difficult time. Many people with Alzheimer's become restless, agitated, and irritable around dinnertime, often referred to as "sundowning" syndrome. Getting the person to go to bed and stay there may require some advance planning.

- Encourage exercise during the day and limit daytime napping, but make sure that the person gets adequate rest during the day because fatigue can increase the likelihood of late afternoon restlessness.
- Try to schedule physically demanding activities earlier in the day. For example, bathing could be done in the morning, or the largest family meal could be served at midday.
- Set a quiet, peaceful tone in the evening to encourage sleep. Keep the lights dim, eliminate loud noises, even play soothing music if the person seems to enjoy it.
- Try to keep bedtime at a similar time each evening. Developing a bedtime routine may help.
- Limit caffeine.
- Use night-lights in the bedroom, hall, and bathroom if the darkness is frightening or disorienting.

## ***Hallucinations and Delusions***

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As the disease progresses, a person with Alzheimer's disease may experience hallucinations and/or delusions. Hallucinations are when the person sees, hears, smells, tastes, or feels something that is not there. Delusions are false beliefs that the person thinks are real.

- Sometimes hallucinations and delusions are signs of physical illness. Keep track of what the person is experiencing and discuss it with the doctor.
- Avoid arguing with the person about what he or she sees or hears. Try to respond to the feelings he or she is expressing. Comfort the person if he or she is afraid.
- Try to distract the person to another topic or activity. Sometimes moving to another room or going outside for a walk may help.
- Turn off the television set when violent or disturbing programs are on. The person with Alzheimer's may not be able to distinguish television programming from reality.
- Make sure the person is safe and does not have access to anything he or she could use to harm anyone.
- Discuss with the doctor any illness the person has had or medicines he or she is taking. Sometimes an illness or medicine may cause hallucinations or delusions.

## *Wandering*

Keeping the person safe is one of the most important aspects of caregiving. Some people with Alzheimer's disease have a tendency to wander away from their home or their caregiver. Knowing how to limit wandering can protect a person from getting lost.

- Make sure that the person carries some kind of identification or wears a medical bracelet.
- Consider enrolling the person in the Alzheimer's Association Safe Return program if the program is available in your area (see page 21 for more information on contacting the Association). If the person gets lost and is unable to communicate adequately, identification will alert others to the person's medical condition.
- Notify neighbors and local authorities in advance that the person has a tendency to wander.
- Keep a recent photograph or videotape of the person with Alzheimer's to assist police if the person becomes lost.
- Keep doors locked. Consider a keyed deadbolt or an additional lock up high or down low on the door. If the person can open a lock because it is familiar, a new latch or lock may help.
- Install an "announcing system" that chimes when the door opens.

## *Home Safety*

Caregivers of people with Alzheimer's disease often have to look at their homes through new eyes to identify and correct safety risks. Creating a safe environment can prevent many stressful and dangerous situations. The ADEAR Center offers the booklet, *Home Safety for People with Alzheimer's Disease*, which lists many helpful tips. See page 20 for information on how to contact the ADEAR Center.

- Install secure locks on all outside windows and doors, especially if the person is prone to wandering. Remove the locks on bathroom doors to prevent the person from accidentally locking himself or herself in.
- Use childproof latches on kitchen cabinets and anyplace where cleaning supplies or other chemicals are kept.
- Label medications and keep them locked up. Also make sure knives, lighters and matches, and guns are secured and out of reach.
- Keep the house free from clutter. Remove scatter rugs and anything else that might contribute to a fall.
- Make sure lighting is good both inside and outside the home.
- Be alert to and address kitchen-safety issues, such as the person forgetting to turn off the stove after cooking. Consider installing an automatic shut-off switch on the stove to prevent burns or fire.
- Be sure to secure or put away anything that could cause danger, both inside and outside the house.

## *Driving*

Making the decision that a person with Alzheimer's is no longer safe to drive is difficult, and it needs to be communicated carefully and sensitively. Even though the person may be upset by the loss of independence, safety must be the priority.

- Look for clues that safe driving is no longer possible, including getting lost in familiar places, driving too fast or too slow, disregarding traffic signs, or getting angry or confused.
- Be sensitive to the person's feelings about losing the ability to drive, but be firm in your request that he or she no longer do so. Be consistent—don't allow the person to drive on "good days" but forbid it on "bad days."
- Ask the doctor to help. The person may view the doctor as an authority and be willing to stop driving. The doctor also can contact the Department of Motor Vehicles and request that the person be reevaluated.
- If necessary, take the car keys. If just having keys is important to the person, substitute a different set of keys.
- If all else fails, disable the car or move it to a location where the person cannot see it or gain access to it.
- Ask family or friends to drive the person or find out about services that help people with disabilities get around their community.

## *Visiting the Doctor*

It is important that the person with Alzheimer's disease receive regular medical care. Advance planning can help the trip to the doctor's office go more smoothly.

- Try to schedule the appointment for the person's best time of day. Also, ask the office staff what time of day the office is least crowded.
- Let the office staff know in advance that this person may be confused because of Alzheimer's disease. Ask them for help to make the visit go smoothly.
- Don't tell the person about the appointment until the day of the visit or even shortly before it is time to go. Be positive and matter-of-fact.
- Bring along something for the person to eat and drink and any materials or activities that he or she enjoys.
- Have a friend or another family member go with you on the trip, so that one of you can be with the person while the other speaks with the doctor.
- Take a brief summary listing the person's medical history, primary care doctor, and current medications.

## *Coping with Holidays*

Holidays are bittersweet for many Alzheimer's disease caregivers. The happy memories of the past contrast with the difficulties of the present, and extra demands on time and energy can seem overwhelming. Finding a balance between rest and activity can help.

- Keep or adapt family traditions that are important to you. Include the person with Alzheimer's as much as possible.
- Recognize that things will be different, and be realistic about what you can do.
- Encourage friends and family to visit. Limit the number of visitors at one time, and try to schedule visits during the time of day when the person is at his or her best.
- Avoid crowds, changes in routine, and strange places that may cause confusion or agitation.
- Do your best to enjoy yourself. Try to find time for the holiday things you like to do.
- Ask a friend or family member to spend time with the person while you are out.
- At larger gatherings such as weddings or family reunions, try to have a space available where the person can rest, be alone, or spend some time with a smaller number of people, if needed.

## ***Visiting a Person with Alzheimer's Disease***

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Visitors are important to people with Alzheimer's. They may not always remember who the visitors are, but the human connection has value. Here are some ideas to share with someone who is planning to visit a person with the disease.

- Plan the visit for the time of day when the person with Alzheimer's is at his or her best.
- Consider bringing along an activity, such as something familiar to read or photo albums to look at, but be prepared to skip it if necessary.
- Be calm and quiet. Avoid using a loud tone of voice or talking to the person as if he or she were a child.
- Respect the person's personal space and don't get too close.
- Try to establish eye contact and call the person by name to get his or her attention.
- Remind the person who you are if he or she doesn't seem to recognize you.
- Don't argue if the person is confused. Respond to the feelings you hear being communicated, and distract the person to a different topic if necessary.
- Remember not to take it personally if the person doesn't recognize you, is unkind, or responds angrily. He or she is reacting out of confusion.

## *Choosing a Nursing Home*

For many caregivers, there comes a point when they are no longer able to take care of their loved one at home. Choosing a residential care facility—a group home, assisted living facility, or nursing home—is a big decision, and it can be hard to know where to start.

- It's helpful to gather information about services and options before the need actually arises. This gives you time to explore fully all the possibilities before making a decision.
- Determine what facilities are in your area. Doctors, friends and relatives, hospital social workers, and religious organizations may be able to help you identify specific facilities.
- Make a list of questions you would like to ask the staff. Think about what is important to you, such as activity programs, transportation, or special units for people with Alzheimer's disease.
- Contact the places that interest you and make an appointment to visit. Talk to the administration, nursing staff, and residents.
- Observe the way the facility runs and how residents are treated. You may want to drop by again unannounced to see if your impressions are the same.

- Find out what kinds of programs and services are offered for people with Alzheimer's and their families. Ask about staff training in dementia care, and check to see what the policy is about family participation in planning patient care.
- Check on room availability, cost and method of payment, and participation in Medicare or Medicaid. You may want to place your name on a waiting list even if you are not ready to make an immediate decision about long-term care.
- Once you have made a decision, be sure you understand the terms of the contract and financial agreement. You may want to have a lawyer review the documents with you before signing.
- Moving is a big change for both the person with Alzheimer's disease and the caregiver. A social worker may be able to help you plan for and adjust to the move. It is important to have support during this difficult transition.

## *For More Information*

Many organizations offer information for caregivers. To learn more about support groups, services, research, and additional publications, you may wish to contact the following:

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

P.O. Box 8250

Silver Spring, MD 20907-8250

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

*www.nia.nih.gov/Alzheimers*

The National Institute on Aging's ADEAR Center offers information and publications for families, caregivers, and professionals on diagnosis, treatment, patient care, caregiver needs, long-term care, education and training, and research related to Alzheimer's disease. Staff members answer telephone, email, and written requests and make referrals to local and national resources. The ADEAR website offers free, online publications in English and Spanish; email alert and online *Connections* newsletter subscriptions; an Alzheimer's disease clinical trials database; the Alzheimer's Disease Library database; and more.

**Alzheimer's Association**

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

The Alzheimer's Association is a national, nonprofit association with a network of local chapters that provide education and support for people diagnosed with Alzheimer's disease, their families, and caregivers. The Association also supports research on Alzheimer's.

**Alzheimer's Foundation of America**

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

The Alzheimer's Foundation of America provides care and services to individuals confronting dementia and to their caregivers and families through member organizations dedicated to improving quality of life. Services include a toll-free hotline, consumer publications and other educational materials, and conferences and workshops.

### **Children of Aging Parents**

P.O. Box 167

Richboro, PA 18954-0167

1-800-227-7294 (toll-free)

*www.caps4caregivers.org*

This nonprofit group provides information and materials for adult children caring for their older parents. Caregivers of people with Alzheimer's disease also may find this information helpful.

### **Eldercare Locator**

1-800-677-1116 (toll-free)

*www.eldercare.gov*

Eldercare Locator is a nationwide directory-assistance service helping older people and their caregivers locate local support and resources. It is funded by the U.S. Administration on Aging (AoA). AoA's website at *www.aoa.gov* offers information about caregiving, working with and providing services to people with Alzheimer's, and where to look for support and assistance.

### **Family Caregiver Alliance**

180 Montgomery Street, Suite 1100

San Francisco, CA 94104

1-800-445-8106 (toll-free)

*www.caregiver.org*

Family Caregiver Alliance is a nonprofit organization that offers support services and information for people caring for adults with Alzheimer's, stroke, traumatic brain injuries, and other cognitive disorders. Programs and services include an information clearinghouse for FCA's publications.

**National Institute on Aging Information Center**

P.O. Box 8057

Gaithersburg, MD 20898-8057

1-800-222-2225 (toll-free)

1-800-222-4225 (TTY/toll-free)

*www.nia.nih.gov*

*www.nia.nih.gov/Espanol*

The NIA Information Center offers a variety of information about health and aging. To order publications in English or Spanish or to sign up for regular email alerts, visit *www.nia.nih.gov/HealthInformation*. Visit NIHSeniorHealth (*www.nihseniorhealth.gov*), a senior-friendly website from NIA and the National Library of Medicine. This website has health information for older adults. Special features make it simple to use. For example, you can click on a button to have the text read out loud or to make the type larger.

**National Family Caregivers Association**

10400 Connecticut Avenue, Suite 500

Kensington, MD 20895-3944

1-800-896-3650 (toll-free)

*www.thefamilycaregiver.org*

The National Family Caregivers Association helps educate and support people who care for loved ones with chronic illness, disability, or the frailties of old age. The Association offers an online library of information and educational materials, workshops, and other resources.

### **National Hospice and Palliative Care Organization**

1731 King Street, Suite 100

Alexandria, VA 22314

1-800-658-8898 (toll-free)

*www.nhpco.org*

This nonprofit organization works to enhance the quality of life for people who are terminally ill. It provides information, resources, and referrals to local hospice services and offers publications and online resources.

### **Simon Foundation for Continence**

P.O. Box 815

Wilmette, IL 60091

1-800-237-4666 (toll-free)

*www.simonfoundation.org*

The Simon Foundation for Continence helps individuals with incontinence, their families, and the health professionals who provide their care. The Foundation provides books, pamphlets, tapes, self-help groups, and other resources.

### **Well Spouse Association**

63 West Main Street, Suite H

Freehold, NJ 07728

1-800-838-0879 (toll-free)

*www.wellspouse.org*

This nonprofit membership organization gives support to spouses and partners of the chronically ill and/or disabled. It offers support groups and a newsletter.

The National Institute on Aging gratefully acknowledges the following Alzheimer's Disease Centers for their valuable contributions of information in preparation of this *Caregiver Guide*:

Duke University Joseph and Kathleen Bryan  
Alzheimer's Disease Research Center

The Johns Hopkins University Alzheimer's Disease Center

Contact the ADEAR Center for additional Alzheimer's disease information, including the free publication *Caring for a Person With Alzheimer's Disease: Your Easy-to-Use Guide* from the National Institute on Aging.



Alzheimer's Disease Education and Referral (ADEAR) Center  
1-800-438-4380  
[www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers)

The ADEAR Center is a service of the  
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National Institutes of Health

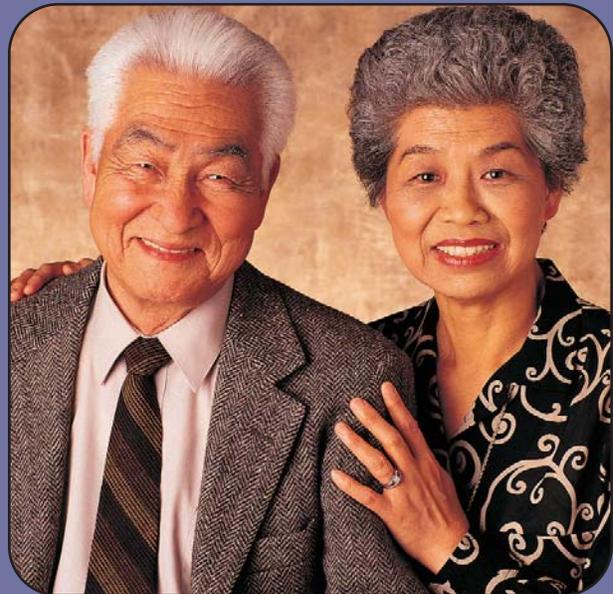


U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
National Institutes of Health  
National Institute on Aging

NIH Publication No. 01-4013

March 2010

# Understanding Alzheimer's Disease



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# About this booklet

Do you have questions about Alzheimer's disease? Please read this booklet. It tells you about:

- Alzheimer's disease (pronounced Allz-high-merz di-zeez)
- The signs of Alzheimer's disease
- Why it is so important to see your doctor early
- Treatment for the disease
- How to get help if you are caring for someone with Alzheimer's disease



## **Helen's story:**

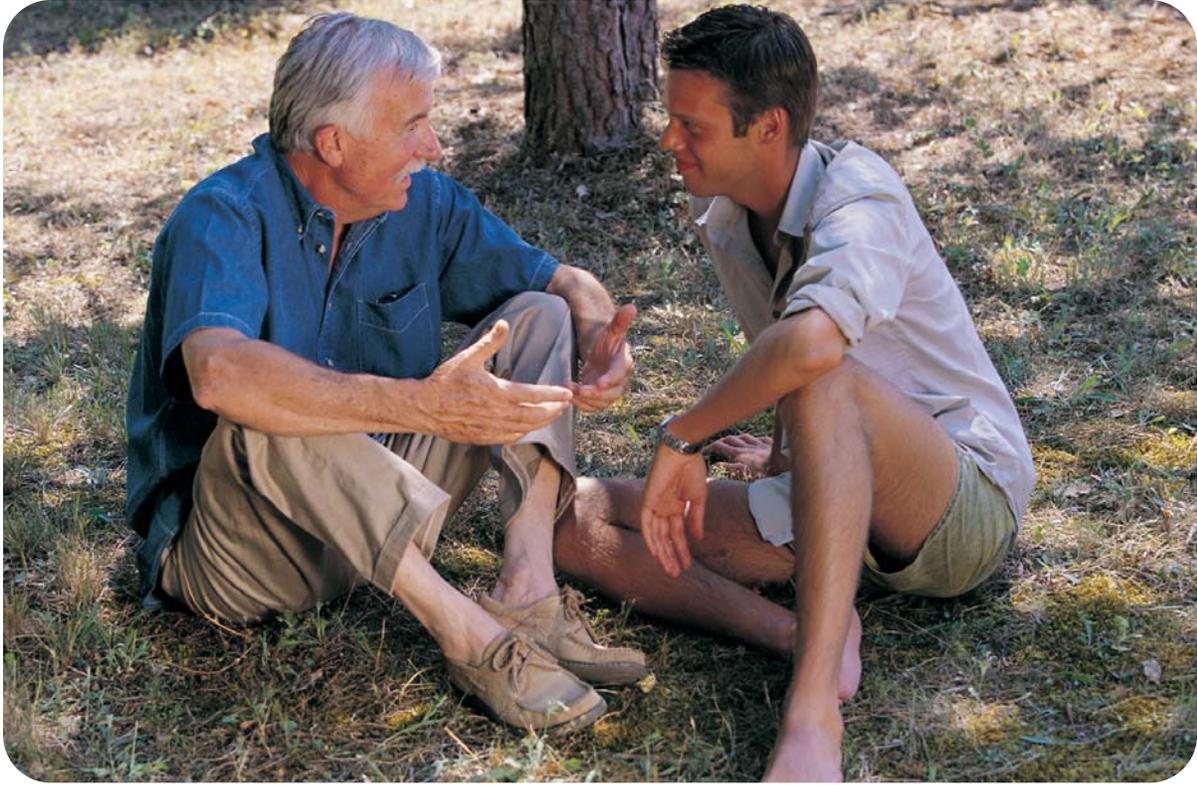
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“I have Alzheimer’s disease. It took me a long time before I could even say the words. When the doctor first told me, I felt like my life was over. And for a while, I did get very depressed. But, my doctor told me about medicine I could take. She said it would slow down my memory loss for a while. I know it’s not a cure. Still, it feels good to do something. Also, my family has been wonderful. They are helping me plan for the care I’ll need. I have decided to take each day as it comes. I want to live my life as fully as I can.”

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Family members can help you plan for your care.



You may have lots of questions about Alzheimer's disease.

### **John's story:**

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“I have friends whose parents have Alzheimer's disease. I never thought it would happen to someone in my family. It catches you by surprise. It takes some time to figure out what you need to do. Mostly, I was upset and worried. I had so many questions. What is Alzheimer's disease? Can it be treated? How is the disease going to affect my father? Will I be able to care for him? Where can I go for help?”

---

**This booklet will help answer your questions about Alzheimer's disease.**

## What is Alzheimer's disease?

Alzheimer's disease is an illness of the brain. It causes large numbers of nerve cells in the brain to die. This affects your ability to remember things and think clearly. Doctors don't know what causes the disease. They do know that it usually begins after age 60 and nearly half of people age 85 and older may have Alzheimer's. However, it is not a normal part of aging.



Alzheimer's disease usually affects people over 60.

## What happens when you have Alzheimer's disease?

The disease often starts slowly. In fact, some people don't know they have Alzheimer's disease. They blame their forgetfulness on old age. However, over time, their memory problems get much worse. People with Alzheimer's lose the ability to drive a car, cook a meal, or even read a newspaper. They may get lost easily and find even simple things confusing. Some people become worried, angry, or violent. At some point, people with Alzheimer's disease may need someone to take care of all their needs (feeding, bathing, etc.) at home or in a nursing home.

# Signs of Alzheimer's disease

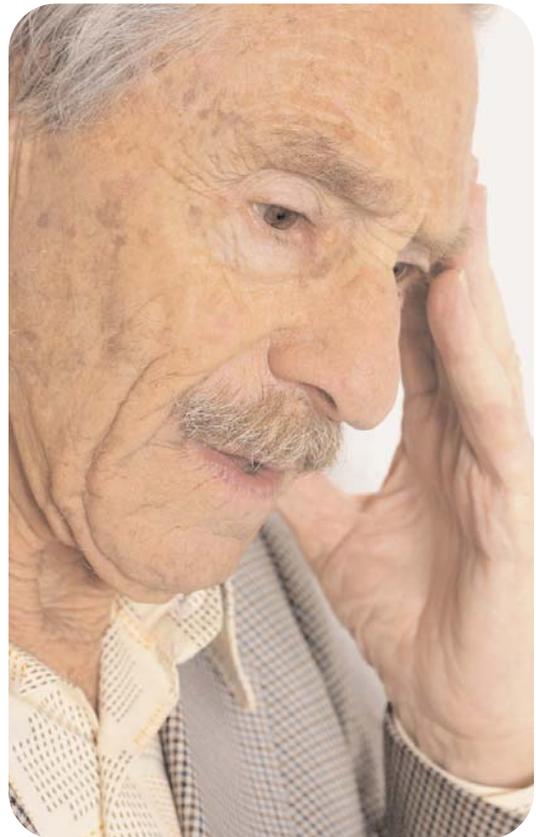
It's really important to know the signs of Alzheimer's disease. If you know the signs, you can get help right away. Listed below are the early signs of Alzheimer's and the later signs that show up after you have had the disease for a while.

## Early signs

- Trouble remembering recent events.
- Problems remembering names of people and places.
- Trouble solving simple math problems.

## Later signs

- Forget how to brush your teeth or comb your hair.
- Cannot remember the names of common things such as desk, house, apple, etc.
- Wander away from home.



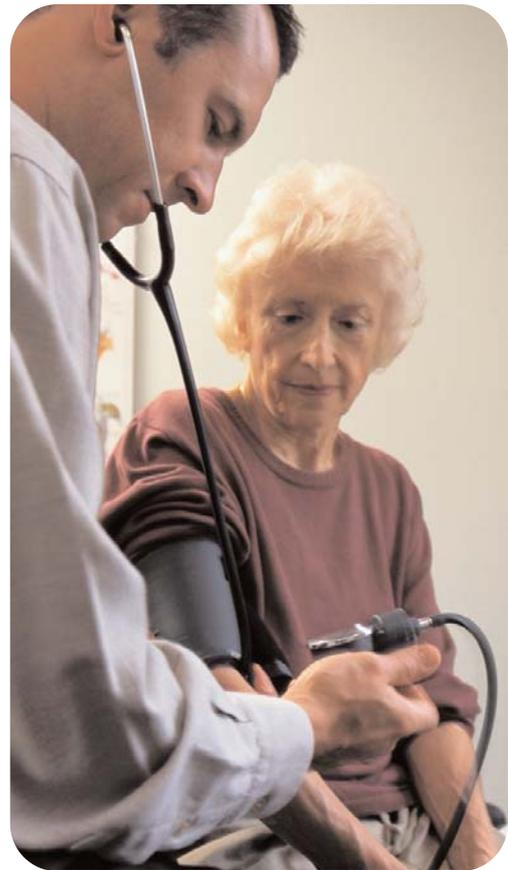
Trouble remembering recent events may be an early sign of Alzheimer's disease.

## See your doctor early

If you or someone in your family thinks your forgetfulness is getting in the way of your normal routine, it's time to see your doctor. **Seeing the doctor early means you can find out what's causing you to be forgetful.** If you have Alzheimer's, finding the disease early gives you and your family more time to talk about and plan for your treatment and care.

Your doctor may do the following things to help diagnose Alzheimer's disease:

- Check on your general health
- Ask questions about your family's health
- Talk to someone in your family about your memory problems
- Ask how well you can do everyday things like driving, writing a check, and talking with friends and family
- Test your memory, problem solving, counting, and language skills
- Do medical tests — such as checking your blood and urine
- Do brain scans, also called CAT scans, that show pictures of your brain



See your doctor as soon as you begin to have memory problems.

## Other illnesses that cause Alzheimer-like signs

You need to know that there are some illnesses and problems that may look like Alzheimer's, but are caused by other problems.

These include:

- Bad reaction to certain medicines
- Depression
- Not eating enough healthy foods, or too few vitamins and minerals in your body
- Brain tumors
- Blood vessel disease
- Thyroid problems

The point is to get checked out by your doctor. Don't let fear stop you from seeing your doctor. You can get help.

Some of these illnesses can be treated. Once treated, your confusion and memory loss should go away.

## Treatment for Alzheimer's disease

There are medicines that can treat the symptoms of Alzheimer's. However, there is no cure. Some medicines keep your memory loss and other symptoms from getting worse for a time. These medicines work best if Alzheimer's disease is found early. Other medicines work to help you sleep better or feel less worried and depressed. These medicines don't directly treat the disease. They do help you feel more comfortable.



Some medications can help treat Alzheimer's disease.

# What about research on Alzheimer's disease?

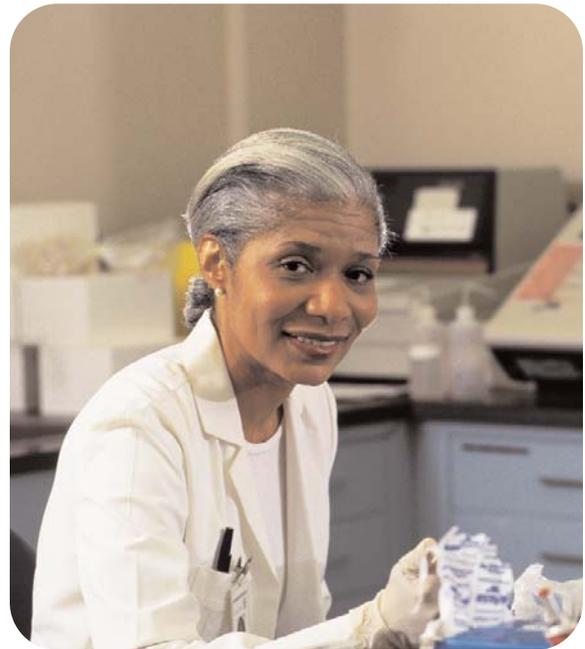
Researchers are working very hard to find new and better treatments for this disease. They are doing research with people who have different kinds of memory problems to learn the best way to treat Alzheimer's. They also are looking at how to prevent Alzheimer's, slow the disease, and reduce the symptoms.

## Clinical trials

**Clinical trials are research studies that help doctors learn which treatments work best.**

Healthy people and people with Alzheimer's may be able to take part in clinical trials.

To find out more about these studies, contact the Alzheimer's Disease Education and Referral (ADEAR) Center at **1-800-438-4380**, or visit the ADEAR Center Website at **[www.alzheimers.nia.nih.gov](http://www.alzheimers.nia.nih.gov)**.



You can learn more about clinical

## Is there help for caregivers?

Yes. If you are caring for someone with Alzheimer's disease, you may feel overwhelmed. It can take all your time and energy. There is help for you. Learn about support groups, adult day-care programs, home healthcare services, and other helpful resources. You need to take care of yourself in order to take care of someone with Alzheimer's disease. The Alzheimer's Association has chapters across the country that can help. Also, the ADEAR Center has two booklets that may be helpful: "The Caregiver Guide" and "Home Safety."

**See page 11 for more information and resources.**



Caregivers need help and

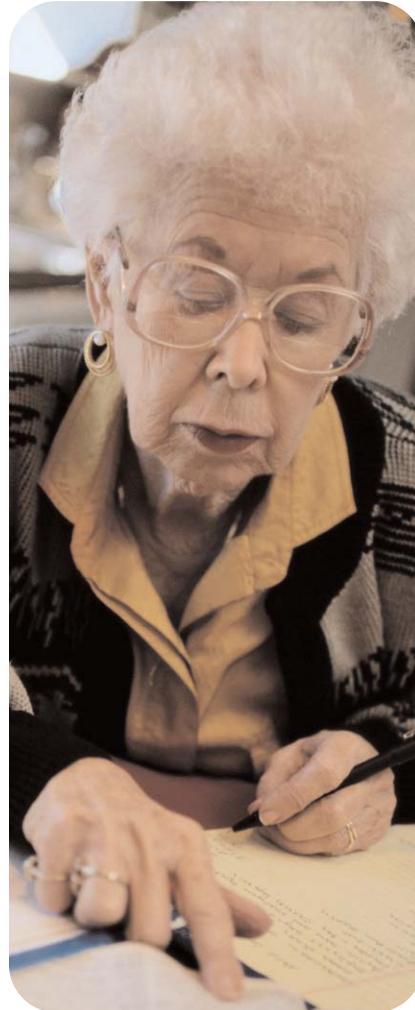


# Where can I get more information?

Contact the following organizations to learn about support groups, services, publications on Alzheimer's disease, research centers, and studies:

**Alzheimer's Association**  
**225 N. Michigan Avenue,**  
**Suite 1700**  
**Chicago, IL 60601**  
**Phone: 1-800-272-3900**  
**Website: [www.alz.org](http://www.alz.org)**

The Alzheimer's Association is a nonprofit organization offering information and support services to people with Alzheimer's disease and their families. Call to find out where to get help in your area.



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

**P.O. Box 8250**

**Silver Spring, MD 20907-8250**

**Phone: 1-800-438-4380**

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

The Alzheimer's Disease Education and Referral (ADEAR) Center offers information on diagnosis, treatment, patient care, caregiver needs, long-term care, and research related to Alzheimer's disease. Staff can refer you to local and national resources. The Center is a service of the National Institute on Aging, part of the Federal Government's National Institutes of Health.

**Eldercare Locator**

**Phone: 1-800-677-1116**

**Website: [www.eldercare.gov](http://www.eldercare.gov)**

Families often need information about community resources, such as home care, adult day care, and nursing homes. Contact the Eldercare Locator to find these resources in your area. The Eldercare Locator is a service of the Administration on Aging. It is funded by the Federal Government.



Call for more information on Alzheimer's disease.

**For copies of this booklet, contact:**

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

**P.O. Box 8250**

**Silver Spring, MD 20907-8250**

**Phone: 1-800-438-4380**

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



**U.S DEPARTMENT OF HEALTH AND HUMAN SERVICES**

Public Health Service

National Institutes of Health

National Institute on Aging

NIH Publication No. 06-5441

June 2007

# Understanding Memory Loss

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What to do when you  
have trouble remembering

From the National Institute on Aging



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# Introduction

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We've all forgotten a name, where we put our keys, or if we locked the front door. It's normal to forget things once in a while. However, forgetting how to make change, use the telephone, or find your way home may be signs of a more serious memory problem.

## This booklet will help you learn about:

- the difference between mild forgetfulness and more serious memory problems
- causes of memory problems and how they can be treated
- how to cope with serious memory problems

## Tips about using the booklet

Use the Table of Contents to help you find things quickly. Also, we put some medical terms in bold, such as **brain scan**. You can find how to say these words and what they mean in the “Words to know” section on page 24.

## Mary's story



Mary couldn't find her car keys. She looked on the hook just inside the front door. They weren't there. She searched in her purse. No luck. Finally, she found them on her desk. Yesterday, she forgot her neighbor's name. Her memory was playing tricks on her. She was starting to worry about it.

She decided to see her doctor. After a complete check-up, her doctor said that Mary was fine. Her forgetfulness was just a normal part of getting older. The doctor suggested that Mary take a class, play cards with friends, or help out at the local school to sharpen her memory.

# Differences between mild forgetfulness and more serious memory problems

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## What is mild forgetfulness?

It is true that some of us get more forgetful as we age. It may take longer to learn new things, remember certain words, or find our glasses. These changes are often signs of mild forgetfulness, not serious memory problems.

See your doctor if you're worried about your forgetfulness. Tell him or her about your concerns. Be sure to make a follow-up appointment to check your memory in the next 6 months to a year. If you think you might forget, ask a family member, friend, or the doctor's office to remind you.

## What can I do about mild forgetfulness?

You can do many things to help keep your memory sharp and stay alert. Look at the list on page 6 for some helpful ideas.

## Here are some ways to help your memory:

- Learn a new skill.
- Volunteer in your community, at a school, or at your place of worship.
- Spend time with friends and family.
- Use memory tools such as big calendars, to-do lists, and notes to yourself.
- Put your wallet or purse, keys, and glasses in the same place each day.
- Get lots of rest.
- Exercise and eat well.
- Don't drink a lot of alcohol.
- Get help if you feel depressed for weeks at a time.



Spending time with friends and family may help.

## What is a serious memory problem?

Serious memory problems make it hard to do everyday things. For example, you may find it hard to drive, shop, or even talk with a friend. Signs of serious memory problems may include:

- asking the same questions over and over again
- getting lost in places you know well
- not being able to follow directions
- becoming more confused about time, people, and places
- not taking care of yourself—eating poorly, not bathing, or being unsafe

## What can I do about serious memory problems?

See your doctor if you are having any of the problems listed above. It's important to find out what might be causing a serious memory problem. Once you know the cause, you can get the right treatment.



Talk with your doctor if you think you have a serious memory problem.

## Al's story



Al didn't know what was happening. He was having a hard time remembering things. He wasn't eating or sleeping well and didn't want to see friends. He was confused and irritable.

His wife was worried. She took him to the doctor. It turned out that Al was having a bad reaction to one of his medicines. Once his doctor changed the medicine, Al felt more like himself.

# Serious memory problems— causes and treatments

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Many things can cause serious memory problems, such as blood clots, depression, and Alzheimer’s disease. Read below to learn more about causes and treatments of serious memory problems.

## Medical conditions

Certain medical conditions can cause serious memory problems. These problems should go away once you get treatment. Some medical conditions that may cause memory problems are:

- bad reaction to certain medicines
- depression
- not eating enough healthy foods, or too few vitamins and minerals in your body
- drinking too much alcohol
- blood clots or tumors in the brain
- head injury, such as a concussion from a fall or accident
- thyroid, kidney, or liver problems

## Treatment for medical conditions

These medical conditions are serious. See your doctor for treatment.

# Gloria's story



Gloria was feeling sad all the time. She just wanted to sleep all day and night. She was becoming really forgetful, too. Gloria's nephew Bob was afraid something was very wrong. He took her to see a doctor. The doctor said she had depression and needed to take medicine and see a counselor.

After 3 months, Bob could see the change in his aunt. She was eating and sleeping better. Gloria also was spending more time with friends and doing volunteer work.

## Emotional problems

Some emotional problems in older people can cause serious memory problems. Feeling sad, lonely, worried, or bored can cause you to be confused and forgetful.

### Treatment for emotional problems

- You may need to see a doctor or counselor for treatment. Once you get help, your memory problems should get better.
- Being active, spending more time with family and friends, and learning new skills also can help you feel better and improve your memory.



Being active can help you feel better.

## Joe's story



Joe was almost 74. He was still working part-time. He noticed that he was becoming more forgetful at work. He felt frustrated that it was so hard to find the right words to describe something. His boss told him that he missed a couple of meetings. He started to wonder if he had a serious problem.

Joe's wife took him to get a complete health check-up. His doctor told Joe that he had mild cognitive impairment, also called MCI. The doctor said there was no treatment for MCI, but that he would keep a close watch on Joe's memory and thinking skills. Joe felt better knowing there was a reason for his memory problems.

## Mild cognitive impairment

(pronounced mild **kog-ni-tiv im-pair-ment**)

As some people grow older, they have more memory problems than other people their age. This condition is called **mild cognitive impairment**, or MCI. People with MCI can take care of themselves and do their normal activities.

MCI memory problems may include:

- losing things often
- forgetting to go to events and appointments
- having more trouble coming up with words than other people of the same age

Your doctor can do thinking, memory, and language tests to see if you have MCI. He or she also may suggest that you see a specialist for more tests. Because MCI may be an early sign of Alzheimer's disease, it's really important to see your doctor or specialist every 6 to 12 months. See page 15 for more about Alzheimer's disease.

### Treatment for MCI

- At this time, there is no proven treatment for MCI. Your doctor can check to see if you have any changes in your memory or thinking skills over time.
- You may want to try to keep your memory sharp. The list on page 6 suggests some ways to help your memory.

## Anna's story



Anna's mother was still going strong at 85. She kept busy with friends and church activities. But lately, Anna had noticed changes. Her mother was becoming more forgetful and confused. Also, she was spending a lot of time alone in her house. One day, her mom got lost on her way home from shopping.

Anna knew it was time to get help. She took her mom to the doctor. Anna was really upset to learn that her mom had early-stage Alzheimer's disease. It's been tough, but learning about treatment choices, what to expect in the future, and how to live with the disease has helped the whole family. They're taking one day at a time.

# Alzheimer's disease

(pronounced **Allz**-high-merz duh-**zeez**)

**Alzheimer's disease** causes serious memory problems. The signs of Alzheimer's disease begin slowly and get worse over time. This is because changes in the brain cause large numbers of brain cells to die.

It may look like simple forgetfulness at first, but over time, people with Alzheimer's disease have trouble thinking clearly. They find it hard to do everyday things like shopping, driving, and cooking. As the illness gets worse, people with Alzheimer's disease may need someone to take care of all their needs at home or in a nursing home. These needs may include feeding, bathing, and dressing.

## Treatment for Alzheimer's disease

- Taking certain medicines can help a person in the early or middle stages of Alzheimer's disease. These medicines can keep symptoms, such as memory loss, from getting worse for a time. The medicines can have side effects and may not work for everyone. Talk with your doctor about side effects or other concerns you may have.
- Other medicines can help if you are worried, depressed, or having problems sleeping.

See page 22 to learn where families can go for help and information.

## Sam's story



Sam was an active 70-year-old who felt healthy. He couldn't believe it when, all of a sudden, he couldn't remember what somebody told him 5 minutes ago.

He went for a check-up and had some tests, including a brain scan. After reviewing the test results, the doctor told him that his forgetfulness was caused by small strokes. These strokes had damaged some of his brain cells. She said his problem was called vascular dementia.

The doctor told Sam that she couldn't cure his memory problems. But, she could give him medicine to control his high blood pressure. This medicine also would lower his chances of having more strokes.

## Vascular dementia

(pronounced **vas-kue-ler duh-men-shuh**)

Many people have never heard of **vascular dementia**. Like Alzheimer's disease, it is a medical condition that causes serious memory problems. Unlike Alzheimer's disease, signs of vascular dementia may appear suddenly. This is because the memory loss and confusion are caused by small strokes or changes in the blood supply to the brain. If the strokes stop, you may get better or stay the same for a long time. If you have more strokes, you may get worse.

### Treatment for vascular dementia

You can take steps to lower your chances of having more strokes. These steps include:

- Control your high blood pressure.
- Treat your high cholesterol.
- Take care of your diabetes.
- Stop smoking.



Get your blood pressure checked each time you see the doctor.

# Help for serious memory problems

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## What can I do if I'm worried about my memory?

See your doctor. If your doctor thinks your memory problems are serious, you may need to have a complete health check-up. The doctor will review your medicines and may test your blood and urine. You also may need to take tests that check your memory, problem solving, counting, and language skills.

In addition, the doctor may suggest a **brain scan**. Pictures from the scan can show normal and problem areas in the brain. Once the doctor finds out what is causing your memory problems, ask about the best treatment for you.



Doctors can do brain scans to check for some causes of memory problems.

## What can family members do to help?

If your family member or friend has a serious memory problem, you can help the person live as normal a life as possible. You can help the person stay active, go places, and keep up everyday routines. You can remind the person of the time of day, where he or she lives, and what is happening at home and in the world. You also can help the person remember to take medicine or visit the doctor.

Some families use the following things to help with memory problems:

- big calendars to highlight important dates and events
- lists of the plans for each day
- notes about safety in the home
- written directions for using common household items (most people with Alzheimer's disease can still read)



Family members and friends can help people with serious memory problems live as normal a life as possible.

## Clinical trials and studies

People with Alzheimer's disease, MCI, or a family history of Alzheimer's may be able to take part in clinical trials, a type of research study. Healthy people with no memory problems and no family history of Alzheimer's also may be able to take part in clinical trials.

Joining a clinical trial or other research study is a way to help fight Alzheimer's disease. To find out more about clinical trials:

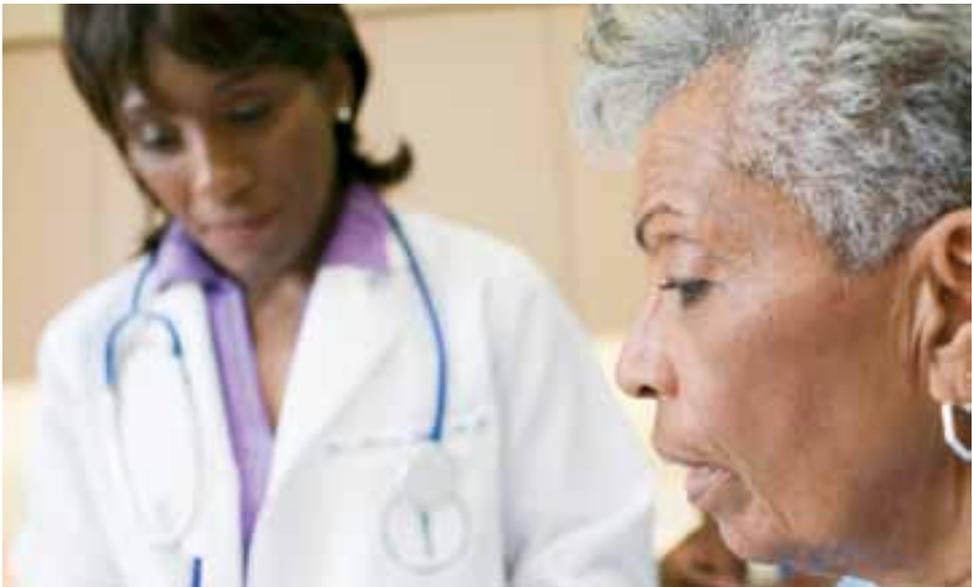
- Call the Alzheimer's Disease Education and Referral (ADEAR) Center at **1-800-438-4380**. It's a free call.
- Visit the ADEAR Center website at [www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers).
- Check out [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov).

# What you need to know

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- ❑ There are differences between normal forgetfulness and more serious memory problems.
- ❑ It's important to understand the causes of memory problems and how they can be treated.
- ❑ You can get help for mild and serious memory problems.

**See your doctor if you are worried about your memory.**  
It's important to find out what is causing your memory problems.



It's important to find out what is causing your memory problems.

# Where can I get more information?

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Contact the following organizations to learn more about memory loss. They can give you information about support groups and services, and publications on Alzheimer's disease. They can also give you information about research centers and clinical trials and studies.

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

P.O. Box 8250

Silver Spring, MD 20907-8250

Phone: **1-800-438-4380**

Website: **[www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers)**

The Alzheimer's Disease Education and Referral (ADEAR) Center offers information on diagnosis, treatment, patient care, caregiver needs, long-term care, and research related to Alzheimer's disease. Staff can refer you to local and national resources. The Center is a service of the National Institute on Aging, part of the Federal Government's National Institutes of Health.

## **Alzheimer's Association**

Phone: **1-800-272-3900**

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

The Alzheimer's Association is a nonprofit organization offering information and support services to people with Alzheimer's disease and their families. Call or visit their website to find out where to get help in your area.

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

Phone: **1-866-232-8484**

Website: **[www.alzfdn.org](http://www.alzfdn.org)**

This foundation serves people with dementia and their caregivers and families. Services include a toll-free hotline, publications and other materials, and conferences and workshops.

## **Eldercare Locator**

Phone: **1-800-677-1116**

Website: **[www.eldercare.gov](http://www.eldercare.gov)**

Families often need information about community resources, such as home care, adult day care, and nursing homes. Contact the Eldercare Locator to find these resources in your area. The Eldercare Locator is a service of the Administration on Aging. It is funded by the Federal Government.

# Words to know

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## Alzheimer's disease

(pronounced **Allz**-high-merz duh-**zeez**)

A disease that causes large numbers of nerve cells in the brain to die. These changes make it hard for a person to remember things, have clear thinking, and make good judgments. The symptoms begin slowly and get worse over time.

## Brain scan

A type of test that shows pictures of normal and problem areas of the brain.

## Mild cognitive impairment

(pronounced mild **kog**-ni-tiv im-**pair**-ment)

Also called MCI. It is a medical condition that causes people to have more memory problems than other people their age. The signs of MCI are not as severe as those of Alzheimer's disease. They include losing things often, forgetting to go to events and appointments, and having more trouble coming up with the right words than other people the same age.

## Vascular dementia

(pronounced **vas**-kue-ler duh-**men**-shuh)

A medical condition caused by small strokes or changes in the brain's blood supply. Signs can appear suddenly. These signs include changes in memory, language, thinking skills, and mood.

**For copies of this booklet, contact:**

Alzheimer's Disease Education and Referral Center  
P.O. Box 8250  
Silver Spring, MD 20907-8250

Phone: **1-800-438-4380**

Website: **[www.nia.nih.gov/Alzheimers](http://www.nia.nih.gov/Alzheimers)**



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