

Healthy Steps: Alzheimer's Disease and Dementias

Alzheimer's disease (AD) is the most common form of dementia (a brain disorder that seriously affects a person's ability to carry out daily activities) among older people. It involves the parts of the brain that control thought, memory, and language. Every day scientists learn more, but right now the causes of AD are still unknown, and there is no cure.

AD is named after Dr. Alois Alzheimer, a German doctor. In 1906, Dr. Alzheimer noticed changes in the brain tissue of a woman who had died of an unusual mental illness. He found abnormal clumps (now called amyloid plaques) and tangled bundles of fibers (now called neurofibrillary tangles). Today, these plaques and tangles in the brain are considered hallmarks of AD.

Scientists also have found other brain changes in people with AD. There is a loss of nerve cells in areas of the brain that are vital to memory and other mental abilities. There also are lower levels of chemicals in the brain that carry complex messages back and forth between nerve cells. AD may disrupt normal thinking and memory by blocking these messages between nerve cells.

Alzheimer's disease is an age-related and irreversible brain disorder that occurs gradually and results in memory loss, behavior and personality changes, and a decline in thinking abilities. These losses are related to the breakdown of the connections between nerve cells in the brain and the eventual death of many of these cells. The course of this disease varies from person to person, as does the rate of decline. On average, patients with AD live for 8 to 10 years after they are diagnosed, though the disease can last for up to 20 years.

AD is part of a group of disorders (termed dementias) that are characterized by cognitive and behavioral problems. AD advances progressively, from mild forgetfulness to a severe loss of mental function. In most people with AD, symptoms first appear after age 60. The earliest symptoms characteristically include loss of recent memory, later compounded by faulty judgment, and changes in personality. Often, people in the initial stages of AD think less clearly and tend to be easily confused. Later in the disease, they may forget how to do simple tasks, such as how to dress themselves or eat with proper utensils. Eventually, people with AD lose the capacity to function on their own and become completely dependent on other people for their everyday care. Finally, the disease becomes so debilitating that patients are bedridden and likely to develop other illnesses and infections. Most commonly, people with AD die of pneumonia.

Although the risk of developing AD increases with age, AD and dementia symptoms are not a part of normal aging. AD and other dementing disorders are caused by diseases that affect the brain. In the absence of disease, the human brain often can function well into the tenth decade of life.

What is Dementia?

Dementia is the loss of intellectual functions (such as thinking, remembering and reasoning) of sufficient severity to interfere with a person's daily functioning. It is not a disease in itself, but rather a group of symptoms which may accompany certain diseases or physical conditions. The cause and rate of progression of dementias vary. Some of the more well known diseases that produce dementia include Alzheimer's disease, multi infarct dementia, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease and Parkinson's disease. Other conditions which may cause or mimic dementia include depression, brain tumors, nutritional deficiencies,

head injuries, hydrocephalus, infections (AIDS, meningitis, syphilis), drug reactions and thyroid problems. It is imperative that all persons experiencing memory deficits or confusion undergo a thorough diagnostic workup. This requires examination by a physician experienced in the diagnosis of dementing disorders and detailed laboratory testing. The examination should include a reevaluation of all medications. This process will help the patient obtain treatment for reversible conditions, aid the patient and family in planning future care, and provide important medical information for future generations.

Sometimes older people have emotional problems that can be mistaken for dementia. Feeling sad, lonely, worried, or bored may be more common for older people facing retirement or coping with the death of a spouse, relative, or friend. Adapting to these changes leaves some people feeling confused or forgetful. Emotional problems can be eased by supportive friends and family, or by professional help from a doctor or counselor.

What is Multi-Infarct Dementia (MID)?

In multi-infarct dementia, a series of small strokes or changes in the brain's blood supply may result in the death of brain tissue. The location in the brain where the small strokes occur determines the seriousness of the problem and the symptoms that arise. Symptoms that begin suddenly may be a sign of this kind of dementia. People with multi-infarct dementia are likely to show signs of improvement or remain stable for long periods of time, then quickly develop new symptoms if more strokes occur. In many people with multi-infarct dementia, high blood pressure is to blame. One of the most important reasons for controlling high blood pressure is to prevent strokes.

AD is the most common cause of dementia among people age 65 and older. It presents a major health problem for the United States because of its enormous impact on individuals, families, the health care system, and society as a whole. Scientists estimate that up to 4.5 million people currently suffer with the disease, more than 100,000 in Arkansas, and the prevalence (the number of people with the disease at any one time) doubles every 5 years beyond age 65.

These numbers are significant now and will become even more so in the future because of dramatic increases in life expectancy since the early 1900s. Researchers estimate that by 2050, 13.2 million Americans will have AD if current population trends continue and no preventive treatments become available. Approximately 4 million Americans are 85 years old or older, and this age group is the fastest growing segment of the population. It also is the group with the highest risk of AD. The U.S. Census Bureau estimates that nearly 19 million Americans will be aged 85 and older by the year 2050. Some experts who study population trends suggest that the number could be even greater. This trend is not only apparent in the U.S. but also worldwide. As more and more people live longer, the number of people affected by diseases of aging, including AD, will continue to grow. For example, one study shows that nearly half of all people age 85 and older have some form of dementia.

The increasing number of people with AD and the costs associated with the disease mean that AD puts a heavy economic burden on society. The annual national direct and indirect costs of caring for people with AD are estimated to be as high as \$100 billion.

AD's impact is seen not only in the numbers who develop the disease and the cost to society, but also in its effects on people with the disease, their families, friends and caregivers. Slightly more than half of AD patients receive care at home, while the remainder are cared for in a variety of health care institutions. During their years of caregiving, these spouses, relatives, and friends experience emotional, physical, and financial stress. They watch their loved ones become more and more forgetful, frustrated, and confused. Eventually, the person with AD will not even recognize his or her nearest and dearest relatives and friends.

Caregivers-most of whom are women-must juggle child care, jobs, and other responsibilities with caring for relatives with AD who cannot function on their own. As the disease runs its course and the abilities of people

with AD steadily decline, family members face difficult decisions about the long-term care of their loved ones. Frequently, they have no choice but to place their relative in a nursing home. The numbers of caregivers and their needs can be expected to grow significantly as the population ages and as the number of people with AD increases.

Alzheimer's disease: more pieces of the puzzle fall into place

In normal aging, nerve cells in the brain are not lost in large numbers. In contrast, AD causes many nerve cells to stop functioning, lose connections with other nerve cells, and die. At first, AD destroys neurons in parts of the brain that control memory, including the hippocampus (a structure deep in the brain that helps to encode short-term memories) and related structures. As nerve cells in the hippocampus stop working properly, short-term memory fails, and often, a person's ability to do easy and familiar tasks begins to decline. AD later attacks the cerebral cortex, particularly the areas responsible for language and reasoning. At this point, AD begins to take away language skills and changes a person's ability to make judgments. Personality changes also may occur. Emotional outbursts and disturbing behaviors, such as wandering and agitation, begin to occur and become more and more frequent as the disease continues its course. Eventually, many other areas of the brain are involved, all these brain regions atrophy (shrink and lose function), and the person with AD becomes bedridden, incontinent, totally helpless, and unresponsive to the outside world.

What Are the Main Characteristics of AD?

The brain in AD is abnormal in three ways:

Amyloid Plaques

In AD, plaques develop first in areas of the brain used for memory and other cognitive functions. They consist of largely insoluble (cannot be dissolved) deposits of beta-amyloid – a protein fragment snipped from a larger protein called amyloid precursor protein (APP) – intermingled with portions of neurons (nerve cells) and with non-nerve cells such as microglia (cells that surround and digest damaged cells or foreign substances that cause inflammation) and astrocytes (glial cells that serve to support and nourish neurons). Plaques are found in the spaces between the brain's nerve cells. Although researchers still do not know whether amyloid plaques themselves cause AD or whether they are a by-product of the AD process, there is evidence that amyloid deposition may be a central process in the disease. Certainly, changes in the structure of the APP protein can cause AD, as shown in one inherited form of AD, which is caused by mutations in the gene that contains instructions for making the APP protein. Recent work has revealed much about the nature of beta-amyloid and the ways in which it may be toxic to neurons, the processes by which plaques form and are deposited in the brain, and ways in which the numbers of plaques can be reduced.

Neurofibrillary Tangles

The second hallmark of AD consists of abnormal collections of twisted threads found inside nerve cells. The chief component of these tangles is one form of a protein called tau. In the central nervous system, tau proteins are best known for their ability to bind and help stabilize microtubules, which are one constituent of the cell's internal support structure, or skeleton.

In healthy neurons, microtubules form structures like train tracks, which guide nutrients and molecules from the bodies of the cells down to the ends of the axon. Tau normally holds together the "railroad ties" or connector pieces of the microtubule tracks. However, in AD tau is changed chemically, and this altered tau twists into paired helical filaments – two threads of tau wound around each other. These filaments aggregate to form neurofibrillary tangles. When this happens, the tau no longer holds the railroad tracks together and the microtubules fall apart. This collapse of the transport system first may result in malfunctions in communication between nerve cells and later may lead to neuronal death that contributes to the development of dementia.

Loss of Connections Between Cells and Cell Death

The third major pathological feature of AD is the gradual loss of connections between neurons and eventually, neuron death. As plaques and tangles proliferate, they damage neurons to the point that they cannot function properly or communicate with each other. Eventually, they die. As this process continues and spreads through the brain, affected regions begin to shrink. By the final stage of AD, plaques and tangles are widespread, and brain tissue has shrunk significantly, a process called brain atrophy.

What Causes AD?

Scientists do not yet fully understand what causes AD. There probably is not one single cause, but several factors that affect each person differently. Age is the most important known risk factor for AD. The number of people with the disease doubles every 5 years beyond age 65.

Family history is another risk factor. Scientists believe that genetics may play a role in many AD cases. For example, familial AD, a rare form of AD that usually occurs between the ages of 30 and 60, can be inherited. However, in the more common form of AD, which occurs later in life, no obvious family pattern is seen. One risk factor for this type of AD is a protein called apolipoprotein E (apoE). Everyone has apoE, which helps carry cholesterol in the blood. The apoE gene has three forms. One seems to protect a person from AD, and another seems to make a person more likely to develop the disease. Other genes that increase the risk of AD or that protect against AD probably remain to be discovered.

Scientists still need to learn a lot more about what causes AD. In addition to genetics and apoE, they are studying education, diet, environment, and viruses to learn what role they might play in the development of this disease.

How is AD Diagnosed?

Today, the only definite way to diagnose AD is to find out whether there are plaques and tangles in brain tissue. To look at brain tissue, doctors must wait until they do an autopsy, which is an examination of the body done after a person dies. Therefore, doctors must make a diagnosis of "possible" or "probable" AD.

At specialized centers, doctors can diagnose AD correctly up to 90 percent of the time. Doctors use several tools to diagnose "probable" AD:

- **A complete medical history** includes information about the person's general health, past medical problems, and any difficulties the person has carrying out daily activities.
- **Medical tests** - such as tests of blood, urine, or spinal fluid - help the doctor find other possible diseases causing the symptoms.
- **Neuropsychological tests** measure memory, problem solving, attention, counting, and language.
- **Brain scans** allow the doctor to look at a picture of the brain to see if anything does not look normal.

Information from the medical history and test results help the doctor rule out other possible causes of the person's symptoms. For example, thyroid problems, drug reactions, depression, brain tumors, and blood vessel disease in the brain can cause AD-like symptoms. Some of these other conditions can be treated successfully.

What drugs are currently available to treat AD?

No treatment can stop AD. However, for some people in the early and middle stages of the disease, the drugs tacrine (Cognex), donepezil (Aricept), rivastigmine (Exelon), or galantamine (Reminyl) may help prevent some symptoms from becoming worse for a limited time. Also, some medicines may help control behavioral symptoms of AD such as sleeplessness, agitation, wandering, anxiety, and depression. Treating these symptoms often makes patients more comfortable and makes their care easier for caregivers.

The fifth approved medication, known as Namenda® (memantine), is an N-methyl D-aspartate (NMDA) antagonist. It is prescribed for the treatment of moderate to severe AD. Studies have shown that the main effect of Namenda® is to delay progression of some of the symptoms of moderate to severe AD. The medication may allow patients to maintain certain daily functions a little longer. For example, Namenda® may help a patient in the later stages of AD maintain his or her ability to go to the bathroom independently for several more months, a benefit for both patients and caregivers.

Alzheimer's Disease and Parkinson's Disease: Two Diseases or One?

While Alzheimer's disease and Parkinson's disease (PD) are always classified as different diseases, a growing body of evidence demonstrates a number of common physical signs and neuroanatomy. For example, some AD patients have problems with movement, the most obvious symptom of PD. AD patients can also show changes in the substantia nigra—a place in the brain controlling certain types of movements—whose neurons are severely depleted in PD. Some AD patients demonstrate Lewy bodies, a typical marker for neuron pathology that is found in PD but in different brain regions than in AD.

Similarly, many PD patients develop dementia and have neurofibrillary tangles and senile plaques like those found in AD. A further indication of overlap is Lewy body disease, a neurodegenerative disorder whose clinical signs occupy a middle ground between AD on the one hand and PD on the other. Furthermore, one population on the island of Guam also shows a constellation of signs that are common to both types of disease.

Often, it is not possible, on either clinical or neuropathologic examination, to make a clear diagnostic distinction between the two diseases. On a statistical basis, the numbers of individuals showing signs of both diseases is surprisingly high. Because of this crossover of anatomical and physical signs, some clinicians have suggested that AD and PD are the same disease occurring over a broad spectrum. An alternative notion is that the two diseases simply co-exist in the same brain. As scientists conduct more research into these two diseases and the possible overlaps in their etiologies, the growing knowledge base may help to explain the development of many neurological diseases and point the way to common therapeutic approaches. This also applies to research on other dementias, for example, those caused by tau mutations and by other forms of amyloid such as prions.

Clues to Healthy Aging Found in Lifestyles

It is clear that genes, environment, and lifestyle all affect the way our brains age. One of the major reasons for studying aging is to find factors that will help us to grow older in a healthy way and to retain normal and active cognitive function for as long as possible. Evidence from studies in mice and humans is accumulating that early life events and our lifestyles may play an important role in the aging of our brains, the degree to which we retain normal cognitive function, and perhaps also our chances of developing AD.

Physical Activity

Recent studies have shown that light to moderate physical activity, such as walking, results in a gain, or perhaps less loss, in some aspects of cognitive function in humans. The mechanisms that may help with cognitive function are difficult to study in the human, so researchers have turned to animal models to understand what is happening in the brain in the older individual. They are beginning to be able to link changes in the brains of animals to changes in cognitive function.

Scientists have only recently learned that in certain brain regions, new neurons are born, even in older age. This was a surprising finding because for more than 100 years it was believed that all of the neurons a person will ever have are produced by the time infancy ends. Studies done 2 years ago demonstrated that new neurons are added continuously in the hippocampus of the adult brain in rodents, non-human primates, and humans. In rodents, the number of new cells varies, with numbers increasing with exercise and environmental enrichment and decreasing with old age and some forms of stress. Voluntary physical activity in mice, such as running in an exercise wheel, increases the number of new neurons in the hippocampus.

New data in a mouse model have shown that running not only increased the numbers of neurons in the hippocampus, but also helped with spatial memory (that is, how the animals oriented themselves to their environment). Brains were studied both for changes in neuron number and for long-term potentiation (LTP). LTP is a complex form of electrical activity believed to be one of the factors important in the formation of memory in the hippocampus. Running helped the mice perform better in a maze, increased the numbers of neurons in the hippocampus, and selectively enhanced LTP, all of which may in turn have had a positive impact on memory function. Although at present the studies are only correlative, they suggest that physical activity can regulate nerve cell division in the hippocampus in the adult animal and improve learning. It may even be possible to stimulate brain repair mechanisms by exercising. Thus, physical activity may be one way to maintain or even improve cognitive performance as we age. Whether or not it would influence the risk of developing AD pathology is another question.

Healthful Eating Throughout Life

For generations, mothers have exhorted their children to eat their fruits and vegetables. Folklore has taught us that fruits and vegetables are good for us, but evidence on why this is so is only now emerging. Much of the data in the scientific literature on the effects of fruits and vegetables have come from studies on aging animals.

A recent animal study by researchers at the University of Colorado Health Sciences Center and the USDA Human Nutrition Research Center on Aging, Tufts University, Boston, reported that a diet rich in spinach, strawberries, or blueberries can reduce age-related deficits in specific neurotransmitter systems in the brain. In addition, the spinach diet improved learning in a test of motor function. Motor learning is important for adaptation to changes in the environment as well as being key to recovery from stroke and spinal cord injury.

The seven warning signs of Alzheimer's disease are:

1. Asking the same question over and over again.
2. Repeating the same story, word for word, again and again.
3. Forgetting how to cook, or how to make repairs, or how to play cards- activities that were previously done with ease and regularity.
4. Losing one's ability to pay bills or balance one's checkbook.
5. Getting lost in familiar surroundings, or misplacing household objects.
6. Neglecting to bathe, or wearing the same clothes over and over again, while insisting that they have taken a bath or that their clothes are still clean.
7. Relying on someone else, such as a spouse, to make decisions or answer questions they previously would have handled themselves.

Alzheimer's disease develops slowly and causes changes in the brain long before there are obvious changes in a person's memory, thinking, use of words or behavior. Stages and changes the person will go through are outlined below.

Common Changes in Mild AD

- Loses spark or zest for life - does not start anything.
- Loses recent memory without a change in appearance or casual conversation.
- Loses judgment about money.
- Has difficulty with new learning and making new memories.
- Has trouble finding words - may substitute or make up words that sound like or mean something like the forgotten word.
- May stop talking to avoid making mistakes.
- Has shorter attention span and less motivation to stay with an activity.
- Easily loses way going to familiar places.
- Resists change or new things.

- Has trouble organizing and thinking logically.
- Asks repetitive questions.
- Withdraws, loses interest, is irritable, not as sensitive to others' feelings, uncharacteristically angry when frustrated or tired.
- Won't make decisions. For example, when asked what she wants to eat, says "I'll have what she is having."
- Takes longer to do routine chores and becomes upset if rushed or if something unexpected happens.
- Forgets to pay, pays too much, or forgets how to pay - may hand the checkout person a wallet instead of the correct amount of money.
- Forgets to eat, eats only one kind of food, or eats constantly.
- Loses or misplaces things by hiding them in odd places or forgets where things go, such as putting clothes in the dishwasher.
- Constantly checks, searches or hoards things of no value.

Common Changes in Moderate AD

- Changes in behavior, concern for appearance, hygiene, and sleep become more noticeable.
- Mixes up identity of people, such as thinking a son is a brother or that a wife is a stranger.
- Poor judgment creates safety issues when left alone - may wander and risk exposure, poisoning, falls, self-neglect or exploitation.
- Has trouble recognizing familiar people and own objects; may take things that belong to others.
- Continuously repeats stories, favorite words, statements, or motions like tearing tissues.
- Has restless, repetitive movements in late afternoon or evening, such as pacing, trying doorknobs, fingering draperies.
- Cannot organize thoughts or follow logical explanations.
- Has trouble following written notes or completing tasks.
- Makes up stories to fill in gaps in memory. For example might say, "Mama will come for me when she gets off work."
- May be able to read but cannot formulate the correct response to a written request.
- May accuse, threaten, curse, fidget or behave inappropriately, such as kicking, hitting, biting, screaming or grabbing.
- May become sloppy or forget manners.
- May see, hear, smell, or taste things that are not there.
- May accuse spouse of an affair or family members of stealing.
- Naps frequently or awakens at night believing it is time to go to work.
- Has more difficulty positioning the body to use the toilet or sit in a chair.
- May think mirror image is following him or television story is happening to her.
- Needs help finding the toilet, using the shower, remembering to drink, and dressing for the weather or occasion.
- Exhibits inappropriate sexual behavior, such as mistaking another individual for a spouse. Forgets what is private behavior, and may disrobe or masturbate in public.

Common Changes in Severe AD

- Doesn't recognize self or close family.
- Speaks in gibberish, is mute, or is difficult to understand.
- May refuse to eat, chokes, or forgets to swallow.
- May repetitively cry out, pat or touch everything.
- Loses control of bowel and bladder.
- Loses weight and skin becomes thin and tears easily.

- May look uncomfortable or cry out when transferred or touched.
- Forgets how to walk or is too unsteady or weak to stand alone.
- May have seizures, frequent infections, falls.
- May groan, scream or mumble loudly.
- Sleeps more.
- Needs total assistance for all activities of daily living.

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 AD 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. The Alzheimer's Disease Education & Referral Center provides some suggestions to consider when faced with difficult aspects of caring for a person with AD. The site: <http://www.alzheimers.org/careguide.htm#dealing>

University of Arkansas, United States Department of Agriculture, County Governments Cooperating

The Arkansas Cooperative Extension Service offers its Programs to all eligible persons regardless of race, color, national origin, religion, gender, age, disability, marital or veteran status, or any other legally protected status, and is an Equal Opportunity Employer.