

ALZHEIMER'S DISEASE GOALS AND OBJECTIVES

Course Description

"Alzheimer's Disease" is a home study continuing education course for rehabilitation professionals. This course presents updated information about Alzheimer's Disease including sections on pathophysiology, etiology, symptomology, diagnosis, treatment, caregiving, and safety.

Course Rationale

The purpose of this course is to present current information about Alzheimer's Disease. Both therapists and therapy assistants will find this information pertinent and useful when creating and implementing rehabilitation programs and home safety programs that address the challenges and needs specific to individuals with AD.

Course Goals and Objectives

Upon completion of this course, the therapist or assistant will be able to

1. recognize the societal and economic impact of AD
2. list the neuro-physiologic changes associated with AD
3. recognize the current theories relating to AD etiology
4. identify associated risk factors for AD
5. list the symptoms of AD including its effects upon cognitive abilities required for safe and effective rehabilitative care.
6. recognize current mechanisms utilized to diagnose AD
7. differentiate all of the current options available for treating AD
8. recognize the responsibilities and challenges associated with being a caregiver
9. create a safe home environment for individuals with AD
10. identify the resources available for AD patients and their families

Course Instructor

Michael Niss PT

Target Audience

Physical therapists, physical therapist assistants, occupational therapists, and occupational therapist assistants

Course Educational Level

This course is applicable for introductory learners.

Course Prerequisites

None

Criteria for issuance of Continuing Education Credits

A documented score of 70% or greater on the written post-test.

Continuing Education Credits

Four (4) hours of continuing education credit (4 NBCOT PDUs/4 contact hours)

AOTA - .4 AOTA CEU, Category 1: Domain of OT – Client Factors, Context

Determination of Continuing Education Contact Hours

"Alzheimer's Disease" has been established to be a 4 hour continuing education program. This determination is based on an accepted standard for home-based self-study courses of 12 pages of text (12 pt font) per hour. The complete instructional text for this course is 52 pages (excluding References and Post-Test).

ALZHEIMER'S DISEASE OUTLINE

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Overview

Alzheimer's disease (AD) is the most common form of dementia 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.

The disease usually begins after age 60, and risk goes up with age. While younger people also may get AD, it is much less common. About 3 percent of men and women ages 65 to 74 have AD, and nearly half of those age 85 and older may have the disease. It is important to note, however, that AD is not a normal part of aging.

Morbidity

AD is a slow disease, starting with mild memory problems and ending with severe brain damage. The course the disease takes and how fast changes occur vary from person to person. On average, AD patients live from 8 to 10 years after they are diagnosed, though the disease can last for as many as 20 years.

Dementia

The term "dementia" describes a group of symptoms that are caused by changes in brain function. Dementia symptoms may include asking the same questions repeatedly; becoming lost in familiar places; being unable to follow directions; getting disoriented about time, people, and places; and neglecting personal safety, hygiene, and nutrition. People with dementia lose their abilities at different rates.

The Impact of Alzheimer's Disease

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 million people currently have the disease, and the prevalence (the number of people with the disease at any one time) doubles

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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 expectancies since the turn of the century. Furthermore, the group over 85 - the group with the highest risk of AD - is the fastest growing group in the population. Researchers estimate that by 2050, 14 million Americans will have Alzheimer's disease if current population trends continue and no preventive treatments become available (Hebert et al., 2001).

The increasing number of people with AD and the costs associated with the disease mean that AD puts a heavy economic burden on society.

More than 34 million people are now age 65 or older. This number is 13 percent of the total population of the U.S. The percentage of people over age 65 will increase rapidly over the next few years as the "baby boom" generation reaches 65. Slightly more than half of those with AD are cared for at home, while the rest are in different kinds of care facilities. The estimated annual cost of caring for one person with AD in 1996 was between \$18,400 and \$36,100, depending on how advanced the disease was and whether or not the person was at home. The cost of care has been steadily rising since then. The annual national direct and indirect costs of caring for AD patients are estimated to be as much as \$100 billion (Ernst and Hay, 1994; Ernst et al., 1997; Huang et al., 1988). The cost of care is not only financial. Families, friends, and caregivers struggle with great emotional and physical stress as they cope with the physical and mental changes in their loved ones. Caregivers must juggle many responsibilities and adjust to new and changing roles. As the disease gets worse and caring at home becomes increasingly difficult, family members face difficult decisions about long-term care. The number of caregivers - and their needs - will steadily grow as our population ages and the number of people with AD increases.

Pathophysiology

The Aging Brain

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

- Some neurons shrink, especially large ones in areas important to learning, memory, planning, and other complex mental activities.
- Tangles and plaques develop in neurons and surrounding areas (though in much smaller amounts than in AD).
- Damage by free radicals increases
- Inflammation also increases.

As a result of these changes, healthy older people may notice a modest decline in their ability to learn new things and retrieve information, such as remembering

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names. They may perform worse on complex tasks of attention, learning, and memory. However, if given enough time to perform the task, the scores of healthy people in their 70s and 80s are often the same as those of young adults. As they age, adults often improve their vocabulary and other forms of verbal knowledge.

Many investigators are now focused on understanding more fully these changes in normal aging and their effects on memory and thinking. For example, scientists have examined whether older adults differ from younger adults in the types of information they use to make decisions and their actual decision-making processes. Scientists found that older adults' memory and decision accuracy improved when they perceived the task to be personally relevant or when they were held accountable for their performance (Hess et al., 2001). Other studies comparing the performance of older and younger adults on memory tasks also showed that when older adults were given materials that engaged their emotional interest, their performance on memory tests equaled that of young adults (Rahhal et al., 2001). Other work shows that older adults perform better on most memory tasks at their optimal time of day. This time is determined by a biological clock that appears to shift toward the morning as a person ages (West et al., 2002). These results further reinforce the growing understanding that many factors besides age influence memory and cognitive ability.

By identifying the changes that occur in normal aging, investigators hope to be able to understand the transformation from healthy aging to Alzheimer's disease. In addition, learning more about the very earliest stages of the disease process may open doors to treatments that may delay the onset of the disease or prevent its progression.

Neuron repair

Unlike most cells, which have a fairly short lifespan, nerve cells, which are generated in the fetus or a short time after birth, live a long time. Brain neurons can live for up to 100 years or longer. In an adult, when neurons die because of disease or injury, they are not usually replaced. Recent research, however, shows that in a few brain regions, new neurons can be born, even in the old brain.

To prevent their own death, living neurons must constantly maintain and remodel themselves. If cell cleanup and repair slows down or stops for any reason, the nerve cell cannot function well, and eventually it dies.

Alzheimer's disease disrupts each of the three processes that keep neurons healthy: communication, metabolism, and repair. This disruption causes certain 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.

Beta-Amyloid Plaques and Neurofibrillary Tangles

The brains of AD patients have an abundance of two abnormal structures - beta amyloid plaques and neurofibrillary tangles. This is especially true in certain regions of the brain that are important in memory. Plaques are dense, mostly insoluble deposits of protein and cellular material outside and around the neurons. Tangles are insoluble twisted fibers that build up inside the nerve cell. Though many older people develop some plaques and tangles, the brains of AD patients have them to a much greater extent. Scientists have known about plaques and tangles for many years, but recent research has shown much about what they are made of, how they form, and their possible roles in AD.

Beta-Amyloid Plaques - Plaques are made of beta-amyloid, a protein fragment snipped from a larger protein called amyloid precursor protein (APP). APP is associated with the cell membrane. After it is made, APP sticks through the neuron's membrane, partly inside and partly outside the cell. Enzymes act on the APP and cut it into fragments of protein, one of which is called beta-amyloid. The beta-amyloid fragments then begin coming together into clumps outside the cell, and join together with other molecules and non-nerve cells to form insoluble plaques.

In AD, plaques develop in the hippocampus, a structure deep in the brain that helps to encode memories, and in other areas of the cerebral cortex that are used in thinking and making decisions. It is still not known whether beta-amyloid plaques themselves cause AD or whether they are a by-product of the AD process. It is known however, that changes in APP structure can cause a rare, inherited form of AD.

Scientists know that cleavage of APP by two kinds of enzymes - beta-secretases and gamma-secretases - generates the toxic beta-amyloid fragments. Two very similar beta-secretases, BACE1 and BACE2, can generate beta-amyloid. Previous studies demonstrated that the BACE1 enzyme is likely responsible for cleaving one end of the beta-amyloid fragment from APP. However, investigators thought that BACE2 might also be involved. A new study was designed to determine which of the beta-secretases is more important for the production of the toxic beta-amyloid (Cai et al., 2001). In this study, investigators at the Johns Hopkins University School of Medicine developed a transgenic "knockout" mouse in which the gene for the BACE1 enzyme was eliminated. This allowed the team to see whether removing the enzyme would interfere with the production of beta-amyloid. With the enzyme eliminated, beta-amyloid protein fragments no longer were produced in neuronal cultures from the knockout mice. These results suggested that BACE1 was involved in the amyloid-producing activity, and that BACE2 appeared to play a much smaller role in the cleavage of APP in neurons. To further support this conclusion, the investigators also compared the roles of BACE1 and alpha secretase, an enzyme involved in normal, nonpathological processing of APP into soluble products. They found that the two enzymes appear to compete with each other in the processing of APP, further demonstrating that BACE1 is the primary enzyme in the production of beta-amyloid. Many scientists believe that interfering with the deposition of beta-

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amyloid may prevent AD or slow its progression. Because they play key roles in the processing of APP and the resulting deposition of beta-amyloid, both beta- and gamma-secretase activities represent potential targets for drug therapies. The finding that BACE1 is the principal beta-secretase in neurons suggests that scientists might want to focus on the design of therapeutics to inhibit BACE1 activity.

Neurofibrillary Tangles - Healthy neurons have an internal support structure partly made up of structures called microtubules. These microtubules act like tracks, guiding nutrients and molecules from the body of the cell down to the ends of the axon and back. A special kind of protein, tau, makes the microtubules stable. In AD, tau is changed chemically. It begins to pair with other threads of tau and they become tangled up together. When this happens, the microtubules disintegrate, collapsing the neuron's transport system. This may result first in malfunctions in communication between neurons and later in the death of the cells.

Etiology

Genetics

Scientists have made enormous strides in the past two decades in unraveling the genetic components of AD and related dementias. For example, we now know that mutations of particular genes on three chromosomes (1, 14, and 21) virtually always lead to early-onset AD. In addition, mutations in the tau gene on chromosome 17 cause frontotemporal dementia and related diseases. These discoveries are helping to broaden our understanding of how mutations in particular genes cause changes in cellular pathways that eventually cause different kinds of dementia. For example, in a recent study, investigators at the University of Connecticut Health Sciences Center examined the ways in which a mutation in the presenilin-1 gene found on chromosomes 14 might affect the cellular structure of neurons during development. They found that mutated presenilin-1 interferes with the ability of brain cells to regulate and stabilize growing neurons by promoting the formation of neurofibrillary tangles, and interfering with brain receptors that help determine the fate of cells during development (Pigino et al., 2001).

We also know that slightly different forms of the APOE gene on chromosome 19 can influence a person's risk of developing late-onset AD. However, the APOE-e4 allele of this gene may explain only about 10 to 15 percent of the genetic risk of late-onset AD, and it is likely that other major risk factor genes also are involved. The roles that genetic changes play in increasing or decreasing a person's chances of developing late-onset AD are under intense scrutiny by many scientists.

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Three teams of investigators studying late-onset AD published papers recently reporting results of studies investigating one particularly intriguing chromosome - chromosome 10. In the first study, investigators at the Mayo Clinic in Jacksonville, Florida, confirmed a linkage between high levels of beta-amyloid in blood and a region on the long arm of chromosome 10 (Ertekin-Taner et al., 2001). Because beta-amyloid is intimately associated with the neuropathology of AD, the investigators think that genes that elevate these beta-amyloid levels could be risk factor genes for AD. A second team, located at the Washington University School of Medicine, conducted a study on pairs of siblings who had definite or probable AD. They also found a suggestive linkage to AD in the same region of the long arm of chromosome 10 (Myers et al., 2000). In a third analysis, a Harvard Medical School research team focused upon a specific gene called the insulin degrading enzyme (IDE) gene (Bertram et al., 2000). IDE is found in neurons and another type of brain cell called glia, and it acts to degrade beta-amyloid. These investigators found a linkage between one form of IDE, present in a region on the long arm of chromosome 10, with AD. These studies indicate that there may be more than one late-onset AD gene on the long arm of chromosome 10 that affects the risk of developing AD.

Chromosome 10 is of interest for another reason as well. Little is currently known about genes that might influence the age at which AD begins ("age of onset"). Because AD and Parkinson's disease (PD) share some common characteristics, including dementia, Duke University Medical Center investigators performed a genomic screen in the families of 449 AD and 174 PD families to see whether one or more genes controlled age at onset for both diseases. Results showed that this characteristic is highly heritable and that a specific region on chromosome 10 affects age of onset for both diseases (Li et al., 2002b).

Chromosomes 9 and 12 are also stirring interest as possible sites of genes that might affect AD risk. In collaboration with researchers at Washington University School of Medicine and Cardiff University, scientists at NIA have used genetic analysis strategies to find potentially promising regions on these two chromosomes. They are now conducting sequence analyses to pinpoint the locations more exactly (Myers et al. 2002). These investigators also are sequencing genes that might be involved in oxidative stress and lipid metabolism, two other factors thought to be involved in the development of AD.

Scientists at NIA and investigators from Duke University also have recently completed a study designed to examine whether cognitive decline associated with the APOE-e4 allele is different in older African-Americans than in Caucasians (Fillenbaum et al., 2001). The study involved more than 4,000 residents of five adjacent counties in the Piedmont area of North Carolina. Participants were given a brief cognitive function test at the beginning of the study and again 3 years later. The investigators found that participants who had the APOE-e4 allele scored lower on the first test than did those without APOE-e4, and that having the allele increased by 59 percent the odds of cognitive

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decline. However, age and race were not related to performance on the tests.

Lifestyle

Another area that is capturing an increasing amount of attention and interest is the possible influence of education, leisure, physical, and intellectually stimulating activities on the risk of developing AD. The interaction of genetic and lifestyle factors is also of interest. A number of studies over the past few years have provided intriguing hints that these activities may be linked to a reduced risk of AD, and they are consistent with what we know about other health benefits of lifelong physical and intellectual activity.

Several studies in the past year have revealed some clues about the effect of these potentially protective activities. The first study, conducted by a research team at Case Western Reserve University School of Medicine, explored the longstanding notion that high levels of education and occupation are correlated with protection against development of AD (Friedland et al., 2001). Some researchers have speculated that such protective effects occur because these activities may build up brain reserves that delay or buffer against cognitive decline. Others have argued that the protective effect of education is related to its complex associations with economic, medical, and occupational factors. This study attempted to differentiate between these two explanations by investigating the potential protective effects of three general categories of recreational activities. These categories included passive (e.g., watching television), intellectual (e.g., playing chess, solving crossword puzzles), and physical (e.g., bowling, skating) activities. Patients with AD were found to have been much less active than healthy control persons of similar background in terms of both diversity and intensity of recreational activities engaged in during early and middle adulthood. These differences were not explained by differing educational or income levels, age, or gender. People who were relatively inactive in midlife had a 250 percent increased risk of developing AD. Differences were greatest for intellectual activities, but were significant for passive and physical activities as well. This study suggests that engaging in physical and intellectual activities may buffer against cognitive decline and that underactivity is related to increased risk of AD.

A recent study by scientists at the University of Washington in Seattle explored how environmental risk may interact with the APOE genotype to clarify the possible relationships between early life environment and the development of AD (Mocerri et al., 2001). The researchers used information from Census data to index socioeconomic risk through measures of the father's occupation, parental age, household size, number of siblings, and birth order. They found that the risk of AD increased among individuals whose fathers were unskilled manual workers or laborers compared to those whose fathers had non-manual occupations, but this increased risk was significant only among individuals who carried the APOE-e4 allele. Therefore, compared to those with neither risk factor, the risk for Alzheimer's disease was greatly elevated when both the genetic and the

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environmental risk factors were present. These findings highlight some intriguing clues about the possibility that the APOE-e4 allele may modify any relationship between early-life environmental factors and the development of Alzheimer's disease.

Cholesterol and Homocysteine

A third exciting area of research is providing data about factors that may protect against or increase the risk of AD. In recent years, a number of studies have suggested a connection between AD and cholesterol in the blood. For example, the APOE-e4 allele is a variant of the APOE gene, which codes apolipoprotein E, a protein that helps to carry cholesterol in the blood. Test tube studies also have shown that blood cholesterol increases production of beta-amyloid from its APP precursor, and animal studies show a relationship between blood cholesterol and brain plaque levels in transgenic mice. Epidemiologic studies linking vascular risk factors to dementia have lent further support to this relationship. Many questions remain about the relationship between blood cholesterol and AD, but these intriguing findings have spurred new research and led scientists to hypothesize that drugs that lower blood cholesterol might also lower risk of developing dementia and AD.

Two recent observational studies examined changes in AD risk with prescription of statins, the most commonly prescribed cholesterol-lowering drugs. Both studies have stirred considerable interest because they showed a significant reduction in dementia risk correlated with individuals who take these drugs. In the first study, a research team at the Boston University School of Medicine, the University of Massachusetts Medical School, and Harvard School of Public Health analyzed data on more than 1,300 people in the United Kingdom (Jick et al., 2000). They found that people with high cholesterol who were prescribed statins had a risk of dementia 70 percent lower than those who did not have high cholesterol (or hyperlipidemia) or who were not on lipid-lowering treatment. The effect was similar regardless of the specific statin prescribed. People with high cholesterol who were prescribed a non-statin drug or those who remained untreated did not have reduced risk for dementia, suggesting that the effect was not due to lowering lipid levels per se.

Investigators at Loyola University Medical School in Maywood, IL, conducted a second study, which involved cases listed in a three-hospital database in the U.S. This study showed a relationship between either lovastatin or pravastatin prescription and a 60 to 73 percent lowered risk of developing AD (Wolozin et al., 2000). This relationship was not found with non-statin medications for hypertension or cardiovascular disease.

A recent epidemiologic study from investigators at Boston University, based on data from the Framingham Heart Study, also found that elevated levels of an amino acid called homocysteine, a risk factor for heart disease, are associated with an increased risk of developing AD (Seshadri et al., 2002). Investigators at

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NIA have shown in transgenic mice that high homocysteine levels make neurons vulnerable to dysfunction and death (Kruman et al., 2002). The relationship between AD and homocysteine is particularly interesting because blood levels of homocysteine can be reduced by increasing intake of folic acid and vitamins B6 and B12. These findings have led the NIA to fund a multicenter, randomized, placebo-controlled clinical trial, currently underway, to determine whether reducing homocysteine levels through high-dose supplements of folate and vitamins B6 and B12 will slow the rate of decline in people with AD.

Tau

In studying tau and what can go wrong, investigators have found that tau abnormalities are also central to other rare neurodegenerative diseases. These diseases, called tauopathies, include frontotemporal dementia, Pick's disease, supranuclear palsy, and corticobasal degeneration. They share a number of characteristics, but also each has distinct features that set them apart from each other and from AD. Characteristic signs and symptoms include changes in personality, social behavior, and language ability; difficulties in thinking and making decisions; poor coordination and balance; psychiatric symptoms; and dementia. Recent advances include the discovery of mutations in the tau gene that cause one tauopathy called frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17). The development of several mouse models that produce tau tangles, will allow researchers to address the many questions that remain about these diseases.

Oxidative Damage from Free Radicals

Another promising area of investigation relates to a longstanding theory of aging. This theory suggests that over time, damage from a kind of molecule called a free radical can build up in neurons, causing a loss in function. Free radicals can help cells in certain ways, such as fighting infection. However, too many can injure cells because they are very active and can readily change other nearby molecules, such as those in the neuron's cell membrane or in DNA. The resulting molecules can set off a chain reaction, releasing even more free radicals that can further damage neurons. This kind of damage is called oxidative damage. It may contribute to AD by upsetting the delicate machinery that controls the flow of substances in and out of the cell. 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. Some epidemiological and laboratory studies suggest that anti-oxidants from dietary supplements or food may provide some protection against developing AD. Other studies suggest that low calorie diets may protect against the development of AD by slowing down metabolic rates.

Inflammation

Another set of hints about the causes of AD points to inflammation in the brain. Because cells and compounds that are known to be involved in inflammation are found in AD plaques, some researchers think it may play a role in AD.

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They disagree, though, on whether inflammation is a good or a bad thing. Some think it is harmful - that it sets off a vicious cycle of events that ultimately causes neurons to die. Evidence from many studies supports this idea.

Other scientists believe that some aspects of the inflammatory process may be helpful - that they are part of a healing process in the brain. For example, certain inflammatory processes may play a role in combating the accumulation of plaques. Many studies are now underway to examine the different parts of the inflammatory process more fully and their effects on AD.

Aluminum

Certain aluminum compounds have been found to be an important component of the neurological damage characteristics of Alzheimer's Disease. Much research over the last decade has focused on the role of aluminum in the development of this disease. At this point, its role is still not clearly defined. Since AD is a chronic disease which may take a long time to develop, long-term exposure is the most important measure of intake. Long-term exposure is easiest to estimate for drinking water exposures. Epidemiological studies attempting to link AD with exposures in drinking water have been inconclusive and contradictory. Thus, the significance of increased aluminum intake with regard to onset of AD has not been determined.

Aluminum is one of the most abundant elements found in the environment. Therefore, human exposure to this metal is common and unavoidable. However, intake is relatively low because this element is highly insoluble in many of its naturally occurring forms. The significance of environmental contact with aluminum is further diminished by the fact that less than 1% of that taken into the body orally is absorbed from the gastrointestinal tract.

The average human intake is estimated to be between 30 and 50 mg per day. This intake comes primarily from foods, drinking water, and pharmaceuticals. Based on the maximum levels reported in drinking water, less than 1/4 of the total intake comes from water. Some common food additives contain aluminum. Due to certain additives, processed cheese and cornbread are two major contributors to high aluminum exposures in the American diet. With regard to pharmaceuticals, some common over-the-counter medications such as antacids and buffered aspirin contain aluminum to increase the daily intake significantly.

Over the last few years, there has been concern about the exposures resulting from leaching of aluminum from cookware and beverage cans. However, as a general rule, this contributes a relatively small amount to the total daily intake. Aluminum beverage cans are usually coated with a polymer to minimize such leaching. Leaching from aluminum cookware becomes potentially significant only when cooking highly basic or acidic foods.

Copper and Zinc

Additional work in beta-amyloid has built on earlier studies indicating that the amount of copper and zinc is increased in the cortex of brains from individuals who have died of AD. These metals are concentrated in beta-amyloid plaques. Although controversial, some scientists believe that beta-amyloid possesses binding sites for copper and zinc that enhance the resistance of beta-amyloid to breakdown by enzymes and encourage its tendency to clump together to form plaques. In a new study, investigators in Australia, Sweden, Germany, and the U.S., led by scientists at the Massachusetts General Hospital, treated 12-month-old transgenic mice with orally administered clioquinol for 12 weeks (Cherny et al., 2001). Clioquinol is a chemical that binds metals such as copper and zinc and removes them from body tissues. The team found that treatment with clioquinol reversed the deposition of beta-amyloid in the brain of the transgenic mice with AD. The amyloid plaque surface area was significantly reduced and membrane-associated beta-amyloid in brain tissue decreased by 65 percent. In fact, two of the six animals treated with clioquinol had no sedimentable beta-amyloid, and no beta-amyloid could be detected using very specific and sensitive immunological techniques. Twenty older transgenic mice (21 months of age) treated at a higher dose for just 9 weeks also were examined. After this treatment, sedimentable brain beta-amyloid decreased by 49 percent and the study team found an overall clearance of beta-amyloid from the brain. Clioquinol did not cause decreased levels of APP nor did it result in decreased levels of a protein involved in neuron-neuron communication, suggesting that it was not toxic to brain tissue. Despite these encouraging findings, safety issues in this therapy still need to be addressed in human studies, as small amounts of these metals are necessary for many chemical reactions in the body.

Symptoms of AD

As Alzheimer's disease makes inroads into memory and mental abilities, it also begins to change a person's emotions and behaviors. Between 70 to 90 percent of people with Alzheimer's disease eventually develop one or more behavioral symptoms. These 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.

Unlike a stroke, in which damage to part of the brain occurs all at once, the damage of Alzheimer's disease spreads slowly over time and affects many different parts of the brain. Even small tasks require the brain to engage in a complex process that can involve more than one region of the brain. If this process is disrupted, the person may not be able to do the task or may act in a strange or inappropriate way.

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Behavioral symptoms are one of the hardest aspects of the disease for families and other caregivers to deal with. They are emotional and upsetting. They are also a visible sign of the terrible change that has taken place in the person with AD.

The seven warning signs of Alzheimer's disease

If someone has several or even most of these symptoms, it does not mean they definitely have the disease. It does mean they should be thoroughly examined by a medical specialist trained in evaluating memory disorders, such as a neurologist or a psychiatrist, or by a comprehensive memory disorder clinic, with an entire team of expert knowledge about memory problems.

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.

Stages of AD

Although the course of AD is not the same in every patient, symptoms seem to develop over the same general stages.

Preclinical AD

AD begins in the entorhinal cortex, which is near the hippocampus and has direct connections to it. It then proceeds to the hippocampus, the structure that is essential to the formation of short-term and long-term memories. Affected

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regions begin to atrophy (shrink). These brain changes probably start 10 to 20 years before any visible signs and symptoms appear.

Mild Cognitive Impairment

As they get older, some people develop memory problems greater than those expected for their age. However, these problems do not necessarily meet all the accepted criteria for AD. For example, a person with memory problems might not experience the personality changes or difficulties in making decisions experienced by those with AD. These people are thought to have mild cognitive impairment (MCI) with memory loss. In certain studies, about 40 percent of these individuals develop AD within 3 years. Other people with MCI, however, have not progressed to AD, even after 8 years.

Some scientists think MCI with memory loss is often a very early stage of AD. One recent study provided some support for this notion (Morris et al., 2001). In this study, researchers at the Washington University School of Medicine in St. Louis, Missouri, examined 404 people who had either mild memory loss (classified as MCI) or no memory problems. These participants agreed to have annual memory assessments, and 42 agreed to donate their brains to the study after death. The 227 people with MCI were placed into one of three categories that reflected the researchers' degree of confidence that the subtle signs of memory loss might indicate the onset of AD. The categories were: "fairly confident" of dementia, "suspicious" of dementia, and "uncertain" of dementia. The volunteers were reassessed annually for up to 9 1/2 years. After 5 years, AD symptoms had developed in 7 percent of the healthy volunteers, 20 percent of the individuals in the "uncertain" group, 36 percent of those in the "suspicious" group, and 60 percent of those in the "fairly confident" group. By 9 1/2 years, all the volunteers with the most severe form of MCI had developed the clinical symptoms of AD. In studying the donated brain tissue of those who died, investigators also found that 21 of the 25 volunteers who originally were diagnosed with MCI had damage to brain tissue that was characteristic of AD. The investigators interpreted these findings to mean that MCI is an early stage of AD.

Mild AD

As the disease begins to affect the cerebral cortex, memory loss continues and changes in other cognitive abilities emerge. The clinical diagnosis of AD is usually made during this stage. Signs of mild AD can include:

- 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.

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- 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.

The growing numbers of plaques and tangles first damage areas of brain that control memory, language, and reasoning. It is not until later in the disease that physical abilities decline. This leads to a situation in mild AD in which a person seems 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 because the early signs can be confused with changes that can happen normally with aging. Accepting these signs and deciding to go for diagnostic tests can be a big hurdle for patients and families to cross.

Moderate AD

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

- 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.

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- 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.

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 these processes are disturbed, and this is 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 is 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 around her can be strange and frightening. Sticking close to a trusted and familiar caregiver may be the only thing that makes sense and provides security. Taking off clothes may seem reasonable to a person with AD who feels hot and doesn't understand or remember that undressing in public is not acceptable.

Severe AD

In the last stage of AD, plaques and tangles are widespread throughout the brain, and areas of the brain have atrophied further. Patients cannot recognize family and loved ones or communicate in any way. They are completely dependent on others for care. All sense of self seems to vanish. Other symptoms can include:

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- Lack of bladder and bowel control
- 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 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.

At the end, patients may be in bed much or all of the time. Most people with AD die from other illnesses, frequently aspiration pneumonia. This type of pneumonia happens when a person is not able to swallow properly and breathes food or liquids into the lungs.

Diagnosis

Currently, experienced physicians can diagnose AD with up to 90 percent accuracy. However, we are still some distance from the ultimate goal - a reliable, valid, inexpensive, and early diagnostic marker.

Early diagnosis has several advantages. For example, many conditions cause symptoms that mimic those of Alzheimer's disease. Finding out early that the problem isn't AD but is something else, can spur people into getting treatment for the real condition. For the small percentage of dementias that are treatable or even reversible, early diagnosis increases the chances of successful treatment.

Even when the cause of the dementia turns out to be Alzheimer's disease, it's good to find out sooner rather than later. One benefit is medical. The drugs now available to treat AD can help some people maintain their mental abilities for months to years, though they do not change the underlying course of the disease.

Other benefits are practical. The sooner the person with AD and family know, the more time they have to make future living arrangements, handle financial matters, establish a durable power of attorney, deal with other legal issues, create a support network, or even make plans to join a research study. Being able to participate for as long as possible in making decisions about the present and future is important to many people with AD.

Current Tools for Diagnosing AD

A definitive diagnosis of Alzheimer's disease is still only possible after death, during an autopsy, when the plaques and tangles can actually be seen. But with the tools now available, experienced physicians can be pretty confident about making an accurate diagnosis in a living person. A comprehensive assessment for Alzheimer's disease usually includes all of the following.

- **Detailed Patient History** - How and when symptoms developed. The patient's and his or her family's overall medical condition and history. An assessment of the patient's emotional state and living environment.
- **Interview of family members or close friends** - People close to the patient 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.
- **Physical and neurological examinations and laboratory tests** - Blood and other medical tests help determine neurological functioning and identify possible non-AD causes of dementia.

Biological Markers and Oxidative Stress

Scientists are also trying to discover whether biological markers exist that could indicate early changes in the brain associated with AD. Understanding more about these markers - what they are, how they function, and how and when their levels change - will help investigators answer questions about the cause and development of AD and may lead one day to treatments to delay or prevent the onset of the disease.

One long-standing theory of aging and neurodegeneration is that damage from highly reactive molecules called oxygen free radicals can build up in neurons over time. If unchecked, this oxidative stress can modify or damage cellular molecules such as proteins, lipids, and nucleic acids. In the AD brain, in particular, such damage has been observed, especially in the late stages, when both beta-amyloid plaques and neurofibrillary tangles are present. However, scientists do not know whether the oxidative stress causes or results from the process of beta-amyloid plaque formation. A number of markers of oxidative stress have been measured in the cerebrospinal fluid (CSF) of people with AD, but for most of these markers, the amounts found in those with AD and in cognitively healthy individuals overlap substantially.

Scientists have suggested that the extent to which lipids in the central nervous system have been affected by free radical oxidative stress can be assessed by measuring body levels of a newly described class of lipids - the isoprostanes (iP). Isoprostanes are formed by the addition of oxygen to particular lipids. In a new study, researchers at the University of Pennsylvania School of Medicine worked with transgenic mice to see whether iP accumulation might be a useful biomarker of plaque pathology (Praticò et al., 2001). Over 14 months, these investigators

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compared the amount of a particular iP in urine, blood, CSF, and brain from transgenic mice and a control group of mice at different ages. Results showed that after the age of 6 months, the amounts of iP in the two groups began to diverge, and differences in all the fluids and tissues increased in parallel with age. Because iP is chemically stable and can be measured in plasma, urine, or CSF, it may have utility as a diagnostic tool and to monitor development of pathology in AD or other neuro- degenerative diseases in which oxidative stress has been implicated.

Cornell University investigators also used CSF to hunt for biological markers of AD. These researchers used state-of-the-art protein analysis tools to identify changes in the composition of CSF that correlate with Alzheimer's disease (Choe et al., 2002). Using this approach, the investigators identified a panel of nine proteins that demonstrate altered expression in patients with Alzheimer's disease. When taken together, these proteins suggest the clinical state of Alzheimer's disease. This study is one of the first to use a multiple-marker assay for the presence of Alzheimer's disease based on changes in CSF composition. In the future, a biomarker assay like this may help to improve the accuracy of AD diagnosis.

A study from a research team at the University of Kentucky Sanders-Brown Center on Aging examined the possibility that a marker of oxidative stress in DNA may identify persons with neurodegenerative disorders such as Alzheimer's disease (Lovell and Markesbery, 2001). This marker of DNA oxidative stress is called 8-hydroxy-2'-deoxyguanosine (8-OHG). It is formed by oxidation of one of the four building blocks (bases) that make up DNA strands. In normal cells, not very much oxidation of this base takes place, and the cell is able to repair the DNA by removing the 8-OHG. The 8-OHG is then found free in the cell. In AD, two changes to this process seem to take place. First, a high level of oxidative stress causes more of the 8-OHG to be formed in the DNA. Second, the repair process is much less efficient, so less of the oxidized base is removed from the DNA and found free in the cell. After comparing people with AD and cognitively healthy individuals, the University of Kentucky investigators found that the ratio of DNA-bound 8-OHG to free 8-OHG increased 100-fold in the patients with AD. The investigators suggest that this marker of DNA oxidation mirrors brain degeneration and might be a useful indicator of disease progression.

Neuroimaging

Investigators are continuing to use neuroimaging techniques, such as magnetic resonance imaging (MRI) and positron emission tomography (PET), to assess whether it is possible to measure aspects of brain structure or function that will identify those people who are at risk of AD before they develop the symptoms of the disease. Over the past year, results from a number of promising longitudinal neuroimaging studies have been published. These studies have expanded our understanding of the potential usefulness of imaging techniques for research and diagnostic purposes as well as increased our knowledge about early AD changes

in the brain.

For example, it is well known that the hippocampus, a region of the brain important for learning and short-term memory, is affected early in the course of AD. Using a series of MRI scans, researchers at the Mayo Clinic documented for the first time the rate of hippocampal atrophy in patients with MCI (Jack et al., 2000). In this study, the investigators grouped participants into those who were cognitively healthy, those who had MCI, and those who had probable AD. Each participant had an MRI at the beginning of the study and another one later during the course of the study. The percent change in hippocampal volume was measured for each participant. Within the cognitively healthy and MCI groups, those who declined clinically over time had a significantly greater volume loss than those who remained clinically stable. These results correlated the rate of change in hippocampal volume and change in cognitive status. The data also suggest that it should be possible to distinguish stable from declining members of a group, both in persons showing early symptoms and in those who have not yet shown symptoms. The research team concluded from this study that serial hippocampal volume measurements may be a useful tool to monitor the efficacy of therapeutic interventions in clinical trials for both progression and prevention of AD, and that they may also be a way to identify people with MCI who will not progress to AD.

Neuropathological studies have shown that neurons die in the entorhinal cortex (EC), another brain region involved in memory function, even earlier than in the hippocampus (Kordower et al., 2001; Price et al., 2001). Several studies using MRI have shown that patients with AD and MCI also have reduced EC volumes as compared with cognitively normal older adults. Some researchers have found that changes in EC volume are better than hippocampal volume for distinguishing individuals with AD from those with MCI (Du et al., 2001). Others have found that conversion to dementia from MCI is better predicted by volume of the EC, as opposed to the hippocampus (Dickerson et al., 2001). Further study of the time course of change in the hippocampus, EC, and other structures will help delineate which brain regions are best for diagnosing AD early and following its progression.

A research team from the New York University School of Medicine has recently published the first longitudinal PET imaging study of cognitively healthy elderly declining to MCI (deLeon et al., 2001). The investigators in this study found that decreased glucose metabolism in the EC at baseline was the most accurate predictor of conversion from normal cognition to MCI. That is, changes in the EC were seen before cognitive decline and before changes in metabolism in other parts of the brain. Reduced glucose metabolism in the EC accurately predicted declining cognitive function in 83 percent of study participants who got worse, and accurately predicted non-decline in 85 percent of participants who remained cognitively healthy after 3 years. At the follow-up PET evaluation in those who had progressed to MCI, reduced glucose metabolism was also seen in the

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hippocampus and temporal neocortex, a development also seen in AD. In addition, those who experienced cognitive decline and were carriers of the APOE-e4 allele) showed especially marked reductions over time in glucose metabolism in the temporal neocortex. This finding is consistent with earlier reports by other investigators that showed reductions in temporal cortex metabolism of APOE-e4 carriers compared to persons without APOE-e4.

It is important to note that using PET to identify persons at risk of developing MCI and AD is still at the experimental stage, and a number of longitudinal studies will need to be completed and analyzed before its potential can be usefully evaluated.

Neuropsychology

Several research teams have hypothesized that performance on specific cognitive tests might predict whether an individual will develop AD. For example, in one recent study, Boston University investigators gave 1,076 participants in the ongoing Framingham Heart Study a series of cognitive tests every 2 years for up to 22 years (Elias et al., 2000). At the time of the first tests, participants were at least 65 years old. None had had a stroke or dementia. The investigators found that lower scores in a number of areas - learning new things, recall, retention, and abstract reasoning - obtained during any time period that a participant did not have dementia were associated with the later development of AD. The study team also found that a detectable lowering of cognitive functioning preceded the appearance of AD by many years. Changes in abstract reasoning ability and capacity to retain verbal information were the strongest predictors of AD when there was a long interval between the initial assessment and development of AD.

A smaller study of cognitively normal elders and people with mild memory difficulty, conducted by investigators at Massachusetts General Hospital and Harvard Medical School, also showed that neuropsychological tests can predict the development of AD to some extent (Albert et al., 2001). Of the 20 neuropsychological measures used in the initial tests given in this study, four were useful in discriminating those who converted to a diagnosis of probable AD from those who did not. Tests of memory and executive functions (such as the ability to reason and make decisions) had the most power to discriminate between those who were likely to develop AD and those who were not.

Based on the results of these and similar neuropsychological studies, the Quality Standards Subcommittee of the American Academy of Neurology has developed clinical practice guidelines for clinicians who work with patients with memory complaints (Petersen et al., 2001). The guidelines recommend that clinicians use general cognitive screening instruments, such as the Mini-Mental State Examination, and neuropsychological tests to evaluate and monitor patients with MCI. These tests may help clinicians assess the degree of cognitive impairment and help them detect signs that might indicate the development of dementia.

The Mini Mental State Examination (MMSE) - is the most commonly used test for complaints of memory problems or when a diagnosis of dementia is being considered.

The MMSE is a series of questions and tests, each of which scores points if answered correctly. If every answer is correct, a maximum score of 30 points is possible. People with Alzheimer's disease generally score 26 points or less.

Section 1: Orientation

The first 10 points are gained for giving the correct date and location.

For example:

What is the day of the week?
What year was last year?
What is the street name?
What building are we in?

Section 2: Memory (part 1)

The first part of the memory test evaluates short-term memory. The patient is given the names of three objects to remember - table, ball and pen, for example. They are then be asked to repeat the three names, scoring 1 point for each object correctly recalled (3 points maximum).

Section 3: Attention and calculation

The next part of the MMSE tests the ability to concentrate on a tricky task. For example, the patient may be asked to count backwards by 5 starting at 50. One point is given for each correct subtraction, with a maximum of 5 points.

Section 4: Memory (part 2)

The patient is asked to recall the three items from Section 2. The attention and calculation section may have been quite a stressful experience, so this can be tricky. One point is given for each correctly recalled object.

Section 5: Language, writing and drawing

The final part of the test makes an assessment of spoken and written language, and the ability to write and copy.

The person being tested is shown two everyday items - a hammer and a crayon, for example - and asked to name them. One point is scored for each correct answer.

The patient is then asked to say aloud a tongue-twister sentence such as 'Pass the peas please'. One point is scored for correctly repeating the sentence.

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The patient is then given a piece of paper, and asked to carry out a three-step process:

For example:

'Take this paper in your hand' (1 point);

'Fold it in half' (1 point);

'Place it on this chair' (1 point).

One point is gained for each correctly completed step.

A card is then shown with an instruction for a simple task - 'Clap your hands'.

One point is scored for a correct response.

The next stage of the test is to write a sentence on a piece of paper. The sentence needs to make sense. One point is scored for an acceptable sentence.

Finally, the ability to copy a design of two intersecting shapes is assessed. One point is awarded for correctly copying it. All angles on both figures must be present, and the figures must have one overlapping angle.

APOE Testing

A blood test is available that can identify which apoE alleles a person has. However, because the apoE4 gene is only a risk factor for AD, this blood test cannot tell whether a person will develop AD or not. In diagnosing AD, apoE testing is not a common practice. Instead of a yes or no answer, the best information a person can get from this genetic test for apoE is maybe or maybe not. Although some people want to know whether they will get AD later in life, this type of prediction is not yet possible. In fact, some researchers believe that screening measures may never be able to predict AD with 100 percent accuracy.

In a research setting, apoE testing may be used to identify study volunteers who may be at a higher risk of getting AD. In this way, researchers can look for early brain changes in some patients. This test also helps researchers compare the effectiveness of treatments for patients with different apoE profiles. Most researchers believe that the apoE test is useful for studying AD risk in large groups of people but not for determining one person's individual risk. Predictive screening in otherwise healthy people will be useful if an accurate/reliable test is developed and effective ways to treat or prevent AD are available.

Criteria for "Probable" Alzheimer's Disease

Because no simple and reliable biological test for AD is available, the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Association together established criteria to help physicians diagnose AD. These criteria also help physicians distinguish between AD and other forms of dementia. "Probable" Alzheimer's disease is determined when a person has:

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- Dementia confirmed by clinical and neuropsychological examination
- Progressive worsening of memory and other mental functioning
- No disturbances of consciousness (no "blacking out")
- Symptoms beginning between ages 40 and 90
- No other disorders that might account for the dementia

As they get older, some people develop a memory deficit greater than that expected for their age. However, other aspects of cognition are not affected, so these people do not meet all the accepted criteria for AD. Thus, they are said to have "mild cognitive impairment" (MCI). About 40 percent of these individuals will develop AD within 3 years. Others, however, do not seem to progress to AD.

Treatment

It has become clear that there probably isn't a "magic bullet" that will, by itself, prevent or cure AD. However, scientists are identifying a number of interventions that can be used to reduce risk and treat the disease. Today, it is estimated that the National Institute on Aging, other NIH Institutes, and private industry are conducting clinical trials on around 30 compounds that may be active against AD.

Medications

Five prescription drugs currently are approved by the U.S. Food and Drug Administration to treat people who have been diagnosed with Alzheimer's disease (AD). Treating the symptoms of AD can provide patients with comfort, dignity, and independence for a longer period of time and can encourage and assist their caregivers as well. It is important to understand that none of these medications stops the disease itself.

Treatment for Mild to Moderate AD

Four of these medications are called cholinesterase inhibitors. These drugs are prescribed for the treatment of mild to moderate AD. They may help delay or prevent symptoms from becoming worse for a limited time and may help control some behavioral symptoms. The medications are: Reminyl® (galantamine), Exelon® (rivastigmine), Aricept® (donepezil), and Cognex® (tacrine). Scientists do not yet fully understand how cholinesterase inhibitors work to treat AD, but current research indicates that they prevent the breakdown of acetylcholine, a brain chemical believed to be important for memory and thinking. As AD progresses, the brain produces less and less acetylcholine; therefore, cholinesterase inhibitors may eventually lose their effect.

No published study directly compares these drugs. Because all four work in a similar way, it is not expected that switching from one of these drugs to another will produce significantly different results. However, an AD patient may respond

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better to one drug than another. Cognex® (tacrine) is no longer actively marketed by the manufacturer.

Treatment for Moderate to Severe AD

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.

Namenda® is believed to work by regulating glutamate, another important brain chemical that, when produced in excessive amounts, may lead to brain cell death. Because NMDA antagonists work very differently from cholinesterase inhibitors, the two types of drugs can be prescribed in combination.

Dosage and Side Effects

Doctors usually start patients at low drug doses and gradually increase the dosage based on how well a patient tolerates the drug. There is some evidence that certain patients may benefit from higher doses of the cholinesterase inhibitor medications. However, the higher the dose, the more likely are side effects. The recommended effective dosage of Namenda® is 20 mg/day after the patient has successfully tolerated lower doses. Some additional differences among these medications are summarized in the following table. .

DRUG NAME	DRUG TYPE AND TREATMENT	MANUFACTURER'S RECOMMENDED DOSAGE	COMMON SIDE EFFECTS	POSSIBLE DRUG INTERACTIONS
Namenda® (memantine) Blocks the toxic effects associated with excess glutamate and regulates glutamate activation.	N-methyl D-aspartate (NMDA) antagonist prescribed to treat symptoms of moderate to severe AD	<ul style="list-style-type: none">• 5 mg, once a day• Increase to 10 mg/day (5 mg twice a day), 15 mg/day (5 mg and 10 mg as separate doses), and 20 mg/day (10 mg twice a day) at minimum of one week intervals if well tolerated.	Dizziness, headache, constipation, confusion	Other NMDA antagonist medications, including amantadine, an antiviral used to treat the flu, dextromethorphan, prescribed to relieve coughs due to colds or flu, and ketamine, sometimes used as an anesthetic, have not been systematically evaluated and should be used with caution in combination with this medication.

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<p>Reminyl® (galantamine)</p> <p>Prevents the breakdown of acetylcholine and stimulates nicotinic receptors to release more acetylcholine in the brain.</p>	<p>Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate AD</p>	<ul style="list-style-type: none"> • 4mg, twice a day (8mg/day) • Increase by 8mg/day after 4 weeks to 8mg, twice a day (16mg/day) if well tolerated. • After another 4 weeks, increase to 12mg, twice a day (24mg/day) if well tolerated. 	<p>Nausea, vomiting, diarrhea, weight loss</p>	<p>Some antidepressants such as paroxetine, amitriptyline, fluoxetine, fluvoxamine, and other drugs with anticholinergic action may cause retention of excess Reminyl in the body, leading to complications; NSAIDs should be used with caution in combination with this medication.*</p>
<p>Exelon® (rivastigmine)</p> <p>Prevents the breakdown of acetylcholine and butyrylcholine (a brain chemical similar to acetylcholine) in the brain.</p>	<p>Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate AD</p>	<ul style="list-style-type: none"> • 1.5mg, twice a day (3mg/day) • Increase by 3mg/day every 2 weeks to 6mg, twice a day (12mg/day) if well tolerated. 	<p>Nausea, vomiting, weight loss, upset stomach, muscle weakness</p>	<p>None observed in laboratory studies; NSAIDs should be used with caution in combination with this medication.*</p>
<p>Aricept® (donepezil)</p> <p>Prevents the breakdown of acetylcholine in the brain.</p>	<p>Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate AD</p>	<ul style="list-style-type: none"> • 5mg, once a day • Increase after 4-6 weeks to 10mg, once a day if well tolerated. 	<p>Nausea, diarrhea, vomiting</p>	<p>None observed in laboratory studies; NSAIDs should be used with caution in combination with this medication.*</p>
<p>Cognex® (tacrine)</p> <p>Prevents the breakdown of acetylcholine in the brain.</p> <p>Note: Cognex is still available but no longer actively marketed by the manufacturer.</p>	<p>Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate AD</p>	<ul style="list-style-type: none"> • 10mg, four times a day (40mg/day) • Increase by 40mg/day every 4 weeks to 40mg, four times a day (160mg/day), if liver enzyme functions remain normal and if well tolerated. 	<p>Nausea, diarrhea, possible liver damage</p>	<p>NSAIDs should be used with caution in combination with this medication.*</p>

Other Medications

Inflammation of tissue in the brain and overproduction of free radicals are two processes that are thought to be a feature of AD. Scientists are testing two different types of nonsteroidal anti-inflammatory drugs (NSAIDs) to find out if they slow the disease. There is evidence that inflammation in the brain may contribute to AD damage. Scientists believe that anti-inflammatory drugs such as NSAIDs

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might help slow the progression of AD. Rofecoxib (Vioxx) and naproxen (Aleve) are two NSAIDs currently being studied.

Scientists are also conducting clinical trials to see if substances already used to reduce cardiovascular risk factors also help lower AD risk or delay progression of the disease. These trials are testing whether supplementation with folic acid and vitamins B6 and B12 can slow the rate of cognitive decline in cognitively normal men and women, women at increased risk of developing dementia, and people diagnosed with AD. A study of statins, the most common type of cholesterol-lowering drug, is also underway to see whether these drugs can slow the rate of disease progression in AD patients.

Estrogen

Over the past 25 years, laboratory and animal studies, as well as observational studies in women, have suggested that estrogen has some positive effects on brain activity. These findings have created scientific interest in the relationship among estrogen, memory, and cognitive function.

Studies of estrogen in postmenopausal women with mild to moderate AD did not find estrogen beneficial. But, even if estrogen does not slow the progression of the disease in women already affected with AD, scientists thought perhaps menopausal hormone therapy might in some way affect age-related cognitive decline or protect a woman from developing AD. Two types of such therapies have been investigated—the use of estrogen alone in women who have had a hysterectomy and the use of estrogen plus progestin, which reduces the risk of thickening of the lining of the uterus and endometrial cancer, in other women.

In 2002 a large clinical trial showed that combined estrogen/progestin therapy taken daily for just over 5 years increased the risk of heart disease and breast cancer in some women. More recently, a substudy of that trial showed that this same therapy taken daily by women over age 65 actually increased their chance of developing dementia.

Scientists are continuing to evaluate estrogen alone to prevent dementia. This includes an NIA clinical trial of estrogen alone to prevent or delay development of AD in cognitively normal older women with a family history of dementia.

Nerve Growth Factor

Another area of work involves nerve growth factor (NGF). NGF is one of several growth factors in the body that maintain the health of neurons. NGF also promotes the growth of axons and dendrites, the neuron branches that connect with other neurons and that are essential in nerve cells' ability to communicate. Studies have turned up a number of clues that link NGF to the neurons that use acetylcholine as a neurotransmitter, so researchers have been eager to see what happens when NGF is added to aging brain tissue. In animal studies, researchers have been able to reverse most of the age-related neuronal

shrinkage and loss of ability to make acetylcholine. This success has led to a small-scale, privately-funded gene therapy trial that is testing whether this procedure can be done safely in humans and whether it might lessen symptoms of AD.

Nutritional Supplements

Research has shown that vitamin E slows the progress of some consequences of AD by about 7 months. Scientists now are studying vitamin E to learn whether it can prevent or delay AD in patients with mild cognitive impairment (MCI). Recent research suggests that ginkgo biloba, an extract made from the leaves of the ginkgo tree, may be of some help in treating AD symptoms. There is no evidence that ginkgo will cure or prevent AD. Scientists now are trying to find out whether ginkgo biloba can delay or prevent dementia in older people.

Immunization

Immunization is a common practice that protects people against a wide variety of diseases. Scientists questioned whether this might be a useful strategy for AD as well, and the results of their intense work over the last several years illustrate both the promise and the difficulties of this type of research.

In early studies conducted at Elan Pharmaceuticals, scientists worked with transgenic mice that gradually develop beta-amyloid plaques in the brain, injecting them with a vaccine composed of very small amounts of the beta-amyloid peptide, or protein fragment, mixed with another substance known to stimulate the immune system (Schenk et al., 1999). They found that the injections resulted in much less beta-amyloid being deposited in the brains of the mice and better performance on memory tests.

The success of these studies in mice led to preliminary trials in humans, conducted by Elan investigators and teams supported by NIH. These trials tested the vaccine's safety and assessed its effectiveness. In both trials, investigators also measured the immune response in those who received the vaccine. These human trials were halted prematurely in early 2002 because inflammation developed in the brains of some of the participants. The researchers' disappointment was tempered by the fact that the study still provided a wealth of important clinical and pathology data on hundreds of participants and by the recognition that cutting-edge research like this can suffer setbacks.

Simultaneously, other teams of investigators made additional progress in this area by continuing work with several strains of transgenic mice. One research team, from Washington University School of Medicine in St. Louis, found that passively immunizing transgenic mice decreased the deposition of beta-amyloid in the brain and reduced the overall number of plaques (DeMattos, et al., 2001). In other studies, they also found that prolonged administration of anti-beta-amyloid antibody decreased the accumulation of beta-amyloid in plaques and rapidly increased the amount of beta-amyloid in the blood, effectively removing it

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from the brain (DeMattos et al., 2002a; DeMattos et al., 2002b). This is an important finding because it suggests that there may be ways to remove beta-amyloid from the brain without producing adverse side effects.

In conjunction with the researchers at Washington University, scientists with Lilly Research Laboratories in Indianapolis, showed that the antibody therapy rapidly reversed the impairment shown by the transgenic mice in certain learning and memory tasks (Dodart et al., 2002).

Although scientists still have much to learn, this exciting research is helping them understand more fully the steps involved in the metabolism of APP and beta-amyloid, and how beta-amyloid is distributed among body compartments - including blood, cerebrospinal fluid, and brain. This improved understanding may prove central to more effective AD diagnosis and treatment in the future.

Other Approaches

Finally, a number of clinical trials are focusing on the earliest stages of the disease process. For example, scientists are developing drugs that prevent enzymes from clipping beta-amyloid out from APP. Others are working on ways to stop beta-amyloid from clumping together into plaques. Teams of investigators are also studying certain enzymes that seem to be able to break beta-amyloid into pieces after it is released from cells but before it has a chance to form into plaques. Still other scientists are exploring the role of neurotransmitter systems other than acetylcholine, such as glutamate. One especially active area of research involves the possibility that a vaccine might be able to stimulate the immune system into getting rid of plaques once they have formed, stopping beta-amyloid and plaque buildup, or even getting rid of plaques once they have formed.

Caregivers

Perhaps one of the greatest costs of Alzheimer's disease is the physical and emotional toll on family, caregivers, and friends. 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 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.

Although research on caregiver support is still in its early days, a lot is already known about the unique aspects of caregivers' personalities and situations. Certain characteristics seem to make some caregivers more vulnerable to the physical and emotional stresses associated with dementia care. These

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characteristics include being a male spouse, having few breaks from caregiving responsibilities, and having preexisting illnesses.

Caregiver research is also beginning to tease out characteristics of support programs that might be most useful for particular groups of caregivers. For example, peer support programs that link caregivers with trained volunteers who also have been dementia caregivers appear to help. These programs are especially good for caregivers whose social support networks are weak or who are in very stressful situations. Other research has confirmed that the information and problem-solving needs of caregivers evolve over time as the person with AD changes. Support programs can respond by offering services and information geared to different stages of the disease.

One of the most difficult decisions that many families face is whether to place a loved one with Alzheimer's disease 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.

Caring for a Person with AD

The following are some of the challenges faced by AD caregivers:

Physical effort and time commitment: Help with bathing, eating, dressing, and other activities of daily living take a lot of time. As the disease progresses, the need for this kind of help increases. Behavior problems and safety concerns mean that the caregiver is always "on duty," even when not actively helping the person.

Financial costs: The costs of care vary, but can be high depending on whether the person is cared for at home or in a residential care setting and how much help the caregiver has. Many caregivers give up their jobs or cut back on their work hours and this also has financial implications.

Psychological loss: Caregivers often experience a profound sense of loss as the disease slowly takes their husband, wife, parent, or friend. The relationship as it once was gradually ends and plans for the future must be radically changed. Caregivers must come to terms with "the long goodbye."

Negative effects of being a caregiver

- Employment complications
- Emotional distress
- Fatigue and poor physical health
- Social isolation
- Family conflict
- Less time for leisure, self, and other family members

Positive effects of being a caregiver

- 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

Research to Help Families and Caregivers

Investigators are exploring the emotional, psychological, and physical costs of caregiving, and they are investigating ways to ease the burden.

A number of studies are examining the factors that contribute to stress and depression in family caregivers of people with AD. In one study, Case Western Reserve University investigators explored the relationship between depression in the care recipient and in the caregiver (Neundorfer et al., 2001). They found that the well-being of both people is closely related - the more depressed the person with AD was, the more depressed the caregiver also was. Wives of men with AD and caregivers who were themselves in poor health were at particular risk of depression. The researchers concluded that interventions for caregivers are needed early on in the family member's illness and that further research is needed to understand what interventions will sustain the quality of life and physical and mental well-being of the person with AD as well as the caregiver.

A second study examined caregiving stress from a somewhat different angle. We know that the chronic stress resulting from continuously caring for a family member with dementia has been associated with depression, elevated stress hormones, and increased vulnerability to influenza and poor wound healing in older caregivers. However, only recently have the long-term effects of this stressful period for caregivers after the death of the demented spouse been investigated. This study, conducted by a research group at the Houston Veterans Affairs Medical Center, examined the psychological state of spousal caregivers for up to 4 years following the death of the person with dementia (Robinson-Whelen et al., 2001). The former caregivers were compared to a group of caregivers who were still caring for their husbands or wives throughout the study, as well as to a group of non-caregiving age-matched control participants. The investigators found that although former caregivers experienced slight decreases in stress and negative mood after their spouses had died, their emotional state and levels of depression and loneliness had not returned to levels comparable to non-caregivers up to 3 years later. In fact, they remained similar to those of current spousal caregivers, suggesting that the consequences of long-term caregiving may be long-term as well. The investigators also found that social support after the death of the spouse helped more to ensure a positive post-caregiving outcome than support received during the caregiving years. Not

surprisingly, an inability to suppress thoughts of the caregiving years was negatively associated with psychological well-being. Clearly, the needs of caregiving spouses must receive long-term attention. Programs aimed at providing social support and working through the persistent traumatic and stressful thoughts of the prior years of spousal caregiving have the potential to help former caregivers and boost their psychological and physical well-being.

A third study looked at ways to help family caregivers by building on previous research showing that people who exercise benefit in various ways, including reduced stress-induced high blood pressure and improved quality of sleep. This study, conducted by Stanford University Medical School researchers, is the first to examine the role that a regular moderate-intensity exercise program plays in enhancing health and quality of life for women caring for loved ones with dementia (King et al., 2002). A group of 100 women caregivers, aged 49 to 82 years old, received either home-based, telephone-supervised moderate-intensity exercise training or a nutrition education program. Exercise consisted of brisk walking for four 30- to 40-minute sessions per week. Compared with the nutrition education group, exercise participants showed significant improvements in physical activity levels, stress-induced blood pressure reactions, and sleep quality. The nutrition group also benefited through reducing the percentage of total calories from fats and saturated fats and consuming fewer fats, oils, sweets, and high-fat snacks. Both groups reported significant reductions in psychological distress, including depressive symptoms and self-rated stress. This research demonstrates that properly tailored health promotion programs can improve the health and functioning of older women family caregivers.

Communication

Trying to communicate with a person who has AD 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 AD 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.
- 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 AD 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.

Activities of Daily Living

Bathing

While some people with AD 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 AD. 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 AD, 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.
- Arrange the clothes in the order they are to be put on to help the person move through the process.
- Provide clear, step-by-step instructions if the person needs prompting.

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- Choose clothing that is comfortable, easy to get on and off, and easy to care for. Elastic waists and Velcro enclosures minimize struggles with buttons and zippers.

Eating

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

- Ensure a quiet, calm atmosphere for eating. Limiting noise and other distractions may help the person focus on the meal.
- Provide a limited number of choices of food and serve small portions. You may want to offer several small meals throughout the day in place of three larger ones.
- Use straws or cups with lids to make drinking easier.
- Substitute finger foods if the person struggles with utensils. Using a bowl instead of a plate also may help.
- Have healthy snacks on hand. To encourage eating, keep the snacks where they can be seen.
- Visit the dentist regularly to keep mouth and teeth healthy.

Activities

Finding activities that the person with AD 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.

Incontinence

As the disease progresses, many people with AD begin to experience incontinence. 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

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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.
- Always have an extra set of clothing available in case of an accident.

Sleep Problems

For the exhausted caregiver, sleep can't come too soon. For many people with AD, however, nighttime may be a difficult time. Getting the person to go to bed and stay there may require some advance planning.

- 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.
- Encourage exercise during the day and limit daytime napping.
- Restrict access to caffeine late in the day.
- Use night lights in the bedroom, hall, and bathroom if the darkness is frightening or disorienting.

Exercise

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

- Think about what kind of physical activities both enjoy, perhaps walking, swimming, tennis, dancing, or gardening. Determine the time of day and place where this type of activity would work best.
- 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.

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- Allow as much independence as possible, even if it means a less-than-perfect garden or a scoreless tennis match.
- Investigate 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.

Safety Recommendations

People with AD become increasingly unable to take care of themselves. However, individuals will move through the disease in their own unique manner. As a caregiver, you face the ongoing challenge of adapting to each change in the person's behavior and functioning. The following general principles may be helpful.

1. **Think prevention.** It is very difficult to predict what a person with AD might do. Just because something has not yet occurred, does not mean it should not be cause for concern. Even with the best-laid plans, accidents can happen. Therefore, checking the safety of the home will help control some of the potential problems that may create hazardous situations.
2. **Adapt the environment.** It is more effective to change the environment than to change most behaviors. While some AD behaviors can be managed with special medications prescribed by a doctor, many cannot. Changes in an environment must be made to decrease the hazards and stressors that accompany these behavioral and functional changes.
3. **Minimize danger.** By minimizing danger, you can maximize independence. A safe environment can be a less restrictive environment where the person with AD can experience increased security and more mobility.

Supervision

This issue needs careful evaluation and is certainly a safety concern. The following points should be considered.

Does the person with AD:

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- become confused or unpredictable under stress?
- recognize a dangerous situation; for example, fire?
- know how to use the telephone in an emergency?
- know how to get help?
- stay content within the home?
- wander and become disoriented?
- show signs of agitation, depression, or withdrawal when left alone for any period of time?
- attempt to pursue former interests or hobbies that might now warrant supervision such as cooking, appliance repair, or woodworking?

Home Safety Room-By-Room

Prevention begins with a safety check of every room in your home. Use the following room-by-room checklist to identify potential hazards and to record any changes that need to be made. Products or gadgets necessary to improve home safety can be purchased at stores carrying hardware, electronics, medical supplies, and children's items.

Caregivers can make adaptations that modify and simplify without severely disrupting the home. A safe home can be a less stressful home for the person with AD, the caregiver, and family members.

Throughout the Home

- Display emergency numbers and your home address near all telephones.
- Use a telephone answering machine when you cannot answer calls. The person with AD often is unable to take messages or may be a target for telephone exploitation by solicitors. When the answering machine is on, turn down the phone bell to avoid disruptive ringing.
- Install smoke alarms near all bedrooms; check their functioning and batteries frequently.
- Avoid the use of flammable and volatile compounds near gas water heaters. Do not store these materials in an area where a gas pilot light is used.
- Install secure locks on all outside doors and windows.
- Hide a spare house key *outside* in case the person with AD locks you out of the house.

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- Avoid the use of extension cords if possible by placing lamps and appliances close to electrical outlets. Tack extension cords to the baseboards of a room to avoid tripping.
- Cover unused outlets with childproof plugs.
- Place red tape around floor vents, radiators, and other heating devices to deter the person with AD from standing on or touching a hot grid.
- Check all rooms for adequate lighting.
- Place light switches at the top and the bottom of stairs.
- Stairways should have at least one handrail that extends beyond the first and last steps. If possible, stairways should be carpeted or have safety grip strips.
- Keep all medications (prescription and over-the-counter) locked. Each bottle of prescription medicine should be clearly labeled with the patient's name, name of the drug, drug strength, dosage frequency, and expiration date. Child-resistant caps are available if needed.
- Keep all alcohol in a locked cabinet or out of reach of the person with AD. Drinking alcohol can increase confusion.
- If smoking is permitted at all, monitor while the person with AD is smoking. Remove matches, cigarettes, and ashtrays. With these reminders out of sight, the person may forget the desire to smoke.
- Avoid clutter, which can create confusion and danger. Throw out/recycle newspapers and magazines regularly. Keep all walk areas free of furniture.
- Keep plastic bags out of reach. A person with AD may choke or suffocate.
- Remove all guns or other weapons from the home, or safety proof them by installing safety locks or by removing ammunition and firing pins.
- Lock all power tools and machinery in the garage, workroom, or basement.
- Remove all poisonous plants from the home. Check with local nurseries or poison control centers for a list of poisonous plants.
- Keep fish tanks out of reach. The combination of glass, water, electrical pumps, and potentially poisonous aquatic life could be harmful to a curious person with AD.

Outside Approaches to the House

- Keep steps sturdy and textured to prevent falls in wet or icy weather.
- Mark the edges of steps with bright or reflective tape.
- Consider a ramp with handrails into the home rather than steps.
- Eliminate uneven surfaces or walkways, hoses, or other objects that may cause a person to trip.
- Restrict access to a swimming pool by fencing it off with a locked gate, covering it, and keeping it closely supervised when in use. In the patio area, remove the fuel source and fire starters from any grills when not in use, and supervise use when the person with AD is present.
- Place a small bench or table by the entry door to hold parcels while unlocking the door.
- Make sure outside lighting is adequate. Light sensors that turn on lights automatically as you approach the house are available and may be useful. They also may be used in other parts of the home.
- Prune bushes and foliage well away from walkways and doorways.
- Consider a NO SOLICITING sign for the front gate or door.

Entryway

- Remove scatter rugs and throw rugs.
- Use textured strips or nonskid wax on hardwood floors to prevent slipping.

Kitchen

- Install childproof door latches on storage cabinets and drawers designated for breakable or dangerous items. Lock away all household cleaning products, matches, knives, scissors, blades, small appliances, and valued china.
- If prescription or nonprescription drugs are kept in the kitchen, store them in a locked cabinet.
- Remove scatter rugs and foam pads from the floor.
- Remove knobs from the stove, or install an automatic shut-off switch.
- Do not use or store flammable liquids in the kitchen. Lock them in the garage or in an outside storage unit.

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- Keep a night-light in the kitchen.
- Remove or secure the family "junk drawer." A person with AD may eat small items such as matches, hardware, erasers, plastics, etc.
- Remove artificial fruits and vegetables or food-shaped kitchen magnets, which might appear to be edible.
- Insert a drain trap in the kitchen sink to catch anything that may otherwise become lost or clog the plumbing.
- Consider dismantling the garbage disposal. People with AD may place objects or their own hands in the disposal.

Bedroom

- Use a night-light.
- Use an intercom device (often used for infants) to alert you to any noises indicating falls or a need for help. This also is an effective device for bathrooms.
- Remove scatter rugs.
- Remove portable space heaters. If you use portable fans, be sure that objects cannot be placed in the blades.
- Be cautious when using electric mattress pads, electric blankets, electric sheets, and heating pads, all of which may cause burns. Keep controls out of reach.
- Move the bed against the wall for increased security, or place the mattress on the floor.

Bathroom

- Do not leave a severely impaired person with AD alone in the bathroom.
- Remove the lock from the bathroom door to prevent the person with AD from getting locked inside.
- Place nonskid adhesive strips, decals, or mats in the tub and shower. If the bathroom is uncarpeted, consider placing these strips next to the tub, toilet, and sink.
- Use washable wall-to-wall bathroom carpeting to prevent slipping on wet tile floors.
- Use an extended toilet seat with handrails, or install grab bars beside the toilet.

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- Install grab bars in the tub/shower. A grab bar in contrasting color to the wall is easier to see.
- Use a foam rubber faucet cover (often used for small children) in the tub to prevent serious injury should the person with AD fall.
- Use plastic shower stools and a hand-held showerhead to make bathing easier.
- In the shower, tub, and sink, use a single faucet that mixes hot and cold water to avoid burns.
- Adjust the water heater to 120 degrees to avoid scalding tap water.
- Insert drain traps in sinks to catch small items that may be lost or flushed down the drain.
- Store medications (prescription and nonprescription) in a locked cabinet. Check medication dates and throw away outdated medications.
- Remove cleaning products from under the sink, or lock them away.
- Use a night-light.
- Remove small electrical appliances from the bathroom. Cover electrical outlets. If men use electric razors, have them use a mirror outside the bathroom to avoid water contact.

Living Room

- Clear all walk areas of electrical cords.
- Remove scatter rugs or throw rugs. Repair or replace torn carpet.
- Place decals at eye level on sliding glass doors, picture windows, or furniture with large glass panels to identify the glass pane.
- Do not leave the person with AD alone with an open fire in the fireplace, or consider alternative heating sources. Remove matches and cigarette lighters.
- Keep the controls for cable or satellite TV, VCR, and stereo system out of sight.

Laundry Room

- Keep the door to the laundry room locked if possible.
- Lock all laundry products in a cabinet.
- Remove large knobs from the washer and dryer if the person with AD tampers with machinery.

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- Close and latch the doors and lids to the washer and dryer to prevent objects from being placed in the machines.

Home Safety Behavior-By-Behavior

Although a number of behavior and sensory problems may accompany Alzheimer's disease, not every person will experience the disease in exactly the same way. As the disease progresses, particular behavioral changes can create safety problems. The person with AD may or may not have these symptoms. However, should these behaviors occur, the following safety recommendations may help reduce risks.

Wandering

- Remove clutter and clear the pathways from room to room to allow the person with AD to move about more freely.
- Make sure floors provide good traction for walking or pacing. Use nonskid floor wax or leave floors unpolished. Secure all rug edges, eliminate throw rugs, or install nonskid strips. The person with AD should wear nonskid shoes or sneakers.
- Place locks on exit doors high or low on the door out of direct sight. Consider double locks that require a key. Keep a key for yourself and hide one near the door for emergency exit purposes.
- Use loosely fitting doorknob covers so that the cover turns instead of the actual knob. *(Due to the potential hazard they could cause if an emergency exit is needed, locked doors and doorknob covers should be used only when a caregiver is present.)*
- Install safety devices found in hardware stores to limit the distance that windows can be opened.
- If possible, secure the yard with fencing and a locked gate. Use door alarms such as loose bells above the door or devices that ring when the doorknob is touched or the door is opened.
- Divert the attention of the person with AD away from using the door by placing small scenic posters on the door; placing removable gates, curtains, or brightly colored streamers across the door; or wallpapering the door to match any adjoining walls.
- Place STOP, DO NOT ENTER, or CLOSED signs in strategic areas on doors.
- Reduce clues that symbolize departure such as shoes, keys, suitcases, coats, or hats.
- Obtain a medical identification bracelet for the person with AD with the words "memory loss" inscribed along with an emergency telephone number. Place the bracelet on the person's dominant

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hand to limit the possibility of removal, or solder the bracelet closed.

- Place labels in garments to aid in identification. Check with the local Alzheimer's Association about the Safe Return program.
- Keep an article of the person's worn, unwashed clothing in a plastic bag to aid in finding someone with the use of dogs.
- Notify neighbors of the person's potential to wander or become lost. Alert them to contact you or the police immediately if the individual is seen alone and on the move.
- Give local police, neighbors, and relatives a recent picture, along with the name and pertinent information about the person with AD, as a precaution should he or she become lost. Keep extra pictures on hand.
- Consider making an up-to-date home video of the person with AD.
- Do not leave a person with AD who has a history of wandering unattended.

Rummaging/Hiding Things

- Lock up all dangerous or toxic products, or place them out of the person's reach.
- Remove all old or spoiled food from the refrigerator and cupboards. A person with AD may rummage for snacks but may lack the judgment or taste to rule out spoiled foods.
- Simplify the environment by removing clutter or valuable items that could be misplaced, lost, or hidden by the person with AD. These include important papers, checkbooks, charge cards, and jewelry.
- If your yard has a fence with a locked gate, place the mailbox outside the gate. People with AD often hide, lose, or throw away mail. If this is a serious problem, consider obtaining a post office box.
- Create a special place for the person with AD to rummage freely or sort (for example, a chest of drawers, a bag of selected objects, or a basket of clothing to fold or unfold). Often, safety problems occur when the person with AD becomes bored or does not know what to do.
- Provide the person with AD a safe box, treasure chest, or cupboard to store special objects.
- Close access to unused rooms, thereby limiting the opportunity for rummaging and hiding things.

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- Search the house periodically to discover hiding places. Once found, these hiding places can be discreetly and frequently checked.
- Keep all trashcans covered or out of sight. The person with AD may not remember the purpose of the container or may rummage through it.
- Check trash containers them before emptying them in case something has been hidden there or accidentally thrown away.

Hallucinations, Illusions, and Delusions

Due to the complex changes occurring in their brain, people with AD may see or hear things that have no basis in reality. Hallucinations come from within the brain and involve hearing, seeing, or feeling things that are not really there. For example, a person with AD may see children playing in the living room when no children exist. Illusions differ from hallucinations because the person with AD is misinterpreting something that actually does exist. Shadows on the wall may look like people, for example. Delusions are persistent thoughts that the person with AD believes are true but in reality, are not. Often, stealing is suspected, for example, but cannot be verified.

It is important to seek medical evaluation if a person with AD has ongoing disturbing hallucinations, illusions, or delusions. Often, these symptoms can be treated with medication or behavior management techniques. With all of the above symptoms, the following environmental adaptations also may be helpful.

- Paint walls a light color to reflect more light. Use solid colors, which are less confusing to an impaired person than a patterned wall. Large, bold prints (for example, florals in wallpaper or drapes) may cause confusing illusions.
- Make sure there is adequate lighting, and keep extra bulbs handy in a secured place. Dimly lit areas may produce confusing shadows or difficulty with interpreting everyday objects.
- Reduce glare by using soft light or frosted bulbs, partially closing blinds or curtains, and maintaining adequate globes or shades on light fixtures.
- Remove or cover mirrors if they cause the person with AD to become confused or frightened.
- Ask if the person can point to a specific area that is producing confusion. Perhaps one particular aspect of the environment is being misinterpreted.
- Vary the home environment as little as possible to minimize the potential for visual confusion. Keep furniture in the same place.

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- Have the person with AD avoid watching violent or disturbing television programs. The person with AD may believe the story is real.
- Do not confront the person with AD who becomes aggressive. Withdraw and make sure you have access to an exit as needed.

Impairment of the Senses

Alzheimer's disease can cause changes in a person's ability to interpret what they see, hear, taste, feel, or smell, even though the sense organs may still be intact. The person with AD should be evaluated periodically by a physician for any such changes that may be correctable with glasses, dentures, hearing aids, or other treatments.

Vision

People with AD may experience a number of changes in visual abilities. For example, they may lose their ability to comprehend visual images. Although there is nothing physically wrong with their eyes, people with AD may no longer be able to interpret accurately what they see due to changes in their brain. Also, their sense of perception and depth may be altered. These changes can cause safety concerns.

- Create color contrast between floors and walls to help the person see depth. Floor coverings are less visually confusing if they are a solid color.
- Use dishes and placemats in contrasting colors for easier identification.
- Mark the edges of steps with brightly colored strips of tape to outline changes in elevation.
- Place brightly colored signs or simple pictures on important rooms (the bathroom, for example) for easier identification.
- Be aware that a small pet that blends in with the floor or lies in walkways may be a hazard. The person with AD may trip over a small pet.

Smell

A loss or decrease in smell often accompanies Alzheimer's disease.

- Install good quality smoke detectors and check them frequently. The person with AD may not smell smoke or may not associate it with danger.
- Keep refrigerators clear of spoiled foods.

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Touch

People with AD may experience loss of sensation or may no longer be able to interpret feelings of heat, cold, or discomfort.

- Adjust water heaters to 120 degrees to avoid scalding tap water. Most hot water heaters are set at 150 degrees, which can cause burns.
- Color code separate water faucet handles, with red for hot and blue for cold.
- Place a sign on the oven, coffee maker, toaster, crock-pot, iron, or other potentially hot appliances that says DO NOT TOUCH or STOP! VERY HOT. The person with AD should not use appliances without supervision. Unplug appliances when not in use.
- Use a thermometer to tell you whether the water in the bathtub is too hot or too cold.
- Remove furniture or other objects with sharp corners or pad them to reduce potential for injury.

Taste

People with AD may lose taste sensitivity. As their judgment declines, they also may place dangerous or inappropriate things in their mouth.

- If possible, keep a spare set of dentures. If the person keeps removing dentures, check for correct fit.
- Keep all condiments such as salt, sugar, or spices away from easy access if you see the person with AD using excess amounts. Too much salt, sugar, or spice can be irritating to the stomach or cause other health problems.
- Remove or lock up medicine cabinet items such as toothpaste, perfume, lotions, shampoos, rubbing alcohol, or soap, which may look and smell like edible items to the person with AD.
- Consider a childproof latch on the refrigerator, if necessary.
- Keep the poison control number by the telephone. Keep a bottle of Ipecac (vomit inducing) available but use only with instructions from poison control or 911.
- Keep pet litter boxes inaccessible to the person with AD. Do not store pet food in the refrigerator.
- Learn the Heimlich maneuver or other techniques to use in case of choking. Check with your local Red Cross for more information and instruction.

Hearing

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People with AD may have normal hearing, but they may lose their ability to interpret what they hear accurately. This may result in confusion or over-stimulation.

- Avoid excessive noise in the home such as having the stereo and the TV on at the same time.
- Be sensitive to the amount of noise going on outside, and close windows or doors, if necessary.
- Avoid large gatherings of people in the home if the person with AD shows signs of agitation or distress in crowds.
- Check hearing aid batteries and functioning frequently.

Driving

Driving is a complex activity that demands quick reactions, alert senses, and split-second decision-making. For a person with AD, driving becomes increasingly more difficult. Memory loss, impaired judgment, disorientation, impaired visual and spatial perception, slow reaction time, diminished attention span, inability to recognize cues such as stop signs and traffic lights can make driving particularly hazardous.

People with AD who continue to drive can be a danger to themselves, their passengers, and the community at large. As the disease progresses, they lose driving skills and must stop driving. Unfortunately, people with AD often cannot recognize when they should no longer drive. This is a tremendous safety concern. It is extremely important to have the impaired person's driving abilities carefully evaluated.

Warning Signs of Unsafe Driving

Often, it is the caregiver, a family member, neighbor, or friend who becomes aware of the safety hazards. If a person with AD experiences one of more of the following problems, it may be time to limit or stop driving.

Does the person with AD:

- get lost while driving in a familiar location?
- fail to observe traffic signals?
- drive at an inappropriate speed?
- become angry, frustrated, or confused while driving?
- make slow or poor decisions?

Explaining to the person with AD that he or she can no longer drive can be extremely difficult. Loss of driving privileges may represent a tremendous loss of independence, freedom, and identity. It is a significant concern for the person with AD and the caregiver. The issue of not driving may produce anger, denial,

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and grief in the person with AD, as well as guilt and anxiety in the caregiver. Family and concerned professionals need to be both sensitive and firm. Above all, they should be persistent and consistent.

The doctor of a person with AD can assist the family with the task of restricting driving. Talk with the doctor about your concerns. Most people will listen to their doctor. Ask the doctor to advise the person with AD to reduce his or her driving, go for a driving evaluation or test, or stop driving altogether. An increasing number of States have laws requiring physicians to report AD and related disorders to the Department of Motor Vehicles. The Department of Motor Vehicles then is responsible for retesting the at-risk driver. Testing should occur regularly, at least yearly.

When dementia impairs driving and the person with AD continues to insist on driving, a number of different approaches may be necessary. Work as a team with family, friends, and professionals and use a single, simple explanation for the loss of driving ability such as: "You have a memory problem, and it is no longer safe to drive." "You cannot drive because you are on medication." or "The doctor has prescribed that you no longer drive."

- Have the doctor write on a prescription pad DO NOT DRIVE. Ask the doctor to write to the Department of Motor Vehicles or Department of Public Safety saying this person should no longer drive. Show the letter to the person with AD as evidence.
- Offer to drive.
- Walk when possible, and make these outings special events.
- Use public transportation or any special transportation provided by community organizations. Ask about senior discounts or transportation coupons. The person with AD should not take public transportation unsupervised.
- Park the car at a friend's home.
- Hide the car keys.
- Exchange car keys with a set of unusable keys. Some people with AD are in the habit of carrying keys.
- Place a large note under the car hood requesting that any mechanic call you before doing work requested by the person with AD.
- Have a mechanic install a "kill switch" or alarm system that disengages the fuel line to prevent the car from starting.
- Consider selling the car and putting aside the money saved from insurance, repairs, and gasoline for taxi funds.
- Do not leave a person with AD alone in a parked car.

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Natural Disaster Safety

Natural disasters come in many forms and degrees of severity. They seldom give warning, and they call upon good judgment and ability to follow through with crisis plans. People with AD are at a serious disadvantage. Their impairments in memory and reasoning severely limit their ability to act appropriately in crises.

It is always important to have a plan of action in case of fire, earthquake, flood, tornado, or other disasters. Specific home safety precautions may apply and environmental changes may be needed. The American Red Cross is an excellent resource for general safety information and preparedness guides for comprehensive planning. If there is a person with AD in the home, the following precautions apply:

- Get to know your neighbors, and identify specific individuals who would be willing to help in a crisis. Formulate a plan of action with them should the person with AD be unattended during a crisis.
- Give neighbors a list of emergency numbers of caregivers, family members, and primary medical resources.
- Educate neighbors beforehand about the person's specific disabilities, including inability to follow complex instructions, memory loss, impaired judgment, and probable disorientation and confusion. Give examples of some of the simple one-step instructions that the person may be able to follow.
- Have regular emergency drills so that each member of the household has a specific task. Realize that the person with AD cannot be expected to hold any responsibility in the crisis plan and that someone will need to take primary responsibility for supervising the individual.
- Always have at least an extra week's supply of any medical or personal hygiene items critical to the person's welfare, such as:
 - food and water
 - medications
 - incontinence undergarments
 - hearing aid batteries
 - glasses
- Be sure that the person with AD wears an identification bracelet stating "memory loss" should he or she become lost or disoriented during the crisis. Contact your local Alzheimer's Association chapter and enroll the person in the Safe Return program.

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- Under no circumstances should a person with AD be left alone following a natural disaster. Do not count on the individual to stay in one place while you go to get help. Provide plenty of reassurance.

Resources

Alzheimer's Association. 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. Chapters offer referrals to local resources and services, and sponsor support groups and educational programs. Online and print publications are also available.

Alzheimer's Association
225 North Michigan Ave.
Suite 1700
Chicago, IL 60601
Website: www.alz.org

Alzheimer's Disease Cooperative Study. The Alzheimer's Disease Cooperative Study (ADCS) is a cooperative agreement between the National Institute on Aging (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 of 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's Disease Cooperative Study
University of California, San Diego
9500 Gilman Drive - 0949
La Jolla, CA 92093-0949
858-622-5880
Website: <http://antimony.ucsd.edu/>

Alzheimer's Disease Education and Referral (ADEAR) Center. The ADEAR Center, part of the NIA, provides publications and information on AD, including booklets on caregiving, fact sheets and reports on research findings, a database of clinical trials, recommended reading lists, and the Progress Report on Alzheimer's Disease. Information specialists provide referrals to local AD resources.

Alzheimer's Disease Education and Referral (ADEAR) Center
PO Box 8250
Silver Spring, MD 20907
1-800-438-4380
Website: www.alzheimers.org

Children of Aging Parents. Children of Aging Parents is a nonprofit organization that provides information and referrals for nursing homes, retirement communities, elderlaw attorneys, adult day-care centers, medical insurance providers, respite care, assisted living centers, and State and county agencies. Also offered are fact sheets on various topics, a bimonthly newsletter, conferences and workshops, support group referrals, and a speaker's bureau.

Children of Aging Parents
1609 Woodbourne Road, Suite 302A
Levittown, PA 19057-1511
1-800-227-7294
Website: www.caps4caregivers.org

Eldercare Locator. The 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 also features AD information for families, caregivers, and health professionals.

Eldercare Locator
1-800-677-1116
Web site: www.eldercare.gov

Family Caregiving Alliance. The Family Caregiver Alliance (FCA) is a nonprofit organization that offers support services for those caring for adults with AD, stroke, traumatic brain injuries, and other cognitive disorders. FCA programs and services include an Information Clearinghouse for FCA's publications.

Family Caregiving Alliance
690 Market Street, Suite 600

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San Francisco, CA 94104
415-434-3388

National Institute on Aging (NIA). Part of the National Institutes of Health (NIH), the NIA is the Federal government's lead agency for research on AD. NIA also offers information about health and aging, including the Age Page series and the NIA Exercise Kit, which contains an 80-page exercise guide and 48-minute closed-captioned video. Caregivers can find many Age Pages on the website.

National Institute on Aging Information Center
PO Box 8057
Gaithersburg, MD 20898-8057
1-800-222-2225
1-800-222-4225 (TTY)
Website: www.nia.nih.gov

Partnership for Caring. Partnership For Caring (PFC) is a nonprofit organization that works to improve how people die in our society. PFC operates an information hotline dealing with end-of-life issues and provides State-specific living wills, medical powers of attorney, and other information materials. PFC also provides education and consultation services to doctors, nurses, social workers, attorneys, and clergy concerning end-of-life decisions.

Partnership for Caring
1620 Eye Street NW, Suite 202
Washington, DC 20006
1-800-989-9455
Website: www.partnershipforcaring.org

Well Spouse Foundation. Well Spouse Foundation is a nonprofit organization that gives support to spouses and partners of the chronically ill and/or disabled. Well Spouse maintains support groups, publishes a bimonthly newsletter, and helps organize letter writing programs to help members deal with the effects of isolation.

Well Spouse Foundation
63 West Main Street, Suite H
Freehold, NJ 07728
1-800-838-0879
Website: www.wellspouse.org

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ALZHEIMER'S DISEASE

POST-TEST

1. What percentage of people between the ages of 65 – 74 have Alzheimer's Disease?
 - A. 1%
 - B. 3%
 - C. 5%
 - D. 7%

2. The region of the brain most affected during the early stages of AD is the _____. The primary function of this area of the brain is _____.
 - A. parietal lobe, critical thought process
 - B. hippocampus, encoding memory
 - C. frontal lobe, regulating behavior
 - D. cerebellum, coordinating multiple activities

3. Gene mutations of which three chromosomes have been found to cause early-onset AD?
 - A. 1, 14, 17
 - B. 1, 17, 21
 - C. 1, 14, 21
 - D. 14, 17, 21

4. Which of the following is the greatest risk factor for developing AD?
 - A. Educational level
 - B. Gender
 - C. Inactivity during midlife
 - D. Nutrition

5. A therapy patient with mild AD is most likely to exhibit which of the following behaviors?
 - A. Occasionally substitutes words during conversation with therapist.
 - B. Accuses therapy staff of stealing personal items
 - C. Screams or cries out when touched during transfer training
 - D. Believes the person he sees in the mirror during ADL training is following him

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6. Currently, the only way to definitively diagnose Alzheimer's Disease is:
- A. autopsy
 - B. the Mini Mental State Examination
 - C. neuroimaging
 - D. APOE testing
7. Frequently, a patient with AD is able to perform therapy activities better in the morning than in the evening. This phenomenon is known as:
- A. clocking
 - B. nocturnal regression
 - C. phasing
 - D. sundowning
8. A therapy patient who is taking Namenda for early stages of AD should be monitored carefully during gait activities because _____ is a common side effect of the medication.
- A. weakness
 - B. bradykinesia
 - C. tachycardia
 - D. dizziness
9. A person with AD may mistakenly believe that shadows on the wall are really people in the room with them. This is an example of:
- A. Hallucination
 - B. Adaptation
 - C. Illusion
 - D. Delusion
10. Which of the following is true regarding how AD affects the senses?
- A. decreased ability to detect color
 - B. loss or decrease in ability to smell
 - C. hypersensitivity to taste
 - D. diminished hearing