Can Alzheimer's Disease Be Prevented?

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Introduction

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

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

Can We Prevent Complex Diseases Like AD?

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

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

AD Risk Factors We Can't Control

Age

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

Genetics

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

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

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

- APOE ε2, a rarely occurring form, may provide some protection against AD.
- APOE ε3, the most common form, plays a neutral role, neither increasing nor decreasing risk.

- APOE ε4, which occurs in about 40 percent of all people who develop late-onset AD and is present in about 25 to 30 percent of the population, increases risk by lowering the age of onset. Having this allele does not mean that a person will definitely develop AD; it only increases risk. Many people who develop AD do not have an APOE ε4 allele.

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

To Learn More

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

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

The Search for AD Prevention Strategies

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

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

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

Understanding Scientific Findings in the News

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

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

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

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

Assessing Physical Activity

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

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

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

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

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

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

Exploring Dietary Factors

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

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

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

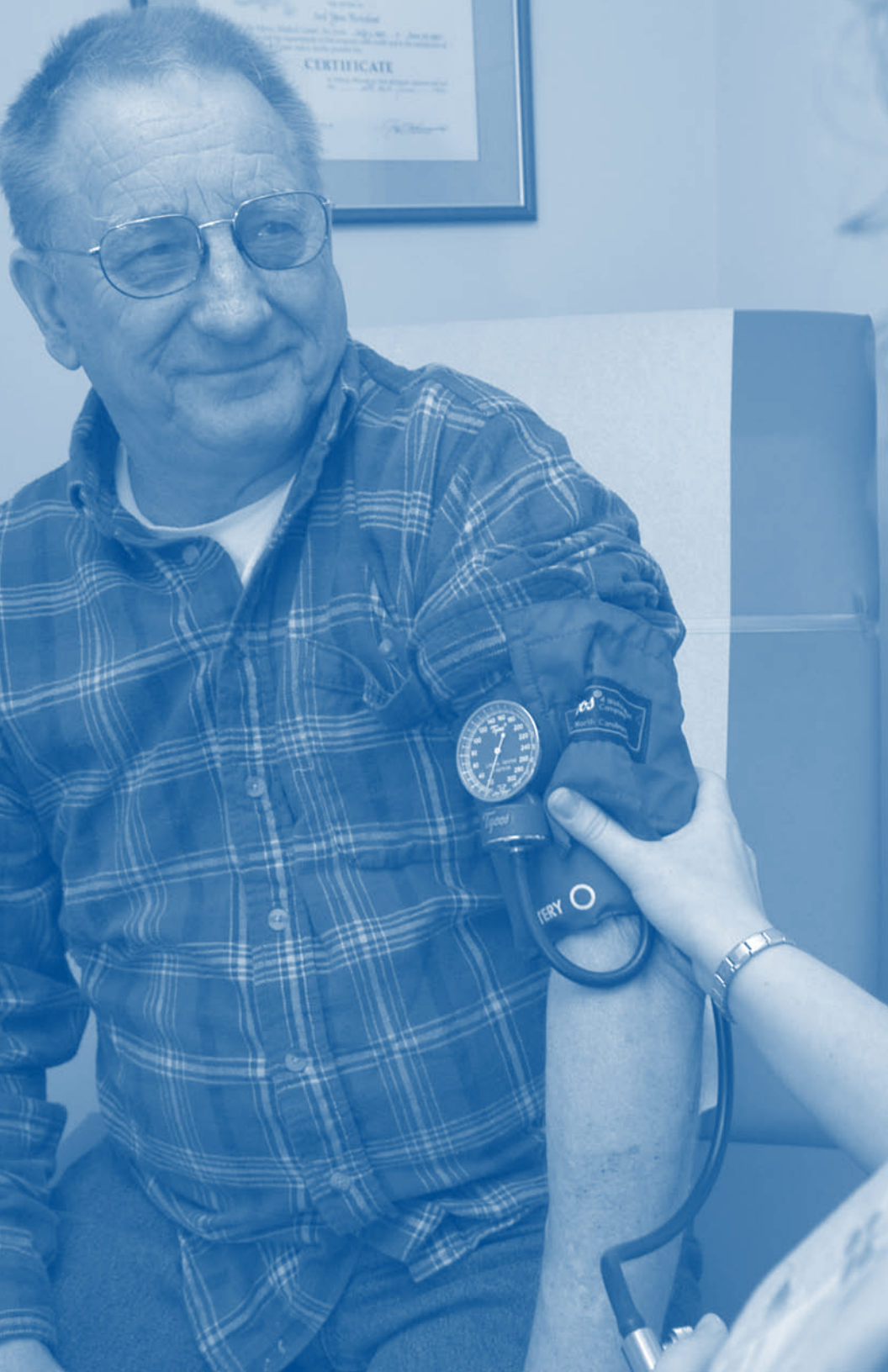
Several epidemiologic studies have shown an association between eating a diet rich in vegetables (especially green leafy vegetables and cruciferous vegetables like broccoli) and a reduced rate of cognitive decline. Researchers speculate that the beneficial effect may come from the antioxidant and folate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

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

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

Investigating Chronic Diseases

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


CERTIFICATE

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

Examining Social Engagement and Intellectually Stimulating Activities

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

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

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

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

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

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

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

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

The Cognitive and Emotional Health Project

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

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

Other Clues to AD Prevention

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

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

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

Antioxidants

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

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

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

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

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

Estrogen

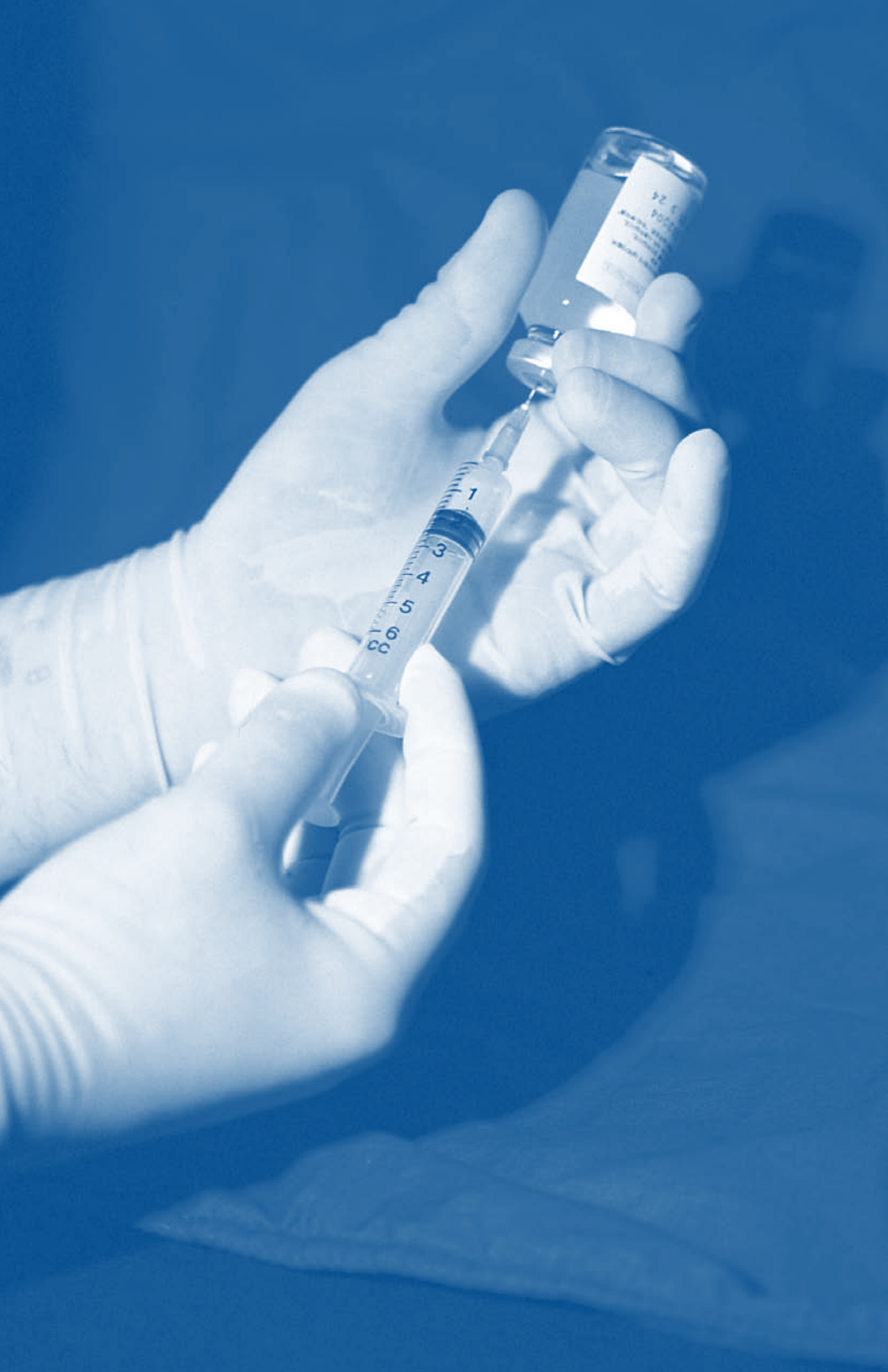
The hormone estrogen is produced by a woman's ovaries during her childbearing years, and its production declines dramatically after menopause. Over the past 25 years, some laboratory and animal research, as well as observational studies in women, have suggested that estrogen may protect the brain. Experts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

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

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

Immunization

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



Other Areas of Research

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

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

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

Technologies Help Scientists Develop Diagnostic Procedures

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

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

So, What Can You Do?

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

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

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

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

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

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

A Final Word of Caution

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

For More Information

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

Alzheimer's Disease Education and Referral (ADEAR) Center
P.O. Box 8250
Silver Spring, MD 20907-8250
800-438-4380 (toll-free)
www.nia.nih.gov/Alzheimers

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

Alzheimer Research Forum
www.alzforum.org

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

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

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

Alzheimer's Disease Cooperative Study
University of California, San Diego
9500 Gilman Drive
La Jolla, CA 92093-0949
858-622-5880
www.adcs.org

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

ClinicalTrials.gov
www.ClinicalTrials.gov

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

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

Alzheimer's Disease Education and Referral (ADEAR) Center

www.nia.nih.gov/Alzheimers

800-438-4380

P.O. Box 8250
Silver Spring, MD 20907-8250

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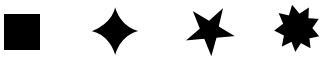

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