

Advances

The Alzheimer's Association Newsletter

Progress in Alzheimer Research and Care

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End of Vaccine Trial Closes a Chapter but Not the Book

Everyone with a personal or professional connection to Alzheimer's disease was disappointed when Elan Corporation and Wyeth-Ayerst Laboratories issued a March 1 press release announcing permanent suspension of their trials of AN-1792, the "Alzheimer vaccine." The developers halted the Phase II trials after 15 of the 300 participants receiving the active drug developed symptoms of brain inflammation. The release noted that most affected participants had improved or recovered, and that the developers were working closely with clinical investigators and regulatory agencies to determine why the symptoms occurred.

According to Bill Thies, PhD, Alzheimer's Association vice president of medical and scientific affairs, "While we all feel the psychological and emotional impact of the trial suspension, from a purely scientific perspective it's probably a minor glitch. Even if this turn of events spelled the end of immunotherapy as a treatment strategy, there are literally thousands of top researchers working on dozens of other approaches." *Target Alzheimer's*, a booklet prepared in 2001 by the Association of the British Pharmaceutical Industry (ABPI), lists more than 30 potential Alzheimer treatments and preventive strategies currently under development at drug companies and academic centers worldwide.

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rx corner

Leteprenim: According to a preliminary report on a Phase II clinical trial of leteprenim potassium (Neotrofin[®]), there was no statistically significant improvement in participants taking leteprenim compared with those taking a placebo (inactive ingredient). NeoTherapeutics, Inc, the maker of the experimental drug, reported that the drug did not meet U.S. Food and Drug Administration requirements for approval as an Alzheimer treatment. Leteprenim is designed to mimic the effects of proteins called nerve growth factors, which play an important role in cell survival, repair, and regeneration.

Memantine: Forest Laboratories, Inc. has announced that it will recruit participants who are already taking one of the FDA-approved Alzheimer drugs to participate in Phase III trials of memantine. This drug may protect brain cells against glutamate, a messenger chemical released in excess amount by cells damaged in Alzheimer's and related disorders. Trial sites throughout the United States are expected to be announced this summer.

For More Information

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Science and Supplements

As to diseases, make a habit of two things—to help, or at least, to do no harm. Hippocrates

This principle from the man who has often been called the founder of Western medicine still guides efforts to develop new medications today. Researchers adhere to that age-old principle in testing new drugs for their safety and efficacy. As scientists engage in the slow, painstaking search for safe new Alzheimer treatments, Alzheimer families may feel compelled to seek more immediate solutions in alternative therapies, such as herbal remedies and other dietary supplements—treatments that generally fall outside of standard practices in modern American medicine.

The interest in alternative therapies is great. The U.S. Food and Drug Administration reports that about 29,000 kinds of dietary supplements are sold in the United States and that American spending on dietary supplements has increased more than fivefold—from more than \$3 billion in 1990 to about \$17 billion in 2000.

In general, scientists in the health research community and proponents of alternative therapies have viewed one another with skepticism. Some common ground is being established, however, in the National Center for Complementary and Alternative Medicine (NCCAM), which was established in 1998 as an agency of the U.S. National Institutes of Health.

Ginkgo Biloba Trials

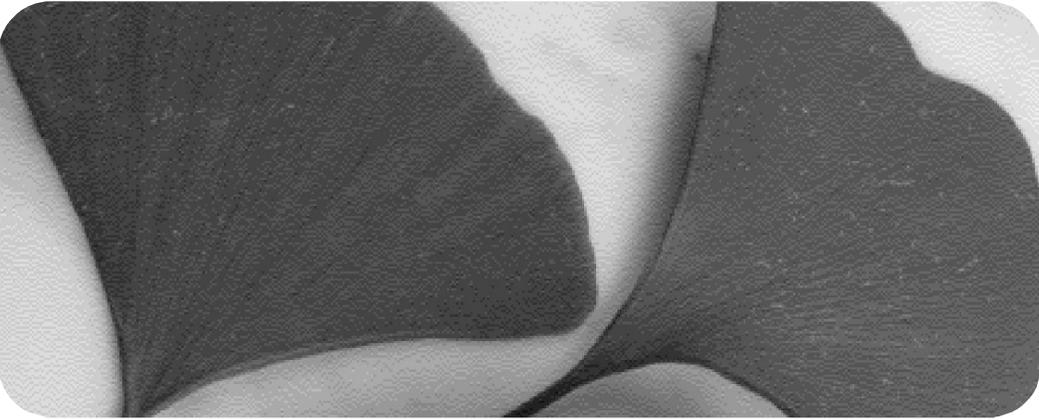
NCCAM and the National Institute on Aging, for example, are currently funding a large, multicenter trial investigating whether *Ginkgo biloba* extract may prevent or delay cognitive decline in older adults. The researchers, led by Steven T. DeKosky, MD, of the University of Pittsburgh, recruited about 3,000 participants who are at least 75 years old and have no cognitive impairment. NCCAM is also funding a much smaller, but similar trial at Oregon Health Sciences University in Portland, for which about 200 participants 85 years and older enrolled.

Ginkgo biloba extract is of interest because it contains several chemical compounds that may have positive effects on brain cells—by possibly reducing inflammation associated with Alzheimer's, attacking toxic oxygen molecules, or enhancing the regulation of chemical messengers in the brain. It has been used for thousands of years in traditional Chinese medicine and is currently being used in some European countries to alleviate cognitivesymptoms associatedwith a number of conditions.

The Value of Scientific Rigor

One might ask why clinical trials are needed to test a substance used as a treatment in China centuries before Hippocrates was even born. The primary reason is that claims about





Ginkgo and dementia are based largely on testimonials, tradition, and a rather small body of scientific research. There is not enough evidence to make claims about whether it is safe and effective—or how much is safe and effective—to treat or prevent Alzheimer’s specifically. The purpose of the six-year, multicenter trial is to determine whether it is effective in preventing Alzheimer’s disease and vascular dementia, how big of an effect it has, and whether it is safe to use over a long period.

The participants have been randomly assigned to either a control group that receives a placebo (inactive ingredient) or the active group that receives the *Ginkgo* extract. The trial is double-blinded, meaning that neither the people administering the medication nor the participants know who is in which group—a way to help ensure that outcomes are not affected by expectations. The cognitive assessments of each participant will include a phone interview every six months and an annual evaluation with a series of exams. At the end of the trial, researchers will compare data from the two groups to determine if the people taking the herbal extract were less likely to develop dementia.

There are other questions about *Ginkgo biloba* that fall outside the scope of current studies. Clinical trials conducted to date have

investigated whether *Ginkgo* can treat people who have dementia. Most of the studies—but not all of them—have shown a statistically significant but modest improvement in some people taking *Ginkgo* extracts. Most of these trials were small, and several have been criticized for being poorly designed. Large, carefully controlled trials are needed to determine whether the extract is effective and what dosage is appropriate.

Another concern is possible interactions between *Ginkgo biloba* and other medications. *Ginkgo*, like aspirin and the prescription drug warfarin, is an anticoagulant, or blood-thinning agent. Some researchers have reported that combining *Ginkgo* extract with aspirin or warfarin can cause internal bleeding.

Testing the Claims and Praise

The effort to address these concerns in rigorous scientific investigations presents a strong contrast to claims often made about this herbal remedy on the Internet and in some publications. Although *Ginkgo* products receive hardy endorsements from various sources, the evidence about the extract’s effectiveness as a treatment is inconclusive, and there is no solid evidence that it cures dementia. *The UC Berkeley Wellness Letter*, reporting on *Ginkgo* in January 1998, noted that even German

and French physicians who prescribe *Ginkgo biloba* “have never claimed miraculous powers for it.”

This past March, Stephen E. Straus, MD, director of NCCAM, presented a lecture titled “Exploring the Scientific Basis of Complementary and Alternative Medicine.” In his address, he noted, “The praise has been unchallenged in this field, and that’s changing. It needs to be challenged by evidence.” The evidence from the current *Ginkgo* trials may provide physicians and consumers with the information they need to make sound decisions about using *Ginkgo* to prevent dementia. The work of NCCAM is to ensure that this research continues in further investigations to understand the potential benefits and risks of other alternative treatments.

For More Information

National Center for Complementary
Alternative Medicine
www.nccam.nih.gov

The Driving Dilemma *When Should a Person with Alzheimer's Relinquish the Car Keys?*

The decision about whether a person in the early stages of Alzheimer's disease should be allowed to drive is a difficult one. Driving is a complex activity that requires quick thinking and reactions, good perception, and split-second decision-making. For the person with Alzheimer's disease, driving becomes a safety issue.

Behind the wheel, the person with Alzheimer's may forget directions and landmarks and become lost, disoriented, and—worse yet—a danger to himself and others. With grandchildren in the car's backseat and wife beside him, R. Swisher, who has Alzheimer's, accelerated into the street, narrowly avoiding being hit broadside by two other cars going 40 miles per hour. Another time, he changed lanes into a car's path.

Despite his wife's insistence that her husband not drive, her fervent pleas were ignored. She writes: "Our primary care physician wrote a 'Do Not Drive' prescription. He refuses to go back to that doctor."

Readers who shared their experiences for this "Dialogue" column said the decision to sell the car or hide the car keys was painful. "This was the first big life change for Mom as a result of Alzheimer's. It made the disease real to us—the point of no return," writes Jane Gaboury, of Alpharetta, Georgia, whose 71-year-old mother Cecile regularly drove through stop signs before ceasing to drive.

"The question of whether or not driving restrictions should be enforced for people with Alzheimer's is simple in theory and difficult in reality," notes Gaboury. "In theory, people who are impaired must not be allowed to drive, whether that impairment is the temporary result of alcohol or of a more permanent condition such as Alzheimer's." Yet caregivers question how family members can determine when the impairment is sufficient to warrant driving restrictions.

The Alzheimer's Association does not believe a diagnosis of Alzheimer's automatically means a person is incapable of driving. Family members must regularly monitor each person's driving ability, says L. Jaime Fitten, MD, who is completing work on a written screening test at the UCLA School of Medicine. The tool is an adaptation of road tests conducted with 100 individuals, including those with Alzheimer's and dementia, other health problems, and healthy senior citizens.

"Not surprisingly, we found that the more complex the driving situation is, the more difficult it was for the person with dementia," says Fitten, professor of psychiatry and biobehavioral sciences, UCLA. "Yet Alzheimer's does not affect all areas of the brain in exactly the same way. Aging—and how we age—is complex.

"It's not so much the age of the individual, but their overall health—whether they have Alzheimer's, arthritis, visual, or hearing problems—that can lead to unsafe driving. More legislation looking at driving and the elderly is needed."

Julie Rankila, of Farmington, Minnesota, agrees. "Saying people with Alzheimer's disease should not drive is too broad of a statement. It's like saying, 'All people over 60 should not drive.' My grandfather, 91, still drives, and he can barely see or hear. The elderly can be just as dangerous on the road as those with Alzheimer's."

Creative Solutions to Not Driving

Julie's father was diagnosed with Alzheimer's at age 53, and not being able to drive was torture for him. Proving the resiliency of caregivers coping with Alzheimer's, the Rankila family purchased a four-wheeler for Dad to drive on familiar, off-road trails. "He now has some semblance of independence and can journey to the store or friends' houses. We know eventually he will be unable to operate this safely, but this has helped ease the transition."

Ross Ward was a traveling artist who drove over 30,000 miles a year for 20 years. "He started getting lost regularly, and when he returned, the car had many mysterious minor dents," writes his wife Carla, who learned of her husband's dementia in February 1998.

Ross, then 57, discovered a creative solution for not driving his beloved Jeep



Cherokee. The New Mexico resident turned it into an “art car,” gluing over 700 pieces of kitschy toys, including Buddha, Barbie, the Power Rangers, and Snow White. He also affixed hundreds of pennies onto the hood to turn his “Jeep” into a “Lincoln.”

Solicit the Support of Others

Ask your physician to advise the person with dementia not to drive and have him or her write a letter or issue a “Do Not Drive” prescription. Learn how to disable a car, or enlist the help of a local mechanic so it will no longer start. You can also have your insurance agent provide documentation that the person with Alzheimer’s no longer has insurance coverage.

But remember that the person with the disease is not necessarily going to understand or abide by the “law” or the decision. After Violet was diagnosed with Alzheimer’s, her physician recommended not driving and her family promptly notified the Arizona department of motor vehicles, which sent a notice of disqualification to the former nurse. Violet threw it away and loaded her car and her belongings into the car and disappeared for three days.

A statewide search by police located Violet 120 miles away. “We were lucky it was December and not July,” write Don and Joanne Lipinski. “The law differs considerably when a child is trying to care for a parent.”

Fitten recommends learning about your state’s driving regulations.

In six states—California, Delaware, Nevada, New Jersey, Oregon, and Pennsylvania—physicians are legally required to report various medical conditions that may affect driving ability. The department of motor vehicles may then revoke the person’s license.

“Driving today is hazardous enough with all of our faculties on the alert,” notes Florida’s Herbert I. Johnson. “We cannot rely on laws and today’s health care restrictions to prevent accidents and loss of life. Common sense must prevail.”

For More Information

Driving and Alzheimer’s Fact Sheet (ED247ZG), first copy, free. 800.272.3900, www.alz.org

Safe Return, 800.272.3900

How Do I Get My Doctor to Listen and Take My Concerns Seriously?

Care consultants in the Contact Center field hundreds of calls each day from caregivers and people grappling with Alzheimer’s disease. One of callers’ top three concerns relates to “doctor-patient” communication, listening, and the best way of getting the answers you so desperately need.

We Want to Hear from You!

Your doctor is busy, and you feel he or she doesn’t listen to your concerns. Yet your doctor is vital to helping you understand the physical and emotional aspects of Alzheimer’s. What types of concerns are you bringing to your physician? What strategies have helped improve communication?

Your experiences could be incorporated into the “Dialogue” article in the fall 2002 *Advances*. Please send your feedback no later than July 5.

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Keeping the Faith Religion, Spirituality Play Central Roles in Lives Affected by Alzheimer's

Given the cognitive and behavioral changes that people with Alzheimer's experience, can religion and spirituality still be a critical part of their lives?

Yes, say experts.

Religious and spiritual beliefs can still be maintained and benefit not only people with the disease but also their caregivers, says one researcher who studies religion and spirituality in the elderly and people with Alzheimer's.

Research and anecdotal reports indicate that people with Alzheimer's often respond to familiar hymns, prayers, and liturgies as well as to visual cues such as clerical collars and crucifixes well into the disease, says Stephen Sapp, PhD, chair of the Department of Religious Studies at the University of Miami.

"I feel strongly that we simply do not know what is really going on in the Alzheimer's person's mind, and we don't know what is being received and processed," he says. "So I advocate continuing to offer input that is meaningful to the person before the disease process leads to what appears to be a significant lack of comprehension."

The terms religion and spirituality mean different things. Sapp says spirituality gives individuals a sense of connectedness to themselves, others, the natural world, and that which transcends all these categories—

a divine force, or God. Spirituality often confronts the question of the meaning of life, he notes.

On the other hand, he says, religion offers specific concepts, symbols, norms, words, rituals, and the like with which to conceptualize, reflect upon, express, and understand connectedness. "In short, religion tends toward the institutionalization or regularization of the spiritual, which we associate with church, synagogue, or mosque."

Sapp, a member of the Alzheimer's Association's Ethics Advisory Panel and founding president of the Association's Greater Miami Chapter, admits he is more inclined toward religion than spirituality. He notes that religion can offer social support, while spirituality may not.

Many religious congregations can and do offer individual and group support to people with Alzheimer's and their family caregivers, he says. By contrast, some forms of contemporary spirituality are more individualistic and thus may be of less help to people with the disease or their caregivers, he adds.

Sapp says religious congregations have important roles to play in the lives of people with Alzheimer's and their caregivers, from providing emotional and spiritual support to taking over the caregiver's role for a few hours.

A member of a church whose husband had recently been institutionalized

because of the severity of his Alzheimer's found that the members of the congregation still showed they cared for her, he says. "The men of the church, who had spent a great deal of time with him in the earlier stages of the illness, continue to perform many of the chores around her house, and the women provide understanding and listening ears."

People of faith take comfort in believing in a God who loves and cares about them, he says. "One benefit of faith in the face of Alzheimer's is that it offers hope in what appears to be a hopeless situation." The Abrahamic faiths all hold out a promise that a better life awaits, he notes. "In the case of Alzheimer's disease, I have seen many people find great solace in it."

However, Sapp says most congregations and clergy in the United States fail to reach out to people with Alzheimer's and their family caregivers. "Clergy attitudes are crucial because in most congregations the recognized leader sets the tone."

He says he has been frustrated in trying to get clergy and congregations involved in Alzheimer programs, which would benefit both groups in ministering to their own members and in serving the broader community. After all, he notes, religious people have an obligation to help others.

Caregivers may be reluctant to bring someone with Alzheimer's to

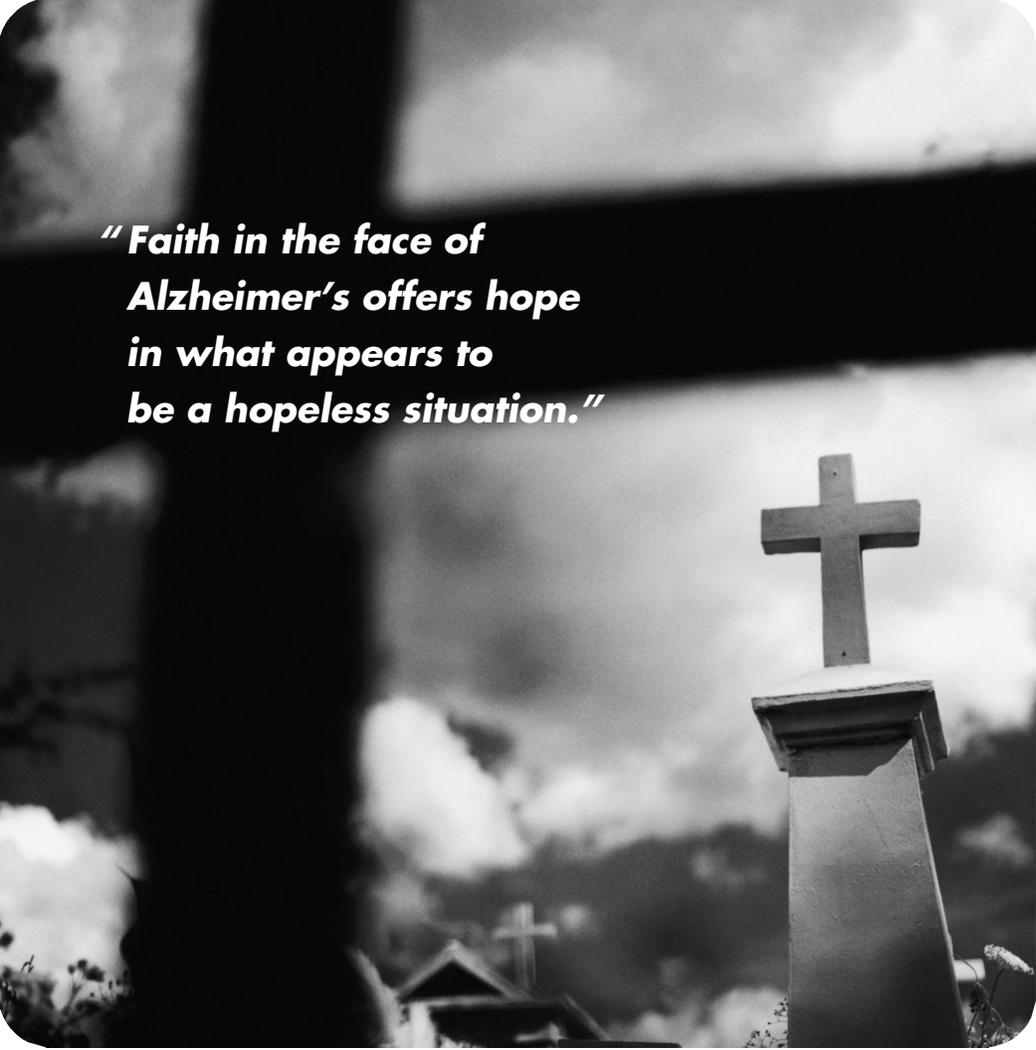


church because they are embarrassed or because the person may disrupt the service by yelling or engaging in other inappropriate behavior. This doesn't have to be a problem, he says. Some churches have special facilities where parents can take noisy children and still participate in worship through audio or video feeds, he says. "Perhaps these could find a new use."

Recent research has found a correlation between spiritual well-being and wellness. Last fall, *Alternative Therapies in Health and Medicine* published a study that suggested that regular meditation and diet contributed to reduced heart disease.

One of the most striking phenomena to hit religious gerontology since Sapp became involved in the field, and one welcomed by most people who work in the area, is the burgeoning research that is seen to demonstrate "scientifically" the effectiveness of religious beliefs and behaviors for health in general and healthy aging in particular, Sapp says.

"Modern science can offer us the means to live longer and healthier lives, but for all its successes and contributions, it is utterly powerless to offer us any meaning to live for," he notes. "The central teachings of the great religious traditions about the inherent value of every human being, whatever the person's condition, can serve as an important counterbalance."



"Faith in the face of Alzheimer's offers hope in what appears to be a hopeless situation."

Q: *Is some degree of memory loss natural as we age?*

A: Physicians once believed that significant memory loss was a normal part of aging, often regarding even Alzheimer's as natural age-related decline. Although experts now recognize severe memory loss as a symptom of serious illness, whether memory inevitably declines to some extent remains an open question. Many people feel that their memory becomes less sharp as they grow older, but determining whether there is any scientific basis for this belief poses an enormous research challenge.

When scientists considered significant memory loss natural, they also believed that aging caused massive brain cell loss. Recent studies using advanced sampling and mathematical modeling techniques suggest that people lose far fewer brain cells than scientists originally believed. These new techniques have also found different patterns of cell loss in the brains of individuals with and without Alzheimer's, confirming that Alzheimer's is not simply "accelerated" aging.

Correcting the misperception that aging significantly reduces brain cells does not reveal whether aging cells continue to function as well as younger ones. Unlike cells in the skin, liver, and other organs, the vast majority of the brain's 20 billion nerve cells do not divide and replenish themselves over time. The ability to learn and remember arises from the capacity to chemically encode information within a stable cell population. This persistence exposes

brain cells to a lifetime of potential stresses and harmful influences.

Information about cell function must come from performance tests, but evaluating memory over the human lifespan creates a huge challenge. Individual variation causes significant overlap in the test results of all age groups. Further, testing separate groups of older and younger people creates a type of error called the "cohort effect." This phenomenon means that one cannot necessarily assume that distinctions between older and younger groups are due to age—the differences may arise because an entire generation was subject to certain conditions that prevailed at a given time but have since changed. Examples include general nutrition, access to health care, typical educational attainment, and the social milieu. Many researchers believe that another factor potentially affecting the performance of seemingly healthy older individuals is that the groups may inadvertently include people in early stages of dementia.

The best way around the limitations of the cohort effect is a longitudinal study, which follows the same individuals over long periods. One of the world's most comprehensive such studies is the Baltimore Longitudinal Study of Aging (BLSA), supported by the U.S. National Institute on Aging. Begun in 1958, the BLSA is following more than 1,200 men and women from their 20s to their 90s.

Preliminary BLSA data suggest that age has complex effects on memory. Although most people over 60 decline in their ability to remember figures and shapes for short periods, vocabulary continues to increase until people reach their 80s. Other widely accepted studies have shown that most older adults experience some slowing in their ability to absorb complex directions and react appropriately.

Although experts expect the BLSA to produce more substantial insights, our current knowledge of what to expect as we age is frustratingly scanty. When people wonder whether some memory loss is normal, another unspoken question is often, "Should I worry about my own memory?" Many experts feel that the most worrisome memory lapses involve lack of awareness that we've forgotten something. Forgetting that you had a lunch date until a friend rings your doorbell is probably less cause for concern than wondering why your friend is at the door and failing to remember the lunch date even with prompting.

Our consultant for this column is Paul D. Coleman, PhD, professor in the Center on Aging and Developmental Biology and director of the Alzheimer's Disease Center at the University of Rochester, Rochester, New York.

Public Policy Forum Inspires Advocates to Make a Difference

A record number of attendees—nearly 600 in all—convened in Washington, D.C., April 27–30, for the Alzheimer’s Association 14th Annual Public Policy Forum.

Titled “Alzheimer Advocacy: A Billion Ways to Make a Difference,” the forum provided caregivers, Association chapter leaders and volunteers, and national staff and board members opportunities to hone their advocacy skills, network with peers, and talk with their representatives on Capitol Hill. Three plenary sessions and 16 workshops addressed such topics as Medicare access, the prescription drug debate, caregiver support, and e-advocacy. Highlights included firsthand accounts from people with Alzheimer’s and their caregivers detailing their struggles and successes living with the disease.

Early-stage Alzheimer’s was the focus of “In Our Own Voice: People with Dementia Speak Out.” Nellie Vega, an advocate with the Association’s Mid-Hudson Chapter diagnosed in January 2001, explained how a harrowing incident played a part in her seeking further medical attention (after initial tests a few years earlier showed no neurological damage). While making French fries in her kitchen, she went to pour salt into the water—only to discover she was about to add kitchen cleanser instead.

Once a case worker for homeless people living with AIDS, Vega keeps her mind

active with a part-time job as a pharmacist technician. Her dedicated advocacy efforts include educating young people about Alzheimer’s: “We have to make the youth aware that this is not an old-timers’ disease. It can happen to anyone.”

“Amyloid, ApoE, and Plaques—Oh My!” offered creative approaches advocates could take to generate excitement about and support for Alzheimer research from national and state legislators. Attendees heard a touching account from Ralph Winn, chair of the Upstate South Carolina Chapter’s public policy committee. The longtime caregiver for his wife, Hazel, who died from Alzheimer’s in January, Winn writes over 100 letters annually to raise money for Memory Walk. He implored the audience to urge elected officials to work for the Alzheimer cause.

“We’re the people who elect them. They’re *our* employees,” Winn stressed. “We can vote them in or out. We’re helping them when we elect them—why not ask them to help us when we need them?”

Held on the steps of the Lincoln Memorial, the Ninth Annual Candlelight Vigil featured a vocal performance of “My Heart Will Go On” by Stacy James, Miss Texas 2001 and an active participant with the Texas Coalition of the Alzheimer’s Association. The inspirational April 29 event served as a rallying point for chapter

delegations that converged on Capitol Hill the following day to attend an Alzheimer’s hearing held by the U.S. Senate Committee on Appropriations—Subcommittee on Labor, Health and Human Services, and Education, and to visit their representatives in Congress.

“I was empowered by meeting with our local legislators and their aides,” said Kathleen Hairston, program director for the Inland Empire Regional Office of the Los Angeles, Riverside, and San Bernardino Counties Chapter. “I now know that there are a billion ways to make a difference for individuals with Alzheimer’s, their families and caregivers, and care professionals.”



Steven McConnell, PhD, left, interim president and CEO, Alzheimer’s Association, poses with board member David Hyde Pierce.



The Candlelight Vigil was an inspirational event.

around the association

New On-line Resource Center on Web

An on-line Resource Center will launch on the Association's public Web site in late June. The Resource Center will house a collection of fact sheets, reading lists, *Advances* articles, and brochures, plus links to more than 100 Web sites.

For More Information www.alz.org

Updated Guidelines for Alzheimer's Management

The Los Angeles, Riverside, and San Bernardino Counties Chapter has been working on ways to improve the quality of health care for people with dementia. Its *Guidelines for Alzheimer's Disease Management*, originally published in 1998, has been updated. The recommendations include a periodic assessment documenting daily function, cognitive status, and behavioral problems; developing an ongoing treatment plan; and discussing the diagnosis, progression, treatment choices, and goals of Alzheimer care both with the person affected by Alzheimer's and their caregivers.

For More Information www.alzla.org or 323.938.3379, ext. 211

New Reading Lists Available

The Benjamin B. Green-Field Library and Resource Center at the national office has produced three new reading lists on subjects related to Alzheimer's disease. The first, *Persons with Alzheimer's Disease*, identifies books, newsletters, and videos with first-person accounts of those grappling with dementia. *Aluminum and Alzheimer's Disease* refers the readers to articles, books, and Web sites on that topic. A final list addresses *Communication* and includes both print and electronic resources compiled for both family and professional caregivers.

For More Information www.alz.org or 800.272.3900 and ask for the library.

ADI Hosts 18th Annual Conference

Alzheimer's Disease International (ADI) will be hosting its 18th annual conference October 23–26, 2002, in Barcelona, Spain. The conference—held in English and Spanish—will bring together researchers, physicians, care providers, staff and volunteers of Alzheimer associations, people with dementia, and their families to explore quality-of-life issues and the global impact of dementia. The conference will also examine the importance of design and architecture in dementia care.

For More Information www.alzheimer2002.com/, email: support@supportserveis.com, or call +34-93-201-7571.

in the news

Medicare Change

This past spring, news media nationwide reported on a recent regulation change by the Centers for Medicare and Medicaid Services. For years, Medicare refused to pay for some medical services for beneficiaries with Alzheimer's solely because of their diagnosis. Now, Medicare cannot use the dementia diagnostic codes alone to deny medical services. The Alzheimer's Association's Medicare Advocacy Project lobbied for the change, which took effect last fall.

Link Between High Cholesterol and Cognitive Decline

In late March, media reported on a new study published in the *Archives of Neurology*, which provides additional evidence of a link between elevated cholesterol levels and an increased risk of cognitive decline. The study suggests that modifiable risk factors known to contribute to cardiovascular disease may also play a role in Alzheimer's, dementia, cognitive decline, or all three.

This study of 1,037 women with coronary heart disease found that lower levels of total cholesterol and low-density lipoprotein (LDL) cholesterol were associated with better cognitive performance and lower risk of impairment. The study also found that the use of statins, a class of drugs used to treat high cholesterol, was associated with a lower occurrence of cognitive impairment.

End of Vaccine Trial Closes a Chapter but Not the Book*continued from page 1*

Thies points out—and many other experts agree—that immunotherapy still holds promise and should not be dismissed as a viable approach to treatment or prevention. Some of the most prominent names in Alzheimer research—including several Association-funded investigators—offered opinions about immunotherapy's future during a March 5 on-line discussion on the Alzheimer Research Forum, a nonprofit Web site for clinicians and scientists. The discussion links to a report from a March 13 Paris conference on Immunization against Alzheimer's and Other Neurodegenerative Diseases hosted by the IPSEN Foundation for Therapeutic Research.

The IPSEN report includes an observation by sources close to the vaccine trials that some individuals who developed brain inflammation had not yet formed antibodies to the vaccine. According to some scientists, this observation suggests that the inflammation may be due to the activity of T cells, a specific type of white blood cell involved in immune response. Bill Thies points out, "If that explanation is right, there are lots of ways around T cell activation."

On-line discussion participants also noted that several of the trial enrollees who developed inflammation were found to have herpes simplex virus type 1 (HSV1) in their cerebrospinal fluid. HSV1, which causes cold sores, is known to exist in a dormant state in the nervous

system of many older adults. If the inflammation occurred because AN-1792 reactivated the virus, giving antiviral drugs along with the vaccine might stave off the reaction.

Other modified immunotherapeutic approaches could focus on refining the vaccine's formulation. AN-1792 was a form of beta-amyloid (A β), the protein fragment that makes up most of the amyloid plaques that are a hallmark of Alzheimer abnormality. A preparation based on a portion of the A β fragment or on anti-amyloid antibodies themselves might be less prone to stimulate inflammation.

An April 8 *Nature Neuroscience* article by Steven M. Paul, MD, and colleagues reported that a single dose of a vaccine based on a genetically engineered amyloid antibody improved memory performance in a mouse model of Alzheimer's disease. While results in mice offer no guarantees of human effectiveness, Elan moved their vaccine into Phase I clinical trials only one year after publishing their first promising results in mice.

Another possibility is that the inflammation might not be undesirable—it could be a beneficial reaction that precedes elimination of amyloid plaques, just as temporary inflammation often precedes healing of a cut. Although it would be unethical to continue administering medication until this issue can be clarified, several forum participants pointed out that the trials are not "really over" even though no more

medication will be given. It is impossible to "unvaccinate" enrollees, and researchers will continue to gain information about the body's reaction to immunization and the significance of inflammation as they continue to monitor trial participants.

While scientists seek further insight into the problems that arose with AN-1792 and explore refined immunotherapeutic approaches, researchers around the world will continue to advance on many other promising treatment and prevention fronts. David Morgan, PhD, from the University of South Florida, summed up the spirit of the Alzheimer Research Forum discussion by observing, "We would all like to see the vaccine work. Still, I am confident that if this one does not succeed, one of the other approaches currently under way will eventually prove beneficial."

For On-line Discussion

Alzheimer Research Forum
www.alzforum.org/members/forums/journal/vaccine/index.html

For an Electronic Version

Target Alzheimer's
www.abpi.org.uk

- 1 Select *ABPI Publications*
- 2 Select *Recently Published*
- 3 Drop down menu appears
- 4 Investigational drugs are listed in the *Summary Table*