Volume 12, Numbers 3-4 **Alzheimer's Disease Education & Referral Center** 2004-05

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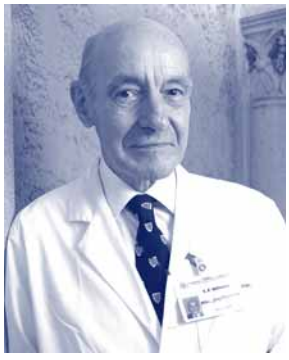
Alzheimer's Disease Centers Program Celebrates 20th Anniversary

The year was 1984. Ronald Reagan was campaigning for his second term in office. Prince and the Revolution had the top pop song, *When Doves Cry*. At the Oscars, *Terms of Endearment* won best picture. The Soviet Union pulled out of the summer Olympic Games. The Detroit Tigers won the World Series. Apple Computer sponsored the first commercial for "personal computers" during the Super Bowl (won by the Chicago Bears). And, leaders at the National Institute on Aging (NIA) decided it was time to develop a national, interdisciplinary research program specifically focused on the causes and course of Alzheimer's disease (AD) and the differences between AD and normal aging.

In the early years, NIA's AD research program faced many hurdles, including a lack of scientific interest and few trained investigators. Funding focused on dementia was also scarce. In fact, in 1975, Robert N. Butler, M.D., the first Director of NIA, could find "only 12 grants across the whole National Institutes of Health (NIH) pertaining to aging and the brain, averaging $60,000 each." Dr. Butler decided that "AD and related dementias were catastrophic diseases that must be identified as major national research priorities." In 1976, an editorial by Robert Katzman, M.D., an influential neurologist then at the Albert Einstein College of Medicine in New York, described AD as a major public heath problem. The following year, three NIH Institutes, the National Institute of Mental Health, the National Institute of Neurological Disorders and Stroke (NINDS), and NIA held a national conference that further focused attention on AD. In the mid-1980s, T. Franklin Williams, M.D., established the Office of Alzheimer's Research at NIA, and with the support of NIH Director James Wyngaarden, M.D., began to consolidate the NIA's coordination of AD research. ""We had come to recognize that Alzheimer's dementia was probably the greatest scourge

Robert N. Butler, M.D., NIA's first Director



T. Franklin Williams, M.D., former Director, NIA

(see ADC Anniversary, page 2)

ADEAR Clinical Trials web pages redesigned

Looking for detailed information such as recruitment status, eligibility criteria, or location for specific AD research studies? The ADEAR Center has redesigned its clinical trials database (www.alzheimers.org/clintrials) to make that search easier. With improved search functions and organization, the revamped database has made AD study information more accessible

(see Clinical Trials Web Pages, page 8)

ADC Anniversary

(from page 1)

and disaster for older people and their families in the United States, and as well the growing potential in our scientific community to address its challenges. We made Alzheimer's research our highest priority", says Dr. Williams. As NIA was assuming the lead Federal research role, the concept of a network of centers that would foster research on Alzheimer's began to germinate. Such a network could create the necessary infrastructure to promote longitudinal clinical-pathological studies; integrate basic and clinical research; standardize clinical assessment tools, methods, and clinical trials; and establish national data banks to share resources for clinical, neuropathological, and genetic studies.

Robert Katzman, M.D., neurologist

First centers formed in 1984

This "center network" concept formed the basis of the creation in 1984 of the legislatively-mandated Alzheimer's Disease Centers (ADCs) program. NIA awarded funding, after applications were submitted and peer-reviewed, to teams of scientists based at five institutions—Harvard University, Johns Hopkins University, Mount Sinai Medical School, the University of California at San Diego, and the University of Southern California. The original centers were called Alzheimer's Disease Research Centers (ADRCs), and their funding awards totaled $3.5 million. Researchers were sent forth on a scientific quest that continues to this day.

Zaven Khachaturian, Ph.D., former Associate Director, Neuroscience and Neuropsychology of Aging Program (NNA) and the first Director of the Office of Alzheimer's Research, is widely regarded as the architect of the ADRC program. Of those early days, Dr. Khachaturian says, "The challenges that NIA faced in launching the national initiative to increase interest in aging and AD research seemed insurmountable; but now it is heartening to see how much of a difference the Institute has made. The successes of NIA's program were largely due to unwavering support and encouragement by Dr. Williams and other NIA staff, primarily Drs. Teresa Radebaugh and Creighton (Tony) Phelps."

Zaven Khachaturian, Ph.D., former Director, Office of Alzheimer's Research at the NIA

A brief history of dementia research: the early days

Dementia did not suddenly appear in society in 1906 when Dr. Alois Alzheimer, using newly-developed silver stains, examined the brain tissue of a 51-year-old German woman and described what we now know as plaques and tangles. In fact, dementia was described as early as 500 BC. Until the late 1800s, clinicians believed that an accumulation of "phlegm" caused "senility," which was simply a symptom of old age. Dr. Alzheimer's patient was diagnosed with a form of mental disorder called "presenile dementia" due to her relative young age. Because of her age, clinicians did not consider the possibility that the plaques and tangles Dr. Alzheimer described could also be the cause of dementia in old age. So, Alzheimer's disease was originally characterized as a *presenile* dementia.

Up until the late 1940s, the medical community widely believed that dementia in old age—*senile* dementia—was a normal part of aging caused by cerebral arteriosclerosis. It was still often termed senility. But researchers in the 1950s and 60s showed that the brains of many patients with *senile* dementia did contain the plaques and tangles of *presenile* dementia and began to investigate their biological structure.

In the 1970s, as neurological research brought further understanding of the structure and function of the brain, scientists observed deficiencies in the neurotransmitter acetylcholine in people with *senile* dementia. Researchers began challenging the common belief that *senile* dementia was a normal part of aging, concluding that the brain pathology was identical to that which Dr. Alzheimer described in *presenile* dementia.

"Alzheimer's disease" became a common term in the late 1970s to describe both the *presenile* and *senile* forms of dementia. Neuroscientists and physicians began using clinical criteria to diagnose AD more frequently, and it became clear that the *senile* form of AD was by far the most prevalent. Emerging technologies and more sophisticated biochemistry techniques were contributing to growing scientific enthusiasm to find the causes of AD, and the increasing numbers of elderly in the population contributed a sense of urgency to do so.

AD coalitions begin forming

In the mid to late 1970s, a coalition of grass-roots AD advocacy groups consisting primarily of involved family members began to influence public policy discussions and rally public interest in the national AD research agenda. In 1980, leaders of the NINDS and NIA met with coalition members, who would establish the Alzheimer's Disease and Related Disorders Association (ADRDA), later named the Alzheimer's Association. By the early 80s, efforts by the ADRDA succeeded in creating a growing public awareness of the incidence and prevalence of AD and the enormous costs borne by society, and they lobbied Congress to provide funding for the NIA to create the ADRC program.

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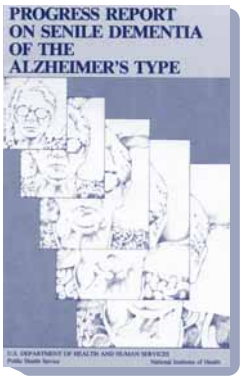
ADCs Contribute Significant AD Research Advances

ADC teams have contributed to many of the most significant AD research discoveries in the past 20 years, including:

- developing new concepts such as MCI, a transitional cognitive state between normal function and mild AD, and helping increase emphasis on evaluation of cognition in normal aging and the transition to MCI and early dementia
- furthering understanding of cellular processes and cholinergic and neurotoxic mechanisms that play key roles in formation of neuritic plaques and neurofibrillary tangles, loss of connections, and cell death
- developing and testing the Alzheimer's Disease Assessment Scale (ADAS) and the Clinical Dementia Rating (CDR), which are instruments for AD screening
- identifying the importance of genetics in development of AD, including identifying the mutations in genes on chromosomes 14, and 1 as major causes of early-onset AD, and identifying the apolipoprotein E4 variant of the apolipoprotein gene on chromosome 19 as a risk factor gene for late-onset AD
- supporting molecular studies and work in related dementias, such as discovering that the α-synuclein protein is deposited in Lewy bodies in AD, Parkinson's disease (PD), and in Lewy body dementia, and recognizing the common properties of other abnormal proteins associated with neurodegenerative diseases such as PD, as well as identifying *tau* mutations on chromosome 17, causing frontotemporal dementia with parkinsonism
- conducting clinicopathological studies, for example, how early memory and cognitive abnormalities correlate with changes in the hippocampus and entorhinal cortex
- organizing neuroimaging studies to define the clinical course, signs, and symptoms of AD, and developing a compound known as Pittsburgh Compound-B (PIB), which penetrates the blood-brain barrier, sticks to amyloid plaques, and permits the level of amyloid to be determined on positron emission tomography (PET) scans of living patients
- identifying potential chemical biomarkers in cerebrospinal fluid and serum in clinically well-characterized individuals, including *tau,* amyloid, isoprostanes, and lipids
- helping to define the contributions of cardiovascular and cerebrovascular diseases and other comorbidities such as diabetes in the development and severity of AD
- creating transgenic mouse models expressing specific mutated genes, including amyloid precursor protein (APP), presenilin 1, apoE alleles, and *tau* proteins, as well as gene knockout models such as BACE, which allow scientists to study cellular pathologies so that treatments can be developed to retard or prevent their formation
- supporting studies of inflammatory mechanisms and the role of oxidative stress, calcium, glutamate, and mitochondrial dysfunction
- helping recruit African Americans, Caribbean Hispanics, Mexican Americans, Native Americans, and Chinese Americans for multi-cultural studies
- defining models for caregiver support groups; examining the relationship between caregiver stress and depression; studying how AD affects driving skills; improving behavior management; discussing competency issues, such as loss of financial capacity; using telecomputing; and adapting strategies for managing patients with late-stage dementia
- supporting population studies, such as the Religious Orders Study and the Nun Study
- participating in many ongoing trials examining promising therapies and prevention

Mission of the ADRC program

The cadre of scientists at the first five ADRCs became the foundation of a network that today reaches across the country and has grown to 30 institutions. Their mission is to promote research, training and education, technology transfer, and collaboration to improve diagnosis, treatment, and overall understanding of AD and related dementias through clinical, pathology, and education cores. Areas of investigation range from the basic mechanisms of AD to managing the symptoms and helping families cope with the effects of the disease. Centers provide investigators and research groups with well-characterized patients and control subjects, family information, and tissue and biological specimens for use in research projects. Early research projects funded by the centers focused on possible causes of AD and changes in brain chemistry. Researchers were looking at calcium transport, glucose metabolism, protein synthesis, accumulation of metals, possible viral agents, genetic factors, and related dementias.



First *Progress Report* on AD, published in 1981.

In 1985, Congress appropriated funds for five additional ADRCs. Duke University, the University of Kentucky, Washington University at St. Louis, the University of Pittsburgh, and the University of Washington joined NIA's growing AD research network as a result of this Request for Application (RFA) competition.

Collaborative approaches

In 1986, the Alzheimer's Disease Patient Registries (ADPR) were established, which included the Consortium to Establish a Registry for Alzheimer's Disease (CERAD), an early collaboration among the centers. Under the leadership of Albert Heyman, M.D., a Duke University neurologist, CERAD standardized the definition, assessment, and profile of AD, and the criteria for pathological diagnosis of AD. These criteria are still widely used. Another ADPR project at the Mayo Clinic provided much of the foundation for the current interest and advances concerning mild cognitive impairment (MCI).

Also in 1986, a small clinical trial showed that a cholinesterase inhibitor called tacrine (later marketed as Cognex) had some promise in treating moderate AD. The Alzheimer's Association worked with NIA, several ADRC directors, and the drug company Warner-Lambert to set up a large, multi-site clinical trial to test tacrine further. This trial provided evidence to the Food and Drug Administration (FDA) that led to approval of tacrine as the first drug specifically targeting AD.

Large clinical trials supported

Collaboration on the tacrine trial also spawned, in 1991, the formation of a consortium of centers and affiliated organizations to test new treatments as they emerge. The consortium, named the Alzheimer's Disease Cooperative Study (ADCS), was created to conduct clinical trials on compounds not of interest to large pharmaceutical companies. This includes drugs that are off patent, drugs that were patented and marketed for another use but might be useful to treat AD, or novel compounds from investigators or small companies that do not have adequate resources to conduct clinical trials. The ADCS program today continues to organize large clinical trials and to develop trial methodologies that are widely used by both academics and industry.

"When the ADC program was created, NIA's leaders hoped that an environment of cooperation would stimulate AD researchers to seek new pathways to scientific discovery and to share their findings. The program has done just that. In the collaborative atmosphere of the centers, specialists in biomedical, behavioral, pathological, and clinical science are studying the causes, and possible prevention of AD, and developing new lines of multidisciplinary research. As scientists at the centers uncover the complexities of dementia, they spark a certain friendly competition with other research scientists throughout the world. Their brilliance and enthusiasm creates an excellent training ground for up and coming investigators, and inspires others to devote their energies to AD research," says Tony Phelps, Ph.D., Program Director, Alzheimer's Disease Centers, NNA.

Cell repository created

In 1989, the NIA, working with the Duke University ADRC, created a genetics cell repository at the Indiana

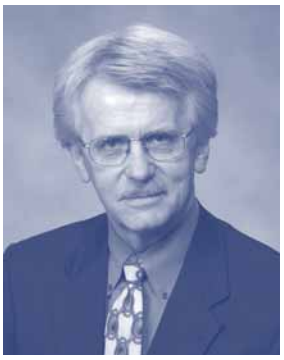
John Growdon, M.D., Director of the Harvard Medical School ADRC in 1984 (and continuing in that role today):

"In the late 1970s and early 1980s, when the ADCs were first envisioned, there was great enthusiasm that we could treat AD. This optimistic spirit was based on the seminal neuroscientific breakthrough linking AD to degeneration of cholinergic neurons in the brain, with resultant deficits in memory-dependent cholinergic neurotransmission. Many of us hoped that correcting the cholinergic deficit would improve AD symptoms, in a way analogous to the beneficial effects of treating the dopaminergic deficiency in Parkinson disease. Although AD neurochemical pathology proved more complex than simple acetylcholine loss, this line of investigation eventually did lead to the approval of acetylcholinesterase inhibitors as standard symptomatic drug treatment for AD today."

University ADC. This repository has grown and is now independently funded and called the National Cell Repository for AD (NCRAD). A cell repository banks DNA and cells and builds a database of family histories and medical records for genetic research. NCRAD provides genetic researchers with cell lines and/or DNA samples from people with well-documented AD and normal controls. Because supplies of DNA are finite and cannot easily be regenerated, NCRAD makes "immortalized" cell lines—cells continuously regenerated in the laboratory from the blood samples—to provide samples for studies searching for AD genes.

Wealth of information in 20 years

"When you look at what we knew in 1984 and what we know now, the research advances contributed by ADC scientists represent remarkable progress. I've witnessed this from within the ADC system as a research scientist and from my vantage point at NIA," says Marcelle Morrison-Bogorad, Ph.D., Director, NNA program. Dr. Morrison-Bogorad came to NIA in 1996 from the University of Texas Southwestern Medical Center at Dallas, where she did research on protective proteins in AD brains and was a professor of neurology. "Almost every day, this collective research system adds new understanding of what happens in the brain before and after the symptoms of AD appear. In 20 years we've made giant strides and added an immense wealth of information."



Ronald C. Petersen, M.D., Ph.D., Director, Mayo Clinic Alzheimer's Disease Center:
"The ADC program has been very successful from the perspective of clinical or patient-oriented research, bringing together basic scientists and clinicians to address the same issues. As these research avenues converge, we are now focusing on a much earlier stage in the disease process than we were 20 years ago. By intervening at an earlier stage, such as mild cognitive impairment, hopefully, we will be able to prevent subsequent damage."

Core Centers and Satellite Clinics established

Starting in 1990, the NIA began to fund Alzheimer's Disease Core Centers (ADCCs) to expand and diversify the program geographically. Core Centers do not include the large research projects conducted by ADRCs. At that time, all of the centers were also asked to develop a strategy to recruit minority and ethnically diverse research subjects. Several centers created satellite diagnostic and treatment clinics targeting minority, rural, or other underserved populations. Over time, the program has grown to include 26 such satellites, helping accelerate minority patient enrollment to increase the heterogeneity of the research pool, and helping to ensure that research results would be applicable to minorities as well as to Caucasians.

Collecting and pooling data

The National Alzheimer's Coordinating Center (NACC) was established in 1999 to provide access to larger, standardized data sets collected from the ADCs and to allow characterization of the rarer and mixed phenotypes and genetic and ethnic differences in the patient mix. NACC enables researchers to pool patient information more effectively as they study the unique aspects and subtypes of this complex and heterogeneous disease process. The NACC has data on thousands of subjects and offers qualified AD researchers website access to data sets. It has awarded 13 competitive grants to groups of centers, and NIA has issued two RFAs to conduct collaborative project using patient records and specimens for research projects.

Beginning in 1996, the centers' application process was changed, allowing new applicants to compete with existing centers for funding. While always peer-reviewed, once funded, the centers did not compete directly with other centers until 1996. By 2004, the program had grown to 30 centers, with funding of $46.9 million (10.3% of NIA's AD budget that year). More than 60,000 patients and healthy control subjects have been

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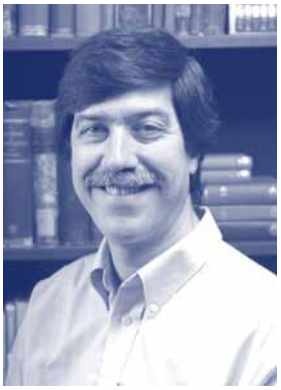

David Bennett, M.D., Director, Rush-Presbyterian-St. Lukes Alzheimer's Disease Center:
"It has become apparent that AD is a complex function of numerous genetic and environmental risk factors that cause or interact with a variety of pathologic, biochemical, and molecular changes in the brain. Despite its complexity, we have witnessed the development of symptomatic therapies for the disease, and potential disease modifying agents are currently in clinical trials. However, the major challenge for the future is disease prevention. Meeting this challenge requires large, longitudinal, multidisciplinary studies that can simultaneously address the myriad factors involved in the disease, and large primary prevention trials. As the NIA has already started to invest in these kinds of studies, I anticipate that strategies for disease prevention will be discovered over the next 20 years. As the steward of biomedical research for the nation, the NIH has orchestrated stunning successes with infectious disease, cardiovascular disease, and cancer. There is every reason to hope for and expect similar successes with AD and other common health problems of older persons."

Lisa Gwyther, MSW, CCSW, Associate Clinical Professor, Department of Psychiatry and Behavioral Sciences at the Joseph and Kathleen Bryan Alzheimer's Disease Center, Duke University:

"ADC education directors strategically leveraged their collaborative creativity over the last 20 years to develop and, more importantly, sustain relationships with key decision-makers and partners in 'hard-to-convince' communities. The ADC education cores create and test culturally acceptable, user-friendly media and materials to answer the 'so-what's' of Alzheimer's research in family-centered, clinically and socially meaningful ways. We have opened doors to earlier diagnosis, care, and research participation for a slowly expanding, influential new constituency of extraordinary 'ordinary' families from diverse ethnic, cultural, and regional groups."

enrolled in ADC programs, and more than 7,000 autopsies have been performed, with the brain material stored in brain banks.

Of cores, of cores…

In addition to an administrative core, clinical core, and a neuropathology core, each center has an education core, which helps recruit and retain subjects for trials, spearheads outreach programs to educate families, and supports innovative staff development to improve clinical skills through training workshops, seminars, and continuing education programs.

Physician education includes lectures, grand rounds, and mini-residencies or internships to help practicing physicians gain skills in assessing, treating, and managing dementia patients. Educational programs often are held in conjunction with State and local agencies and the Alzheimer's Association. In addition to providing private research funds, Association chapters work closely with many of the scientists and other health professionals based at the centers.

Improving information flow

Changes in how the centers function and improvements in information flow were among the suggestions from panels of researchers and outside experts during planning workshops held in 2001 and 2002. Among the recommendations:

- permit greater flexibility in structure of the individual centers to take advantage of local resources and tailor the center's organization to emphasize local interests and expertise. For example, it was suggested that centers might enroll and follow special patient populations such as people living in retirement communities or nursing home residents, rather than studying only clinic populations
- permit contracts with an organization such as the Alzheimer's Association for educational services, or with another center to provide neuropathological evaluations
- continue and accelerate standardized clinical data collection across centers to promote better collaborative clinical studies
- promote better use and increased sharing of tissue and data resources among the centers and the general scientific community
- concentrate cutting-edge research more on the transition from normal aging to MCI and to AD instead of later stages of AD, and focus on comparisons to and overlap with other neurodegenerative diseases

These recommendations were implemented in the succeeding center RFAs. Importantly, efforts were accelerated to establish a universal data set (UDS) among the centers, so that patients enrolled at all centers would be assessed in a standardized manner. The UDS will go into operation in 2005 and will permit even better collaborative research projects among centers and other scientists.

New and ongoing projects

In 2003, the NIA launched a major new initiative to speed the process of creating a large repository of DNA and cell lines from families with multiple cases of late-onset (over age 65) AD. The centers are playing a significant role to recruit families, collect clinical data and blood samples, and provide blood to NCRAD so that DNA and cell lines can be made available to all qualified researchers. The goal of the study, called the Late-Onset Alzheimer's Disease study (also known as the AD Genetics Initiative), is to identify remaining risk factor genes and possible environmental factors, and the interactions of genes and the environment.

In 2004, NIA announced the Alzheimer's Disease Neuroimaging Initiative (ADNI), another multi-center initiative. The 5-year study will use neuroimaging (magnetic resonance imaging or MRI, and positron emission tomography or PET) to identify biomarkers of disease progression to help measure effectiveness of therapies under study in clinical trials. Most of the ADCs are participating in the initiative, which is a partnership among the NIA/NIH, academic investigators, the FDA, and, through the Foundation for NIH, the pharmaceutical and imaging equipment industries, the Alzheimer's Association, and the Institute for the Study of Aging.

ADC grants continue today

The NIA is committing about $16 million in Fiscal Year 2005 to fund 13 new and/or competing renewal ADC grants for a 5-year period. As in previous years, each ADC grant will also support small pilot projects often designed to determine whether a larger study has promise.

Steven DeKosky, M.D., Director, University of Pittsburgh Alzheimer's Disease Center:
"The establishment of the program by the NIA and the research by the centers' investigators laid the foundation for incredible advances in our understanding of diagnosis, clinical course, and pathobiology of AD. It is important to remember that when the ADRC program began, very little was known about AD, especially about how to devise interventions that might slow down the progression of the disease or lead to prevention. Research from individual centers and, even more powerfully, collaborations among the ADCs led to improved methods of diagnosis, high certainty of diagnostic accuracy, advances in our understanding of the genetics of the disease, development of transgenic models for certain aspects of AD, and most importantly avenues for therapeutic intervention that are emerging from the laboratories and are now being tested in patients. We have progressed, in large part due to the centers' work, from symptomatic therapies to specific treatments aimed at the primary pathology of the disease. A national infrastructure was established with the centers that is now clearly prepared to initiate trials of new medications in a minimal time by true experts in the field. After working in this field for over 20 years and understanding how little we knew at the beginning, it is both astounding and hopeful that we've come this far. And we have a large number of medications and strategies to try in our efforts to vanquish this disease."

The ADCs play a major role in AD research. "This program continues to fulfill its initial goals of attracting outstanding investigators to the field of research in AD and aging, as well as increasing the quality and quantity of research. We've helped develop medications that ease symptoms and improve quality of life, and working with the Alzheimer's Association, helped reduce the stigma of AD in society. Our current large initiatives will help us uncover some of the complexity surrounding the causes of AD and learn more about the possibility of reversing or preventing it. We're very excited with the public-private partnership model and the shape of our future research direction. We've had great successes so far but are mindful that answers to some of our fundamental questions remain elusive. We will continue our strong commitment and focus," commented Richard J. Hodes, M.D., Director, NIA.

For more information:

- National Institutes of Health – www.nih.gov
- National Institute on Aging – www.nia.nih.gov
- Alzheimer's Disease Education and Referral (ADEAR) Center – www.alzheimers.org
- National Cell Repository for AD – http://ncrad.iu.edu
- National Alzheimer's Coordinating Center – www.alz.washington.edu
- NIA AD Genetics Initiative – www.NIAgeneticsinitiative.org
- Alzheimer's Disease Cooperative Study – http://adcs.ucsd.edu
- Alzheimer's Association – www.alz.org

Alzheimer's Disease Centers

Alabama

University of Alabama at Birmingham
Website: http://main.uab.edu/show.asp?durki=11627
Telephone: 205-934-2178

Arizona

Sun Health Research Institute/Arizona Consortium
Website: http://alzheimers.sbs.arizona.edu
Telephone: 602-239-6999

Arkansas

University of Arkansas for Medical Sciences
Website: http://alzheimer.uams.edu
Telephone: 501-603-1294

California

Stanford University
Website: http://alzheimer.stanford.edu
Telephone: 650-852-3287

University of California, Davis
Website: http://alzheimer.ucdavis.edu
Telephone: 916-734-5496

University of California, Irvine
Website: www.alz.uci.edu
Telephone: 949-824-5847

University of California, Los Angeles
Website: www.adc.ucla.edu
Telephone: 310-825-8908

University of California, San Diego
Website: http://adrc.ucsd.edu
Telephone: 858-622-5800

University of California, San Francisco
Website: http://memory.ucsf.edu
Telephone: 415-476-6880

University of Southern California
Website: www.usc.edu/dept/gero/ADRC
Telephone: 323-442-3020

Illinois

Northwestern University
Website: www.brain.northwestern.edu
Telephone: 312-908-9339

Rush-Presbyterian-St. Lukes Medical Center
Website: www.rush.edu/patients/radc/index.html
Telephone: 312-942-4463

Indiana

Indiana University
Website: http://iadc.iupui.edu
Telephone: 317-278-2030

Kentucky

University of Kentucky
Website: www.mc.uky.edu/coa/ADRC/adrc.htm
Telephone: 859-323-6040

Maryland

The Johns Hopkins Medical Institutions
Website: www.alzresearch.org
Telephone: 410-955-5632

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Massachusetts

Boston University
Website: www.bu.edu/alzresearch
Telephone: 617-638-5368

Harvard Medical School/Massachusetts General Hospital
Website: www.madrc.org
Telephone: 617-726-3987

Michigan

University of Michigan
Website: http://sitemaker.med.umich.edu/madrc
Telephone: 734-764-2190

Minnesota

Mayo Clinic
Website: http://mayoresearch.mayo.edu/mayo/research/alzheimers_center/
Telephone: 507-284-1324

Missouri

Washington University
Website: www.alzheimer.wustl.edu/adrc2
Telephone: 314-286-2881

New York

Columbia University
Website: www.cumc.columbia.edu/dept/taub/index.html
Telephone: 212-305-1818

Mount Sinai School of Medicine/Bronx VA Medical Center
Website: www.mssm.edu/psychiatry/adrc
Telephone: 212-241-8329

New York University
Website: http://aging.med.nyu.edu
Telephone: 212-263-5700

North Carolina

Duke University
Website: http://adrc.mc.duke.edu/
Telephone: 1-866-444-2372

Ohio

Case Western Reserve University
Website: www.memoryandagingcenter.org
Telephone: 1-800-252-5048

Oregon

Oregon Health and Science University
Website: www.ohsu.edu/som-alzheimers
Telephone: 503-494-6976

Pennsylvania

University of Pennsylvania
Website: www.uphs.upenn.edu/cndr
Telephone: 215-662-4708

University of Pittsburgh
Website: www.adrc.pitt.edu
Telephone: 412-692-2700

Texas

University of Texas, Southwestern Medical Center
Website: www2.swmed.edu/alzheimer
Telephone: 214-648-7444

Washington

University of Washington
Website: http://depts.washington.edu/adrcweb
Telephone: 206-277-3281

Clinical Trials Web Pages

(from page 1)

and readable. The web page includes AD treatment and prevention clinical trials sponsored by the NIA as well as other institutes, organizations, and industries. These clinical trials are also available on the National Institutes of Health clinical trials website (www.ClinicalTrials.gov); however, the ADEAR database provides focused searching for AD trials only and includes additional information.

The search page now has "hot" buttons, including "Open Trials" for all those currently recruiting participants, "New Trials" added in the last 30 days, and "In the News" for trials featured in the media. Other search options, which can be selected separately or in combination, include searching by the location of the research center, either city or State, or by entering a zip code to find all centers within a selected range. Or a person's age, condition, and/or disease stage can be entered to find only those trials that match his/her needs. Another option is to search for a clinical trial based upon the type of treatment being studied, using drop-down lists that display names of treatments by intervention type, drug (including separate brand and generic name lists), device, behavior management, or gene transfer.

These options automatically search for currently recruiting trials. However, trials that have been closed or completed can also be searched using these same features by checking a box to include studies no longer recruiting.

Once you select a clinical trial, detailed information for that trial is displayed. These details are now reorganized into sections to make it easier to pinpoint specific items, such as qualifications for participation. Site information lists the location and contact person for research centers. If a specific search method was used, the sites meeting the criteria used to search for the trial are listed first, followed by the complete list of participating research centers. The end of each record includes resources for additional information with links to the National Library of Medicine's PubMed abstract or citation of relevant articles, when available.

Like any website, the Clinical Trials web page is a work in progress. Additional improvements are already in the works. These include expanding the "In the News" page to include links to news releases and other pertinent information, adding FAQs (Frequently Asked Questions) about clinical trials, and adding a keyword search function. Questions and comments are welcome; please send them via e-mail to trials@alzheimers.org.

CHID Highlights

CHID Highlights describes materials recently added to the Alzheimer's disease file of the Combined Health Information Database (CHID). The items selected represent topics and formats of general interest to readers of *Connections* and ADEAR Center users or their clients. Please order directly from the source listed for each item. Journal articles are available in many university and medical school libraries. CHID is accessible on the Internet at www.chid.nih.gov, by following the link at www.alzheimers.org, or by following the National Library of Medicine's link to CHID at www.nlm.nih.gov/medlineplus/databases.html.

Designing for Safety

Complete Guide to Alzheimer's Proofing Your Home. 2nd. ed. 2000

Warner, M.L.

Available from Ageless Design, The Alzheimer's Store, 12633 159th Court North, Jupiter, FL 33478. Phone: 1-800-752-3238; Fax: 561-744-9572. Website: www.alzstore.com. PRICE: $29.95

"How can I set up my home to provide an efficient, safe, and thoughtful living environment that is sensitive to the needs of my loved one? How can I satisfy my own needs for peace and privacy and well-being?" asks author Mark Warner in this second edition of his popular guide. While not a caregiving guide, the book provides room-by-room tips on how to set up your home to make caring for a person with AD easier, and it includes a number of discussions on how to rearrange the home environment to deal with some of the behavioral issues associated with AD. Detailed information is presented about how to modify interior and exterior spaces, including all types of rooms, hallways, stairs, doors, windows, storage sheds, garages, patios, decks, and the yard. Warner, an architect who created the Ageless Design company to assist with environmental and safety design and products for older people, suggests modifications to help with various AD-related problems. These include cognitive impairment (memory loss, difficulty finding things, disorientation to time and place, misinterpretations, fears, and depression), behavioral problems, difficulties with activities of daily living, wandering, incontinence, and mobility problems. The book is for both home caregivers and the health care professionals who work with people with AD living at home. It also includes an extensive directory of products and manufacturers.

AD Photo Essay

Alive With Alzheimer's. 2004

Greenblat, C.S.

Available from the University of Chicago Press, 1427 East 60th Street, Chicago, IL 60637. Phone: 773-702-7700; Fax: 773-702-9756. Website: www.press.uchicago.edu. PRICE: $27.50

This small book contains 85 photographs taken by Cathy Stein Greenblat at the Silverado Senior Living center in Escondido, California. Sensitive and deeply moving, the photographs are of people who are in various stages of AD. The images are accompanied by poignant captions and quotes, as well as touching biographies. The text and accompanying photographs demonstrate that people with AD can be very "alive" during their remaining years in an institution. The book discusses the strides the caregiving industry is taking to provide personalized and individual attention, and highlights the positive aspects of patients' lifestyles at Silverado. Volunteers and caregivers participate in songs and dances with the elderly, and the staff help support patients in making their own decisions, such as where to go on an outing or whether they would like a pet. This book is testimony to the fact that institutionalized AD patients can thrive within a stimulating environment for some time.

Selecting an SCU

How to Select a Special Care Unit: A Consumer's Guide to Special Care Units for Persons With Dementia. 2002

Kansas Department on Aging

Available from the Kansas Department on Aging, 503 South Kansas Avenue, Topeka, KS 66603. Phone: 1-800-432-3535; 785-296-4986. Website: www.agingkansas.org/kdoa/publications/requestform.htm. PRICE: free

This fact sheet is intended to help caregivers and families of a dementia patient choose a special care unit (SCU) within an adult care facility for their loved one. Published by the Kansas Department on Aging, the fact sheet offers a brief background on AD and other dementias and describes how caregivers can evaluate SCUs. Other sections in the booklet discuss the typical SCU environment, daily resident care, the possible cost to place a person with dementia in an SCU, and certain cost options.

MCI: Aging to AD

Mild Cognitive Impairment: Aging to Alzheimer's Disease. 2003

Petersen, R.C., ed.

Available from Oxford University Press, Inc., 198 Madison Avenue, New York, NY 10016. Phone: 1-800-451-7556. Website: www.oup-usa.org. PRICE: $55

Editor Ronald Petersen, Ph.D., M.D., Director of the Alzheimer's Disease Center at the Mayo Clinic, is well-

known to experts in the AD research field. His work in identifying mild cognitive impairment (MCI) continues to be of enormous importance in advancing AD research. This book presents an up-to-date review of MCI and its relationship to AD. Dr. Petersen has enlisted the aid of several other research leaders, who contribute chapters that discuss:

- the heterogeneity and controversial aspects of MCI,
- clinical features and research criteria for MCI,
- neuropsychiatric symptoms in AD
- cognitive aging and normative neuropsychology,
- optimizing cognitive test norms for detection of preclinical AD,
- magnetic resonance imaging to characterize early AD,
- neuropathological changes in normal aging, MCI, and AD, and
- treatment of MCI and prospects for prevention of AD.

Validation Technique

Validation Breakthrough: Simple Techniques for Communicating With People With "Alzheimer's-Type Dementia." 2nd ed. 2003

Feil, N.

Available from the Health Professions Press, P.O. Box 10624, Baltimore, MD 21285-0624. Phone: 1-888-337-8808; Fax: 410-337-8539. Website: www.healthpropress.com. PRICE: $29.95

In the *Validation Breakthrough*, author Naomi Feil states that "all people are unique and must be treated as individuals," and "all people are valuable, no matter how disoriented they are." She lists the following as some of the principles on which validation theory and practice are based, and which she advocates should be the basis for communicating with "old-old" people (defined here as those over age 75) who have dementia:

- "Painful feelings that are expressed, acknowledged, and validated by a trusted listener will diminish."
- "Painful feelings that are ignored or suppressed will gain strength and can become 'toxic'."
- "When present reality becomes painful, some old-old survive by retreating and stimulating memories of the past."

Feil describes the normal process of aging and development, and the characteristics of what she terms the "Resolution Stage of life." She presents case histories of people in progressive stages of resolution (malorientation, time confusion, repetitive motion, and vegetation) and shows how using the validation technique helped both these individuals and their caregivers. Feil discusses the use of validation with people with early-onset AD, research on the effects of validation, and the differences between validation and other interventions. She explains how to set up and conduct validation groups and answers frequently asked questions.

Mental Fitness

Memory Fitness: A Guide for Successful Aging. 2004

Einstein, G.O.; McDaniel, M.A.

Available from the Yale University Press, P.O. Box 209040, New Haven, CT 06520-9040. Phone: 203-432-0163; Fax: 203-432-8485. Website: www.yalebooks.com. PRICE: $17 paperback, $35 hardback

NIA grantees Gilles Einstein, Ph.D., and Mark McDaniel, Ph.D., have added to the growing body of literature on mental fitness and mental exercising with this guide to the effects of aging on memory and how to maintain or improve memory as you age. They provide an overview of how memory works and how memory processes change with age, forgetting and memory distortions, working memory and avoiding distractions, and strategies to facilitate retrieval. Countering the common belief that "the more one repeats information, the better that information will be remembered… experiments that have directly tested this theory clearly indicate that continuous rote rehearsal is not a very effective way to remember and learn new information," the authors provide a series of strategies to improve memory and learn complex material. They include advice for remembering things that are tough to remember, and remembering to remember (prospective remembering). The authors further suggest lifestyle adjustments that improve mental powers and memory and discuss the effects of stress, depression, illness, and medications on memory. A chapter discusses AD, including possible causes, treatment, advice for caregivers, and resources for additional information and support.

Coping with Behaviors

Fact Sheet: Caregiver's Guide to Understanding Dementia Behaviors. 2004

Available from the Family Caregiver Alliance, National Center on Caregiving, 180 Montgomery Street, Suite 1100, San Francisco, CA 94104. Phone: 1-800-445-8106 or 415-434-3388; Fax: 415-434-3508. Website: www.caregiver.org. PRICE: free online access, $1 for print copy

California-based Family Caregiver Alliance (FCA) has added to its long list of helpful publications with this new fact sheet offering practical strategies for dealing with people with dementia. It provides tips for improving communication, for instance:

- "Set a positive mood for interaction."
- "Get the person's attention."
- "State your message clearly."
- "Ask simple, answerable questions."
- "Break down activities into a series of steps."

General guidelines for coping with difficult behaviors are followed by suggestions for specific problems such as wandering, incontinence, agitation, repetitive speech or actions, paranoia, sleeplessness and sundowning, eating, bathing, dressing, and hallucinations.

For a complete listing of upcoming conferences, please visit: www.alzheimers.org/calendar

April 9-16, 2005

American Academy of Neurology Annual Meeting, Miami Beach, FL

Contact:
American Academy of Neurology
1080 Montreal Avenue
Saint Paul, MN 55116
Telephone: 1-800-879-1960 or 651-695-2717
Fax: 651-695-2791
Website: http://am.aan.com

May 11-13, 2005

Living with Dementia - Positive Solutions: Alzheimer's Australia National Conference, Sydney, Australia

Contact:
Conference Secretariat
c/o Event Planners Australia
P.O. Box 1280
Milton, Queensland 4064
Australia
Fax: +61 (0) 7 3858 5510
Website:
www.alzheimersconference2005.com

May 19-20, 2005

Alzheimer's Disease: Update on Research, Treatment, and Care, San Diego, CA

Contact:
Alzheimer's Disease Research Center
UC San Diego
Telephone: 858-622-5850
E-mail: jcollier@ucsd.edu
Website: http://cme.ucsd.edu/events.cfm?cat_id=1

June 9-12, 2005

American Association of Neuropathologists Annual Meeting, Arlington, VA

Contact:
Office of Secretary-Treasurer
Dr. George Perry
Institute of Pathology
Case Western Reserve University
2095 Adelbert Road
Cleveland, OH 44106
Telephone: 216-368-2488
Fax: 216-368-8964
E-mail: aanp@cwru.edu
Website: http://www.aanp-jnen.com

June 18-21, 2005

International Conference on Prevention of Dementia, Washington, DC

Contact:
Alzheimer's Association
225 N. Michigan Avenue
Suite 1700
Chicago, IL 60601
Telephone: 1-800-272-3900
E-mail: prevention@alz.org
Website: www.alz.org

June 20-22, 2005

Dementia: Molecules to Management, Brisbane, Queensland, Australia

Contact:
Australian Society for Geriatric Medicine
c/o Organisers Australia
P.O. Box 1237
Milton, Queensland 4064
Australia
Telephone: +61 (0)7 3371 0333
E-mail: asgm@orgaus.com.au
Website: www.asgm.org.au

July 26-29, 2005

13th Annual Dementia Care Conference, Chicago, IL

Contact:
Alzheimer's Association
225 N. Michigan Avenue
Suite 1700
Chicago, IL 60601
Telephone: 1-800-272-3900
Website: www.alz.org

September 25-28, 2005

American Neurological Association Annual Meeting, San Diego, CA

Contact:
American Neurological Association
5841 Cedar Lake Road
Suite 204
Minneapolis, MN 55416
Telephone: 952-545-6284
Fax: 952-545-6073
E-mail: ana@llmsi.com
Website: www.aneuroa.org

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