

FOCUS ON RESEARCH

ADRC researchers confirm Alzheimer's disease begins years prior to diagnosis, as early as 50 years old

By Dana Martin and Elizabeth Sharpe

Although we commonly think of Alzheimer's disease (AD) as a disease of old age, studies have shown that AD is actually a progressive illness which begins years prior to diagnosis. Identifying people at increased risk of developing Alzheimer's disease, when they have not yet developed symptoms of the disease, is important. Not only is it important for the benefit of those individuals at high risk, but also for researchers to better develop and test new preventative therapeutics, says ADRC Associate Director Dr. Elaine Peskind. But identifying these individuals is a difficult task, considering how little is still known about how and when Alzheimer's disease begins.

Peskind and her collaborators are working to uncover pieces of this mystery. In July 2008, Peskind will present results from a recent cross-sectional study of 308 mentally healthy volunteers between 21 and 100 years of age at the International Conference on Alzheimer's Disease in Chicago, results that were not only surprising, says Peskind,

but downright scary.

Peskind was lead author of a landmark study of 184 healthy volunteers published in the July 2006 issue of the Archives of Neurology. The results of the study suggested that amyloid plaques characteristic of Alzheimer's disease may start forming between 50 and 60 years of age, much earlier than previously assumed.

By the age of 85, nearly half the population has dementia, and at least 70 percent of those cases are Alzheimer's disease. The



Elaine Peskind, M.D.

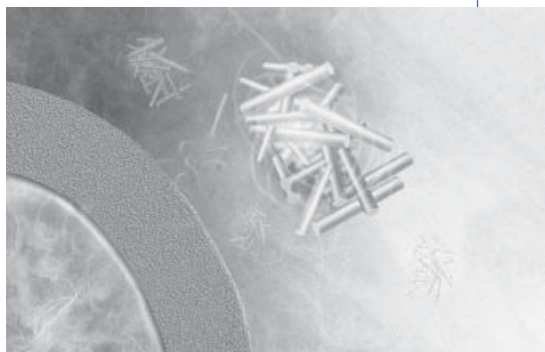
Associate Director of the University of Washington Alzheimer's Disease Research Center located at the VA Puget Sound Health Care System in Seattle.

disease is clearly age-related, says Peskind. Every five years after the age of 65, the disease doubles in prevalence. But what's scary, says Peskind, is that the slowly evolving process leading to the disease is beginning much, much earlier. Between the ages of 50 and 60 something happens, she says, explaining the "something" is like flipping a switch, a period when the action starts and a transformation takes place. Peskind and researchers from six medical centers are trying to uncover that "something" in the disease process.

In the previously published study, they looked at what happens across the adult life span to one of the most studied markers for Alzheimer's disease, amyloid beta 42 (A β ⁴²), and how this protein is affected by age and the presence of one form of apolipoprotein E (APOE*4), a genetic risk factor for Alzheimer's disease. Amyloid beta 42 is the toxic form of amyloid that makes up brain

Continued on page 2 →

plaques in Alzheimer's disease. In the just-finished, larger study using 308 volunteers, Peskind and researchers from four of the original six sites confirmed that APOE*4 had a



Beta amyloid plaque

Strands of beta amyloid stick together into clumps in the brain, then join with other molecules and non-nerve cells to form insoluble plaques.

(Illustration courtesy of the National Institute on Aging.)

very strong effect on the levels of cerebrospinal fluid amyloid beta 42 ($A\beta^{42}$) in both men and women. Cerebrospinal fluid is the clear fluid that the brain literally “floats” in. The fluid is inside and outside the brain and runs down around the spinal cord, too. Previous studies have shown that cerebrospinal fluid $A\beta^{42}$ levels decrease in patients with Alzheimer's disease and $A\beta^{42}$ levels in the brain increase. These studies used mouse models of Alzheimer's disease and positron emission tomography (PET) imaging of living humans with and without Alzheimer's disease using the Pittsburgh compound. PET

imaging using the Pittsburgh compound, which is only used for research, produces a color-enhanced image of the brain which highlights areas in the brain where the Pittsburgh compound attaches to amyloid plaques. Cerebrospinal fluid $A\beta^{42}$ levels likely go down because $A\beta^{42}$ is being deposited into plaques in the brain. Plaques work like a trap for the $A\beta^{42}$; they pull the $A\beta^{42}$ out of the spinal fluid.

How did a person's age, gender, and the presence of apolipoprotein E (APOE*4) influence the levels of cerebrospinal fluid $A\beta^{42}$? University researchers in

Washington, California, Oregon, Pennsylvania, and Indiana analyzed results of cerebrospinal fluid samples from men younger than 60 years old in the study. They found the levels of cerebrospinal fluid $A\beta^{42}$ decreased slightly, but not significantly, regardless of APOE*4. Men in the study who were older than 60 years of age and who had the APOE*4 also had significantly lower levels of cerebrospinal fluid $A\beta^{42}$.

Women in the study had a different pattern than men. Prior to age 50, cerebrospinal fluid $A\beta^{42}$ levels were constant in all the women. There was no change. After the age of

50, however, cerebrospinal fluid $A\beta^{42}$ levels decreased significantly for the women in the study who had APOE*4 when compared to the women in the study who did not have APOE*4.

Peskind cautions against assuming that having APOE*4 means a person will definitely develop Alzheimer's disease. People without APOE*4 have also been diagnosed with the disease. Half of Alzheimer's patients do not have an APOE*4 gene at all. Results of this study support previous epidemiological findings that APOE*4 causes earlier onset of Alzheimer's disease. Individuals with APOE*4 will develop the disease about ten or fifteen years earlier than those without the APOE*4. So, if the same individual without APOE*4 would be diagnosed with Alzheimer's disease by the age of 85, then the individual with APOE*4 would likely be diagnosed by the age of 70 or 75.

The results of the study also show $A\beta^{42}$ deposits in the brain may be already starting between the ages of 50 and 60, a period in which most individuals are cognitively normal. So, researching preventive therapies at the age of 65 or older is too late. To determine therapeutic benefits, Peskind says, we've got to be

Continued on page 3 →

investigating long-term effects of preventive therapies on people as young as 45.

Peskind adds that more research is needed and a follow-up study will be done, including an enhanced study on healthy individuals between the ages of

45 and 60. She says volunteers are needed here in Seattle to take part in the enhanced study. ❖

For more information on the study and to participate, call the ADRC Research Line at 1-800-317-5382.

Sources:

Results of the latest study will be presented at the International Conference on Alzheimer's Disease in July 2008 (abstract title: "Age and APOE Related CSF AD Biomarker Changes in Normal Controls"). Researchers include Ge Li, Douglas R. Galasko, Joseph F. Quinn, Jeffrey A. Kaye, Christopher M. Clark, Martin R. Farlow, Charles DeCarli, Murray A. Raskind, Eric C. Petrie, James Leverenz, Jane Shofer, Gerard D. Schellenberg, Barbara Cottrell, and Elaine R. Peskind.

Results of the original study were published in volume 63 of the Archives of Neurology: "Age and Apolipoprotein E*4 Allele Effects on Cerebrospinal Fluid Beta-Amyloid 42 in Adults With Normal Cognition." Researchers on the study included: Elaine R. Peskind, Ge Li, Jane Shofer, Joseph F. Quinn, Jeffrey A. Kaye, Chris M. Clark, Martin R. Farlow, Charles DeCarli, Murray A. Raskind, Gerard D. Schellenberg, Virginia M.Y. Lee, and Douglas R. Galasko.

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The University of Washington ADRC Support Fund is used to help support

new junior faculty investigators with strong credentials in the field of Alzheimer's disease research. This fund also helps enhance the research infrastructure of the ADRC by providing funding for the purchase of scientific equipment, supplies, training and numerous other opportunities that would otherwise not be available, as federal dollars are not able to fully support the growing research in Alzheimer's disease.

For more information regarding the Alzheimer's Disease Research Center Program Support Fund, please contact Victoria Hoyt, ADRC Program Coordinator, at 206-764-2749, or toll-free at 1-800-329-8387, ext. 6-2749 or by e-mail at Victoria.Hoyt@va.gov

Checks should be made out to ADRC and addressed to: VAPSHCS (S-116-MIRECC) Attn: Viki Hoyt, 1660 S. Columbian Way, Seattle, WA 98108

EVENT

**Caregiving Training Conference
Monday, June 2, 2008 - Tukwila Community Center**

Learn practical caregiving skills and strategies. This full-day training conference on Monday, June 2 allows you to choose from many helpful workshops based on your needs as a caregiver. Held at the Tukwila Community Center in Tukwila, Washington. Pre-registration is required and space is limited.

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Meet Rebecca Logsdon

A rainy Tuesday morning has just turned sunny, when Dimensions sits down with Dr. Rebecca Logsdon, co-director of the Alzheimer's Disease Research Center's Education Core and research professor in the UW School of Nursing.

Dr. Logsdon wears an infectious smile. She's been up early this morning and already walked Jake, her 13-year old mixed border collie-lab who would be 65 in human years. "He still thinks he's a puppy," adds Logsdon, a subtle indication that Logsdon believes practicing healthy habits improves one's state of mind and quality of life, and that the adage applies to everyone, Jake included.

In the 25 years Logsdon has worked as a clinical psychologist, primarily with older adults, she says a lot has changed. She first came to the UW in 1986 as a postdoctoral fellow and worked with Drs. Linda Teri and Burton Reifler in the Geriatric and Family Services Clinic and the Alzheimer's Disease Research Center. At the time, a diagnosis of Alzheimer's disease was often viewed as a "death sentence," with little that could be done to improve the life of the diagnosed person. Today, much has changed. Alzheimer's disease is increasingly viewed as a chronic

illness a person lives with. Medications and psychosocial treatments have been developed to improve cognitive, behavioral, and emotional functioning in individuals who have been diagnosed with the disease. Recently lifestyle changes and healthy habits like physical exercise, good nutrition, maintaining social involvement, and staying engaged in cognitively stimulating activities have emerged as important to delaying the onset of dementia as well as improving quality of life throughout the course of the disease.

Logsdon's clinical and research focus is on maintaining a good quality of life for individuals with dementia and their caregivers. With her colleagues, Dr. Linda Teri and Dr. Susan McCurry, she has conducted research on psychosocial treatments for depression, anxiety, agitation, sleep disturbances, and inactivity for individuals at all stages of dementia. Some of her most rewarding work, Logsdon says, is the work she does with community partners like the Alzheimer's Association of Western & Central Washington, local senior centers, the Department of Social and Health Services, and adult day centers. These collaborations with community partners help ensure the research gets translated into practical applications, explains Logsdon.

When Logsdon first graduated with a master's degree in vocational rehabilitation counseling, she

worked for five years in Oklahoma City with young people who were mentally ill. After she went back to school for her doctoral training, she started working with older adults with cognitive impairments. She was impressed by the growing need for psychologists to work with these individuals and their families and by the difference that counseling, education, and support could make for them. When she had the opportunity to come to the UW for postdoctoral training with the ADRC, she jumped on the chance, and has been here ever since.

As a clinical psychologist, Logsdon can cite research to support the importance of balancing work and family responsibilities with mental and physical needs. Satisfying the latter needs gives a person the resilience and mental reserves for daily responsibilities. Logsdon points out she's the same as everyone else; she finds it hard to schedule personal time between her other commitments.

But she knows the importance of balance, because she makes the time in her busy life to swim five days a week on a master's swim team. She even competes in swim meets a few times a year, and in the summer, she can be found trying out her strokes on Lake Washington. When she's not swimming, she may be out hiking, renewing mental reserves in the yoga she practices, or rejuvenating creative energies in the knitting projects she's started.

Undoubtedly, Dr. Rebecca Logsdon is someone who practices what she preaches. ❖

SEEKING VOLUNTEERS

Alzheimer's Disease Research Center
University of Washington
Veterans Affairs Puget Sound Health Care System

This spring the Alzheimer's Disease Research Center (ADRC) will be enrolling research participants in several new investigational treatment studies. Finding treatments that actually change the disease process in the body is the focus of this new research.

Currently the only available prescriptions for the treatment of Alzheimer's disease are medications that are mostly aimed at helping with the symptoms of Alzheimer's disease such as memory loss and trouble thinking.

Investigational drugs are now being studied to see if they will slow down or stop the changes that occur in the brains of people with this disease. The ADRC is currently screening potential participants for these studies which will begin enrollment during the next six months. Research participation will

not cost you anything, and is open to all members of the public. Some research participants will receive a placebo (a treatment without active medication) for at least some portion of the research.

To participate, individuals must:

- Be age 50 or older
- Have a diagnosis of mild to moderate Alzheimer's disease
- Be living at home (one study will allow residents of assisted living centers to participate)
- Have a companion who can accompany the participant to all research visits

All research visits are at the Seattle Veterans Affairs Medical Center on Beacon Hill. For more information, please call the UW Alzheimer's Disease Research Center at: 206-764-2069 or 1-800-317-5382.

Seeking Families with a History of Alzheimer's Disease

The Genetics Program at the University of Washington Alzheimer's Disease Research Center is collaborating with other Alzheimer's Disease Research Centers on a new initiative sponsored by the National Institute on Aging to better understand genetic factors in late onset familial Alzheimer's Disease. Families are being sought with two or more living affected individuals with onset of dementia at age 60 or later. Participation would involve a phone interview, review of medical records, and a blood sample. For further information, please contact Malia Rumbaugh at 206-277-6645 or toll free 800-821-7967, or email maliarum@u.washington.edu.

Concerned About Yours, or a Loved One's Memory?

The UW Memory Health Research Center offers free memory screenings and physical exams for men 60 years and older. You may also qualify for a six month hormone treatment study. Please contact Christina: 206-277-1155 www.uwmemoryhealth.org

University of Washington and the Veteran's Administration Healthcare System - Memory Wellness Program

To learn more about any of these studies, please call Seattle: 206-764-2809, or Tacoma: 253-583-2011.

STUDY SUBJECT	DESCRIPTION	CANDIDATE CRITERIA	TIME / PROCEDURE
MEAL: Macronutrient effects on Alzheimer's disease	Examines the effects of high saturated fat diet vs. low saturated fat diet on memory.	Healthy individuals age 55 years and older with and without memory problems.	5 weeks during which the participant will make 8 visits to the clinic.
NOREPI: Insulin, Norepinephrine and working memory	Explores the effects of insulin and norepinephrine (hormones associated with glucose metabolism) on working memory.	Healthy individuals age 55 years and older with or without memory problems.	7 clinic visits, each lasting approximately 3 hours spaced 2-6 weeks apart.
RECALL: Rosiglitazone Effects on Cognitive Abilities in Later Life	Effectiveness of rosiglitazone (an oral diabetic medication) in improving memory in older adults with mild memory impairment.	Healthy individuals age 55 years and older with mild cognitive impairment (MCI).	20 months, during which the participant will be asked to make 12 visits to the clinic.
REFLECT: Effect of Rosiglitazone as additional therapy to acetyl-cholinesterase inhibitors on cognition	Examines the effectiveness of rosiglitazone (Avandia) as additional therapy to acetyl-cholinesterase inhibitors (Aricept, Razadyne, Exelon) on subjects with Alzheimer's disease.	Healthy individuals age 55 years and older with mild to moderate Alzheimer's disease.	54 weeks during which the participant will make 10 clinic visits.
SMELL: Spray Nasal Insulin to Fight Forgetfulness	Looks at the beneficial effects of a nasal spray on memory for older adults with memory loss.	Healthy individuals age 55 years and older with mild cognitive impairment (MCI) or early Alzheimer's.	4 months during which the participant will be asked to make 8 visits to the clinic.
TRIM: Triglycerides and Insulin in Memory	Explores the influence of increased dietary fat on glucose and insulin metabolism, memory and biological markers associated with Alzheimer's.	Healthy individuals age 55 years and older with and without memory problems.	6 visits to the clinic in which each visit is between 2 to 6 weeks apart.

Legal and Financial Planning

What you need to know when someone you love has Alzheimer's disease.



We often wait too long to take care of the legal and financial issues once an older relative has been diagnosed with Alzheimer's disease (AD). However, many of these decisions should be made before one's judgment or decision-making skills become impaired. Sometimes the patient or the caregiver is not emotionally ready to confront legal or financial issues but it is important to do so.

Most people have specific wishes and desires concerning their healthcare, end-of-life decisions and even how they want their belongings distributed. To ensure that one's wishes are carried out, communication is essential because cognitive impairment affects one's ability to think clearly, and legal documents must be prepared and executed when the individual still has legal capacity. The earlier one makes these decisions, the better. Ideally, one will have experts who can advise them. Attorneys, geriatric care managers or social workers, financial or estate planners and of course, a trusted loved one can all be helpful. It is a good idea to work with an attorney when preparing documents such as wills, giving power of attorney, or to establish or manage a trust.

What is a will? It is the most familiar financial planning document. It dictates how a person's assets and estate will be distributed among the beneficiaries or heirs. An individual must have "testamentary capacity" (the legal ability to make a will) in order to make a valid will. Obviously, it is best if one has a valid will long before a diagnosis of AD is made, but if not, a newly diagnosed AD patient must move quickly to make or update a will and secure his/her estate before decision-making skills become too impaired.

Other areas that an attorney may also discuss are estate planning, end-of-life issues such as preparing a Living Will, having a "Do Not Resuscitate" order in one's medical records, executing Durable Power of Attorney for healthcare and finances. Depending on the size of one's estate, Living Trusts can be established and funerals can be planned (the cost of pre-paying one's funeral will not be calculated in the spend down needed to qualify for Medicaid, for example). Remember that even if one has executed all of these documents, they should be revisited from time to time in case adjustments are needed because situations change over time. Copies of important documents

should be kept in a safe but accessible place.

Geriatric care managers can help deal with sensitive or difficult medical or social issues. They can evaluate one's needs, provide a care plan, evaluate in-home care options, long-term care options, make referrals and coordinate medical services. Geriatric care managers are especially helpful if the patient does not live near family members who can help.

While legal help can be expensive, there are many services available to low income families in most states. Check with the local Area Agency on Aging, the state Legal Aid Bureau, the state Bar Association, and other local nonprofit agencies or social services agencies that provide an umbrella of services or referrals to agencies that offer low or no-cost services. Templates for wills, living wills, and power of attorney can often be downloaded from state government websites.

Facing AD is hard enough without all the planning that must also be done. Confronting tough questions about one's future healthcare, care options, end-of-life wishes and legal affairs early on can help increase both the

patient's and family's sense of empowerment and control. The information below contains some helpful information and resources for legal and financial concerns. ❖

This information was adapted from the ADEAR newsletter, Connections, Vol. 15, Number 1-2.

Legal and Financial Planning Documents

Durable Power of Attorney for Health Care

Gives a designated person the authority to make healthcare decisions on behalf of the patient, when patients can not speak for themselves.

Living Will

Describes and instructs healthcare staff how the patient wants end-of-life healthcare managed.

Do Not Resuscitate Form

Instructs healthcare staff not to perform specified life-saving or other heroic measures at end of life.

Will

Indicates how a person's assets and estate will be distributed among beneficiaries after his/her death.

Durable Power of Attorney for Finances

Gives a designated person the authority to make legal/financial decisions on behalf of the patient when the patient is incapacitated.

Living Trust

Describes how a person wants to allocate funds and settlements.

Q&A

Anger... and what to do with it.



The following essay reflects on the important question of handling one's anger as a caregiver while watching a loved one's descent into Alzheimer's disease.

By Malia Rumbaugh, MS, CGC

I just got off the phone with Grace¹, whose husband's family is enrolled in our research study. She and others in the family spent most of the night at the bedside of her brother-in-law during his last hours. A sister in this family also died of Alzheimer's just a few weeks ago and Grace's husband is in the moderate stages of the disease. So why was she calling me? While regular updates are very helpful, it is amazing that amidst the devastation of this disease, people reach out to participate in research.

But why? In our genetic studies, we can't promise any direct benefit to our participants. Why add to the tremendous burden of this disease? Of course, the reasons are as individual as our participants. For some, the drive to help others is as natural as breathing. For others it is the fear that catches in the throat; that this might happen to their children or their grandchildren. There is also the desire for a redemption of sorts, to see something good come out of something bad.

Lately though, I've been thinking about anger. Anger gets a bad rap

and can certainly be destructive. Most of us were raised to be polite, well mannered and considerate people. Some of us even are that way most of the time. Yet how can we not be angry at this disease? As we watch it erode thoughts, memories, personality and so much of what we hold dear in each other, I think anger is a reasonable response. The key is what we do with it.

Mahatma Gandhi is probably not the first person to come to mind when you think of anger, but he knew it well. As he said:

"I have learned through bitter experience the one supreme lesson to conserve my anger, and as heat conserved is transmuted into energy, even so our anger controlled can be transmuted into a power which can move the world."²
- Gandhi

I think this is what I see sometimes in our research participants and their families. It's that glint in their eyes, that steely note in their voice. It hints at a determination to beat this disease even if they themselves may not know the victory. And whatever your reasons for participating, it is because of people like you that we will find a cure. ❖

1. Not her real name.
2. Gandhi the Man, by Eknath Easwaran, Nilgiri Press.

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23RD ANNUAL ALZHEIMER'S DISEASE PUBLIC FORUM

Wednesday, June 18, 2008 - 6:30 to 8:30 p.m.
University of Washington Kane Hall Auditorium 220

Presentations by UW ADRC Research Faculty:

*Medication Treatment of
Disruptive Agitation in
Alzheimer's Disease and
Related Disorders*

Murray A. Raskind, MD

Professor and Vice-Chairman,
Dept. of Psychiatry and Behavioral
Sciences, UW School
of Medicine; Director,
UW Alzheimer's Disease
Research Center; and
Director, Mental Health
Service, VA Puget
Sound Health Care
System



*Enhancing Care for People
with Dementia: Advances
in Non-pharmacological
Treatments*

Linda Teri, PhD

Professor and Interim Vice-Chair
Dept. of Psychosocial and
Community Health;
Director, Northwest
Research Group on Aging,
University of Washington
School of Nursing; and
Founding Director of the
UW deTornyay Center for
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- ★ Complimentary parking available in the Central Plaza Garage located at 15th Ave. NE and NE 41st St. with direct elevator access to Kane Hall. Mention that you are attending the Alzheimer's Public Forum at the gate.
- ★ For additional information visit the ADRC website: www.uwadrc.org or call 206-221-6563.

Sponsored by the University of Washington Alzheimer's Disease Research Center (ADRC), Friends of Alzheimer's Research, The Western Washington Chapter of the Alzheimer's Association, The Alzheimer Society of Washington, and the UW School of Nursing de Tornyay Center for Healthy Aging. The University of Washington is committed to providing access, equal opportunity and reasonable accommodation in its services, programs, activities, education and employment for individuals with disabilities. To request disability accommodation contact the Disability Services Office at least ten days in advance at: 206.543.6450/V, 206.543.6452/TTY, 206.685.7264 (FAX), or e-mail at dso@u.washington.edu