



PATHWAYS

Moving Toward a Cure

Fall 2008



Steven T. DeKosky, MD

Director Accepts New Position, Bids Farewell to Pittsburgh ADRC

I have been affiliated with the Alzheimer Disease Research Center (ADRC) since I came to the University of Pittsburgh in 1990, and I've been director of the center since 1994. Over the years, our accuracy of diagnosis has exceeded 95 percent, and Pitt investigators

have made major contributions to the field of dementia research, such as the following:

- the discovery of Pittsburgh Compound B (PIB) by Bill Klunk and Chet Mathis
- a better understanding of the pathological progression of Alzheimer's disease (AD) through the use of positron-emission tomography (PET) and magnetic resonance imaging (MRI)
- progress in the genetics of AD; neuropsychiatry; and behavioral changes in the disease, including depression and psychotic symptoms
- understanding neuropathology and the fundamental mechanisms of the changes in the brain

Pitt investigators also have studied the earliest signs of Alzheimer's disease, termed mild cognitive impairment (MCI), as well as the pressures and stresses on the caregivers of people with AD and the care partners of people with MCI. All in all, Pitt's ADRC has been an international leader in research and care in dementia, and we are proud of the center's faculty and staff accomplishments.

In August 2008, I accepted a position as vice president and dean of the School of Medicine at the University of Virginia. While my new position brings wonderful opportunities in a number of

areas of medical education and research, it has been very difficult to leave a program in which I've been so invested and to leave so many friends and colleagues.



Oscar Lopez, MD
ADRC Director



William Klunk, MD, PhD
ADRC Codirector

Oscar Lopez and Bill Klunk will assume the leadership of Pitt's ADRC. You will read more about the new codirectors in the next issue of *Pathways*.

I urge you to continue your support of the ADRC, and I thank all of our patients and families for their faith in our care and research programs and our faculty, staff, and students for their wonderful collegiality and collaboration.

We will be establishing a memory disorders clinic at the University of Virginia that will be a satellite of the Pitt ADRC in order to expand our research and aid in the center's continuing excellence and leadership.

I look forward to continuing our search for better treatments and a cure for AD and the other dementias we diagnose and treat. And I will always treasure my relationship with Pittsburgh and all of you.

With my best regards,

Steven T. DeKosky
Steve DeKosky

Planning Ahead: Basic Legal Matters

By Patricia L. Henderson, MS, LPC, CRC

Addressing basic legal matters is something that many people are concerned about—especially those who may be experiencing early signs of cognitive impairment.

As cognitive impairment progresses, there may be a time when the person who is affected is unable to make financial or medical decisions on his or her own. Consulting with a professional, such as an elder law attorney, can help you to prepare for this time.

There are several key documents to consider having in place.

A will is a legal document that tells others how you would like your property to be distributed upon your death.

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A **living will** is a written set of instructions expressing your wishes regarding medical care in the event that you cannot speak for yourself. This document is designed specifically for making end-of-life decisions. It is sometimes called a care directive, meaning that it is the part of an advance directive that tells others how you would like to be cared for under certain circumstances. It provides an opportunity to express your preferences regarding the use of devices such as ventilators and feeding tubes.

A **power of attorney (POA)** gives decision-making authority to an individual who you trust to speak on your behalf when you are unable to do so. There are limited POAs. For example, if you leave the country for a vacation or for an extended period of time, you may need a decision maker to assist you with managing your finances. Upon your return, the POA ends.

A **durable POA** is a special kind of POA in which decision-making authority takes effect (and remains in effect) because an individual with significant cognitive impairment or altered consciousness is unable to make, or convey to others, decisions. Durable POAs can address financial and/or health care decisions. Durable POA documents that address health care decisions are sometimes referred to as the proxy directive portion of an advance directive.

Some people will name one person as a durable POA for both their financial and health care decisions. These duties also can be divided. For example, if one adult child has a medical background and a second child is an accountant, an individual may want to split the decision-making duties based on the children's backgrounds.

It is important to prepare these documents while you are still as healthy as possible. An attorney cannot assist in preparing documents for people who do not understand that they are giving their decision-making authority to someone else.

The American Bar Association in your area can refer you to an elder law attorney who specializes in such issues. In Pittsburgh, there is a lawyer referral service available by calling 412-261-5555. Your Alzheimer Disease Research Center social worker also can offer referrals to elder law attorneys in your area. Note that while estate planning requires the involvement of an attorney, legal counsel is not necessarily required to prepare advance directives.

alzheimer's  association®



**The Alzheimer's Association
24-hour helpline**

provides reliable information and support to all who need it. Call the toll-free hotline anytime, day or night, at

1-800-272-3900.

Volunteers Needed for Research Studies

RAGE Inhibitor Study

Description

Many proteins surround the amyloid plaques in Alzheimer's disease (AD) patients. One of the proteins, receptor for advanced glycation endpoints, called RAGE for short, binds to amyloid and may promote inflammation and lead to nerve cell damage. Researchers found that by inhibiting the RAGE protein, plaque formation could be reduced in animal models.

Study Phase

Phase 2

Study Length

18 months

Study Requirements

- Age 50 or older
- Diagnosis of probable AD
- Caregiver or family member must be able to attend all clinic visits with patient
- Are currently taking AD medication (Aricept, Exelon, or Razadyne)
- Do not have type 1 or type 2 diabetes

Pittsburgh Compound B (PIB) Study

Description

This study will use PET imaging to determine how amyloid changes across stages of severity in Alzheimer's disease (AD) and whether amyloid is present in elderly individuals without memory problems.

Study Length

Varies

Study Requirements

- 30 years of age or older
- Healthy individuals or diagnosis of probable AD or
- Diagnosis of mild cognitive impairment

Compensation

Up to \$200 per year

Bapineuzumab Study

Description

Bapineuzumab is a humanized monoclonal antibody that binds to and clears beta-amyloid peptide and is designed to provide antibodies to beta-amyloid directly to the patient. Bapineuzumab is given as a series of injections. This approach is called passive immunization.

Study Phase

Phase 3

Study Length

18 months

Study Requirements

- Diagnosis of probable AD
- 50–88 years of age
- Caregiver or family member must be able to attend all clinic visits with patient

Glaucoma Study

Description

Glaucoma is an eye disease that leads to loss of vision. Previous studies have shown a risk of peripheral (side) and central vision problems in patients with Alzheimer's disease (AD). This study aims to investigate the structures inside the eye that are involved with peripheral and central vision problems in patients with AD to identify any possible links to glaucoma. Studying the disease and noting the prevalence of glaucoma in AD populations could shed some light on the mechanism and possible treatment modalities for glaucoma.

Study Length

One 60-minute visit (approximate)

Study Requirements

- 60 years of age or older
- Diagnosis of AD

If you are interested in the PIB Study, contact Claire McConaha at 412-692-2727 or mccconahacw@upmc.edu; for the Bapineuzumab, RAGE Inhibitor, and Glaucoma studies, contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.

In Memoriam



The University of Pittsburgh Alzheimer Disease Research Center thanks the following individuals and companies for their generous donations received February 1, 2008–June 30, 2008.

In Memory of Janey Barton

David and Douglas Dick
Mr. and Mrs. James Ferry
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In Memory of Florence Birsch

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In Memory of Marie Kovacic

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Stephen and Roberta Friedland
Dale and Lynn Lazar

*Your contributions are greatly appreciated
and help to support research and education
in the area of Alzheimer's disease. You can
remember or honor a loved one by using
the envelope enclosed in this newsletter to
send in your donation.*

ADRC Mission

The overall objective of the ADRC is to study the pathophysiology (changes in the brain) of Alzheimer's disease (AD) with the aim of improving the reliability of diagnosis of AD and developing effective treatment strategies. The ADRC is funded by the National Institute on Aging and, as part of its research program, provides a comprehensive outpatient evaluation, including medical, neurological, psychiatric, social, and cognitive assessments. A major focus of the ADRC is a commitment by individuals to participate in additional ADRC research studies. Individuals enrolled at the ADRC are encouraged to participate in additional studies in order to be followed by the center.

If you no longer wish
to receive future
issues of *Pathways*,
please contact
MaryAnn Oakley at
412-692-2721 or
oakleym@upmc.edu.

Congratulations

to Elise Weamer for earning her
Master of Public Health degree at
the University of Pittsburgh
Graduate School of Public Health
in April 2008. Way to go!



Topics at Noon Series

Noon-1 p.m.
ADRC Conference Room—S439
4 South UPMC Montefiore
200 Lothrop Street
Pittsburgh, PA 15213

Thursday, November 6, 2008

“Medication IQ: Maximizing
Medication Adherence Among
the Elderly”

Anthony Zuccolotto, BS,
president and CEO
Amy Eschman, MS
Gretchen Archer, MBA
Psychology Software Tools, Inc.

Thursday, December 11, 2008

“Measuring Reliable Change over Time
in Cognitive Test Scores”

Beth Snitz, PhD, research associate
Department of Neurology
University of Pittsburgh School of
Medicine

*Light refreshments will be served.
Registration is not required. For more
information, call 412-692-2700. CME
and CMU credits are available.*

Volunteer Studies for Caregivers

Making Sense of MCI: Patient and Family Perspectives Study

Description

The purpose of this study is to learn how those diagnosed with mild cognitive impairment (MCI) and their family members make sense of—or come to terms with—their symptoms and diagnosis.

Study Length

A one-time interview lasting approximately 45 minutes

Study Requirements

Diagnosis of MCI and a family member willing to answer questions about the person with MCI

CEAD Project: Characterizing the Experience of Alzheimer's Disease Study

Description

The purpose of this research study is to learn more about suffering in patients with Alzheimer's disease and related dementias (ADRD) and the impact of patient suffering on family caregivers. The study uses one-on-one interviews with people who have ADRD and their family members.

Study Length

Initial interviews and follow-up interviews one year later

Study Requirements

Spouse, partner, or family member of an individual diagnosed with ADRD

Self-Management and Resource Training (SMART) Study

Description

This study is designed to determine if a self-management (educational) program strengthens the personal resources (physical and/or mental) of men and women living with a family member who has mild cognitive impairment (MCI) or dementia.

Study Length

Three months

Study Requirements

Spouse or living partner of an individual diagnosed with MCI, Alzheimer's disease, or a related dementia

For more information about the caregiver studies, contact MaryAnn Oakley at 412-692-2721 or oakleym@upmc.edu.

Staff Spotlight

Administrative Coordinator

Kathie Savage

Ask Kathie Savage to name her duties for the Alzheimer Disease Research Center (ADRC) and the answer will depend on what day it is. Some days she helps to prepare documentation for clinical trials. Other days she might help to coordinate research studies and payment for participants. She is involved in funding efforts, too, helping to prepare annual progress reports and grant applications.

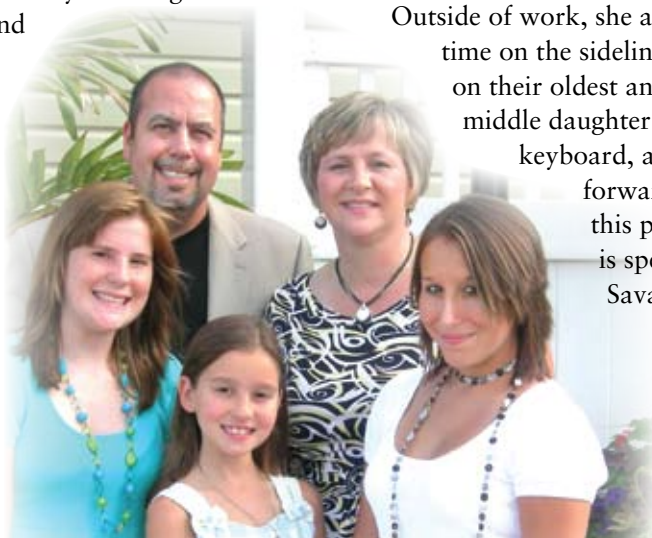
In fact, Savage's job as administrative coordinator puts her in contact with all the physicians and clinical staff at the ADRC, as well as with the center's administrator, Leslie Dunn.

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"I enjoy all the people I work with," she says, "and I enjoy being involved with a program that is so vital in helping families and patients with dementia."

Savage first came to the University of Pittsburgh in 1984 as a temporary employee in the Department of Epidemiology. She later worked with critical care physicians and cardiologists before joining the ADRC 15 years ago. Savage earned her associate's degree from Duff's Business Institute and has completed coursework toward her bachelor's degree at Pitt and the Community College of Allegheny County.

Outside of work, she and her husband spend a lot of time on the sidelines of the soccer field, cheering on their oldest and youngest daughters. Their middle daughter prefers acoustic guitar and a keyboard, and everyone in the house looks forward to family movie night. "At this point in my life, my main hobby is spending time with my kids," Savage says.



Pictured clockwise are Mike and Kathie Savage with their three daughters.

Pitt Researchers Present Work at ICAD 2008

University of Pittsburgh Alzheimer Disease Research Center (ADRC) researchers were well represented at the Alzheimer's Association International Conference on Alzheimer's Disease 2008 (ICAD 2008), which took place in Chicago, Ill., at McCormick Place, Lake Side Center, July 26–31.

One of the strengths of Pitt's ADRC has been its groundbreaking research on imaging brain amyloid deposits. Chet Mathis, PhD, coinventor of the amyloid PET tracer Pittsburgh Compound B (PIB), presented a summary of research from the more than 40 centers around the world that use PIB. He also discussed work using newer versions of PIB that will help to bring this technology into common clinical use.

William Klunk, MD, PhD, the other coinventor, discussed studies designed to find the earliest evidence of amyloid accumulation that often can be found years before any symptoms of memory impairment.

Other work from Pitt's ADRC included presentations on changes in brain size in people with amyloid deposits (Julie Price),

the specific types of amyloid labeled by PIB (Milos Ikonovic), correlations between amyloid and brain metabolism (Ann Cohen), and amyloid in dementias other than Alzheimer's (David Wolk).

Steven DeKosky, MD, who recently stepped down as director of the University's ADRC to become vice president and dean of the medical school at the University of Virginia, received the Zaven Khachaturian Award, which is given to an individual whose "compelling vision, selfless dedication and most extraordinary achievement have significantly advanced the field of Alzheimer science."

ICAD 2008 was the largest gathering of international leaders in Alzheimer's disease research and care ever convened. More than 5,000 researchers from 60 countries shared groundbreaking information and resources on the cause, diagnosis, treatment, and prevention of Alzheimer's and related disorders.

As a part of the association's research program, ICAD serves as a catalyst for generating new knowledge about dementia and fostering a

vital, collegial research community. Conference highlights, obtained from the Alzheimer's Association Web site, 2008, included the following:

- Results from clinical trials of three potential Alzheimer's therapies raise hope for new and better treatments of the disease.
- Lifestyle factors contribute to lowering and raising the risk of Alzheimer's disease.
- Markers in blood and spinal fluid and a new imaging agent show promise for early detection of Alzheimer's disease.
- Four Alzheimer's clinical trials address a variety of treatment targets: amyloid, tau, and synapse formation.
- Eighteen-month Phase 3 trial results for tarenflurbil (Flurizan): Myriad Genetics, Inc. announced that its Phase 3 trial of tarenflurbil (Flurizan) had failed to achieve statistical significance on either of its two primary end points and that the company was abandoning development of the compound for Alzheimer's disease.

More information regarding ICAD presentations can be found by visiting the ICAD Web site at www.alz.org/icad.

ADRC Investigator Presentations at ICAD 2008

"Amyloid Imaging: Developments, Challenges, Future Directions"

C.A. Mathis

"Gray Matter Changes in Cognitively Normal Control Subjects with PIB Retention"

J.C. Price, J.A. James, H.J. Aizenstein, D.A. Wolk, O.L. Lopez, K.L. Dunfee, R.D. Nebes, J.A. Saxton, B.E. Snitz, E.M. Halligan, A.D. Cohen, C.A. Mathis, W.E. Klunk, S.T. DeKosky

"Cerebellar Amyloid in a Case of Early Onset Dementia with a Presenilin-1 Mutation: Correlation to Clinical Phenotype"

D.I. Kaufer, H. Yuen, S.T. DeKosky, W.E. Klunk

"Classification of Amyloid-positivity in Cognitively Normal Elderly Controls: Comparison of Objective Approaches with Visual Reads"

W.E. Klunk, A.D. Cohen, J.C. Price, C.A. Mathis, D.A. Wolk, J.M. Mountz, L.A. Weissfeld, S.K. Ziolk, R.D. Nebes, H.J. Aizenstein, J.A. Saxton, B.E. Snitz, P. Houck, E.M. Halligan, S.T. DeKosky

"Correlation of Amyloid Deposition with Local and Distal Glucose Metabolism in Cognitively Normal Elderly, MCI and AD"

A.D. Cohen, S. Ziolk, H.J. Aizenstein, R.D. Nebes, J.A. Saxton, C.A. Mathis, J.C. Price, W.Bi, L.A. Weissfeld, B.E. Snitz, E.M. Halligan, S.T. DeKosky, W.E. Klunk

"Differential Labeling of Amyloid Plaques and Tangles with 6-CN-PIB: Implications for In Vivo PIB PET Imaging"

M.D. Ikonovic, E.E. Abrahamson, W.E. Klunk, C.A. Mathis, J.C. Price, R.L. Hamilton, S.T. DeKosky

"Amyloid Imaging in Dementias of Uncertain Etiology with Pittsburgh Compound B"

D.A. Wolk, W.E. Klunk, J.C. Price, J.A. Saxton, O.L. Lopez, B.J. Lopresti, C.A. Mathis, S.T. DeKosky

"Risk of Incident Dementia in the Pittsburgh Cardiovascular Health Cognition Study (CHS) over 12–14 years of Follow-up"

L.H. Kuller, O.L. Lopez, A.B. Newman, Y. Chang

"Effectiveness and Safety of Donepezil in Hispanic Patients with Mild to Moderate Alzheimer's Disease: A 12-week Open-label Study"

O.L. Lopez, J.A. Mackell, Y. Sun, L.M. Kasslow, Y. Xu, H. Li



University of Pittsburgh

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Moving Toward a Cure

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Ask the Medical Professional

Q: I have Alzheimer's disease. Does that mean my children and grandchildren will get it, too?

A: Essentially the answer is no. Alzheimer's disease (AD) is not automatically passed on to children and grandchildren, but there are rare cases in which AD has been inherited. There are a few families around the world that have been identified as having this familial form of AD. In these cases, the disease surfaces early—in the 30s, 40s, or 50s—and half of the children of an affected parent will inherit it.

The majority of individuals diagnosed with AD, however, have what is known as late-onset AD. In late-onset AD, the disease usually starts after age 65. The children and grandchildren of these individuals have some increased risk of eventually developing AD, but there is not a predictable pattern of inheritance. There may be some component of genetic risk along with environmental and lifestyle risk factors that contribute to the development of the disease, but the strongest risk factor for developing AD is advancing age. More simply put, the older one gets, the more at risk one is for developing AD. With the current aging of the baby boomers, researchers continue to work more diligently than ever to move forward in search of new treatments for and the prevention of Alzheimer's disease.

