



ALZHEIMER'S DISEASE CENTER



"Dedicated to improving the health, well-being and quality of life of patients and their families."

QUARTERLY

## Wanted: One Thousand Dedicated Families

The National Institute on Aging has launched the LOAD (Late Onset Alzheimer's Disease) study, a nationwide effort to learn more about the genes that cause Alzheimer's disease. The focus of the study is to discover genes that increase the risk of developing the most common form of Alzheimer's disease, late-onset Alzheimer's disease, that is Alzheimer's disease diagnosed at 60 years or older.

This is big science dedicated to answering a big question. Discovering the genes associated with the most common form of Alzheimer's disease is a first step to targeting the mechanisms that cause the death of brain cells and to predict who is at risk for the disease.

This ambitious effort funded by the National Institute on Aging and supported by the Alzheimer's Association seeks to recruit 1000 families nationwide with two or more brothers or sisters who developed Alzheimer's disease after age 60. Families are asked to provide blood samples and to complete a telephone or in-person interview. Participants can live anywhere in the United States, and can be seen at any one of the participating Alzheimer's Disease Centers around the country.

To date, over 300 families have participated in the LOAD study. Why? Why should a family take on the hassles of a family history, exams and blood testing?

We spoke with one family who recently joined the LOAD study. With 2 brothers and 1 sister enrolled in

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## A Message From the Publisher

"Alzheimer's disease is a disease of families." This is the slogan of our Age of Memory.

This issue of the *Quarterly* takes on this slogan. We report on the LOAD study - a national effort to discover the genes that contribute to the pathologic cascade that leads to nerve cell death. Our knowledge of these mechanisms serves as targets for therapeutic interventions. This knowledge will also help us better understand who is at risk for developing Alzheimer's disease and thus the target of early intervention (see pages 1 and 6).

But a family is much more than the sum of its genes. Biology is who we are, but biology is not our destiny. Family means people who are bound by love, trust and sacrifice. We know these intangible forces are working when people start to tell stories to each other: "*Do you remember that time...*" We use stories to make sense of the world, especially when we feel that the world around us is falling apart.

In this issue we introduce two ways to tell stories: gathering a family history (see page 2) and telling children what is Alzheimer's disease (see page 3). One day, we may cure Alzheimer's disease. Let us rededicate our selves to making sure that along the way to that glorious day we make our families stronger.

Jason Karlawish

### SUMMER 2004 QUARTERLY

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# Putting Together the Stories of the Generations

By Kara Krissel, MPH

As the summer months have arrived, many families will gather at reunions, picnics or vacations. These gatherings are perfect opportunities to start sharing the stories that are the family history. One way to look at that history is by drawing the family tree.

Family trees are a useful way to organize and tell the stories of the generations. They are also valuable tools to collect and record a family's health history.

A detailed family health history can provide a map for future health, and can sometimes reveal what medical conditions a family may be at risk for, and knowing can sometimes be half the battle. For example, people at increased risk for cardiovascular disease, may be able to reduce their risk through exercise and diet. A medical history is also important when a physician is evaluating a patient for a diagnosis of Alzheimer's disease or a related neurodegenerative disease, as different types or forms of the disease have genetic, or hereditary, components.

One way to record a family history is by drawing a type of family tree called a "pedigree." This is a tool often used by health professionals to document a family's health history. An example of a pedigree is below. Keep in mind, a family tree can also be recorded without drawing a pedigree. A simple written list of family members with information such as age/date of birth, medical conditions, ethnic/national background, is another option. It is also important to

keep documents related to medical evaluations, births and deaths in a safe and retrievable location.

References:

If you are interested in reading more about how to record your family history please visit the National Society of Genetic Counselors website: [www.nsgc.org](http://www.nsgc.org). This website describes how to collect your family history, who should be included and what information to include. It also provides a guide to drawing pedigrees.

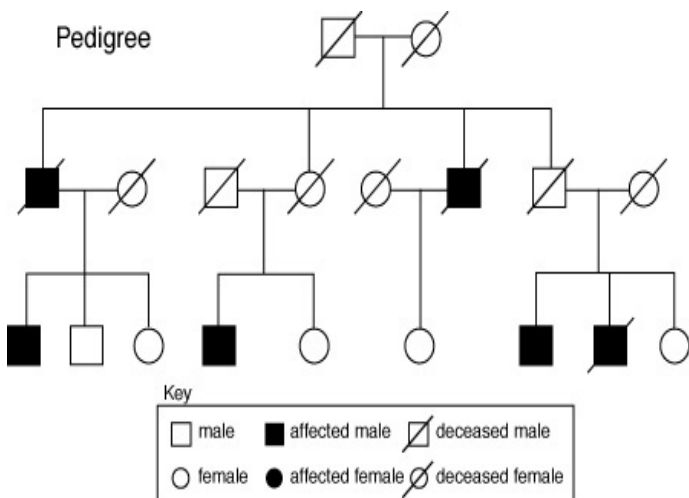
## Research Update: The *VALID* Study (*VAL*proate In *Dementia*)

VALID is a research study testing to see if Valproate (an anti-seizure drug) is effective in delaying, modulating or even preventing difficult behaviors in mild to moderate stage Alzheimer's disease. The study is suitable for patients who have not experienced agitation or psychosis, two of the common behavioral changes seen in Alzheimer's disease, but are at risk to develop them by virtue of their diagnosis.

Recent evidence suggests the possibility that Valproate can protect cells from damage by stressors. It therefore has the potential to slow the rate of Alzheimer's disease progression by favorably altering the pathology. Some of the patients will undergo MRI scans to examine hoped-for differences in brain structure between treated and untreated patients.

35 sites nationwide are participating in the VALID study. We are currently recruiting patients for the 26-month study at our Memory Disorders Clinic.

Interested in learning more about this study? Please contact Jennifer Chase, Clinical Research Coordinator by email at [jchase@mail.med.upenn.edu](mailto:jchase@mail.med.upenn.edu) or by telephone at 215-349-5903.





# Alzheimer's Disease Across the Generations

What's wrong with Grandma? The answer we give to a child struggling to understand their grandparent's dementia reveals how the world of adults portrays the disease to children.

Alzheimers is a disease of families. But there is one member of a family we rarely think of in this context: children, the stereotypical vulnerable innocents, who are to be protected from life's harms and perils. How then do we portray Alzheimer's disease to them? Do we hide it? Lie? Make a joke out of it? Our answer to the question "what's wrong with grandma?" reveals what we fear and what we hope for.

Several books eloquently portray Alzheimer's disease to innocence. The message is candor. The stories describe Alzheimer's disease as a "disease of the brain that some people get when they are older." The symptoms of memory loss, confusion, and anger are told from a child's perspective. We, the reader follow the characters through a series of emotions fear, anger, sadness and even guilt. Other questions soon follow, "will I get it?", "what will happen next?", "is this my fault?", "what can I do to help?"

In these stories, we see the affect Alzheimer's disease has on the unique bond between a grandparent and a grandchild. Ann Frantti's book, *Grandma's Cobwebs*, portrays this bond through the eyes of a child named Clair. Clair experiences a range of emo-

tions upon learning of her grandmother's disease, but true to the nature of childhood, she discovers a way to make her grandmother laugh. In Maria Shriver's book, Kate helps her grandfather remember names of family members by putting together a photo album scrapbook. While Tamika inspires a sense of hope with an old newspaper clipping from her grandmother's past, in Linda Jacobs Altman's book, *Singing with Momma Lou*. All of these books convey the same bittersweet message: the innocent possess a sense of resilience that can only thrive on honesty and open communication.

Experiencing a loved one progress through the stages of Alzheimer's disease is a challenging and emotional experience for families. How we share this experience with children adds additional challenges. These stories are a colorful look at Alzheimer's disease, and serve as a means to open up communication with children. Children who can identify with Clair, Kate and Tamika may in turn come to terms with a grandpar-ents' illness.

Books reviewed for this article:

*Grandma's Cobwebs*  
By Ann Frantti. Illustrations by Sergey Sachkov. 2002. Dagney Publishing (includes an educational supplement) on sale at Amazon.com and dagneypublishing.com

*Remember Me? ¿Te acuerdas de mí?*  
*Alzheimer's Through the Eyes of a Child*  
By Sue Glass. Illustrations W. Yunker. 2003. Raven Tree Press LLC (A story in English and Spanish) on sale at Amazon.com and BarnesandNoble.com

*Singing with Momma Lou*  
By Linda Jacobs Altman. Illustrations by Larry Johnson. 2002. Lee and Low Books Inc. on sale at Amazon.com and BarnesandNoble.com

*What's Happening to Grandpa?*  
By Maria Shriver. Illustrations by Sandra Speidel. 2004. Little, Brown and Company and Warner Books on sale at Amazon.com and BarnesandNoble.com

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• **How can families help children cope with Alzheimer's disease**

- • Maintain open lines of communication
- • Offer comfort and support
- • Provide opportunities for them to express their feelings
- • Let them know their feelings are normal
- • Educate them about the disease and encourage them to ask questions
- • Respond honestly to questions

• Taken from the Alzheimer's Association fact sheet: Helping children and teens understand Alzheimer's disease.  
• [www.alz.org/Resources/FactSheets/Brochure\\_Children\\_Teens.pdf](http://www.alz.org/Resources/FactSheets/Brochure_Children_Teens.pdf)

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# Wanted: One Thousand Dedicated Families

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the study, this family is dedicated to Alzheimer's disease research. When asked why they decided to participate, Mrs. S replied,

"it was a no brainer... a simple blood test and answering some questions seemed a small price to pay for assisting in the process of finding out if genes play a role in the disease."

Mrs. S is the primary carer for her 90-year-old father. Both her father and uncle have been diagnosed with Alzheimer's disease. Her father is the eldest of a blended generation of six brothers and sisters, five living. Bonded by marriage, family S is approaching Alzheimer's disease as a family affair, with the next generation of eight, Mrs. S included, actively involved in their father's and uncle's care. "Hopefully my family can benefit from the study's results as can all families," she says.

When speaking with Mr. S, brother of and primary carer for the second sibling enrolled in the study, it is obvious how dedicated this family really is, not only to the Alzheimer's community, but also to each other. "He is very enjoyable to be with", he says. "When he goes to the senior center, I miss him."

Below, Mrs. S describes her families experience with Alzheimer's disease and explains why they decided to participate in this "LOADed" research study.

## **Q: How Does Alzheimer's Disease Affect Your Family?**

A: My father has Alzheimer's as does his younger brother. My father has had the disease for about a

decade and during that time my mother has struggled greatly with the loss of her soul and help mate. She feels his loss every day of her life and is depressed about it. My brother is disturbed that his father does not always know who he is or the names of his grandchildren. My brother also worries that one day he too will fall victim to the disease. My father now lives with me and that has been an adjustment for my husband and teenage daughters. We can no longer freely make plans without first considering dad's welfare. I am now responsible for meeting dad's every need, which is as great a responsibility as caring for a young child. On the flip side, my father continues to be a loving person whose presence in our home is a gift.

## **Wanted: One Thousand Dedicated Families to Join the LOAD Study**

### **Who can participate?**

Families with at least 3 members who can donate blood and provide a family history, including:

- Two siblings (brothers or sisters) who developed Alzheimer's disease after age 60

### **AND**

- Another family member over 60 who does not have any memory loss OR a family member over age 50 who may have memory loss.

### **How can I find out more?**

If you are interested in learning more about the LOAD study or if you are not sure your family is eligible, please contact:

**Contacts:** Beth Wood and Jennifer Farmer

**Telephone:** 215-614-0937

**Email:** [mccarty@mail.med.upenn.edu](mailto:mccarty@mail.med.upenn.edu)

For more information, you can also visit the National Cell Repository for Alzheimer's Disease (NCRAD) website at [www.ncrad.org](http://www.ncrad.org)

## **Q: They say that Alzheimer's disease is a disease of families. Do you believe that and why?**

A: Sure, it is a disease of the family because every member is impacted in his own way. It calls upon families to come together to do what must be done, as our family is doing, but it also can pull families apart.

## **Q: How did you and your family learn about the Late Onset Alzheimer's disease (LOAD) study?**

A: My uncle heard about the study through his involvement with Penn's Memory Disorders Clinic. He men-

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## News Briefs From Penn's ADC

### Events:

#### **Symposium to discuss the latest Frontotemporal Dementia (FTD) research**

International experts will discuss the state-of-the-science of frontotemporal dementia at a two-day forum held on July 15-16 at the University of Pennsylvania. This is a satellite meeting to the 9<sup>th</sup> International Conference on Alzheimer's Disease and Related Disorders. This forum will feature topics such as overviews of progressive aphasia and social/personality disorder; structural, functional, and biochemical imaging; CSF tau and other biomarkers; animal models of tauopathies; genetic studies of FTD; and effects of FTDP-17 mutations on tau structure and function. For more information please visit: [www.uphs.upenn.edu/cndr](http://www.uphs.upenn.edu/cndr).

#### **Save the date! Friday, September 24. Penn's Second Annual Conference for Families**

The Alzheimer's Disease Center will host a conference for families. For more information, please visit ([www.uphs.upenn.edu/ADC](http://www.uphs.upenn.edu/ADC)) or contact Kara Krissel by email at [karakris@mail.med.upenn.edu](mailto:karakris@mail.med.upenn.edu) or phone 215-573-4634. Registration brochures will also be mailed to *Quarterly* recipients this summer.

### Staff news:

#### **Farwell...**

This summer, we say farewell to Tanya Nagahawatte, research assistant and Bryan James, research specialist. Tanya will be starting medical school at Drexel University, and Bryan will begin a doctoral program in epidemiology and aging at Johns Hopkins University.

#### **...Welcome**

We welcome Emily Murphy. Emily has joined our team as a research assistant working with Dr. Jason Karlawish.

### Staff Awards and Honors:

#### **Virginia M.-Y. Lee, PhD, MBA awarded the 2004 Founders Distinguished Senior Scholar Award**

Virginia M.-Y. Lee, PhD, MBA, Co-director of Penn's Center for Neurodegenerative Disease Research, was awarded the 2004 Founders Distinguished Senior Scholar Award by the American Association of University Women (AAUW) Educational Foundation. This

Award honors a woman scholar for a lifetime of outstanding research, college/ university teaching, publications, and positive impact upon women in her profession and in the community.

#### **Valerie Cotter, MSN, CRNP selected as 2004 Fellow American Academy of Nurse Practitioners (FAANP)**

Valerie Cotter, MSN, CRNP, Education Director of the Alzheimer's Disease Center and Nurse Practitioner at the Memory Disorders Clinic has been selected as a fellow in the American Academy of Nurse Practitioners for 2004. This program was established by the American Academy of Nurse Practitioners in 2000 to recognize nurse practitioner leaders who have made outstanding contributions to health care through clinical practice, research, education or policy.

#### **John Q Trojanowski, MD, PhD awarded the 2005 Rous-Whipple Award**

John Q Trojanowski, MD, PhD was awarded the 2005 Rous-Whipple Award by the American Society for Investigative Pathology. The Rous-Whipple Award is given to a pathologist with a distinguished career in research and continued productivity at the time of the award.

### News and updates:

#### **The Latino Memory Disorders Satellite Clinic has a new address**

In April 2004, our Latino satellite clinic moved to a new location. The clinic is now located at the Maria de Los Santos Health Center, at 452 West Allegheny Avenue, Philadelphia, PA. The Clinic Director is Dr. Milagros Soto. For more information or to schedule an appointment contact Carmen María Lebrón, Administrative Assistant at (215) 614-1829

#### **The Institute on Aging celebrates its' 25<sup>th</sup> anniversary**

The Institute on Aging celebrated its 25<sup>th</sup> Anniversary at its annual Retreat with Poster Session on May 25<sup>th</sup>. Vincent Cristofalo, PhD, the founding Director of the Center for the Study of Aging (CSA) at Penn, was the Sylvan M. Cohen Visiting Scholar and spoke to a standing-room-only audience in Houston Hall. He was followed by Sarah Kagan, PhD, RN, who was the Penn presenter. Also featured this year was a judged poster session which encompassed entries from 73 participants.



# What Have We Learned From the Genes You Have Given Us?

## A research update from the CNDR

By Jennifer Farmer MS, Certified Genetic Counselor

*The Center for Neurodegenerative Disease Research (CNDR) is the home of the Alzheimer's Disease Center's Pathology Core. Its mission is to conduct multidisciplinary clinical and basic research that increases understanding of the causes and mechanisms of Alzheimer's disease and related neurodegenerative diseases.*

Thanks to the patients, family members, and friends of the Alzheimer's Disease Center, we have collected family histories and DNA samples from 135 families for our genetic studies. As a result of this information, we have begun to discover multiple genes associated with Alzheimer's disease (AD) and related conditions. Understanding the role of genes in their normal and abnormal forms brings us one step closer to understanding the underlying disease process of neurodegenerative conditions. This will open new areas of research to develop ways to diagnose, treat or even prevent the disease.

DNA (deoxyribonucleic acid) is a chemical that is the most basic unit of genetic information that helps to define individual genes. A helpful analogy is to think of a gene as a word and every letter in the word is a unit of DNA. DNA sequencing is the determination of the precise pattern of DNA in a gene. In our analogy, DNA sequencing can be compared to the act of spelling out a word letter by letter. In particular, the sequence or spelling of DNA in the Presenilin 1 (PS1) gene and the tau gene has been determined. This is important because it allows us, in the research laboratory, to check an individual's PS1 or tau gene for the correct sequence. To continue the analogy – we are able to do a spell check of the PS1 and tau to be sure that they have been coded correctly. A misspelling or error in the DNA sequence in a gene is called a mutation.

Every gene is important because it codes for a protein that serves an important function in the body. PS1 is one of four known genes that are currently associated with AD. PS1, along with Presenilin 2 (PS2) and amyloid precursor protein (APP), has been linked with the early-onset form of AD. Early-onset AD (EOAD) is defined by an age of onset before age 65 and is often

associated with family history of early onset AD. The cause for early onset AD has been linked to one of these genes in many families when multiple family members in several generations have had the condition. This means that mutations, or changes, in these genes have been identified in such families. Approximately 1% to 10% of AD patients have early-onset, therefore these changes are rare and are not associated with the much more common late-onset form of AD.

The fourth gene associated with AD is the ApolipoproteinE (APOE) gene. APOE is the only known gene identified that plays a role in the more common form of AD. Different variations of the APOE gene have been identified, and one type, called APOE4, does not cause LOAD but can increase a person's risk. LOAD refers to Late-Onset Alzheimer's Disease, and it is the most common form of the disease. In this issue of the *Quarterly*, the LOAD study is highlighted. One of the goals of this study is to identify additional genes for this form of the disease.

Tau is a protein that is commonly found in nerve cells in the brain. Mutations in the tau gene can cause abnormal amounts of the protein to build-up in the brain, and have been linked to frontotemporal dementia (FTD) in a few families.

The genetic research in the CNDR focuses on studying the DNA sequence of genes like PS1 and tau in patients and families with Alzheimer's disease and related conditions, such as FTD. In families where there is a genetic or inherited cause for a neurodegenerative disease, the genetic research can sometimes facilitate genetic testing. Genetic testing can then be used for diagnosis or determining risk in unaffected family members.

A final note, it is important to remember that the majority of individuals with AD and FTD do not have a hereditary condition. Less than 10% of individuals with these conditions have a mutation in a single gene like PS1 or tau that causes their disease.

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# ADC QUARTERLY



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## Research Opportunities at Penn's Alzheimer's Disease Center:

### Studies to develop new treatments

- A study to compare the benefits of three medications currently approved for Alzheimer's disease
- A clinical trial of a new investigational drug for Alzheimer's disease
- A study to determine if taking Zocor (a cholesterol lowering drug) can slow the progression of Alzheimer's disease
- A study to determine if taking high doses of three vitamins can slow the progression of Alzheimer's disease
- A study to evaluate if the drug Valproate can slow down the emergence of problematic behaviors and the progression of Alzheimer's disease (see page 2)

### Diagnostic studies

- A study to determine if a measure of brain waves generated in response to sound can detect the presence of Alzheimer's disease
- A longitudinal study to search for the presence of specific proteins that mark the presence of Alzheimer's pathology at a time when the symptoms are too mild for the disease to be detected by clinical examination

To learn more about these and other research opportunities contact Jennifer Chase, clinical research coordinator at 215-349-5903 or email her at [jchase@mail.med.upenn.edu](mailto:jchase@mail.med.upenn.edu).

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