

## The National Cell Repository for Alzheimer's Disease

(NCRAD) is a data and specimen collection source for families with Alzheimer disease (AD) or serious memory loss. Families having two or more living individuals with memory loss are encouraged to participate. We would like to thank the hundreds of families nationwide who are already participating in the National Cell Repository. Many family members have provided blood samples, which researchers use to study Alzheimer's disease (AD) and other related diseases. Our hope is that, through the efforts of our participants, we will one day unravel the mystery of devastating diseases, like AD. We are always eager to accept new families to help us move toward this goal.



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SCHOOL OF MEDICINE

### National Cell Repository for Alzheimer's Disease

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# NCRAD Update

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## NCRAD and LOAD Attend Conference

By Dolly Reyes, Columbia University and Jennifer Williamson-Catania, M.S., Columbia University

The International Conference on Alzheimer's Disease (ICAD) 2008 was held July 26-31 in Chicago, IL. This conference, sponsored by the Alzheimer's Association, is considered the largest gathering of Alzheimer's disease (AD) and dementia researchers. This year more than 5400 researchers met to discuss clinical drug trials, neuroimaging, diagnosis, treatment and genetics. In response to the increasing population of AD patients and the current pace of research, the Alzheimer's Association is making this important meeting normally held every other year, an annual event. The next conference will be held in Vienna, Austria, in 2009.

The mission of ICAD is to facilitate the communication and collaboration of researchers working on the common goal of understanding Alzheimer's disease in order to provide more

effective treatments or to develop strategies to prevent the disease. The NCRAD (National Cell Repository for Alzheimer's Disease) and the NIA LOAD (Late Onset Alzheimer's Disease Genetics Initiative) teams attend this conference to promote the important resource we have developed with the participation of hundreds of families. Academic, non-profit and commercial researchers may use this resource.

Both local and international clinicians are interested in recruiting families for research participation and studying the genetic underpinnings of AD and other dementias. Interestingly, many researchers and clinicians noted the importance of longitudinal assessments of families and the neuropathological diagnoses via brain donation. These same physicians noted the challenges of developing a resource like NCRAD and are pleased to discover they can apply to use the clinical, neuropathological and genetic data from the NCRAD and LOAD studies to support their research.

# Discussing Genetic Issues With Your Family

This article has been excerpted from the Association of Frontotemporal Dementia website ([www.ftd-picks.org](http://www.ftd-picks.org)) and the chapter "The Role of Genetics - A Piece in the FTD Puzzle" by Jennifer M. Farmer and Elisabeth McCarty-Wood in "What if it's Not Alzheimer's", edited by Lisa Radin and Gary Radin (Prometheus Books, 2008).

**G**enetic issues present a difficult dichotomy within a family. Your genes are what make you unique: no one else in the world has the same exact combination of genes that you do. Yet, you share 50% of your genes with each of your first-degree relatives (parents, siblings, and children). So any genetic issue is both extremely personal and common to all blood relatives.

For this reason, discussing genetic risk can be extremely difficult, even within the most supportive families. When the disorder in question is an adult-onset, progressive, neurological disease like Alzheimer's disease (AD) or Frontotemporal Dementia (FTD), the issues can be even more complicated. The patient's children are often raising their own families, and at the prime of their careers. None of these individuals will want to hear that they might be at risk for the disorder that is afflicting their loved one.

What can a caregiver do regarding communicating potential genetic risk to family members? To what extent is this your responsibility? While there is no one answer for every circumstance, here are some general guidelines and tools to help.

- Meet with a genetic counselor or have a serious discussion with your neurologist about the patient's family history and the likelihood that dementia's like AD or FTD might be inherited in the family. This is especially important if you have a high level of concern based on family lore about older relatives. This professional can help separate fact from "fiction" and, if there is valid reason for concern, they will devise a plan to get more information.
- If the patient's children or grandchildren are under age 18, there is no rush to have the discussion. Because

diseases like AD and FTD do not present a risk this early in life, no clinician would perform a genetic test on a minor; the policy is to test only adults who can understand the complicated issues involved and thus give truly informed consent. As with all complex, emotional issues, it is best to follow a child's lead, letting them know that you welcome their questions and making a judgment call as to how much information they are ready to know at any given time.

- Broach the subject with adult members of the immediate family. Chances are that if there is some family history, these people have been wondering about heritability, but have not wanted to broach the subject themselves. Perhaps they are worried about appearing to have selfish concerns about the future, when you are dealing with the daily demands of your loved one. Opening the door to the topic will give them permission to pick up on the discussion if they want to.
- There are different ways to introduce the topic. You could share copies of a letter from the neurologist that outlines the possibility that AD or FTD is being inherited in the family. Use the exercise of researching the family history to introduce the topic with relatives who may have more information about ancestors. Remember, it is OK that you do not have the answers to all of the questions; often it can be comforting just to know that others in the family have the same concerns.
- People within the family may react very differently to the subject. Some will want to talk about it; others may be scared and get angry. This is normal, and you should remember that they are not reacting to you, but to the threat of the disease. The best you can do is to let them know that there is a support

network, and professionals who can help them find answers if and when they want to.

- Different members of the family will choose different paths to address this risk. Some will ignore it; some will want to discuss it with family; still others will pursue professional advice in private. It is important to know that a geneticist or genetic counselor will hold each individual's consultation in the strictest confidence. Information is not shared with other family members without an individual's consent.

You may not know which course each of your relatives takes. All that is important is for you to know that you opened the door to let each of them address it in his or her own way.

## The Importance of Your Family Medical History

When a physician or healthcare provider is evaluating a patient for a diagnosis of a dementing disease like AD or FTD or another similar neurodegenerative condition, information regarding the family history can help determine a diagnosis. Thus, a detailed family history is a valuable diagnostic tool. It is worth the time and effort to contact relatives and obtain the most accurate details of family structure and medical information. A complete family history that describes family structure and health history contains a lot of information. It is important to document the information in a meaningful way that is accessible and easy to read. (For more information on the importance of knowing your family's health history, and tools to help you gather and organize the information, see the U.S. Surgeon General's Family History Initiative at [www.hhs.gov/familyhistory](http://www.hhs.gov/familyhistory).)

Geneticists and genetic counselors create a pedigree, which is a graphic

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# Aging, Alzheimer Disease and Driving



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**D**riving ability can begin to deteriorate around age 55 for many people. This is normal since aging affects hearing, sight, distance and depth perception and reaction time. Because of these changes, many older drivers start to change their driving habits around the same time. For example, they may not drive at night as much, avoid rush hours and other similar changes. What happens though when an older person's cognitive skills begin to decline due to Alzheimer's disease (AD)? One significant symptom of AD is decline in judgement and reasoning skills. A typical driver makes 20 decisions per mile, with less than half a second to act to avoid a collision. After all, driving is very complicated. Therefore, as we age and our reaction time slows down, it is understandable that driving may become more difficult. It is not easy to make all of those decisions so quickly. But for a person with AD, decision making is even more difficult. Indeed, as many family members know, the decline in reasoning and judgement is also why it is often very difficult, if not impossible, to rationally discuss giving up driving.

How should one discuss driving with a parent, spouse or other relative? It is important to understand that driving represents independence to most people, so don't think it will be easy to get someone to give up driving. But on the other hand, if they are no longer safe behind the wheel, it must be done.

## The following are some warning signs that can indicate there may be a problem:

- Anxiety, feeling uncomfortable and nervous or fearful while driving.
- Lack of concentration. Dents and scrapes on the car or on fences, mailboxes, garage doors, curbs, etc. Discovering damages but cannot explain them.
- Less control of muscles making it harder to push down on the pedals or turn the steering wheel.
- Medical conditions or medications begin to affect the ability to handle a car safely.
- Having a difficult time controlling anger, sadness or other emotions that can affect driving.
- Friends or relatives do not want them to drive, for fear they will hurt themselves or others.
- Frequent traffic citations or constantly being stopped by the police in the last year or two.



- Close calls, almost crashing due to distractions or lack of proper judgment at intersections, in traffic, or on highway entrances/exit ramps.
- Getting lost. Having trouble remembering directions. Getting lost on routes that were once familiar.
- Difficulty in turning around to check over shoulder while backing up or changing lanes.
- Slower responses to unexpected situations such as children or animals darting into traffic.

If you suspect a problem with someone's driving, it is important that you speak to them, other family members, and their physicians to determine if further action needs to be taken.

## When is the best time to talk about driving with an older person?

The best case scenario is to have a discussion about driving before it becomes an issue. For example, retirement may be a good time to bring it up. Possible things to discuss with an older loved one is selecting a safer car, their plans for getting to and from the grocery, doctors' appointments, social outings, church and so on. The following suggestions may help begin the conversation:

- Always start such difficult discussions by stressing your concern for their well-being and base it on things you have observed.
- Acknowledge that driving is important and you want to help them remain as independent and functional as possible.
- Acknowledge the person's strengths. They didn't get this far without the proper driving skills.
- Be positive and supportive, not bossy or critical when discussing driving concerns. It will not help if you alienate them or make them angry.

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## Discussing Genetic Issues with Your Family > continued from page 2

description of family structure and health history, to record information collected from patients and families. Determining the quantity and quality of information to collect can be difficult. Ideally, one should research at least three generations of relatives, which includes:

- First-degree relatives: children, siblings, and parents
- Second-degree relatives: half siblings, aunts, uncles, nieces, nephews, grandparents, grandchildren
- Third-degree relatives: cousins

The type of medical information to obtain on relatives can include:

- Vital Status (Living or deceased)
- Age (Date of birth)
- Age at death
- Cause of death
- Autopsy (if one was performed)
- Pregnancy, miscarriages and stillbirths
- Infertility
- Individuals with previous genetics evaluation
- Environmental exposures
- Radiation, alcohol or drug abuse, tobacco use
- Birth defects
- Mental retardation
- Deafness, blindness
- Chronic childhood illness
- Cancer
- Neurological conditions (e.g. epilepsy, migraines, strokes, multiple sclerosis, Parkinson's

- disease, ALS (Lou Gehrig's disease)
- Mental illness (e.g. bipolar disorder, schizophrenia, OCD)
- Dementia (Alzheimer's disease, senility)
- Ages of diagnosis for all of the above

When going back and obtaining medical information from previous generations, it is important to note that many of the medical terms we use today, such as Alzheimer disease or FTD, were not used. Therefore, many individuals with neurodegenerative conditions would have been told that they had "dementia" or "senility". In such cases, it can be useful to try and gather more descriptive information. For example, it is useful to ask if the individual had problems speaking as a first symptom, or if he/she had a personality or behavior change. It is also important to try and determine an estimate for the age of onset.

Another way to determine diagnosis in deceased relatives is to inquire about autopsy. If an individual had an autopsy, the autopsy records (as well as other records, MRI reports and brain biopsies) can be requested and these records can be most informative. Confirmation of diagnoses with medical records from previous evaluations and laboratory studies is also crucial.

The family medical history, or pedigree, can be a powerful diagnostic tool to a clinician evaluating a patient. The

pedigree can be utilized as a diagnostic tool in the following ways:

- establish pattern of inheritance;
- identify individuals in the family at-risk for the condition;
- determine strategies for genetic testing; and
- help screen for medical risks (such as cancer and heart disease).

Family history information needs to be respected and treated appropriately by healthcare providers and individual family members. Contacting relatives and asking about personal information is not an easy task. Navigating through the complex interpersonal relationships and personalities in a family can be emotionally difficult and stressful. This is a give-and-take process. When calling a relative, it is important to state your intentions or reason for collecting the information. Offer to re-contact family members with information that you learn about your loved one's diagnosis and how it may affect them. Respect an individual's right for privacy. If you go through the effort of obtaining a family history, be sure to document the information clearly and secure it in a location that is accessible to other family members and future generations.

*Adapted from The Association for Frontotemporal Dementia's website: <http://www.ftd-picks.org/?p=learnmore.genetics>*

## Aging, Alzheimer Disease and Driving > continued from page 3

- Have these conversations early and often.

***If you are afraid of driving with them, they should not be driving.***

### How does one make the decision to give up driving all together?

This is an individual decision based on each person's level of decline. There is no one easy answer. It may be easier if they give up driving in stages. The following ideas have helped others ease into giving up the car.

- Reduce driving at night, during bad weather and during high traffic times.
- Drive only regular, familiar routes in the middle of day.
- Help them plan their route and stick to it.
- Enlist the help of other family members, friends and neighbors-have a driving schedule.
- Encourage carpooling.

- Have the doctor write a prescription for no more driving.
- Walk or take public transportation with them. If they see you doing it, they may be more likely to follow.
- Register them in the Alzheimer's Association Safe Return program. Call 1-800-272-3900.
- Some families have found that selling the car made it easier but others have reported that getting rid of the car too early was a mistake. Assess the situation carefully and remember, you know your loved one best.

### Recommended Resources

**Alzheimer's Association Safe Return**  
1-800-272-3900

**AARP Driver safety classes**  
1-888-AARP-NOW



# Research Opportunities

## Delaying the Progression of Driving Impairment in Individuals with Mild Alzheimer's Disease

- Purpose: To determine whether the medication memantine delays the progression of driving impairment in patients with mild Alzheimer's Disease.
- Eligibility: Subjects with clinical diagnosis of mild Alzheimer's Disease over the age of 60.
- Locations: FL
- Contact: Lori Fisher, M.A.  
PH: 1-561-297-0502  
E-mail: lfisher8@fau.edu

## The Genetics of Late Alzheimer's Disease (LOAD)

- Purpose: To identify families with multiple members diagnosed with late-onset Alzheimer's Disease. Families will be characterized clinically and blood samples will be collected to establish cell lines. If a blood sample is not available, autopsy samples will be collected for DNA extraction and storage. Our goal is to recruit 1,000 families over the course of the study. Clinical and demographic data from these families will be collected at the local site and coded data, without identifiers, will be sent and included in a national database of families with Alzheimer's Disease. This database, along with the biological samples, will be housed at the National Cell Repository for Alzheimer's Disease (NCRAD) at Indiana University.
- Eligibility: Two siblings (brothers or sisters) who developed AD after the age of 60 and another family member over 50 who may have memory loss or a family member over 60 who does not have any memory loss. Participants can live anywhere in the U.S. and can be of any racial or ethnic background.
- Locations: (sites in following states, but participation is open to subjects all over the United States)  
FL, IL, IN, MN, MO, NY, PA, TX, WA
- Contact: 1-800-526-2839  
E-mail: alzstudy@iupui.edu

## Depression in Alzheimer's Disease

- Purpose: To demonstrate whether the medication sertraline (Zoloft®) helps people with Alzheimer's disease. Through this study we hope to find out if treating depression can slow the progression of Alzheimer's disease.
- Eligibility: People who suffer from memory loss, Alzheimer's disease, and symptoms of depression. Participants must also be accompanied by their caregiver.
- Locations: CA, MD, NY, PA, SC
- Contact: Ann Morrison, PhD, RN  
PH: 1-410-614-4605  
E-mail: amorris7@jhmi.edu

## Raloxifene for Women with Alzheimer's Disease

- Purpose: To determine whether Raloxifene, a selective estrogen receptor modulator (SERM), improves cognitive function in women with Alzheimer's disease.
- Eligibility: Women 60 years and older with clinical diagnosis of AD.
- Locations: CA, IL, IN
- Contact: Narinder Bolara  
PH: 1-650-721-3308  
E-mail: nbolaria@stanford.edu

## Anti-Oxidant Treatment of Alzheimer's Disease

- Purpose: To examine the safety and effectiveness of two anti-oxidant treatment regimens in patients with mild to moderate Alzheimer's disease. The anti-oxidant treatments include vitamin E+ C+ alpha -lipoic acid, and Coenzyme Q (CoQ).
- Eligibility: Ages 60-85, Both Genders, Diagnosis of probable Alzheimer's Disease
- Locations: AL, AZ, CA, FL, NY, OH, OR, PA, SC, WA
- Contact: ADCS Anti-Oxidant Study webpage [http://adcs.ucsd.edu/Anti-Oxidant\\_protocol.htm](http://adcs.ucsd.edu/Anti-Oxidant_protocol.htm) or Linda Mandelco E-mail: [linda.mandelco@med.va.gov](mailto:linda.mandelco@med.va.gov)

## Prevention of Alzheimer's Disease by Vitamin E and Selenium (PREADVISE)

- Purpose: As a prevention trial, PREADVISE is trying to find out if taking selenium and/or Vitamin E supplements can help to prevent memory loss and dementia such as Alzheimer's disease.
- Eligibility: Ages: 60 - 90, Male. Accepts Healthy Volunteers
- Locations: AL, AK, CA, CO, DC, FL, GA, IA, KS, KY, MD, MA, MI, MN, MS, MO, MT, NE, NV, NJ, NY, OH, OK, PA, SD, TN, TX, WA, WI, Canada, Puerto Rico
- Contact: Cecil R. Runyons  
PH: 1-859-257-1412 Ext. 235  
E-mail: [preadvise@lsv.uky.edu](mailto:preadvise@lsv.uky.edu)

## GIFT: Genetic Investigation in Frontotemporal Dementia and Alzheimer's Disease

- Purpose: To perform DNA studies to evaluate the genetic contribution to Alzheimer's Disease (AD) and Frontotemporal Dementia (FTD). Using a microarray-based approach, 80 genes related to neurodegeneration will be resequenced in order to identify rare mutations or risk-associated genetic variants.
- Eligibility: Subjects with clinical diagnosis of AD or FTD. Healthy volunteers.
- Locations: CA, GA
- Contact: GIFT webpage <http://geschwindlab.neurology.ucla.edu/gift>

Autopsy is still the only way to definitively diagnose the specific kind of dementia affecting an individual. Please contact us if you are interested in pursuing an autopsy for a family member with dementia.

For more information call **1-800-526-2839** or email [alzstudy@iupui.edu](mailto:alzstudy@iupui.edu)

We appreciate your support in helping us unravel the mystery of devastating diseases, like Alzheimer's.

## Sources for Information and Support

### \* **Alzheimer's Association**

<http://www.alz.org>

Tel: 312-335-8700 or 800-272-3900

### **Alzheimer's Disease Education and Referral Center (ADEAR)**

<http://www.nia.nih.gov/Alzheimers>

Tel: 301-495-3311 or 800-438-4380

\* ADEAR lists all 29 Alzheimer's Disease Centers (ADCs) and their contact information.

### **Family Caregiver Alliance**

<http://www.caregiver.org>

Tel: 415-434-3388 or 800-445-8106

### **National Parkinson Foundation**

<http://www.parkinson.org/>

Tel: 305-547-6666 or 800-327-4545

### **Parkinson's Disease Foundation (PDF)**

[www.pdf.org](http://www.pdf.org)

Tel: 212-923-4700 or 800-457-6676

### **Society for Progressive Supranuclear Palsy**

<http://www.psp.org>

Tel: 410-486-3330 or 800-457-4777

### **National Organization for Rare Disorders (NORD)**

<http://www.rarediseases.org>

Tel: 203-746-6518 or 800-999-NORD (6673)

### **Center for Disease Control and Prevention (CDCP)**

<http://www.cdc.gov>

Tel: 800-311-3435

### **Creutzfeldt- Jakob Foundation Inc.**

<http://cjd.foundation.org>

\* **ClinicalTrials.gov** is a registry of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals.  
<http://www.clinicaltrials.gov/>  
No phone number

\* These are good sources for research opportunities in your area.



## Telephone Cognitive Assessment

By Kelly Horner, NCRAD Coordinator, IUPUI

The goal of NCRAD is to help researchers identify the genes that contribute to Alzheimer's disease and other related dementias. To help researchers achieve this goal, we have implemented a new aspect of our study. In this article, we will share with you some of the details of this new protocol and how you and your family members might be able to participate.

Changes in memory can occur at any time, and in some instances may be an early symptom of possible Alzheimer's disease. There has been extensive research by a number of different scientists who have sought to study these early memory changes. NCRAD is eager to help scientists who want to better understand the relationship between normal memory changes and those changes that might precede Alzheimer's disease or related dementias.

To help scientists perform these studies, NCRAD has selected a short series of memory tests that can be administered over the telephone. NCRAD coordinators will be contacting family members who are over the age of 60 and have donated blood samples to NCRAD. Due to the large number of families involved with NCRAD and the time required to complete the memory questions by telephone, we will be sending out notices to families on a rolling basis. So, individuals should not worry if they are not contacted immediately.

**NCRAD is eager to help scientists who want to better understand the relationship between normal memory changes and those changes that might precede Alzheimer's disease or related dementias.**

We are asking family members who may or may not have some memory difficulty to consider completing these brief memory tests. These questions will typically take about 20-30 minutes to complete, and are best completed when the individual is in a quiet location and will not be disturbed while the questions are being answered. Because this is part of a research study, we will not be able to provide individuals any results concerning their test performance or the performance of other family members.

It is only through the active participation of families with Alzheimer's disease or related dementias that we will be able to unravel the genetics of dementia. NCRAD is very hopeful that the data we are able to collect through these memory tests will help increase the usefulness of the NCRAD study samples.

If you have any questions, please feel free to contact NCRAD staff at 1-800-526-2839 or by email at [alzstudy@iupui.edu](mailto:alzstudy@iupui.edu).