

The National Cell Repository

is a repository for families with Alzheimer's Disease or severe 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.

**National Cell Repository
for Alzheimer's Disease
Department of Medical Genetics**

975 West Walnut St ■ IB 130
Indianapolis, IN 46202-5251
Phone: 1-800-526-2839
E-mail: alzstudy@iupui.edu
www.ncrad.org

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NCRAD Update

Newsletter of the National Cell Repository for Alzheimer's Disease Volume 5 ■ August 2004



Does Staying Active Offer Protection Against Dementia?

By Daniel Rexroth, Psy.D., Visiting Assistant Clinical Professor
Indiana University School of Medicine

One of the most frequently asked questions by family members is “**Does staying physically and mentally active help protect someone from getting Alzheimer's disease?**” This question has received considerable attention recently. An article published by Verghese and colleagues in the *New England Journal of Medicine* (June, 2003) studied whether cognitive or physical activity helped protect individuals from dementia. They studied individuals over the age of 75 whose activity level ranged from “not active” to “active daily” on a variety of cognitive or physical activities. The cognitive activities that were studied included reading books or newspapers, writing for pleasure, doing crossword puzzles, playing board games or cards, participating in organized group discussions, and playing musical instruments. The physical activities included tennis or golf, swimming, bicycling, dancing, team games, walking for exercise, climbing more than two flights of stairs, doing housework, and babysitting. The frequency of participation in these types of activities was rated for each individual studied.

The number of times a participant engaged in cognitive activities each week was found to be related to their risk of getting dementia five years later. Participants who later developed dementia participated in significantly fewer cognitively challenging activities. Interestingly, the 33% of the group that was the most cognitively active had a 63% less risk of dementia. Participating in one activity per week was associated with a 7% drop in one's risk for dementia. Among the cognitive activities listed,

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Questions From You

Q. Are Alzheimer's disease and dementia the same thing?

A. "Dementia" is a general term that means someone has trouble with their memory and thinking. There are many different things that can cause dementia. Alzheimer's disease is the most common kind of dementia, but 1/3 of dementia cases are caused by something else. One of the first things a doctor will do when evaluating dementia is to make sure that the memory and thinking problems are not the result of medication side effects, metabolic or hormone imbalances, vitamin deficiency, or infection. Some of the other common causes of dementia are vascular dementia and Lewy body dementia. In vascular dementia, the memory and thinking problems are caused by strokes or circulation problems in the brain. Lewy body dementia has some similarities with both Alzheimer's disease and Parkinson's disease: persons with this condition may have problems with attention and

sense of direction; hallucinations; Parkinson's-like symptoms of trouble walking, slowness, or stiffness; or fluctuations in their thinking or motor skills. Individuals with brain damage from head trauma can also have dementia. Other less common kinds of dementia include Pick's disease, in which deterioration of the frontal lobes of the brain causes changes in personality, behavior, and motivation; or normal pressure hydrocephalus, in which a buildup of fluid in the brain causes decreased memory, difficulty walking, and trouble with bladder control.

Since there are so many different things that can cause problems with memory and thinking, it is always a good idea to get checked out by a doctor if you are noticing these symptoms.

Ann Marie Hake, M.D.
Clinical Assistant Professor, Department of Neurology
Indiana University School of Medicine

Staying Active

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reading, playing board games, and playing musical instruments were generally found to be associated with a lowered risk of dementia. Physical activity did not seem to affect whether a person later developed the disease although other recent studies have found physical activity to protect against incident dementia (Wilson, et al., Neurology, 2002). These findings were found to be true even after accounting for the participant's age, gender, educational level, base-line cognitive status, and the presence or absence of chronic medical illness.

While participation in cognitive activities has been found to stave off dementia in this and other studies, the reason for this is less clear. One theory is that participating in challenging mental activities helps one build a "cognitive reserve." This reserve then acts as a safeguard that provides protection in the early stages of the disease. Another theory takes into consideration that the brain is

an instrument that is always changing. According to this theory, participating in challenging cognitive activities keeps the brain active and changing in a positive manner that helps prevent "decay" from occurring. A third theory is that dementia is a process that actually begins much earlier in life even though it's effects are not seen until late-life. This theory would argue that participating in challenging mental activities does not help stave off the disease but that those who are likely to get dementia are less likely to participate in these activities. In other words, these activities do not protect one from the disease; rather the disease makes it less likely that one would participate in these activities.

While it is difficult to know for sure how staying cognitively and physically active influences one's risk of dementia, we do know that keeping fit, both physically and cognitively, cannot hurt you. So keep up those activities.

Interesting Facts About AD

Provided by the Alzheimer's Association

- An estimated 4.5 million Americans have Alzheimer's disease
- The average lifetime cost of care for an individual with Alzheimer's is \$174,000
- Increasing age is the greatest risk factor for Alzheimer's. One in ten individuals over 65 and nearly half of those over 85 are affected
- Finding a treatment that could delay onset by five years could reduce the number of individuals with Alzheimer's disease by nearly 50 percent after 50 years
- Half of all nursing home residents have Alzheimer's disease or a related disorder
- From the time of diagnosis, people with Alzheimer's disease survive about half as long as those of similar age without dementia. Average survival time is affected by age at diagnosis and severity of other medical conditions.

The Brain and Alzheimer's Disease

By Tatiana Foroud, Ph.D. and Bernardino Ghetti, M.D.
Indiana University School of Medicine

During the past few decades, a great deal has been learned about the changes that occur in the brain of individuals who have late-onset Alzheimer's disease. While a diagnosis of Alzheimer's disease is often suspected while an individual is alive, the diagnosis can only be confirmed through careful examination of the brain after death.

The lack of communication between nerve cells (neurons) is the fundamental cause for the memory loss that is so characteristic of Alzheimer's disease. The two main pathologic abnormalities observed in the brain of patients with Alzheimer's disease are the senile (neuritic) plaques (see figure A) and the neurofibrillary tangles (see figure B). These abnormalities can only be seen with the aid of a microscope.

The core of the amyloid plaques contains a large amount of a protein called beta amyloid. The plaques are located in the space between the cell bodies of neurons. Typically, plaques are located in a part of the brain called the hippocampus, where memories are encoded, and in other regions of the cerebral cortex that are important for thinking and making decisions. The amyloid plaques are dense and do not dissolve. As an individual's disease worsens, the number of plaques increases and their distribution in the brain will often spread.

In contrast to amyloid plaques, which are located outside the neurons, neurofibrillary tangles are found inside the brain cells. In healthy cells, microtubules are involved in the transport of material inside cells. Tau is a protein that works with microtubules in this transport system. In Alzheimer's disease, tau is severely altered and begins to clump together to form tangles. As a consequence, there is an impairment of the transport system that eventually contributes to the death of the cell.

The presence of amyloid plaques and neurofibrillary tangles may be found in individuals who did not have any detectable

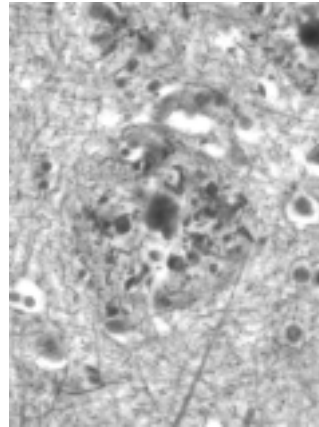


Figure A Senile plaque

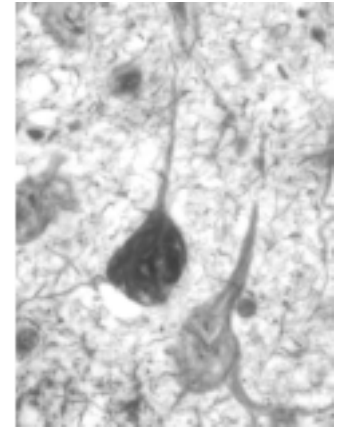


Figure B Neurofibrillary tangle

clinical symptoms of Alzheimer's disease during their lifetime. Therefore, it is critical to document the number of amyloid plaques and neurofibrillary tangles and where they are located in the brain. Neuropathologists have established several classification systems whereby they can grade the severity of the amyloid plaques and neurofibrillary tangles.

The National Cell Repository for Alzheimer's Disease has encouraged participants to consider examination of the brain at death. Through careful study, neuropathologists can definitively diagnose Alzheimer's disease if they observe the expected changes in the brain. The neuropathologist may in some instances learn that the individual did not have Alzheimer's disease but instead had another condition, related to Alzheimer's disease. It is also very valuable to examine the brain of an individual who did not show any symptoms of memory loss during life. This can be important knowledge for the family.

If you are interested in learning more about autopsy, please contact NCRAD at alzstudy@iupui.edu or 1-800-526-2839.

*Check Out Our
New Website!*

www.ncrad.org

The new NCRAD website, www.ncrad.org, is an online information center for anyone seeking information on the National Cell Repository for Alzheimer's Disease. The site has information for families wanting to get involved with NCRAD and the new NIA Alzheimer's Disease Genetics Study, links to related sites, and information on how to contact NCRAD staff.

There is also information on this website for researchers and coordinators who are involved in the NIA Alzheimer's Disease Genetics Study or who are interested in obtaining samples from NCRAD. The researcher and coordinator section of the website is password protected and only available to qualified researchers.

New Studies as Part of the National Cell Repository for Alzheimer's Disease

By Tatiana Foroud, Ph.D.
Indiana University School of Medicine

Changes in memory can occur at any time and in some instances may be an early finding 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. The National Cell Repository for Alzheimer's Disease 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.

To help scientists perform these studies, the coordinators at the National Cell Repository for Alzheimer's Disease, as well as other study staff involved in Alzheimer's disease research nationwide, participated in a training session that selected a short series of memory tests that can be administered either

in person or over the telephone. These questions will typically take about 30 minutes to complete. We hope to invite family members participating in the National Cell Repository for Alzheimer's Disease to participate in this new phase of our research study. We plan to contact family members to find a convenient time when we could ask you a series of questions. It will be important that individuals are seated in a quiet part of their home or office with minimal distraction. Because this is a research study, we will not be able to provide individuals any results of these tests. We hope to be able to administer these tests to individuals participating in our studies every few years.

As always, it is only through the active participation of families with Alzheimer's disease that we are able to make important strides that help us understand the genes that increase or decrease our risk for Alzheimer's disease.

RECOGNIZE THESE NAMES?

It is important to know that anyone can develop Alzheimer's disease; it discriminates against no one. Below is a list of famous people who have been diagnosed with AD.



Heston

Charlton Heston

Ronald Reagan

Norman Rockwell

Winston Churchill

Sugar Ray Robinson

Vincente Minnelli

E.B. White

Rita Hayworth

Charles Bronson

Aaron Copland



Robinson

NCRAD Attends Alzheimer's Disease Educational Conference

As in past years, the National Cell Repository for Alzheimer's Disease had a booth at The 12th National Alzheimer's Disease Educational Conference and, for the first time, The 9th International Conference on Alzheimer's Disease and Related Disorders held in Philadelphia, Pennsylvania July 17-21. The conferences gave NCRAD an opportunity to recruit both families and researchers to be a part of this vital research project. All three NCRAD coordinators (Michele Goodman, Valerie Parks, and Jessica Showalter) were present.

At the 12th National AD Educational Conference, the NCRAD staff was available to answer questions and provide study material to families interested in participating in our research studies designed to identify the genes that contribute to Alzheimer's disease. During the 9th International Conference on AD and Related Disorders, a three day event, the staff from NCRAD spoke with researchers from around the world who are studying Alzheimer's disease. Hundreds of researchers stopped by our booth and many expressed interest in using NCRAD samples to assist them in their research.

The staff from the National Institutes on Aging, including Drs. Marcelle Morrison-Bogorad, Tony Phelps and Marilyn Miller, were on hand to discuss the importance of the National Cell Repository for Alzheimer's Disease for genetics research.

Research Opportunities

Cholesterol Lowering Agent to Slow Progression (CLASP) of Alzheimer's Disease Study

- Purpose: To investigate the safety and effectiveness of simvastatin (a cholesterol lowering drug or statin) to slow the progression of AD.
- Eligibility: Ages 50+ with mild to moderate AD
- Locations: AL, AZ, CA, CT, DC, FL, GA, IL, IN, KY, MA, MI, MN, MS, MO, NY, NC, OR, PA, RI, SC, TX, VT, WA
- Contact: NCRAD staff
PH: 800-526-2839 (toll free)
E-mail: alzstudy@iupui.edu

VITAL – VITamins to Slow Alzheimer's Disease (Homocysteine study)

- Purpose: To determine whether reduction of homocysteine levels with high-dose folic acid, B6, and B12 supplementation will slow the rate of cognitive decline in persons with AD.
- Eligibility: Ages 55+ with probable AD
- Locations: AL, AZ, CA, CT, DC, FL, GA, IL, IN, MA, MI, NV, NJ, NY, OH, OR, PA, RI, SC, TX
- Contact: NCRAD staff
PH: 800-526-2839 (toll free)
E-mail: alzstudy@iupui.edu

Alzheimer's Disease Anti-Inflammatory Prevention Trial (ADAPT)

- Purpose: To study the ability of naproxen and celecoxib (non-steroidal anti-inflammatory medications) to delay or prevent the onset of AD and age-related cognitive decline.
- Eligibility: Healthy, ages 70+, family history of dementia (i.e. AD)
- Locations: AZ, FL, MD, MA, NY, WA
- Contact: Janette Negele,
PH: 206-277-6548,
E-mail: jnegele@washington.edu

Treatment of Agitation/Psychosis in Dementia/Parkinsonism (TAP/DAP)

- Purpose: To determine the efficacy (as well as safety, tolerability, and influence on parkinsonism) of quetiapine and donepezil, used alone or in combination, for the treatment of psychosis and/or agitation in patients with primary dementia complicated by coexistent parkinsonism.
- Eligibility: 50+, both genders, diagnosis of AD, symptoms of psychosis, agitation, parkinsonism
- Locations: AL, AZ, CA, GA, IL, MD, MA, MI, NV, NY, PA, TX, VT, WA
- Contact: Kimberly Schafer, M.S.
PH: (858) 622-5863
E-mail: kschafer@ucsd.edu

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

Valproate in Dementia (VALID)

- Purpose: To demonstrate whether valproate therapy delays the emergence of agitation and/or psychosis in outpatients with probable Alzheimer's disease (AD) who have not experienced agitation and psychosis in their illness. A secondary aim is to determine whether valproate therapy delays the progression of cognitive and functional measures of illness. This trial will also assess the tolerability and safety of low-dose, long-term valproate therapy.

- Eligibility: Ages 55 - 90 with probable AD
- Locations: CA, CT, DC, FL, GA, IL, MI, MO, NV, NY, OH, PA, RI, SC, TN, TX, VT, VA
- Contact: Laura Jakimovich, RN, MS
PH: 585-760-6578
E-mail: laura_jakimovich@urmc.rochester.edu

Huperzine A in Alzheimer's Disease

- Purpose: To evaluate the safety and efficacy of the Chinese herb huperzine A in the treatment of Alzheimer's disease (AD) in a randomized controlled trial of its effect on cognitive function.
- Eligibility: Age 55 + with probable AD, stable condition 3 months prior to screening. If interested, speak with contact about other eligibility requirements.
- Locations: AL, CA, DC, FL, GA, IL, NV, NJ, NY, NC, OR, PA, SC, TX
- Contact: Carolyn Ward, MSPH
PH: 202-784-6671
E-mail: jnegele@washington.edu

Did You Know?

- NCRAD has had participants from all 50 states.
- We have even had participants from Canada, Nigeria, Argentina, Guam, Puerto Rico, Philippines, Germany and Japan.
- Over 4500 participants have provided blood samples.
- Approximately 50 researchers are using NCRAD samples for their research.
- We have researchers located in Canada, Germany, Wales, and England.

Sources for Information and Support

Alzheimer's Association

<http://www.alz.org>
Tel: 312-335-8700 800-272-3900

Alzheimer's Disease Education and Referral Center (ADEAR)

<http://www.alzheimers.org>
Tel: 301-495-3311 800-438-4380
‡ ADEAR lists all 29 Alzheimer Disease Centers (ADCs) and their contact information.

Depression and Related Affective Disorders Association

<http://www.med.jhu.edu/drada>
Tel: 410-955-4647

Family Caregiver Alliance

<http://www.caregiver.org>
Tel: 415-434-3388 800-445-8106

National Parkinson Foundation

<http://www.parkinson.org/>
Tel: 305-547-6666 800-327-4545

Parkinson's Disease Foundation (PDF)

<http://www.parkinsons-foundation.org>
Tel: 212-923-4700, 800-457-6676

Society for Progressive Supranuclear Palsy

<http://www.psp.org>
Tel: 410-486-3330 800-457-4777

National Organization for Rare Disorders (NORD)

<http://www.rarediseases.org>
Tel: 203-746-6518 800-999-NORD (6673)

Centers for Disease Control and Prevention (CDCP)

<http://www.cdc.gov>
Tel: 800-311-3435

Creutzfeldt-Jakob (CJD) Foundation Inc.

<http://cjd.foundation.org>
Tel: 954-704-0519 305-891-7579

10 Signs of AD

1. Memory loss.
2. Difficulty performing familiar tasks.
3. Problems with language.
4. Disorientation to time and place.
5. Poor or decreased judgment.
6. Problems with abstract thinking.
7. Misplacing things.
8. Changes in mood or behavior.
9. Changes in personality.
10. Loss of initiative.

If you recognize several of these warning signs in yourself or a loved one, the Alzheimer's Association recommends consulting a physician. Early diagnosis of Alzheimer's disease or other disorders causing dementia is an important step in getting appropriate treatment, care, and support services.

For more information, call the Alzheimer's Association at (800) 272-3900.



INDIANA UNIVERSITY
SCHOOL OF MEDICINE

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975 West Walnut Street • IB 130
Indianapolis, Indiana 46202-5251