Volume 10 Issue 2

Winter 2003/2004

INDIANA ALZHEIMER DISEASE CENTER NEWSLETTER
INDIANA UNIVERSITY SCHOOL OF MEDICINE

Reflections

Does Staying Active Offer Protection Against Dementia?

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 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, 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.

Save the Dates…..
January 21, 2004
February 9th, 2004
February 11, 2004

See pages 8 and 9 for more details.

Does Staying Active Offer Protection Against Dementia?

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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 affects 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.

Memantine—A New Treatment for AD

Ann Marie Hake, M.D., Clinical Assistant Professor, Department of Neurology, IUSM

For the past 11 years, Alzheimer disease (AD) has been treated with cholinesterase inhibitors - tacrine (Cognex), donepezil (Aricept), rivastigmine (Exelon), and galantamine (Reminyl) - a group of medications that help memory by increasing the amounts of the brain chemical acetylcholine. 2004 will mark the beginning of a new era in the treatment of AD when a new drug becomes available in January. Approved by the FDA for the treatment of moderate to severe-stage AD in October 2003, memantine works by keeping excessive calcium from flowing into nerve cells in the brain while the nerve cells are at rest. When it is time for the nerve cell to be activated, memantine moves aside and allows the calcium to enter the cell. By allowing calcium into the nerve cell only during cell activation, memantine essentially reduces "background noise" in the brain and allows nerve cell signals to be transmitted more clearly. Memantine has been available for several years in Europe under the brand names "Ebixa", "Axura", and "Akatinol". Forest Pharmaceuticals will market memantine in the United States under the brand name "Namenda". In clinical trials, patients with moderate to severe-stage AD who were taking memantine declined at a slower rate than the patients on placebo (sugar pill). The most common side effects seen with memantine were dizziness, headache, confusion, and constipation, although most patients tolerated the medication without any problems. Taking memantine at the same time as a cholinesterase inhibitor did not decrease the effectiveness of either drug or cause any drug interactions, and it is expected that most people will take memantine in addition to the AD medications they are already taking. The starting dose for memantine is 5 mg daily; it is increased by 5 mg each week up to the target dose of 10 mg twice a day.

10 Warning Signs of Alzheimer Disease From the Alzheimer's Association

1. Recent memory loss that affects job skills
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

To Take Hormones or Not to Take Hormones?

Siu Hui, Ph.D., Biostatistician Indiana ADC

Some earlier studies have suggested that postmenopausal women who have chosen to be on hormone replacement therapy may have reduced cognitive decline. But this was not supported by the results of two recent clinical trials in which women were randomly assigned to take either estrogen or a placebo pill. In the first study of hysterectomized women with mild to moderate Alzheimer disease, the cognitive function of those assigned to hormone replacement therapy declined at least as fast as those assigned to placebo.[1] In the more recent Women's Health Initiative Memory Study, about 4500 women age 65 or older and free of dementia were randomly assigned to hormone replacement with estrogen plus progesterone or to placebo. The women receiving hormone replacement actually have a slightly greater cognitive decline and develop dementia more often than the women taking placebo.[2,3] There is no evidence that hormone replacement should be used to slow down cognitive decline or to prevent the onset of Alzheimer disease.

Other randomized studies have shown that hormone replacement therapy does not reduce your risk of some other major health problems. Indeed the Women's Health Initiative study shows that estrogen plus progesterone increases the risk of coronary heart disease, stroke, pulmonary embolism, and breast cancer, although the combination therapy reduces the risk of colorectal cancer and hip fracture.[4] So if you're going through menopause and suffering from hot flashes, what should you do? Most medical experts now recommend that hormone replacement therapy should not be used long-term for prevention of chronic diseases. Rather, it could be used for short-term relief of menopausal symptoms, especially hot flashes. There are non-hormonal treatments, such as clonidine and a class of antidepressants called selective serotonin reuptake inhibitors (SSRI), but they are generally less effective than hormone replacement in symptom relief. The use of soy products and other herbal supplements has at best inconsistent benefits.[5] Women who are considering treatments for their menopausal symptoms should discuss the various options with their physicians.

References:

1 Mulnard R et al., JAMA 2000, 283:1007-15.
2 Rapp SR et al. JAMA 2003, 289:2663-72.
3 Shumaker SA et al. JAMA 2003, 289:2651-62.
4 Writing Group for the Women's Health Initiative Investigators, JAMA 2002, 288:321-33.
5 Brewer D et al., J. Family Practice, 2003, 54:324-5.

Preventing Falls

Falls are a major source of concern for older people and their caregivers. While not all falls can be prevented, there are ways to reduce the chance of falling:

- Regular exercise is the most important as it increases flexibility and strengthens extremities.
- Most falls occur at home, keep floors clean.
- Remove small throw rugs.
- Use safety equipment in bathrooms.
- Wear shoes with good support.
- Have the doctor review your medicines regularly.
- Have your vision checked on a regular basis.
- Report any changes such as dizziness or blurred vision to your doctor right away.

Why Is Genetics An Important Area Of AD Research?

Tatiana Foroud, Ph.D.
Associate Professor of Medical and Molecular Genetics, Indiana University School of Medicine

During the past decade, many scientists have been carefully examining the role of genes in Alzheimer disease (AD). Through the careful comparison of the genetic material (deoxyribonucleic acid, DNA) inherited by family members who develop AD and those who do not, researchers have been able to identify three genes which have been implicated in AD. Changes in the DNA sequence of any of these three genes, presenilin 1 (PS1), presenilin 2 (PS2) and amyloid precursor protein (APP), can result in AD. Most individuals with an altered DNA sequence in these genes will develop AD at an earlier age, typically before the age of 60 years. Since most people develop AD at an older age, only 5% of individuals with AD have a mutation, or DNA sequence change, in one of these three genes.

A fourth gene, Apolipoprotein E (APOE), has been found to be an important gene in later onset AD. The DNA sequence of the APOE gene has been carefully studied and it has been shown that there are three relatively common forms or sequences of this gene. These have been termed APOE2, APOE3 and APOE4. Studies from many different researchers have shown that individuals who have inherited at least one copy of the APOE4 sequence are at higher risk of developing AD as compared to individuals who have only the APOE3 sequence, which is the most common. Individuals who have inherited at least one copy of the APOE2 sequence are at lower risk of developing AD as compared with those having inherited only the APOE3 sequence. Individuals who have inherited an APOE4 sequence are at higher risk of developing AD; however, unlike the DNA sequences in the PS1, PS2 and APP gene which can cause AD, the APOE4 sequence is considered a **risk factor rather than a cause of AD.** Thus, there are individuals who have inherited the APOE4 sequence but do not develop AD.

The search for genes that increase or decrease the risk for AD is an important area of scientific research. It is hoped that through the identification of these genes, researchers will be able to develop drugs that can counteract the negative effects of these genes. Some researchers are pursuing alternate approaches to develop treatments that might delay or improve the symptoms of AD. Some have attempted to use stem cell research. This is a very different type of research from that which seeks to identify genes that increase the risk of AD. The goal of stem cell research is to potentially replace the cells in the brain that have been altered and died. The promise of stem cell replacement as a treatment for AD is likely to be decades away.

Unfortunately, the media has called the search for genes and the use of stem cells as “genetic research”. Some have used the terms stem cell research and cloning interchangeably. No researchers have proposed to clone individuals as a means of treatment for AD. We must wait to see whether stem cell research will prove a useful therapy in AD. In the meantime, the identification of genes has been an immediate focus for many researchers who hope that this might more rapidly lead to better treatments for AD.

In order to identify genes increasing or decreasing the risk for AD, researchers must have DNA samples from individuals diagnosed with AD. It is also often important to have DNA from individuals who do not have AD. One of the easiest ways to obtain DNA is from a blood sample. To participate in research designed to identify the genes contributing to AD, individuals will typically be asked to provide medical records or complete a clinical evaluation to assess whether or not the individual has symptoms of memory loss or AD. In addition, individuals will also be asked for a blood sample, which will often be used to obtain DNA. Thus, through these relatively similar steps, individuals and families can provide critical information for researchers seeking to understand the genetics of AD.

Combination Therapy of Donepezil and Vitamin E in Alzheimer's Disease

Martin Farlow, M.D.
Director, IADC Clinical Core, Professor and Vice-Chairman for Research
Department of Neurology, Indiana University School of Medicine

Dr. Klatte and colleagues examined the rate of Alzheimer disease (AD) progression in patients followed through their facilities taking donepezil and vitamin E between the years 1997 and 2001, as compared to those not taking these medications between the years 1988 and 1996. The rate of deterioration was greater in patients who had not taken medications from 1988 to 1996. The implication from this study is that donepezil and/or vitamin E or the combination of both result in slowing disease progression. The problem is that several other factors which may contribute to the progression of AD have been modified or improved in the last decade and one of these other factors may be contributing to this slowed rate of progression in the more recently treated patients. In favor of this possibility, a number of double-blind placebo-controlled treatments for AD have recently been negative, and the problem has not been lack of drug effect, but rather a failure of expected deterioration to occur in patients in the placebo groups as was commonly seen in studies conducted earlier in the decade. Dr. Klatte and colleagues in the study acknowledged this possibility and mentioned widespread use of non-sedating drugs to control abnormal behaviors. Also, very real possibilities would be general folate supplementation to the diet, which has lowered homocysteine (a risk factor for AD) levels. Also statins which lower cholesterol levels are much more widely used and these drugs could also be slowing AD progression. Both statins and vitamins to delay AD progression are currently being studied in multi-center trials including our IADC. Regardless of the cause, general rates of progression are slowing, so physicians and patients seem to be doing something right. The challenge for most is to recognize which of the above factors is the most effective in modifying the disease and to launch research studies.

NIA Launches a New Alzheimer Disease Family Study

Tatiana Foroud, Ph.D.
Associate Professor of Medical and Molecular Genetics, Indiana University School of Medicine

The National Institute on Aging (NIA), a branch of the National Institutes of Health (NIH) has recently launched a new effort to help researchers identify the genes that play a role in the development of Alzheimer disease (AD). This national effort seeks to recruit 1,000 families with two or more living brothers or sisters who have been diagnosed with AD. Through the participation of such families, scientific researchers will be able to obtain the critical information they need to help them identify the genes that increase the risk for AD.

Family members will be seen at one of the 29 Alzheimer Disease Centers located throughout the United States. In some cases, an AD researcher may come to see a family member. Blood samples from participating individuals will be mailed to the National Cell Repository for Alzheimer Disease (NCRAD) here at Indiana University and stored with those samples from families who have already participated in genetic family studies. The blood sample will be used to obtain DNA (our unique genetic material) to create an immortalized cell line, which is a replenishable source of DNA.

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The faculty and staff of the Indiana Alzheimer Disease Center wish you a happy and peaceful holiday season.

I-CARE About AD Project Update

Susan Abbott, Project Manager

We have launched our new website. Please visit us at www.iupui.edu/~icaread. You can email any questions or comments to icaread@iupui.edu.

Three successful teleconferences have been held, all of which received very positive feedback. Dr. Lammers presented Medications Treatment and Management. Some of the comments we received included *"I think it was great." and "This is all new to me, and I found it very helpful."* The next teleconference is scheduled for February 9, 2004. Call 1-888-575-9624 to register for the teleconference. Jasper was the site of a very successful educational program. Dr. Karl Sash presented Understanding Memory Loss and Aging. The library project is progressing well. After surveying all of the public libraries in the state we have ordered copies of *The Forgetting, Alzheimer's Early Stages, A Dignified Life,* and *Speaking Our Minds* for each of them. The books will be distributed to the libraries during the holidays. Please look for them at your local library.

Thank you to all of our collaborators and program participants.

Holiday Gift Ideas

It is often difficult to figure out what to give at holiday time. If you have a family caregiver on your list, consider giving something that will offer them a much needed break in their day.

- Tickets to a movie, show or concert.
- "Respite visits" to give the caregiver some time off.
- Offer to run errands for the caregiver.
- Dinner out or dinner delivered to the home.
- Books, easy reads that will pass the time but not be to time consuming.
- Housekeeping tasks done or paid visits by a housekeeping service.
- Subscription to a favorite magazine.
- Coupon for 1 day at an adult day care for their loved one.
- Telephone gift coupon for long-distance calls to their friends and family members who live out of town.

For a person with AD or another dementing disorder, consider giving one of the following:

- A gift registration to Safe Return (call the Alzheimer's Association @ 1-888-575-9624).
- Regular visits at home or in the nursing home.
- A stuffed animal to hug.
- A picture album filled with old family photos.
- Exercise equipment such as a stationary bike, or a membership to a swimming pool.
- Comfortable, easy care clothing, slip on or velcro shoes with a non-slip sole.
- Music, tapes or old records.
- Books on tape, or record your own for them.
- Tickets to a musical or concert.
- Favorite foods.
- Home health care equipment, for example, home safety bars installed in the bath or shower.
- Lap robe.
- Bird feeder and bird food.

Do not give gifts that require a lot of care and attention. Keep in mind that expensive or fragile gifts can be broken or lost.

Upcoming Educational Programs

A Radio Segment

Sound Medicine
WFYI 90.1 Public Radio Station

Tune into WFYI at 12:00 noon on Saturday, January 10, 2004 to hear Dr. Mary Guerriero Austrom discuss caregiving and Alzheimer disease.

Contact Susan Abbott at 317-274-4939 for further information.

Caregiver Education

Mary Guerriero Austrom, Ph.D.
Understanding Aging, Memory Loss and AD

Wednesday, February 11, 2004
Ellettsville, IN
4:00 pm-6:00 pm

Contact Mary Ellen Wells
at 812-372-3755 for further information.

Sponsored by the I-CARE About AD Project

Teleconference

Claire Lewis, Elder Law Attorney
Financial and Legal Issues Facing Families Living with AD

An educational program in your living room!

Listen from the comfort of your own home via telephone to a 30 minute presentation about the financial and legal issues facing families living with Alzheimer disease. Discuss your concerns with the attorney during an hour-long question and answer session following the presentation.

Monday, February 9, 2004
7:00-8:30 p.m. (Indianapolis time)

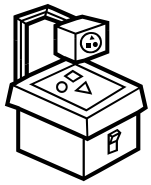
To register for further information contact the Alzheimer's Association at 888-575-9624.

Sponsored by the I-CARE About AD Project

Caregiver Education

Mary Guerriero Austrom, Ph.D.
Understanding Aging, Memory Loss and AD

Thursday, March 11, 2004
Huntington, IN
4:00 pm-6:00 pm



To register or for further information contact Melissa Barile at 260-420-5547.

Upcoming events….

The Forgetting
A Portrait of Alzheimer's

Premiering on PBS/WFYI
January 21, 2004
9:00 p.m.

PBS will present The Forgetting: A Portrait of Alzheimer's. This prime time two-hour national broadcast consists of a 90-minute documentary and half hour follow-up show that will direct viewers to useful resources. The documentary, based on David Shenks's critically-acclaimed book, weaves together the history and science of Alzheimer disease with powerful portrayals of families and individuals facing the disease, and highlights the race to find a cure.

The Indiana Alzheimer Disease Center at the IU School of Medicine is co-sponsoring this event, along with the Alzheimer's Association, CICOA, Family Service, Family Strengthening Coalition, Indiana Hospice and Palliative Care Organization, Senior Corps Senior Companions, and St. Vincent Hospice. Drs. Mary Guerriero Austrom and Hugh Hendrie from the Indiana Alzheimer Disease Center will be among local experts staffing the telephone help-lines on the evening of the broadcast. Please call in with your questions.

NIA Launches a New Alzheimer Disease Family Study

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

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In the coming months, we will be asking all families participating in genetic family studies to help us obtain the most complete information possible so that researchers can find the genes that increase and decrease the risk for AD. We are making an effort to obtain newer medical records for some families. We will also be asking some family members if they would be willing to complete a telephone questionnaire with a NCRAD staff member. As always, we will ask families to consider brain donation, which provides important information for AD research.

We have already had calls from many of you about this new initiative! We are pleased to hear how committed you are to research that will help us to understand AD better. We thank you for your past participation in the NCRAD and look forward to hearing from you. For more information, please call: 1-800-526-2839 or email alzstudy@iupui.edu.

In Memory….

The Indiana University Alzheimer Disease Research Fund gratefully thanks and acknowledges the following individuals for their generous contributions

From July 1, 2003 to present

In Memory of Eula Bowman
Mr. and Mrs. Roger D. Barnhart
Mr. and Mrs. Barbara Braun
Mr. and Mrs. Tom Bynum
Mr. and Mrs. Louis H. Gee
Mr. and Mrs. Brian LaMaster

In Memory of Patrick V. Buanno
Mr. and Mrs. Gerald W. Bishop
Mr. and Mrs. Adolph Brateman
Thomas Francia
Susan K. Johnson
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Beatrice Ochstein
John Rafacz
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Mr. and Mrs. Steven Sternberger
Mr. and Mrs. D.F. Tagtmeyer
Mildred M. Vachon

In Memory of Beverly Koerner
Portfolio Collection Service, Inc.

Benevolent Contributions
Mr. and Mrs. Jerome I. Heyd
Mr. and Mrs. Lawrence G. McCue
Johnson—Weaver Foundation
Mr. and Mrs. John D. Wolszon

In honor of your loved one, please consider a donation in their name.

Your contributions are gratefully accepted and are used to further research and education in the area of Alzheimer disease. Please make checks payable to: IU Foundation/Alzheimer Research. Forward to: 541 Clinical Dr. CL 590, Indiana University, Indianapolis, IN. 46202-5111. Donations to this fund are a wonderful way to remember or honor a loved one. Contributions are tax deductible. Call 317-274-4939 for information on making a bequest or a planned gift to this fund.

Is Alzheimer Disease in your family photo?

If there are two or more living members of your family suffering from serious memory loss, our researchers may be interested in your family.

Please contact the National Cell Repository for Alzheimer Disease (NCRAD) to learn more about this research opportunity.

E-mail NCRAD at alzstudy@iupui.edu or call 317- 274-7360 or 1-800-526-2839.

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INDIANA UNIVERSITY SCHOOL OF MEDICINE
WWW.PATHOLOGY.IUPUI.EDU/AD

Reflections is published by the Indiana Alzheimer Disease Center

EDITOR
Mary Guerriero Austrom, Ph.D.

CO-EDITORS
Bernardino Ghetti, M.D.
Hugh C. Hendrie, M.B., Ch.B.

Contributors in this issue:
Susan M. Abbott
Mary Guerriero Austrom, Ph.D.
Martin R. Farlow, M.D.
Tatiana Foroud, Ph.D.
Ann Marie Hake, M.D.
Siu L. Hui, Ph.D.
Daniel Rexroth, Psy.D.

EDUCATIONAL ASSISTANT
Susan M. Abbott

The editor welcomes your comments and letters
Indiana ADC Educational Core
IU Medical Center
541 Clinical Drive, Suite CL 590
Indianapolis, IN. 46202-5111
317.274.4939
maustrom@iupui.edu

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