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Indiana Alzheimer Disease Center Newsletter
Indiana University School of Medicine
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Reflections

iADC Indiana Alzheimer Disease Center

NIH News: Diabetes Linked to Increased Risk of Alzheimer's Disease in Long-Term Study

~ Reprinted with permission from the Alzheimer's Disease Education and Referral (ADEAR) Center at the National Institute on Aging.

Diabetes mellitus was linked to a 65 percent increased risk of developing Alzheimer's disease (AD), appearing to affect some aspects of cognitive function differently than others in a new study supported by the National Institute on Aging (NIA) at the National Institutes of Health. The findings, from the Rush Alzheimer's Disease Center's Religious Orders Study, add to a developing body of research examining a possible link between diabetes and cognitive decline. The results reported today are among the first to examine how certain cognitive "systems" - memory for words and events, the speed of processing information, and the ability to recognize spatial patterns-- may be affected selectively in people with diabetes.

The research, by Zoe Arvanitakis, M.D., David Bennett, M.D., and colleagues at the Rush University Medical Center in Chicago, IL, appears in the May 2004 issue of the Archives of Neurology. The investigators are part of the institution's Rush Alzheimer's Disease Center, headed by Dr. Bennett. The AD Center is one of 30 across the U.S. supported by the NIA to study and care for Alzheimer's patients.

"The research on a possible link between diabetes and increased risk of AD is intriguing, and this study gives us important additional insights," says Neil Buckholtz, Ph.D., head of the Dementias of Aging Branch in the NIA's neurosciences program. "Further research, some currently underway, will tell us whether therapies for diabetes may in fact play a role in lowering risk of AD or cognitive decline."

824 Catholic nuns, priests, and brothers participating in the Religious Orders Study were followed for an average of 5.5 years. They received detailed clinical evaluations annually, including neuropsychological testing of five cognitive "systems" commonly affected by aging, AD, and other dementias - episodic memory (memory of specific life events), semantic memory (general

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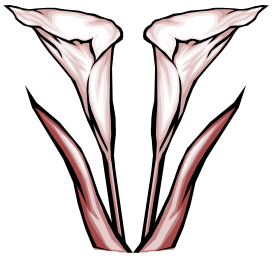

Save the Dates:

Upcoming I-CARE About AD Programs

August 23, 2004

November 8, 2004

November 10, 2004

February 7, 2005

See page 9 for more details.

Diabetes Linked to Increased Risk of AD

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knowledge), working memory (ability to hold and mentally rearrange information), perceptual speed (the speed with which simple perceptual comparisons can be made, such as whether two strings of numbers are the same or different), and visuospatial ability (the ability to recognize spatial patterns).

Over the study period, 151 of the participants had a clinical diagnosis of AD, including 31 who had diabetes. The researchers found a 65 percent increase in the risk of developing AD among those with diabetes compared with people who did not have diabetes.

In measures of cognitive function, only in the area of perceptual speed was there an association with an increased rate of decline over time, by about 44%, when comparing the diabetes and non-diabetes groups. Since stroke-related changes in the brain were found in a previous study to be tied to a decline in perceptual speed, the researchers could not say whether the link between cognitive decline and diabetes appeared because of the changes in the brain associated with Alzheimer's disease or those of some other common age-related condition like stroke or other vascular complications. Studies looking at pathological or brain imaging data would be needed to address these possibilities.

In other areas of cognition, the rate of change over the time period of the study was no different in the two groups. However, at the start of the study, the baseline cognitive function scores of people with diabetes were lower than those of people without diabetes.

"We found that diabetes was related to decline in some cognitive systems but not in others," says Dr. Arvanitakis of Rush, the lead author of the report. "Since all participants have agreed to brain donation at their deaths, we will have the opportunity to examine the pathologic basis of the association of diabetes to cognitive decline." The Rush researchers also expressed their indebtedness to the more than 1,000 nuns, priests, and brothers from across the U.S. participating in the Religious Orders Study.

The NIA is the lead Federal agency conducting and supporting research on Alzheimer's disease and age-related cognitive change. For more information, readers and viewers can visit the NIA's Alzheimer's Disease Education and Referral (ADEAR) Center at http://www.alzheimers.org or call toll-free 1-800-438-4380.

Information on aging generally may be viewed at the NIA's general website at http://www.nia.nih.gov or by calling the NIA Information Center at 1-800-222-2225.

For information on diabetes, see the website of the National Institute on Diabetes, Digestive, and Kidney Diseases (NIDDK), at http://www.niddk.nih.gov, or call the National Diabetes Information Clearinghouse, a service of the NIDDK, at 1-800-860-8747.

10 Warning Signs of Caregiver Stress

~adapted from the Alzheimer's Association

1. **DENIAL** about the disease and its effects on the person who's been diagnosed. "I know Mom's going to get better."

2. **ANGER** at the person with Alzheimer's disease or others; that no effective treatments or cures currently exist; and anger that other people don't understand what's going on. "If he asks me that question one more time I'll scream."

3. **SOCIAL WITHDRAWAL** from friends and activities that once brought pleasure. "I don't care about getting together with the neighbors anymore."

4. **ANXIETY** about facing another day and what the future holds. "What happens when he needs more care that I can provide?"

5. **DEPRESSION** begins to break your spirit and affects your ability to cope. "I don't care anymore."

6. **EXHAUSTION** makes it nearly impossible to complete necessary daily tasks. "I'm too tired for this."

7. **SLEEPLESSNESS** caused by a never-ending list of concerns. "What if she wanders out of the house or falls and hurts herself?"

8. **IRRITABILITY** leads to moodiness and triggers negative responses and reactions. "Leave me alone!"

9. **LACK OF CONCENTRATION** makes it difficult to perform familiar tasks. "I was
so busy, I forgot we had an appointment."

10. **HEALTH PROBLEMS** begin to take their toll, both mentally and physically. "I can't remember the last time I felt good."

If you are experiencing more than 2 of these symptoms please talk to your doctor, call our AD Center @ 317-278-0916 for an appointment, and call the Alzheimer's Association for a list of support group meetings in your area.

Pass this on to a caregiver you know!

Participants Needed for AD Research

~Martha Mendez, R.N., Clinical Core, Indiana ADC

Families Needed for Research on Alzheimer's Disease

Recent estimates indicate that the number of people with Alzheimer's disease (AD) will skyrocket in the next few decades- to as many as 13 million by 2050. Scientists are eager to speed research efforts to understand the causes and risk factors for AD to develop ways to treat or even prevent the disease.

This is a nationwide effort funded by the National Institute on Aging (NIA) and is supported by the Alzheimer's Association that includes 18 NIA-funded Alzheimer's Disease Centers working to identify 1,000 families with at least two siblings who have been diagnosed with late-onset AD (diagnosed at 60 years or older). Qualified researchers across the country have joined efforts to identifying families with multiple members affected with the condition in order to illuminate the underlying disease process of AD, open up novel areas of research, and identify new targets for drug therapy.

Currently, there are four known genes associated with AD. Three of the genes are associated with the early-onset form of the disease. This form of AD is inherited in an autosomal dominant pattern, meaning that the disease develops in family members in multiple generations. Mutations (changes) in these genes, known as presenilin 1 (PS1), presenilin 2 (PS2) and amyloid precursor protein (APP) are rare and are not associated with the much more common late-onset form of AD. The fourth gene associated with Alzheimer's Disease is the apolipoprotein E gene (APOE), which is referred to as a risk-factor or susceptibility gene. The ε4 variant is associated with an increased risk of developing AD.

AD genes as well as the genes for other human diseases have been located by studying families with multiple cases of the disease in question. It is very difficult to locate one risk factor gene out of the 30,000 or so genes that are contained within the human cell. Researchers believe that there are other risk factor genes for AD and they have identified regions in the human genome where these genes lie, but they have not been able to pinpoint exactly where and what these genes are. The further collection and analysis of families with multiple affected individuals will help identify these risk factor genes more clearly.

To be eligible to participate in the study, families must have at least 3 living members who can donate blood, including:

- 2 siblings (brothers or sisters) who developed AD after age 60, and
- Another family member over age 50 who may have memory loss OR a family member over age 60 who does not have any memory loss.
- If a family member is no longer living, but there is frozen autopsy tissue available, then the family may still be eligible.

Participation involves a neurological examination with cognitive testing or collection of medical records and the donation of a blood sample, which will be made into a cell line (a family of cells grown in the laboratory) that will enable the participant's DNA to be available to qualified scientists over many years. The cell lines and DNA will be stored at a centralized repository at Indiana University- the National Cell Repository for AD (NCRAD). Medical, demographic, and family history information will also be collected. There is no cost for those who join the study. An important aspect of the study is the confidential treatment of the genetic information collected from participants, all identifying information such as name and date of birth are removed from all materials.

To participate in the study, families should contact NCRAD toll-free at 1-800-526-2839, or by email alzstudy@iupui.edu. Information is also available through the study Website, www.ncrad.org

Participants Needed …

(Continued from page 4)

You can be a **VITAL** *part of the effort to slow Alzheimer's disease:*

A new nationwide research study—**VITAL** (**Vit**amins to slow **Al**zheimer's disease) - is looking for 400 volunteers to test whether taking high-dose supplements of vitamins B6, B12, and folate will slow the progress of Alzheimer's disease (AD).

People with AD have elevated levels of homocysteine ("ho-mo-SIS-teen") in their blood. Homocysteine is an amino acid that is produced in the human body. High-dose supplements of folate and vitamins B6 can B12 can lower homocysteine levels. Researchers will investigate whether a regimen of these vitamins might also stall the devastating effects of AD.

VITAL is sponsored by the Alzheimer's Disease Cooperative Study at the University of California, San Diego and funded by the National Institute on Aging, part of the U.S. Government's National Institutes of Health.

The **VITAL** study needs volunteers who:

- Have mild to moderate AD
- Are 55 years old or older
- Are fluent in English
- Are on stable medications for at least 4 weeks prior to screening visit
- Have a study partner—a friend or relative who can accompany the volunteer to all clinic visits and answer questions about him/her.

VITAL is a randomized, placebo-controlled research study, including two groups of unequal size: 60% of the participants will be assigned at random to receive daily high-dose supplements and 40% will receive identical placebo (inactive pill). Participants will be assessed regularly by physicians and qualified health care professionals during the 18-month study.

For more information, or to volunteer, call Martha Mendez, R.N. at (317) 278-9773.

How do Genetics and Stress Hormones Affect Memory?

Investigators at the Indiana University Center for Alzheimer's Disease and Related Disorders, 3124 University Hospital Outpatient Center, are seeking research volunteers with and without memory problems to participate in research designed to solve the mystery of how genetics and stress hormones affect memory.

We are looking for male and female volunteers between the ages of 65 and 90 who are:

- In good general health
- Non-smokers
- Without chronic lower back problems
- Living at home or in an assisted living facility

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Participants Needed …

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How do Genetics and Stress Hormones Affect Memory?

(Continued from page 5)

Depending on your qualifications, the study involves:
- 2 visits to the Indiana University Center for Alzheimer's Disease and Related Disorders
- Having one (1) lumbar puncture (spinal tap)
- A blood draw to see which version of a gene you have

Participants will be asked a series of questions that are designed to evaluate memory, thinking capacity and mood. Participants will receive $200 compensation after the lumbar puncture. Risks will be disclosed prior to the study enrollment.

For more information, or to volunteer, call Martha Mendez, R.N. at (317) 278-9773.

Can Cholesterol-Lowering Drugs Help Slow Alzheimer's Disease? Give us a hand to find out.

Cholesterol-lowering drugs (also called "statins") are effective weapons in the fight against heart disease. Now some evidence suggests that statins may also be able to slow the devastating effects of Alzheimer's disease (AD) on the brain.

The Alzheimer's Disease Cooperative Study, a group of research centers sponsored by the U.S. Government's National Institute on Aging, is launching **CLASP** (**C**holesterol **L**owering **A**gent to **S**low **P**rogression of Alzheimer's Disease), a research study to find out more about the effect on AD of one statin, called simvastatin (Zocor).

The **CLASP** study is seeking volunteers who:
- Have mild to moderate AD
- Are age 50 or older
- Speak English
- Do not currently take or need cholesterol-lowering drugs
- Have a study partner—a friend or relative who can accompany the volunteer to all clinic visits and answer questions about him/her.

CLASP is a randomized, placebo-controlled research study. Half of the participants will be assigned at random to receive the experimental drug, the other half will receive placebo (inactive pill). Participants will be assessed regularly by physicians and qualified health care professionals during the 2-year study.

For more information, or to volunteer, call Martha Mendez, R.N. at (317) 278-9773.

Alzheimer's Disease Medications Fact Sheet

~ Reprinted with permission from the Alzheimer's Disease Education and Referral (ADEAR) Center at the National Institute on Aging.

Five prescription drugs currently are approved by the U.S. Food and Drug Administration to treat people who have been diagnosed with Alzheimer's disease (AD). Treating the symptoms of AD can provide patients with comfort, dignity, and independence for a longer period of time and can encourage and assist their caregivers as well. It is important to understand that none of these medications stops the disease itself.

Treatment for Mild to Moderate AD

Four of these medications are called cholinesterase inhibitors. These drugs are prescribed for the treatment of mild to moderate AD. They may help delay or prevent symptoms from becoming worse for a limited time and may help control some behavioral symptoms. The medications are: Reminyl® (galantamine), Exelon® (rivastigmine), Aricept® (donepezil), and Cognex® (tacrine). Scientists do not yet fully understand how cholinesterase inhibitors work to treat AD, but current research indicates that they prevent the breakdown of acetylcholine, a brain chemical believed to be important for memory and thinking. As AD progresses, the brain produces less and less acetylcholine; therefore, cholinesterase inhibitors may eventually lose their effect.

No published study directly compares these drugs. Because all four work in a similar way, it is not expected that switching from one of these drugs to another will produce significantly different results. However, an AD patient may respond better to one drug than another. Cognex® (tacrine) is no longer actively marketed by the manufacturer.

Treatment for Moderate to Severe AD

The fifth approved medication, known as Namenda® (memantine), is an N-methyl D-aspartate NMDA) antagonist. It is prescribed for the treatment of moderate to severe AD. Studies have shown that the main effect of Namenda® is to delay progression of some of the symptoms of moderate to severe AD. The medication may allow patients to maintain certain daily functions a little longer. For example, Namenda® may help a patient in the later stages of AD maintain his or her ability to go to the bathroom independently for several more months, a benefit for both patients and caregivers.

Namenda® is believed to work by regulating glutamate, another important brain chemical that, when produced in excessive amounts, may lead to brain cell death. Because NMDA antagonists work very differently from cholinesterase inhibitors, the two types of drugs can be prescribed in combination.

Dosage and Side Effects

Doctors usually start patients at low drug doses and gradually increase the dosage based on how well a patient tolerates the drug. There is some evidence that certain patients may benefit from higher doses of the cholinesterase inhibitor medications. However, the higher the dose, the more likely are side effects. The recommended effective dosage of Namenda® is 20 mg/day after the patient has successfully tolerated lower doses.

Patients may be drug sensitive in other ways, and they should be monitored when a drug is started. Report any unusual symptoms to the prescribing doctor right away. It is important to follow the doctor's instructions when taking any medication, including vitamins and herbal supplements. Also, let the doctor know before adding or changing any medications.

(Continued on page 8)

AD Medications Fact Sheet (Continued from page 7)

~ Reprinted with permission from the Alzheimer's Disease Education and Referral (ADEAR) Center at the National Institute on Aging.

For More Information

To learn about support groups, services, research centers, and publications about AD, contact the following groups:

Alzheimer's Association
225 N. Michigan Avenue, Suite 1700
Chicago, IL 60601
1-800-272-3900
Website: www.alz.org
This non-profit association supports families and caregivers of patients with AD. Nationwide chapters provide referrals to local resources.

Alzheimer's Disease Education and Referral (ADEAR) Center
PO Box 8250
Silver Spring, MD 20907-8250
1-800-438-4380
Website: www.alzheimers.org
This service of the National Institute on Aging offers information and publications on diagnosis, treatment, patient care, caregiver needs, long-term care, and research related to AD.

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Public Health Service
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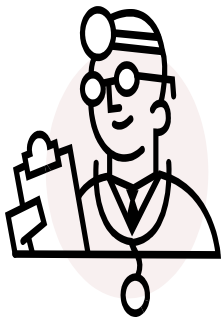
NIH Publication No. 03-3431
January 2004

Ask the Specialist…

Martin R. Farlow, M.D., Leader, Clinical Core, Indiana ADC



Question: If my mom is taking Aricept, should we switch to Nemenda? Is the new drug better?

Answer: If your mother is having adverse effects with Aricept such as nausea, vomiting, diarrhea, then consideration could be given to switching to the new medication which in general does not have the same pattern of cholinergic side effects, particularly gastrointestinal side effects as do the cholinesterase inhibitors. If your mother was doing well on Aricept, consideration could be given to adding Namenda, as one of the large double blind trials that helped gain Namenda FDA approval showed that adding the drug to patients already on established Aricept resulted in significant additional improvement in cognition, function in activities in daily living, and prevention of the new onset of behavioral abnormalities.

Dr. Mary Guerriero Austrom Honored

by Hugh C. Hendrie, M.B, Ch.B., D.Sc. , Associate Director, Indiana ADC

Mary Guerriero Austrom, Ph.D.

During the past academic year, Dr. Mary Austrom, Leader of the IADC Education Core, received two honors from Indiana University. She was a recipient of the Glenn W. Irwin MD, Jr. Experience Excellence Award for outstanding service to the community and was elected a member of the prestigious Faculty Colloquium on Excellence in Teaching in recognition of her distinguished teaching contributions.

In their acknowledgments, the Irwin Award Committee stated:
Dr. Austrom is an extraordinary woman who possesses remarkable charisma and the unique ability to make organizations and groups function more efficiently and effectively. Her service goes well beyond her role as a faculty member. IUPUI and the School of Medicine have benefited greatly from her continued commitment to the Alzheimer's cause and is indeed fortunate to have her leadership and dedication in meeting the needs of the Alzheimer's population in the state of Indiana.

The nominating letter for the FACET award stated:
Dr. Austrom is an extraordinarily creative and talented teacher who has a great ability to motivate and excite her students about learning. She has continuously sought to create new methods and approaches to education. In her collaborative state funded education initiative for caregivers with the Alzheimer's Association, she has developed programs which incorporate distance learning technologies including teleconferences and videoconferences across the 8 IU campuses. In her role as Education Director for our IADC, she has developed a highly innovative teaching manual (train-the-trainer model) for nursing home professionals.

Those who know Mary recognize the appropriateness of these awards and will, I am sure, join our faculty in congratulating her.

I-CARE about AD Project Upcoming Programs

August 23, 2004 - 6:30pm-8:30pm
Dealing with the Emotional Rollercoaster of Caregiving
Speaker - Mary Guerriero Austrom, Ph.D.

November 8, 2004 - 6:30-8:30pm
AD Prevention: How to Maintain Your Brain
Speaker - Hugh C. Hendrie, M.B., Ch.B., D.Sc.

February 7, 2005 - 6:30-8:30 pm
An Overview of Mild Cognitive Impairment and Dementia
Speaker - Fred Unverzagt, Ph.D.

Dr. Mary Guerriero Austrom will be in Terre Haute on November 10, 2004, 4:30p.m.
Caring and Coping through the Holidays
Landsbaum Center for Disease Education, 1433 N. 6 1/2 St., Terre Haute, IN

For more information, or to register, call the IADC Education Core at (317) 274-4939.

In Memory….

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

from January 1, 2004 to present

In Memory of Betty J. Brown
Mr. and Mrs. Tom Armstrong
Mr. and Mrs. Dean Ausban
Mr. and Mrs. Francis Deford
Mr. and Mrs. Ralph Hughes
Francis Humbarger family
Mr. Mike Myers
Mr. and Mrs. Raymond Romein
Mary Carroll & Larry Sparks
Mr. and Mrs. Gordon Stevens
Mr. and Mrs. Lanny Stevens
Ms. Joann Vinnco

In Memory of Bonnie Bruce
The Overhead Door Company

In Memory of Gertrude Burress
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Mr. and Mrs. Bill Davis

In Memory of Victoria Grand
Ms. Sally A. Simic-Auguano

In Memory Odell Gray
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Eta Pi Kappa Sorority
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In Memory of Helen L. Malone
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Ms. Dorothy Coleman
Employees of DFAS-HR/Learning & Development Division
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Mr. and Mrs. Wallace Howard
Ms. Geraldine Sherrell

In Memory of Cleo M. McDivitt
Mr. and Mrs. James Anthony
Ms. Sandra J. Barnes
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In Memory of John P. McGovern
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In Honor of Sarah Roush
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Ms. Mildred S. MacDonald
Dr. and Mrs. Joseph L. Steinem
Ms. Opal Campbell

Inaugural Regional Conference on Alzheimer's Disease

~ Katie Cavanaugh, M.S.

Alzheimer's Disease: Translating Research Into Practice

On June 25, 2004 the Indiana Alzheimer Disease Center hosted the **Inaugural Regional Conference on Alzheimer's Disease** held at the University Conference Center on the IUPUI campus in Indianapolis. Organizers (Mary Guerriero Austrom, Ph.D., Carol J. Farran, D.N. Sc., R.N., Sara Holmes, M.P.H., Darby Morhardt, M.S.W., Tom Meuser, Ph.D., and David Wekstein, Ph.D.) invited faculty from the six Midwest NIA-funded Alzheimer Disease Centers (at Indiana University, University of Kentucky, University of Michigan, Northwestern University, Rush University Medical Center, and Washington University). The conference brought together nationally and internationally renowned clinicians and researchers to translate the latest research findings into a practical format to apply in the clinical setting. The event was an overwhelming success. Future conferences will be hosted by the participating Alzheimer Disease Centers on a rotational basis. Next year—St.

Hugh C. Hendrie, M.B., Ch.B., D.Sc. gave the welcoming address and spoke on risk factors associated with Alzheimer's disease.

William R. Markesbery, M.D. Addressed the current status of Alzheimer's disease research.

Ann Marie Hake, M.D. addressed the latest treatments for AD.

Sandra Weintraub, Ph.D. spoke on profiles of non-AD dementia: Neuro-psychology, Neuroanatomy, and Neuropathology.

Neelum T. Aggarwal, M.D. spoke on mild cognitive impairment and AD.

Organizers David Wekstein, Ph.D. and Mary Guerriero Austrom, Ph.D. with Neelum Aggarwal, M.D.

Hugh Hendrie, M.B., Ch.B., D. Sc., David Wekstein, Ph.D., Neelum Aggarwal, M.D., and Fred Unverzagt, Ph.D.

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.

INDIANA ALZHEIMER DISEASE CENTER NEWSLETTER

INDIANA UNIVERSITY SCHOOL OF MEDICINE

VISIT OUR WEBSITE

WWW.IADC.IUPUI.EDU/

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.

Reflections is published by the Indiana Alzheimer Disease Center

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The editor welcomes your comments and letters

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