Volume 8 Issue 2

Spring 2002

INDIANA ALZHEIMER DISEASE CENTER NEWSLETTER
INDIANA UNIVERSITY SCHOOL OF MEDICINE

Reflections

Dr. Hugh C. Hendrie on Capitol Hill

On February 12, 2002 the Congressional Black Caucus held a press conference and briefing at the U.S. Capitol to raise awareness about Alzheimer disease in the African-American community. Congresswoman Edie Bernice Johnson (D-Tx), Congressman Ed Markey (D-Ma), Delegate Dr. Donna Christian-Christensen (D-VI), Orien Reid, Chair of the National Board of Directors of the Alzheimer's Association, and IU School of Medicine Professor Hugh C. Hendrie addressed members of Congress, their staffs, the media and representatives of the National Institute on Aging. Attending with Dr. Hendrie were Millicent Pettaway, a clinical research nurse with the Indianapolis Study of Health and Aging, Evelyn Mason, a study participant, and Dr. Valerie Smith-Gamble, an assistant professor of clinical psychiatry at the IUSM. Dr. Hendrie and his colleagues discussed their study of Alzheimer disease in African-Americans in Indianapolis and Yoruba in Ibadan, Nigeria.

Representative Johnson, a former nurse, chairs the Congressional Black Caucus. Representative Markey is Co-Chair of the Congressional Task Force on Alzheimer's Disease. Delegate Dr. Christian-Christensen is the first female physician in the history of the U.S. Congress and chairs the Congressional Black Caucus' Health Braintrust.

L to R: Congressman Ed Markey, Congresswoman Edie Bernice Johnson, Orien Reid, Delegate Dr. Donna Christian-Christensen and Dr. Hugh C. Hendrie.

Vaccine Trial for Alzheimer Disease is Stopped

Martin R. Farlow, M.D.

A large, multi-center trial involving approximately 400 to 500 people in Europe and the United States was recently started to see if vaccinating patients with the Abeta protein (the same protein that makes up the core of amyloid plaques in Alzheimer disease) would help in treating the illness. Previous transgenic mouse studies suggested that vaccination could prevent the plaques from forming or even make many of the formed plaques disappear. Unfortunately, 12 individuals have now developed inflammation of the brain (encephalitis) in this trial and the study was stopped. It seems unlikely that it will be restarted soon. This does not mean, however, that in the future antibody approaches to the treatment of Alzheimer disease will not be effective. Indeed, several pharmaceutical companies and institutions are actively pursuing this approach to therapy.

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Therapeutic Research in Alzheimer Disease and Other Cognitive Disorders at Indiana University

Martin R. Farlow, M.D.

Progress has been made over the last decade in treating Alzheimer disease (AD) with four drugs now approved by the FDA and available for treatment. Unfortunately, these medications modestly improve symptoms in some patients but don't stop the underlying disease process. All of the current drugs are cholinesterase inhibitors that work in basically the same way. There is a great need for drugs or other approaches that will work by different mechanisms, both to add to current therapy and also to potentially help those who are not currently benefiting from treatment. The Center for Alzheimer's Disease at Indiana University Hospital in Indianapolis has numerous ongoing programs including several new studies that are actively looking for volunteers to participate. These studies include:

Phase II Alzheimer disease Trial
A drug is being tested that selectively acts on a subset of benzodiazepine receptors in the brain to potentially improve memory and attention. This is a Phase II double-blind, placebo-controlled trial that is looking for patients with mild to moderate stage AD.

Phase II NMDA Receptor Inhibitor Trial
A drug that partially antagonizes the NMDA receptor inhibiting free radicals and potentially preventing the death of neurons is being tested. The Phase II drug study is enrolling patients with mild to moderate stage AD, but allows them to remain on cholinesterase inhibitors.

Severe Stage Dementia Trial
In two large multi-center trials, a drug called memantine has been found to slow progression of AD in patients with moderate to severe stage of this disease. We are recruiting volunteers with AD for a new large multi-center, double-blind, placebo-controlled Phase III trial of this drug. People with moderate to more severe stages of the disease are needed.

Cholinesterase Inhibitor Titration Trial
Volunteers are being recruited for a trial that is underway using one of the available cholinesterase inhibitors; raising the dose either faster or more slowly over time to see which gives the greatest benefit with the fewest side effects.

Shunt Trial
Investigators at Indiana University are recruiting patients for a nationwide trial that involves the implantation of a low flow cerebrospinal fluid shunt. Some previous studies have suggested cerebrospinal fluid drainage may be decreased in patients with AD. It has been hypothesized that this may contribute to the build-up of beta-amyloid plaques. The shunt would increase drainage of cerebrospinal fluid in study subjects. This study allows patients to remain on cholinesterase inhibitor therapy and is recruiting patients in good general health and with mild to moderate stage AD.

Vascular Dementia Trial
Recent data have suggested that many patients with dementia related to strokes may have neurotransmitter deficiencies similar to AD patients and that cholinesterase inhibitors may also be effective in this form of dementia. Two trials are currently enrolling patients with mild to moderate stage dementia related to multiple strokes (vascular dementia), a condition for which there are no approved therapies.

Mild Cognitive Impairment Trial
Patients who do not yet have AD but rather mild cognitive impairment are being recruited for a drug study. Individuals with mild cognitive impairment have memory problems, but are generally not significantly impaired in their activities of daily living. No drugs are currently approved for treating this condition. The drug being tested in this study has shown promise in preliminary research for improving symptoms of memory loss.

Primary Prevention Study with Healthy Elderly
Finally, the Center for Alzheimer's Disease is recruiting **healthy elderly volunteers**, not to participate in a drug study, but rather to help us develop a standardized neuropsychological test battery that will be used in future studies of drugs that would prevent AD from occurring in the first place.

As can be seen by the studies listed above, much effort is going into finding better treatments for these devastating illnesses. With the help of past and future participants and volunteers, rapid progress is being made.

If you are interested in obtaining further information and/or participating in any of these studies, please call 317-278-0916.

Please note: In the last *Reflections* newsletter, article Elderly with Dementia May Face Greater Risk of Alzheimer Disease, should have read: Elderly with Cognitive Impairment May Face Greater Risk of Alzheimer Disease. We apologize for any inconvenience this may have caused.

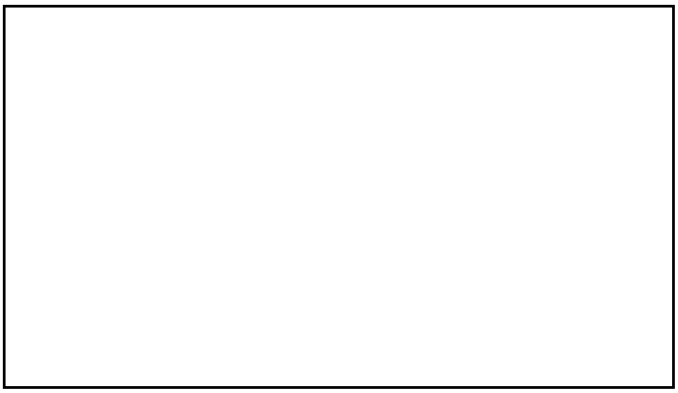
Helping Your Loved One Enjoy the Outdoors Safely

Mary Guerriero Austrom, Ph.D.

Sitting outside or walking and enjoying nature is a wonderful activity for anyone at any age. It can be especially rewarding for people with Alzheimer disease (AD) provided a few simple steps are taken to ensure their safety, whether it is in their own back yard or in the outdoor gardens at a nursing home.

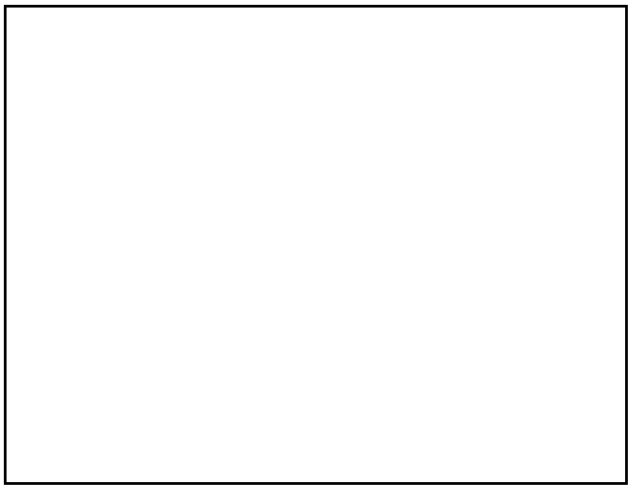
Following are some ideas for creating special outdoor areas as well as tips for safety proofing the garden.

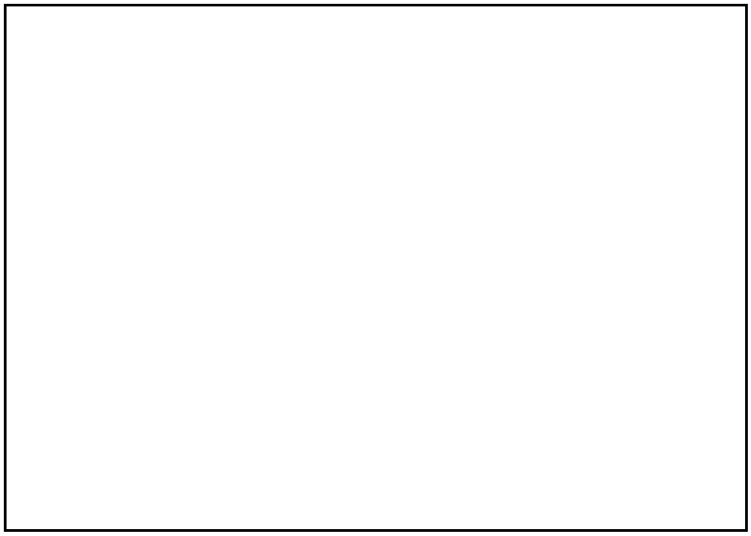
- The garden should be fenced to ensure safety, especially if the person might wander away.
- Make sure there is comfortable seating available. It should be stable and easy to get in and out of. Create a small grouping of seats so that it encourages friends and family members to join him/her and will make visits and conversations easier.
- Place seats away from noisy distracting areas such as air conditioners, which can make conversation difficult.
- Seats should also be protected from the sun and bad weather. In the case of sudden rain shower, the person may not be able to move quickly or could get hurt trying to rush inside.
- Position the seats so that they are easily visible from the inside so that someone can keep an eye on him/her.
- If the person enjoys wildlife install a birdbath and birdfeeder to attract birds and squirrels.
- If they enjoy watching children, place their seat near the sandbox or children's swings.
- If the person enjoys gardening and is still able to participate, plant a vegetable and/or flower garden and encourage them to care for it.
- If the person used to enjoy golf, set up a putting area.
- Eliminate dangerous obstacles in the garden such as garden hoses, tools, or toys left on paths.
- Look for tree roots that may have lifted walkways. Repair winter damage.
- Make sure paths are made of solid materials, especially if the person relies on a cane, walker or wheelchair (stepping stones and gravel are difficult to maneuver).
- Keep thorny bushes and trees such as roses and hawthorns away from paths.
- Remember to use sunscreen and avoid prolonged contact with the sun between 10:00 am and 3:00 pm.
- Drink plenty of fluids to keep hydrated.
- Enjoy the nice weather.



"I really appreciate the presentations because now I know a lot more about science."

"If I ever go to IU Medical School, I will always remember you doctors when I become a famous obstetrician or veterinarian."





"I've always been interested in human bodies and what is inside of them. Now I am sure I want to be a pathologist."

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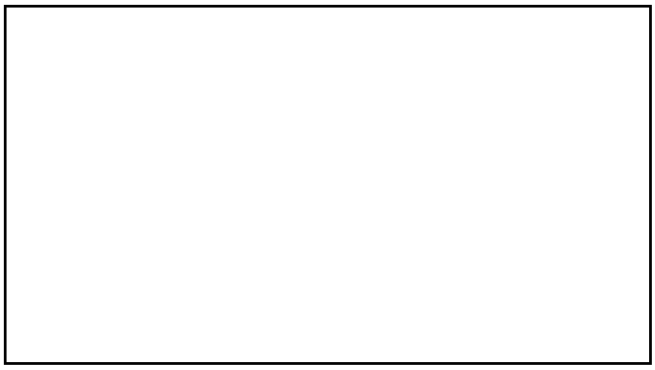
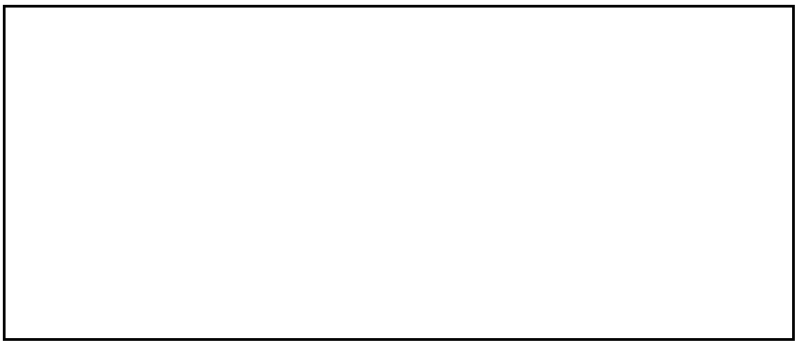
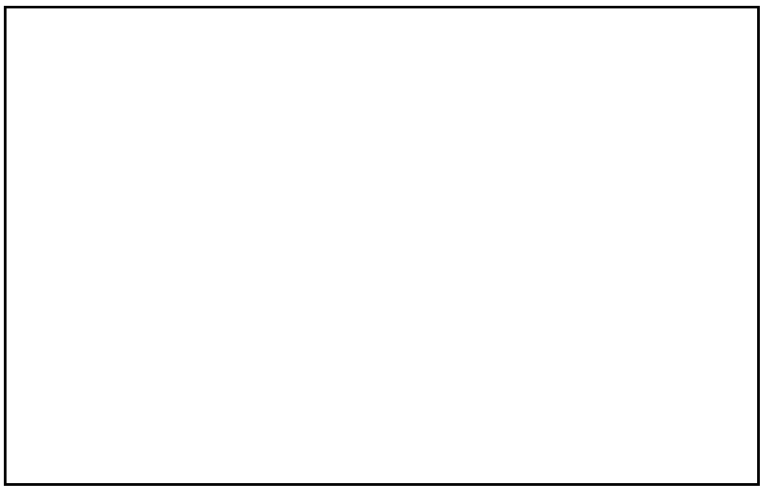


"Thanks a lot for volunteering your time to teaching us at Craig about pathology and cells."

Future Neuroscientists Spend the Day at the Indiana ADC

Science students from Craig Middle School's Immersion Program enjoy the opportunity to explore neuroscience with Drs. Ghetti, Dlouhy and Piccardo





"We talked a lot about genetic diseases, how they affect your body, your actions and your every-day life. One disease was the mad cow disease."

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In Memory....

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

Spring - 2002

In Memory of Barbara Brinduse
Ms. June C. Anderson
Mr. Paul A. Higdon

In Memory of Jean Carlson
Mr. & Mrs. Henry Blazek
Chatham High School Class of 1949
Mr. & Mrs. Paul J. DiPaola
Ms. Doris R. Lissaman
Mr. & Mrs. John G. Pomery
Ms. Jane VanZandt

In Memory of Eileen Clements
Mr. John Clements

In Memory of Ruby A. Penden Fox
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Ms. Luanne M. Wright

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In Memory of Elton M. Rock
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Mrs. Alice Wright
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In Memory of Marjorie J. Wasson
Dr. Charles M. Frankhouser, Jr.
Mr. & Mrs. L'Dea Handy

In Memory of Margaret Wooldred
Atlas Capital Management Corp.

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Ms. Lynette R. Bortis
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World of Wisdom, Inc.

In honor of Memorial Day consider a donation in memory of your loved one, or to honor a brave veteran.

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 Alzheimer's Disease Research Fund. 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 memory loss, our researchers may be interested in your family.
Please contact Jami Stuck to learn more about the National Cell Repository.
317- 274-7360
1-800-526-2839

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You Asked Us…

Q. How and when was Alzheimer disease first discovered?

A. Alzheimer disease (AD) was named after Dr. Alois Alzheimer, who first encountered it in 1901. His patient was only 51 years old, so for a long time people thought that AD affected people before the age of 65 and was therefore called *presenile dementia*. Older people were said to have *senile dementia*. As it turns out, it is really the same disease, no matter how old you are when you get it, however, AD is a lot more common in older people.

When Dr. Alzheimer's patient died in 1906, he examined her brain under the microscope and presented a report of his findings at a psychiatric conference later that year. In 1907, Dr. Alzheimer's paper was published and we have the first report of AD in medical literature. He described both of the abnormalities that are seen in the brains of people with AD, which is why someone named the disease after him in 1911. He discovered that the brain had deposits of a sticky protein called *amyloid* (it was called that because it looked like starch under a microscope, but it's really a protein) that had formed into globs in the brain tissue and damaged the nerve cells around them. The globs of protein and dead nerve cell pieces are called *plaques* and they had been seen in the brains of other patients with similar problems.

Q. What happens in the brain once you get plaques and tangles?

A. In the century since Dr. Alzheimer first described the disease, a lot more has been learned about how plaques form. Brain cells manufacture a long protein called *amyloid precursor protein (APP)* that is then cut up into different pieces. These pieces all have their own jobs, although we are still trying to learn exactly what those jobs are. It is thought that some of the jobs may include protecting the nerve cell and regulating the activity of its genes. The way the APP gets cut up is that after it is made, it starts moving outside of the cell (kind of like a needle and thread being pulled through a piece of cloth.) As it comes through the cell membrane, enzymes called *secretases* are waiting to cut the protein at the appropriate spot. The name of the main enzyme in the normal brain is called *alpha-secretase*, and the pieces formed after it cuts the APP are soluble in water and spinal fluid.

There are also two other enzymes called *beta-secretase* and *gamma-secretase* that can also cut the APP instead of *alpha-secretase*; if they do, the pieces formed are not soluble. The protein formed is called *amyloid beta-protein* (also called *a-beta* or *beta-amyloid*) and it's the sticky protein that gloms together, kills nerve cells, and makes plaques. Everybody makes a little bit of *a-beta*, but usually the body can keep up with it and clear it out before it has a chance to make plaques. When the body can't keep up with it, it starts to build up and plaques start to accumulate. That's why the disease gets more common as people get older.

Dr. Alzheimer was the first person to describe the other thing that goes wrong with nerve cells in AD, *neurofibrillary tangles*. These form when the skeleton of the nerve cell gets twisted and kinked. Some of the tubules that make the cell skeleton are put together like ladders or railroad tracks. If the rungs of the ladder (called *tau* protein) get too much phosphorus stuck to them, the ladder twists and the cell structure collapses. Also, the normal cell uses the tubules as railroad tracks to transport nutrients and the molecules that the cell makes, so if the tubules kink, everything gets derailed and the cell dies.

Both the plaques and the tangles tend to start first in the areas of the brain called the hippocampus and the entorhinal cortex. These parts of the brain are necessary for forming memories. They act like the "save" function on your computer; you can type all you want, but if you don't press "save", it won't be stored on the hard drive and all of your typing will be gone the next time you turn on your computer. As the disease gets worse, the plaques and tangles gradually spread to the rest of the brain.

Q. How old do you have to be to get AD and how long does the disease last?

A. AD occurs most often in elderly people, but there have been a couple of very rare cases described in people in their late teens and twenties. The official estimate of the average length of time that people live after they get diagnosed with AD is 8 years, although I suspect it may be longer now since we are recognizing and diagnosing AD earlier. Some people have lived 25 years or more after diagnosis.

Ann M. Hake, M.D., is a clinical assistant professor of Neurology at I.U. School of Medicine.

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Save the Date: October 4, 2002 Save the Date: October 4, 2002 Save the Date: October 4, 2002

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Alzheimer Disease: Burden, Progress, and Hope

A CME program for physicians
An educational program for families and professionals
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Riley Outpatient Center Auditorium
I.U. School of Medicine
Indianapolis, IN
8:00 a.m. to 4:00 p.m.
Lunch provided
Call 317-274-8353 to register or for additional information.

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