

# Georgetown University Medical Center Memory Disorders Program Semi-Quarterly Newsletter



VOLUME 1, ISSUE 1

NEWSLETTER DATE: NOVEMBER, 2005

## A Second Go Around for the Alzheimer's Vaccine?

Georgetown's Memory Disorders Clinic begins a second generation immunotherapy trial. Georgetown was selected as one of the 30 sites, nationwide to participate in a Phase II trial of a novel treatment. The treatment consists of an antibody that is infused intravenously (a process known as passive immunotherapy).

In Alzheimer's disease, a protein fragment called amyloid accumulates in the brain, leading to the damage to brain cells associated with the symptoms of dementia. Several years ago, Elan Pharmaceuticals developed a vaccine against amyloid that showed great promise in animal testing.

Unfortunately, some humans treated with the vaccine developed a serious complication, and so the vaccine was abandoned. However, Elan has developed an antibody treatment based on the vaccine. The antibody may provide the benefits of the vaccine without the serious risk. It is hoped that repeated infusion of the antibody will lead to clearance of amyloid from the brain.

In order to be eligible to participate in this research study, subjects must have been diagnosed with possible or probable Alzheimer's disease and be in good health. They must be 50 to 85 years of age and may continue to take medications to treat Alzheimer's disease during study

participation. The study will last over two years and the investigational medication will be given as an intravenous infusion once every three months. Memory assessments and MRI scans will be done throughout the study, along with regular blood tests, to monitor for efficacy and safety. A study partner who is with the subject at least five days a week must be able to attend all study visits.

**If you are interested in learning more or participating in the Elan antibody study, please contact Carolyn at 202-784-4771.**

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### The Director's Column:

#### *Dr. Aisen's Opinion: Is Vitamin E Safe? Who should take it?*

Who could be against vitamins? Many people, including much of the medical profession, have long considered taking vitamins to be safe, and to promote health. But in reality, every pill that you take, whether aspirin or vitamins or a prescription drug, carries some risk of harm. That risk must be weighed against the benefits. The only scientifically valid approach to weighing risks versus benefits is to conduct randomized controlled clinical trials. In such trials, participants take an active pill or a placebo, and neither they nor the study staff know which. This allows a truly objective assessment of the effects of the pill.

It is plausible to consider that vitamin E, an antioxidant, might be beneficial for people with Alzheimer's disease (AD), since the disease is thought to involve oxidative stress in the brain. In the mid-1990's, a large randomized controlled trial was conducted to determine the benefits and risks of vitamin E treatment for individuals with AD. The results did in fact demonstrate some benefit (mild slowing of disease progression), and little risk. As a result, the use of vitamin E by people with AD, and, by extension, people worried about the risk of developing AD, became widespread practice.

No additional randomized trials of vitamin E in people with AD have been reported. But several papers were published in the past year that are relevant to this issue. One involved testing the use of vitamin E to reduce the risk of AD in people with mild cognitive impairment; this study showed no benefit. This result suggests that the benefit of vitamin E in the treatment of AD does not extend to people who are at risk but do not have AD. Another trial, this one concerned with the cardiovascular effects of vitamin E, evaluated its use in people with diabetes or vascular disease. This study suggested that there is no cardiovascular benefit, and in fact vitamin E may increase episodes of heart failure (in those who have diabetes or vascular disease).

Finally, a paper reported the result of a meta-analysis of vitamin E trials. This means that the authors combined the results of a number of separate randomized trials of vitamin E (involving different types of people, different doses and duration and treatment) to reach broad conclusions about the effect of vitamin E treatment. This paper suggested that taking high doses of vitamin E (400 international units daily or more) may increase the risk of death. Many experts have criticized the methods and conclusions of this paper.

Story continues on pg2.

## The Director's Column continued...

### Dr. Aisen's Opinion on Vitamin E

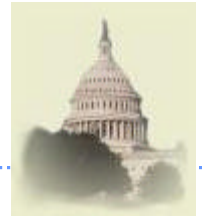
Where does this leave us? The only randomized study of vitamin E in people with AD showed a benefit with little risk. But people who do not have a diagnosis of AD may not benefit from vitamin E. And vitamin E may increase the risk of heart failure in people with diabetes or vascular disease. Medical professionals have had difficulty reconciling these findings.

In our view, the evidence suggests that the benefit of vitamin E treatment outweighs the risk of people with AD, particularly in those who do not have diabetes or vascular disease. But the risks outweigh the benefits in people who have no cognitive impairment, and in those with mild cognitive impairment (MCI). Of course, each person is different, and should reach a decision in consultation with his or her treating clinician. *Written by Paul S. Aisen, MD*

### News from Capitol Hill:

In a huge victory for Alzheimer's Advocates and our Medicaid colleagues, the **Smith (R-OR) - Bingaman (D-NM) amendment to the Budget**

**Resolution passed** on a 52-48 vote on March 17th, 2005. The Smith Bingaman amendment would strike the Medicaid cuts proposed by the Senate Budget Committee and create a Medicaid Commission that would review the Medicaid program and make recommendations to the Congress about necessary changes to the program. This hopefully will have a positive impact on Medicaid beneficiaries, especially those with Alzheimer's disease who rely on Medicaid to pay long term expenses.



### What does Mild Cognitive Impairment (MCI) really mean?

Mild Cognitive Impairment (MCI) is a diagnostic category used to describe people who have memory changes beyond what is normal for their age, but not impaired to such a degree that they experience losses in everyday functional abilities, as a person with dementia does. MCI describes a subtle but measurable memory disorder, and is a transitional state between normal cognitive aging and mild dementia. A diagnosis of MCI means one is able to function at essentially a normal level, despite persistent memory lapses, noticeable to themselves and their family and friends.

The general public tend to confuse what constitutes normal memory and normal forgetfulness in late life. In normal aging, one can learn new things and can consistently recall recent events. Typically, a person with MCI will forget things one would normally remember, like a doctor's appointment, paying taxes, recent conversations, recent events or important events. Mild difficulties in other areas of thinking such as naming objects and complex planning tasks may be present. Sometimes changes in behavior or language and word finding difficulties are

also reported. Usually, other cognitive areas such as judgment and reasoning are not affected. Individuals who suffer from MCI have 5-10 times greater risk of developing dementia than that of cognitively healthy individuals. However, not all individuals with MCI will have a progression to dementia.

MCI is being vigorously researched, however there are currently no treatments that have been FDA approved. The largest MCI treatment study to date has shown that Aricept (Donepezil) does not seem to be helpful in treating MCI.

Georgetown researchers are participating in a clinical research study of the Nicotine patch as a possible treatment for MCI. Nicotine imitates many of the actions of acetylcholine, a chemical substance which acts on brain cells in a specific way that helps us to remember. Preliminary studies have suggested that short term administration of nicotine appears to improve memory in patients with mild memory loss and early Alzheimer's disease. Several decades of research in humans have shown that nicotine stimulation produces improved attention, speed of information processing, reaction time, and sustained attention. Fur-

thermore, nicotine decreases errors on a variety of memory tasks, particularly those that require attention and calculations. Eligible volunteers must be non-smokers and have a diagnosis of MCI. For patients who are not interested in participating in a treatment study, a nontreatment study is now underway: The Alzheimer's Disease Neuroimaging Initiative (ADNI). The goal of this three year NIH sponsored study is to determine whether imaging of the brain (through MRI, PET, or CAT scans) every six months can help predict and monitor the onset and progression of Alzheimer's Disease. In addition to neuroimaging, the study will collect and test blood, and for some participants, cerebral spinal fluid. Normal elderly, people with MCI and people with Alzheimer's Disease are all eligible to participate with a study partner.

~ Written by Kathleen Johnson, RN, MSN, NP

For more information regarding MCI please contact Kathleen at 202-784-5556 or email her at [kbj5@georgetown.edu](mailto:kbj5@georgetown.edu) For additional information regarding the ADNI study please call Kelly at 202-687-0413.

## Research Opportunities at Georgetown's Memory Disorders Program

### Currently Enrolling Studies:

Study Name	Required Diagnosis	Key Inclusion/Exclusion	Study Duration/ Number of Visits	Who to contact
<b>Flurizan</b> (drug study)	Mild Alzheimer's	Must be able to have an MRI or CT Scan	7 visits over 12 months	Carolyn at 202/784-4771
<b>Elan</b> (antibody study)	Mild to Moderate Alzheimer's Disease	Must be able to have an MRI	25 visits over 27 months	Carolyn at 202/784-4771
<b>Huperzine</b> (drug study)	Mild to Moderate Alzheimer's Disease	Patient cannot currently be taking Aricept, Exelon, or	9 visits over 24 weeks	Sally at 202/687-8323
<b>Valproate</b> (drug study)	Moderate Alzheimer's Disease	Patient cannot be experiencing any agitation or psy-	12 visits over 26 months	Sally at 202/687-8323
<b>Nicotine</b> (drug study)	Mild Cognitive Impairment	Patient needs to be a non-smoker	11 visits over 12 months	Kelly 202/687-0413
<b>ADNI</b> (imaging study)	Normal Elderly, MCI and mild to moderate	Must be able to have an MRI	8 visits over 18 months	Kelly 202/687-0413
<b>Statin</b> (drug study)	Mild to Moderate Alzheimer's Disease	Patient must not be taking any lipid lowering medica-	8 visits over 20 months	Kelly at 202/687-0413
<b>Caregiver Communications Study</b>	Mild Alzheimer's Disease /Normal Controls	Must live with someone who can also participate.	2 visits over 12 months	Kris at 202/687-9078
<b>Pfizer</b> (drug study)	Mild Alzheimer's Disease /Normal	Patient cannot currently be taking Aricept, Exelon, or	2-3 visits over 4 months	Ivy at 202/784-0757

### Highlighted Studies:

**Flurizan** - The purpose of this study is to determine the possible benefits of Flurizan, a drug chemically related to nonsteroidal anti-inflammatory Medications. Medications like Flurizan have been shown to reduce levels of beta-amyloid, a protein fragment considered a prime suspect behind cognitive decline in Alzheimer's disease. This study will require memory testing at each study visit, as well as an MRI or CT scan. Participants must be at least 55 years of age and have a diagnosis of probable Mild Alzheimer's Disease and be taking a stable dose of an acetylcholine esterase inhibitor, such as Aricept, Reminyl, or Exelon, for at least 4 months. For more information please contact Carolyn at 202-784-4471.

**Statin** - We are studying the safety and efficacy of simvastatin, a "statin" drug currently used to reduce cholesterol, as an agent to slow progression of Alzheimer's disease. Studies indicate that cholesterol lowering medication may reduce amyloid levels in the brain and lead to cognitive benefits. Participants at least 50 years of age with a diagnosis of mild to moderate Alzheimer's disease, who do not currently require lipid lowering treatments. Study visits occur at 3-6 month intervals over a 20 month period. For more information please call Carolyn at 202-784-4471.

**Valproate** - Valproate is a medication with both anti-seizure and mood stabilizing properties. This study investigates whether valproate therapy delays the emergence of agitation and/or psychosis in outpatients with probable Alzheimer's disease who have never experienced these symptoms throughout their course of illness. It also investigates the hypothesis that Valproate slows disease progression in Alzheimer's disease. Participants must be at least 55 years of age with mild to moderate cognitive impairment of probable Alzheimer's disease. There must be **no history** of present/previous agitation or psychosis requiring psychotropic medication since the illness began. Study visits occur at approximately three monthly intervals over 26 months. For more information please call Carolyn at 202-784-4471.

*Additional Study Information on back*

## Huperzine A - new hope for AD sufferers?

Investigators have been studying huperzine A and its therapeutic potential with increasing intensity for over two decades. It is a naturally occurring cholinesterase inhibitor and is extracted from a traditional Chinese herbal moss named Qian Cheng Ta. It is also known as Jin Bu Huan, meaning "more valuable than gold", and has been used for centuries in China to treat fever and inflammation. Today huperzine A has become a commonly prescribed medication in China for AD. In the US, where huperzine A is not yet approved by the Food and Drug Administration, it is available in health food stores as a natural supplement and is being used by some U.S. clinicians to treat AD.

**What makes it an appealing new treatment?** There is evidence that huperzine A may be more effective than other cholinesterase inhibitors currently in use, and it has additional properties that may make it a beneficial addition to available treatments for AD. Huperzine A has neuroprotective properties, protecting brain cells from glutamate toxicity. Glutamate is a neurochemical that excited nerve cells, but in excess can have toxic effects. Huperzine A also exhibits antioxidant properties (protecting brain cells from oxidative damage) which may be important in the treatment of Alzheimer's disease.

To date several clinical studies with huperzine A have been completed in China with AD sufferers. In these studies huperzine A appears to be effective and well tolerated. Researchers are now eager to extend this work with trials in the US. With the approval and support of the National Institute of Health, Georgetown University is commencing the first US controlled study on the benefits of huperzine A in people with Alzheimer's disease. This is an exciting new study and may provide a new treatment for Alzheimer's sufferers. The study, which is directed by Dr. Aisen, is taking place at 23 sites in the US, with 150 people expected to participate. **The huperzine A trial is currently seeking volunteers.** Participation may be appropriate for people who are interested in natural therapies, and for those who have not found currently approved cholinesterase inhibitors effective or tolerable.

More details on this important trial can be found on the Alzheimer's Disease Educational and Referral Center (ADEAR) website at [www.alzheimers.org](http://www.alzheimers.org) and at the Georgetown University Memory Disorder Program website <http://memory.georgetown.edu>. For additional information on participating in the huperzine A trial at Georgetown University please contact Sally at 202-687-8323.

*Written by Sally Walsh, MD*

## Brain Donation Program

Georgetown Memory Disorders Program has joined teams with and will be collaborating with the Johns Hopkins University Department of pathology to offer brain donation to persons with Alzheimer's disease, related disorders, older people without cognitive impairment, and those with mild cognitive impairment (MCI).

This collaborative effort is part of the GUMC Department of Neurology Memory Disorders Program's initiative to provide comprehensive services and research opportunities throughout the lifespan. The program will assist researchers to better understand the disease processes affecting the brain. A brain donation is the only way to confirm a diagnosis of Alzheimer's disease. Information from autopsy is helpful to researchers working to better understand Alzheimer's disease and to find a cure.

### We are asking for your help in the struggle against Alzheimer's disease.

Consider donating your brain for research after your death. Brain donation is truly a priceless gift for neuroscience researchers combating Alzheimer's and related disorders, as well as millions of families who will be affected by neurodegenerative diseases.



Direct research on post mortem human brain tissue is essential for scientists to gain a better understanding of neurological diseases and can provide insights for the development of new treatments that will benefit future generations. Much of what we know about Alzheimer's can be attributed to the generous donations of families who have coped with this disease. We understand that it is a very personal decision and thoughtful consideration must be given by you and your family. The time to start thinking about donation is now, even though death may be years away. Early discussion with your loved ones and family about your decisions regarding donation will reduce the stress of a decision at the time of death. We are available to answer any questions or concerns you and your family might have. For additional information regarding our brain donation program please contact Carolyn at 202-784-4471.

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## Caregiver Communication Study

**The aim of this study is to develop a new way to observe communication behaviors used by persons with Alzheimer's disease in the home environment. The Communicative Coping Behavior Checklist (CCBC) is an observation checklist to be completed by the caregiver or knowledgeable informant. In addition, to the Alzheimer's disease patients and their caregivers, we are also recruiting healthy volunteer subject pairs. With this research we hope to improve the communicative relationship between the caregiver and the care receiver. The study requires two visits for both the patient and the caregiver. Each visit will last 2 to 2 1/2 hours. For more information please contact Kris at 202-687-9078 or Pamela Saunders, PhD. at 202-784-4771.**

For all clinic information please call Dana:  
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**Visit our website: <http://memory.georgetown.edu>**