



# Alzheimer's Disease Research Center Newsletter

FALL 2008

MEG SEWELL, PH.D.  
EDITOR, DIR. EDUCATION CORE  
MARY SANO, PH.D.  
DIRECTOR, ADRC  
HILLEL GROSSMAN, MD  
MEDICAL DIR., CLINICAL CORE

## Bapineuzumab. It's a hard word to say, but preliminary results look promising.

A major mechanism by which the body fights foreign substances involves the production of antibodies. These antibodies can be produced in the lab and infused like a vaccine. Amyloid plaques in Alzheimer's disease (AD) are a kind of "foreign substance" and the immune system can be instructed to degrade amyloid if properly alerted with antibodies against amyloid (or "anti-amyloid antibodies").

The vaccination can be "active" (vaccination with amyloid plaque material so the body produces its own anti-amyloid antibodies); alternatively, anti-amyloid antibodies created in a lab can be infused into a patient. This is important because the elderly may not respond robustly to active vaccination.

Bapineuzumab, developed by Elan and Wyeth, an example of an anti-amyloid antibody created in a lab, has

been shown in lab animals to reduce levels of amyloid and amyloid plaques. In humans, bapineuzumab was sufficiently tolerated to permit continued investigation. Analyses of Phase II data show favorable trends in cognitive test performance for some subgroups of subjects. Bapineuzumab is now in a Phase III trial, and our ADRC will be participating. The team will be led by Dr. Hillel Grossman who will work closely with research coordinator George Marzloff and other members of our team.

The method of drug delivery—periodic intravenous infusion—relieves subjects and caretakers of daily pill regimens. If this large-scale study can demonstrate bapineuzumab's efficacy and safety (among other analyses), this immunotherapeutic drug could serve as a novel treatment for AD.

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### Bapineuzumab study info:

- \* 18-month study
- \* For those with mild AD
- \* Ages 50-89
- \* IV infusion every 13 weeks for 65 weeks
- \* Clinical assessments continue for 78 weeks
- \* For more information, call 212-241-8329.

## Ask The Expert: Corbett Schimming, M.D. Assistant Professor of Psychiatry, ADRC.

### Q: Does depression cause Alzheimer's disease or does Alzheimer's disease cause depression?

R: There are two schools of thought regarding this issue: one group feels that major depression constitutes a risk factor for developing AD, while others feel that depressive symptoms develop as a response to brain changes seen in early AD. Put simply, some scientists believe that depression speeds along the changes seen in AD, while others believe that depression is a byproduct of these changes.

(Cont'd on page 4)



## Mumbai Corner

Hello! This new section in the newsletter will give us an opportunity to tell you about our exciting research project in Mumbai, India! We'll be bringing you updates and interviews in future issues. Also, you can send us questions about this project and we'll answer them in the next issue. (Questions can be e-mailed to [Kathleen.vandyk@mssm.edu](mailto:Kathleen.vandyk@mssm.edu).)

The "Age-Related Cognitive Loss in Mumbai, India" project was initiated in 2004 by the project's Principal Investigator Dr. Dushyant Purohit, a senior research neuropathologist associated with the ADRC. Funded by the National Institute on Aging and Fogarty International Center of the NIH, the project began with a goal of constructing India's first comprehensive Memory and Aging Research Center at Nair Hospital in Mumbai. Nair Hospital's Memory and Aging Clinic, the clinical hub of the research center, was modeled after our own Memory and Aging center, complete with the standard research recruitment and yearly clinical evaluation and neuropsychological testing. The team of experts that works on this project includes many from our ADRC: Dr. Hillel Grossman, Dr. Margaret Sewell, Dr. Mary Sano, Kathleen Van Dyk, Dr. Daniel Perl and Dr. Purohit.

After four years of hard work developing this center, initially with an R21 development grant, followed by R01 grant funding, the Nair Hospital Memory and Aging Clinic is now fully functioning, complete with dedicated senior faculty members of the Nair Hospital/TN Medical College including Professor A.B. Shah (Neurologist), and Professor Charles Pinto (Psychiatrist), who direct the center with the help of a team of physicians, neuropsychologists and ancillary staff. Like at Mount Sinai, many patients are referred to the clinic from various departments of Nair Hospital and affiliated facilities if they are complaining of memory problems. Some patients are referred by doctors in the community, while some elderly volunteers without memory problems simply enroll for the yearly evaluation to contribute to the research, like some of our ADRC study volunteers do. The clinical evaluation and neuropsychological testing that is completed at the Mumbai clinic is nearly

identical to the yearly evaluation our volunteers receive, allowing for cultural/language based modifications. Thus, the research from these two sites, MSSM and Nair Hospital, offers a remarkable opportunity to study the aging process in two unique groups. The project is also valuable in providing cutting edge training in research and cognitive disorders in India.



An integral part of the research center is the project's Brain Bank/ Neuropathology Laboratory established at the Nair Hospital, similar to the Mount Sinai/ Bronx VA Brain Bank that supports our ADRC. The scope of our work is growing with the addition of facilities in two other local hospitals/medical colleges in Mumbai. A brain tissue donation program is also being set up to inspire and promote the tremendous importance of those research initiatives among research volunteers.

We look forward to bringing you updates as this project grows. Be sure to check out the interview with one of the professionals at the Nair site in the next MSSM ADRC newsletter.



*Pictured above: Investigator-Scientists who established the Memory and Aging Research Center at Nair Hospital, Mumbai. From L to R: Dr. A.B. Shah (Prof of Neurology, Nair Hospital), Dr. J. Deshpande (Prof. of Pathology, Nair Hospital), Dr. D.P. Purohit (Principal Investigator, Associate Prof. of Pathology and Psychiatry at MSSM), Dr. S. N. Oak (Dean of Nair Hospital), Dr. Daniel D. Perl (Prof of Pathology, MSSM), Dr. M. Sano (Prof of Psychiatry, Director of ADRC MSSM), and Dr. C. Pinto (Prof of Psychiatry, Nair Hospital).*

## ADRC NEWS



Congratulations to **Michal Beeri, Ph.D.**, an ADRC researcher pictured left, whose recent research on the link between diabetes and AD was featured at the International Conference on Alzheimer's Disease in Chicago.

Several large-scale studies have shown that those with diabetes have a higher risk of developing AD compared to those without diabetes. On the other hand, previous research showed that people with diabetes had no changes or fewer AD-associated brain lesions than non-diabetics. Dr. Beeri and colleagues hypothesized that the treatment of diabetes with insulin and other drugs may have helped reduce the neuropathological burden of AD and other dementias. This study examined the brains of 124 people with diabetes and 124 without, from the Mount Sinai Brain Bank. Diabetic subjects who were treated with both insulin and with other anti-diabetes medications (oral hypoglycemic agents), had significantly fewer plaques (as much as 80%) than diabetic subjects taking only insulin, only other anti-diabetes medication, or neither, or subjects without diabetes.

These results help to resolve the controversy between clinical findings of increased AD in people with diabetes and minimal changes in AD associated brain lesions. More importantly, these results suggest that the combination of insulin and oral antidiabetic medications may influence AD-associated brain pathology beneficially and point to brain biological pathways (e.g., insulin signaling) that might be used in developing treatment strategies. Results from this study will be published in *Neurology* on September 2, 2008.



Congratulations to our own **Sam Gandy, M.D., Ph.D.**, Mount Sinai Professor of Alzheimer's Research, Associate Director of the Alzheimer's Disease Research Center, Professor of Neurology and Psychiatry, and Chair, National Medical and Scientific Advisory Council of the Alzheimer's Association. UCLA will be awarding him the prestigious Arthur Cherkin Award in Geriatric Medicine in September.

Congratulations to **Tessa Lundquist**, pictured right, one of our ADRC research coordinators, was recently published in June/July 2008 issue of the *American Journal of Alzheimer's Disease and Other Dementias*.

For her senior honors thesis on the topic of young adult's attitudes about Alzheimer's disease, she tested 100 undergraduates with varying levels of contact with the disease. Her question was whether participants with higher levels of contact with someone with AD (such as having a family member afflicted with the disease) would have more positive attitudes about AD than those who had less contact with those with AD.

Results indicated that those who had higher levels of contact with people with AD were more willing to make personal sacrifices for AD (such as donating time or money) than those who had no contact. She concluded that younger people may realize a greater need to support persons with AD if they have been personally affected by the illness through a close relationship.



Tessa graduated in 2007 from the University of Massachusetts Amherst with a B.A. in Psychology.

### Cont'd from page 1: Ask the doc....

A new study by Dr. Robert Wilson and colleagues at the Rush Alzheimer's Disease Center in Chicago helps clarify the question. The researchers tested whether or not depressive symptoms increase during the early stages of AD. They studied a large group of nuns, priests and monks without AD, and looked at the development of both AD and depression in these people over time. Interestingly, they discovered that subjects who went on to develop AD were not more likely to develop depressive symptoms prior to their diagnosis, compared to their counterparts who did not develop AD. Furthermore, this finding was not altered by the subject's age, gender, educational level or personality type. In essence, these findings refute the hypothesis that depressive symptoms develop in response to the AD disease process or as a response to declining function. Rather, it suggests that depressive symptoms are a specific risk factor for AD, not an early sign of its presence.

How might depression place people at risk for AD? Many studies indicate that depressive symptoms may lead to loss of brain tissue. One leading explanation for these degenerative changes links the chronic stress associated with depression to neurobiological changes in the brain. Alternatively, work done here at Mount Sinai by Dr. Michael Rapp and colleagues found increased levels of plaques and tangles (the "calling cards" of AD) in the brains of AD patients with a lifetime history of depression, suggesting an association between depression and the specific pathology of AD.

Identifying and treating depression may be one possible strategy to intervene and help prevent AD. A better understanding of the specific ways depression poses a risk for AD may lead to important new ways of delaying or altering the onset of dementia.

## Upcoming Events

**October 26 2008:** Join us on Sunday morning at Riverside Park at 97th Street for our annual for the Fall Memory Walk with our **NYCARE** team. Last year we raised over \$6,000! Visit [www.alznyc.org](http://www.alznyc.org) for more information. If you'd like to join our team, call Dr. Sewell at 212-241-0188.

**January 2009:** Healthcare professionals are invited to join us for a program called "**Memory complaints: MCI, AD or other causes? Diagnosis, management strategies and research.**" This CME dinner program at Ruths Chris Steak House, is a collaborative effort of **NYCARE**—the Alzheimer's Association joining with the three New York City Alzheimer's Centers: Mount Sinai, Columbia, and New York University. Call Dr. Sewell for more info: 212-241-0188.

## Need a Memory Evaluation?

The ADRC's **Memory and Aging Center (MAC)** provides comprehensive evaluation, treatment, and management for those who have memory complaints.

**Experts:** Our team includes experts in geriatrics, geriatric psychiatry and neuropsychology, neurology, and radiology.

**Quick:** The evaluation can be completed in one visit, including evaluation by a geriatric memory specialist, neuropsychological testing, and neuroimaging.

**Consistent:** Patients see the same clinicians each time, and may choose to be followed on a yearly basis or have their report sent to their primary physician.

*To make an appointment please call our coordinator, at 212-241-1844.*



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## ADRC Studies

### **D-5 Trial for those with Alzheimer's Disease:**

A new study is being conducted to evaluate the safety and effectiveness of an experimental drug known as ELND005, or scyllo-inositol, for the potential treatment of Alzheimer's disease (AD). ELND005 is a disease-modifying agent being tested to determine if it can reduce the progression of AD by breaking down the build-up of amyloid plaques in the brain. Volunteers will receive either active study drug or placebo, an inactive sugar pill, for 18 months, the duration of the study. All participants will be carefully monitored at the research clinic throughout the study. Volunteers are eligible if they meet the following criteria: age 50-85, diagnosis of probable AD, MMSE score 16-26, MRI scan consistent with AD diagnosis and the presence of a caregiver able to attend all study visits. For more information, please call **212-241-5692**. *GCO#08-0449; MSSM IRB approved through 6/16/09.*

### **Trial of a Nutritional Supplement in Alzheimer's Disease:**

We are seeking patients with Alzheimer's disease to participate in a research study on an antioxidant formula containing **resveratrol**. Some study participants will receive the formula and some will receive a placebo (sugar pill). Participation in the study includes memory testing, neurological exams and blood tests. Resveratrol may reduce brain cell damage caused by harmful chemical byproducts. This study is investigating if resveratrol can help the cognition of Alzheimer's disease patients. The study will be conducted over 12 months and is funded by the Alzheimer's Association. For more information, please call **212-241-8329**. *GCO# 05-1394(0001); Principal Investigator: Mary Sano, Ph.D. MSSM approved through 4/30/09.*

### **The Development of NIC5-15 in the Treatment of Alzheimer's Disease**

We are seeking patients with Alzheimer's disease to participate in this randomized, double-blind, placebo-controlled trial of a **dietary supplement**. This supplement has anti-diabetic effects in people and has been shown to improve memory in laboratory animals. It also reduces the production of amyloid in test-tube conditions. Amyloid is the major ingredient of the Alzheimer's plaques. The purpose of the study is to determine whether this product is safe and effective in treating Alzheimer's disease and what dose is best. This natural product (called **NIC5-15**) is found in many foods, including soy beans, and has been already approved by the Food and Drug Administration (FDA) for use as a dietary supplement. For more information, please call **212-241-8329**. *GCO # 05-0090 (0001 01); Hillel Grossman, M.D., Principal Investigator, MSSM IRB approved through 12/19/2008.*

### **RAGE Inhibitor**

Researchers are participating in a nationwide study that will test an experimental treatment, **RAGE Inhibitor**, to target the source of Alzheimer's disease. One of the proteins that surround the amyloid plaques in Alzheimer's disease patients, called receptor for Advanced Glycation Endpoints (RAGE for short) binds to amyloid and may promote nerve cell damage. By inhibiting the RAGE protein, plaque formation could be reduced. Volunteers will receive either active study drug or placebo (inactive pill). All participants will be monitored carefully at the research clinic throughout the study. Participants are eligible to participate if they are age 50 or older and have mild to moderate AD, have not had any serious or unstable diseases within the past three months, do not have Type 1 or Type 2 diabetes and have a reliable caregiver who can accompany them to all study visits. For more information please call **212-659-8885**. *GCO #08-0194 MSSM IRB approved through 5/12/09.*

### **Home-Based Assessment (HBA) study for Memory Protection Research**

We are seeking healthy volunteers, 75 or older, to participate in a nationwide research study to examine methods to evaluate memory and thinking skills from the home. Currently, in order to participate in Alzheimer's Disease research studies, volunteers must visit a clinic to meet with researchers. The Home-Based Assessment study will look at three types of home evaluation methods - a telephone, electronic kiosk or mail-in forms - to determine if there may be a better way to gather study information and track memory and thinking-related changes over time. Participants will be assigned by chance to one of the three methods and their memory and thinking skills will be evaluated using their particular method monthly, quarterly or annually. Participants will also have an in-person screening evaluation visit that will include a physical and neurological exam, a medical history, and some cognitive testing. Participants will also be given a multi-vitamin to be taken twice daily, as the study will examine how well the different methods report pill-taking behavior. At the end of the 4-year study, participants will undergo a final in-person evaluation. For more information, call **212-241-8329**. *GCO#91-208 (13); Jane Martin PhD, Principal Investigator, MSSM IRB approved through 08/31/09.*

*For information about our Brain Tissue Donation Program, please contact Dr. Karen Dahlman at 212-241-2968.*



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ADRC

1 Gustave L. Levy Place, Box 1230  
NY NY 10029

Phone: 212-241-8329

Fax: 212-996-0987

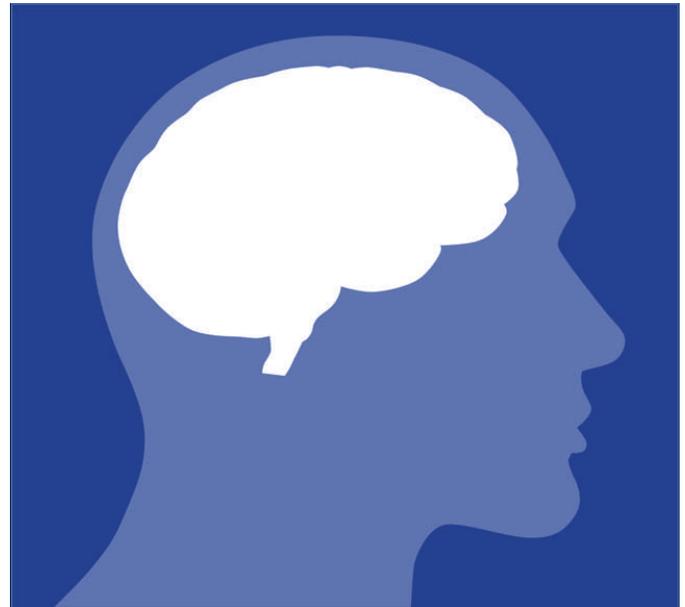
Email: [margaret.sewell@mssm.edu](mailto:margaret.sewell@mssm.edu)

## Surpassing diabetes, Alzheimer's disease is now the 6th leading cause of death in the U.S.

Alzheimer's disease is now the sixth leading cause of death in the United States, according to the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics. With an unprecedented historic population shift of 78 million aging baby boomers in the country and this disease poised to strike 10 million baby boomers—it is clear this escalating epidemic must be addressed now.

“The CDC's announcement that Alzheimer's disease jumped from the seventh to the sixth leading cause of death should serve as a wake-up call to the nation,” said William Thies, Ph.D., vice president of Medical and Scientific Relations at the Alzheimer's Association. “The fact that there are no effective treatments for Alzheimer's has allowed the disease to pass diabetes. It is vitally important that we increase Alzheimer's research funding to slow or stop the progression of this devastating disease.” Although there are several promising drugs currently in Phase III clinical trials, insufficient research funds are committed to research focused on Alzheimer's disease treatment and prevention. The situation is further compounded by the fact that for the past five years, the NIH budget has been essentially flat.

## In the News



If you would like to read the Alzheimer's Association's 2008 *Alzheimer's Disease Facts and Figures* report, it can be downloaded at:  
[www.alz.org/alzheimers\\_disease\\_facts\\_figures.asp](http://www.alz.org/alzheimers_disease_facts_figures.asp)

This article was adapted from  
[www.alz.org/news\\_and\\_events13689.asp](http://www.alz.org/news_and_events13689.asp)

**Is it time  
for your annual  
memory check-up?  
Call 212-241-8329  
today to set up your  
appointment!**