



# MEMORY DISORDERS CLINIC



*"Dedicated to improving the health, well-being  
and quality of life of patients and their  
caregivers."*

## NEWSLETTER

### Want to join the effort to prevent Alzheimer's Disease? Then read on...

by Kris Gravanda

Why wait for the symptoms of Alzheimer's disease? Why not prevent the disease? The benefits of prevention are obvious and highly desirable. But right now, the studies needed to demonstrate the ability of a drug to do this have not been done. And they can't be. Why? In part, this is because researchers do not have the right tools to carry out such a trial. Fortunately, the Alzheimer's Disease Cooperative Study is launching a study to develop the needed tools: the Primary Prevention Instrument Study (*see related story on page 3*).

The benefits of this study to subjects and society are clear. People who participate will get a thorough annual check up of their memory and thinking. In addition, they will be contributing to a national effort to take the first step to design a clinical trial to prevent Alzheimer's disease. The Primary Prevention Instrument Study is the first step to the next big step: a clinical trial to test new drugs.

#### **What does the Primary Prevention Instrument Study involve?**

The study will last four-years. It assesses the usefulness of new or improved paper and pencil tests to measure a person's memory and thinking skills. The study will also compare different methods to collect information from individuals participating in a clinical trial. Participants will be randomly selected to either fill out the pencil and paper tests at-home (and return them to the clinic via Postal Mail) or fill them out in-person at the Memory Disorders Clinic. At least yearly, a subject will receive a thorough assessment at the Memory Disorders Clinic.

#### **Who can enroll in the Primary Prevention Instrument Study?**

This study is open to English or Spanish speaking persons who are at least 75 years of age and who do not have a diagnosis of Alzheimer's disease. Some of the  
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### **Dear Friends of the Memory Disorders Clinic,**

The special focus of this issue of our newsletter is research to advance the standard of care for Alzheimer's disease (AD) and related dementias. Dedicated patients and families at the Memory Disorders Clinic have participated in clinical trials to test more than 10 potential treatments and ways to measure treatment benefits.

In this issue we describe the Primary Prevention Study. The point of this study is to discover the best ways to efficiently conduct a trial to *prevent* Alzheimer's disease. This study is notable for two reasons. It will allow healthy elderly persons the opportunity to receive careful yearly check-ups on their memory and thinking. It will also produce results that will allow researchers to finally begin to study whether drugs prevent AD.

Also in this issue, Jason Karlawish discusses the fragile infrastructure that makes the Primary Prevention Study possible. It's sponsor, the Alzheimer's Disease Cooperative Study, is a federally funded network of dementia researchers who take on important but not-so-profitable questions.

We invite your feedback on this issue. Please send emails to [jennifer@mail.med.upenn.edu](mailto:jennifer@mail.med.upenn.edu) or write to us at:

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## Why did I go into dementia care?

### Kris Gravanda, Clinical Research Coordinator.

By Tanya Nagahawatte

*The following is the second in a series of articles about how the staff at the Memory Disorders Clinic became interested in dementia care.*

Kris Gravanda, our Clinical Research Coordinator, is one of the newest members of the Memory Disorders Clinic (MDC) staff. Kris arrived this summer from Erie, PA. Her decision to move to Philadelphia was primarily driven by the opportunity to work at the Memory Disorders Clinic. As the Clinical Research Coordinator, Kris is responsible for enrolling patients in clinical studies and insuring the smooth operation of those studies.

How did she become interested in dementia care? Her interest started at an early age because of her mother's commitment to community service. Kris often accompanied her mother on visits to a local nursing home. There she realized the unique joy that came from working with older adults. As Kris grew up and went off to college, her personal and career goals took shape around her commitment to elder care.

While in college at Case Western University in Cleveland, Ohio, she volunteered at Menorah Park Retirement Community. There she participated in research on improving the quality of life for people in the community with Alzheimer's disease. This experience had an important impact on her decision to work in dementia care.

"I was fascinated by the fact that overall these were older adults who could function pretty well, but would see me everyday and would never remember who I was. I was just amazed by Alzheimer's disease. I wanted to know everything about it and what was being done to treat it."

This work reinforced her interest in working with older adults and focused her on dementia care. Out of her experience with the residents at the retirement community she became interested in how to preserve and improve their quality of life. She pursued this interest in her academic life. In the spring of 2001, she graduated Magna Cum Laude with a dual degree in Gerontology and Sociology.

Kris has been working at the Memory Disorders Clinic since mid-June running the four clinical trials. She derives much enjoyment from working with patients. In addition, she finds working with their family caregivers

rewarding. By creating the bridge between the participating families and the study requirements, she can ensure that clinical trials are being completed in a timely and scientifically rigorous fashion while at the same time focusing on the personal needs of families. She looks forward to spending time with Memory Disorder Clinic families while facilitating the development of new treatments.

Looking forward, Kris may pursue a business degree focusing in health care management in retirement communities. For now though, Kris hopes to continue to learn about the growing field of geriatrics and dementia as well as learn from the families that come to the Memory Disorders Clinic.

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## Preventing Alzheimer's Disease...

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assessments require information from another person who knows the participant well. Thus, each subject must have a study partner who can take part in some of the assessments and accompany the subject to clinic visits.

### **What are the benefits of joining the Primary Prevention Instrument Study?**

There are a number of benefits to joining the study. Healthcare professionals at the Memory Disorders Clinic will closely assess each participant's memory and thinking at no cost to the participant. In short, each subject, every year receives a thorough assessment of his or her memory and thinking skills. Subjects and their study partner will be reimbursed for expenses incurred from traveling to and from the clinic and receive \$50.00 for completing each annual assessment. During the study, subjects will have the option of joining a book club. When the study is over, subjects have the option of continuing to receive an annual assessment as part of the Memory Disorders Clinic "normal control study." Finally, subjects will also participate in a national effort to set the groundwork for drug studies to prevent dementia.

### **What should an interested person do?**

To learn more about the Primary Prevention Instrument Study call Kris Gravanda, the Clinical Research Coordinator, at 215-349-5903.



## What is the ADCS? Making sense of the alphabet of Alzheimer's disease research.

by Jason H. Karlawish, M.D.

In this issue of the newsletter, Kris Gravanda describes the latest ADCS study (see page 1). Beginning in January 2002, the Alzheimer's Disease Cooperative Study (ADCS) will begin a study to develop valid measures to use in future studies of drugs to prevent Alzheimer's disease. What is the ADCS and why is it doing this trial? These are not simply academic questions. The ADCS stands for a significant commitment of your tax dollars to not-for-profit, patient-centered Alzheimer's disease research. The ADCS is a national organization of researchers dedicated to discovering better ways to treat and even prevent Alzheimer's disease. This network maintains a balance among the forces that motivate and sustain clinical research. The plain fact is that some research questions are important to improve the health and well-being of patients and their families but they are not profitable. Hence, industry will not take up the question. The ADCS does.

### **What is the ADCS?**

The ADCS is a nationwide network of Alzheimer's disease clinical investigators. A National Institute on Aging grant funds the group. The mission of the ADCS is to perform clinical trials of potential treatments for dementia and to develop better ways to measure the benefits of treatments. The ADCS's administrative headquarters is based at the University of California at San Diego. Its 35 study sites are spread across the United States and Canada. One of them is at Penn under the leadership of Christopher Clark and myself.

### **What has the ADCS done?**

In its ten years, the ADCS has been a key contributor to the progress of dementia treatment. The fruits of the ADCS's research include the development of one of the key measurements that researchers use in clinical trials to assess whether a drug treats dementia: the global measure of change. Change on the global assessment is one of the primary endpoints in a clinical trial to establish whether a drug works to treat AD. Another key ADCS project was the study that showed vitamin E slows the progression of Alzheimer's disease. Other significant contributions include studies that showed that estrogen and prednisone do not treat the disease.

Studies that develop instruments to measure dementia progression and investigate whether common drugs like prednisone, estrogen, and vitamins treat AD illustrate

the ADCS' vital role in the worldwide effort to reduce the harms and suffering of AD. The ADCS does not simply replicate the model of useful research that the pharmaceutical industry supports. Instead, it takes on important research that would otherwise fall between the gaps.

### **How does the ADCS fill in the gaps?**

There are at least three ways the ADCS fills in the gaps and thus why it matters. First, the ADCS focuses on investigating the therapeutic potential of drugs that are no longer on patent and that might be widely produced by a number of companies. For example, many companies produce vitamin E. Thus, no one company has an incentive to study whether vitamin E slows dementia. Simply put, why invest the resources in a multi-site clinical trial when the profit of showing your drug treats AD is diluted by all the other manufacturers selling it too?

The other valuable role of the ADCS is that it adheres to the dictum that truth demands freedom. In other words, the results of ADCS research are transparent and widely disseminated. Negative studies are the pariah of clinical research. Biostatisticians are quick to note that these studies that fail to show a significant difference between the intervention such as estrogen and the placebo control group are studies that simply failed to find a difference. In fact, a difference may actually exist. The drug may actually work. But this study failed to detect it. For the owner of a drug, a negative study is "bad press." It does not shine favorable light on the drug. Sometimes these data simply are not published or receive minimal presentation. This often fulfills the goals of business. But it does not fulfill the goal of science that relies on the free and open exchange of information, even "negative" information.

The third valuable role of the ADCS is to develop valid ways to measure whether an intervention treats dementia. These measures are the building blocks of valid and valuable clinical trials. If you cannot measure what is happening, you cannot do a trial. These measures include the pencil and paper interviews that patients and caregivers answer during a clinical trial. These measures establish whether there has been progression. Studies to develop valid measures that record meaningful change are like studies of off patent drugs; they are not the foundation of a for-profit enterprise.

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## What is the ADCS... *Continued from page 3*

Valid measures exist to show whether an intervention treats Alzheimer's disease. But valid measures do not exist to show whether an intervention *prevents* Alzheimer's disease. In other words, the building blocks are not all in place to successfully start one of the most pressing public health issues: the prevention of AD. The ADCS has inaugurated a study to build the foundation for studies of drugs to prevent AD.

### ***Putting it all together: science in the service of society.***

The ADCS serves a number of valuable roles that the business of dementia research does not readily take up. Upcoming ADCS projects include validating instruments to use in a dementia prevention trial, testing whether off patent, common and even over the counter drugs treat AD, and a study of informed consent in dementia research. In sum, these are not the stuff of big money, but they could be big science that contributes to substantial advances in the standard of care.

There is a lesson here. It is the need for the national infrastructure that supports clinical research in a way that properly balances among the emotions and incentives that motivate researchers to go to work every day. What motivates research? The thrill of discovering original knowledge. Fame. Improving the health and well being of people with a disease. And profit. Patent law assures that there is big money in drug development. But if any one of these motivations dominates, the system can fail to investigate potentially valuable questions.

The ADCS network is a vital not-for-profit, publicly funded, transparent network of clinical researchers who take on questions that may not be where the money is, but may be where valuable truth lies.

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## Recent Staff Publications

McGraw-Hill has just published "Advanced Practice Nursing with Older Adults", co-authored by our Education Director and Memory Disorders Clinic clinician, Valerie Cotter, MSN, CRNP and Neville Strumpf, PhD, RN, C, FAAN.

Ms. Cotter and Dr. Strumpf wrote this book because they recognized the need for a comprehensive text for

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## How can you help support the Memory Disorders Clinic?

The Memory Disorders Clinic depends on grants and donations. Our support comes from competitive grants from the National Institutes of Health (NIH), Foundation sponsored programs and individual donations and bequests from patients, families and friends. NIH funding supports the infrastructure of the Center, but individual donations and bequests are critical. They provide flexibility to pursue and sustain new and innovative research, education and care.

### **What can you do to help?**

There are at least five ways you can contribute to the mission of the Memory Disorders Clinic:

- Give a donation to the University of Pennsylvania specifically directed to the Memory Disorders Clinic.
- Volunteer your time at the Memory Disorders Clinic
- Suggest that instead of sending flowers, mourners donate to the Memory Disorders Clinic
- Designate the Memory Disorders Clinic as a beneficiary in your will or life insurance
- Write your senator or congressperson about increasing funding for research on aging.

Gifts of cash, appreciated securities, real estate, personal property, life insurance and other valuable assets may be given outright. In addition, bequests and gifts that provide income to the donor can ensure the future security of the Memory Disorders Clinic. Of course, any size contribution is gratefully accepted.

For more information about our Program Needs, please visit our web site at [www.uphs.upenn.edu/ADC](http://www.uphs.upenn.edu/ADC)

To send a gift, make the check payable to the "Trustees of the University of Pennsylvania" and indicate "Memory Disorders Clinic" in the memo line.

Send the check to:

Alzheimer's Disease Center  
Attention: Program Administrator  
University of Pennsylvania  
3615 Chestnut Street, Room 212  
Philadelphia, PA 19104

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## You can help advance our understanding of the causes and risk factors associated with AD.

By Maria Song

Understanding the causes and risk factors associated with Alzheimer's disease (AD) is an important step toward preventing AD. In other articles in this newsletter we talk about current studies to develop measures to test therapies that prevent AD. Understanding who is at risk for developing AD and why will be vitally important for testing potential therapies, especially therapies to prevent AD.

Apolipoprotein-ε4 (APOE-ε4) is a well-known genetic risk factor associated with increased risk of developing AD. But why this is a risk factor is not well understood. Knowing why can have great benefits. These benefits might include identifying potential strategies for new therapies and better defining persons at risk for AD. We have teamed up with the University of Washington to conduct a study to collect these important data. The study's purpose is to discover if the increased risk of developing AD that is associated with APOE-ε4 is due to its affect on the hormone cortisol. Subjects include cognitively normal persons and persons with AD.

### ***What is APOE and why do we think its affect on cortisol plays a role in developing AD?***

Provocative links exist between AD, the APOE gene and cortisol. Here's what we know so far. There are three types of APOE:ε4, ε3, and ε2, and having the APOE-ε4 gene has been shown to increase the risk of developing AD. We also know that when your body is under stress, APOE limits the production of cortisol, which is a stress hormone. Preliminary studies indicate that individuals with the APOE-ε4 gene tend to have higher levels of cortisol compared to individuals with the other types of APOE. People with AD also have high levels of cortisol. Putting this all together suggests that APOE-ε4 does not limit the production of cortisol as well as other types of APOE and thereby increases the cortisol level in the body. This may in turn be one of the mechanisms for developing AD.

### ***Why should high levels of cortisol increase your risk of developing AD?***

We think that cortisol in high levels may be harmful to nerve and brain cells. Cells that have been harmed by cortisol may be more susceptible to AD. Understanding the relationship between age, cortisol levels and

APOE type will help to explain why and how the APOE-ε4 gene affects the risk of developing AD.

### ***What does the Study involve?***

The study involves just two visits. In the first visit, participants will be asked for some background information, have physical and cognitive exams, and a blood test. If a participant passes all the assessments, he or she will come in for the second visit that involves a lumbar puncture (LP). An LP is a routine medical procedure that allows us to draw Cerebral Spinal Fluid (CSF). A physician inserts a special needle into the lower back to draw the fluid. The procedure causes minimal discomfort since a local anesthetic will be used. It has been done on over 300 patients at the Memory Disorders Clinic.

Additionally 1/3 cup of blood will be collected for storage. The blood will be stored at the University of Pennsylvania as well as in a National Alzheimer's Cooperative Center. The identity of participants will remain confidential. After completing the study, participants will receive \$200.

### ***Who can participate?***

People between the ages 18–90 can participate in this study. We are seeking cognitively normal persons as well as persons with AD.

### ***How can I learn more?***

Interested persons can learn more by calling Maria Song, Research Coordinator, at (215) 662–4377.

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## **Staff Publications...Continued from page 4**

nurse practitioners and students in nurse practitioner programs who care for aging persons. They utilized their 15 years of experience educating advanced practice nurses in the Gerontology Nurse Practitioner Program at the University of Pennsylvania School of Nursing to formulate their ideas and design the book. The book is a unique contribution to gerontological nursing because it underscores the depth and breadth of knowledge needed to engage in independent and collaborative practice. It illustrates the ever-growing body of clinical research focused on older adults, both with and without Alzheimer's disease, and the extraordinary opportunities for advanced practice nursing.



# MDC NEWSLETTER



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of patients and their caregivers."*

## Staff Highlights

### *Dr. Arnold begins a sabbatical...*

October 1st was the beginning of a year-long research sabbatical for Dr. Steven Arnold. During this sabbatical, Dr. Arnold is investigating the molecular neuropathology of neurodegenerative and psychiatric diseases. His work includes developing new automated methods for microscope analysis of tissue and learning novel methods for simultaneously investigating thousands of genes and proteins in the brain that may be abnormally produced in these diseases.

### *... and we wish a warm welcome to Dr. Kohler.*

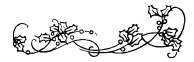
We are very fortunate that on October 1<sup>st</sup> Christian Kohler, MD joined the Memory Disorders Clinic staff. He is caring for Dr. Arnold's patients on Wednesday mornings with Marianne Watson.

Dr. Kohler is a board certified psychiatrist and the Clinical Director of Neuropsychiatry at Penn. He received his medical training from Medizinische Fakultät in Innsbruck, Austria. He completed residency training in psychiatry at Wright State University in Dayton, Ohio, residency training in neurology at the University of Cincinnati, Ohio and a fellowship in neuropsychiatry at the University of Pennsylvania.

Dr. Kohler's research interests involve emotional processing in brainrelated disorders. This includes work on depression and emotion recognition in people with schizophrenia and before and after epilepsy surgery.



*The Memory Disorders Clinic Staff wish  
everyone a happy Holiday Season and joyous  
New Year.*



## Memory Disorders Clinic

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