



# ALZHEIMER'S DISEASE CENTER



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

## NEWSLETTER

### "Excuse me but may we look at your brain?"

by Jennifer Klocinski, MA and Jason Karlawish, MD

One of the keys to understanding a disease is to compare people with the disease to people without the disease. This means that an organized and coherent approach to Alzheimer's disease (AD) research needs to include persons without the disease in addition to persons with the disease. In short, older adults without serious problems with their memory or thinking are vital in our efforts to combat dementing illnesses such as Alzheimer's disease. How? By donating their brains to science. Researchers from institutions around the world use tissue from Penn's

Brain, Tissue and Biological Samples Bank to collaborate on multi-disciplinary research studies. Currently, the tissue program contains just

over 100 brain donations but only 2 of these come from people who do not have dementia. Tissue from individuals who have no symptoms of dementia is in short supply. We have 17 commitments from individuals participating in our Normal Aging Study. We need many more!

Why not use animal brain tissue? Because, only humans can get Alzheimer's disease. This limits researchers to studying human brain tissue to understand the risk factors and causes of AD and to find potential treatments and cures. Although they are somewhat helpful, studies of rats and mice do not provide sufficient information about changes in the brain that are simply due to aging.

Thus, a vital component of research to understand Alzheimer's disease is to study brain tissue from

people without AD, (i.e. normal control subjects). These studies are crucial to our understanding of why some people get AD while others do not. Results from one normal aging research program illustrate how important comparison studies can be. The Nun Study is conducted at the University of Kentucky with members of the School Sisters of Notre Dame. One study participant, Sister Mary appeared to be the model for healthy aging. When she died at the age of 101 she was mentally active. Tests of her memory and thinking had been normal for her age.

To the researcher's surprise her brain tissue at autopsy resembled that of an individual with advanced Alzheimer's disease. How could this be?

After finding 18 similar cases the researchers were able to conclude that the absence of strokes might explain why they did not develop the symptoms of AD.

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***The Normal Aging Study***

- *AD only affects humans so animal studies are not enough*
- *Brain tissue is in short supply*
- *Participants receive an annual "brain check-up" and contribute to AD research*
- *Participants also receive \$25 for each visit to offset transportation costs*

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# MDC, ADC, NIH, NIA..? Making sense of the alphabet of Alzheimer’s disease.

by Jennifer Klocinski, MA

When I began working at the Alzheimer’s Disease Center (ADC) at the University of Pennsylvania the initials and jargon my colleagues tossed about befuddled me: MDC, ADC, CNDR, NIA, NIH. Who do I really work for and how are they related? Now the alphabet of Alzheimer’s disease research makes sense to me, but I suspect many of you are as confused as I was.

## What is the University of Pennsylvania’s ADC?

The ADC is the Alzheimer’s Disease Center. It is one of 29 research centers and 3 affiliates at major medical institutions across the nation. Each is funded by grants from the National Institute on Aging (NIA). The purposes of these centers are to provide a structured way to research Alzheimer’s disease and to create a network to encourage collaboration and sharing of ideas. The funding does not directly finance the research conducted at the ADCs. Instead, it supports the infrastructure to conduct research and foster interdisciplinary collaboration.

The National Institute on Aging mandates that each ADC have four cores: an administrative core, clinical core, neuropathology core and education and information transfer core. These four cores all work together to foster basic, clinical, and behavioral and social science research.

Penn’s ADC was established in 1991. John Q. Trojanowski, MD PhD, a neuropathologist is the director of the ADC and also leads the neuropathology core (an interview with Dr. Trojanowski appears on page 5). Christopher M. Clark, MD, a neurologist, is the ADC’s associate director and directs the clinical core and the Memory Disorders Clinic. Over the past 11 years Penn’s ADC has grown substantially and now has over 30 staff members with diverse training including medicine, psychiatry, bioethics, nursing, sociology, and psychology. The ADC staff also collaborates with researchers throughout the University and around the world. The research has produced over 400 peer-reviewed papers and book chapters.

## What is the MDC?

The MDC is the Memory Disorders Clinic. It along

with a satellite clinic, Clínica para Trastornos de la Memoria, which serves the Latino community, are the home of two ADC cores, the clinical core and the education and information transfer core (EITC). The MDC is an out-patient, clinical practice of the Neurology department of the Hospital of the University of Pennsylvania. The clinicians and staff of the MDC provide diagnosis, medical care, education and social

## ADC ORGANIZATIONAL STRUCTURE

### NATIONAL INSTITUTES OF HEALTH

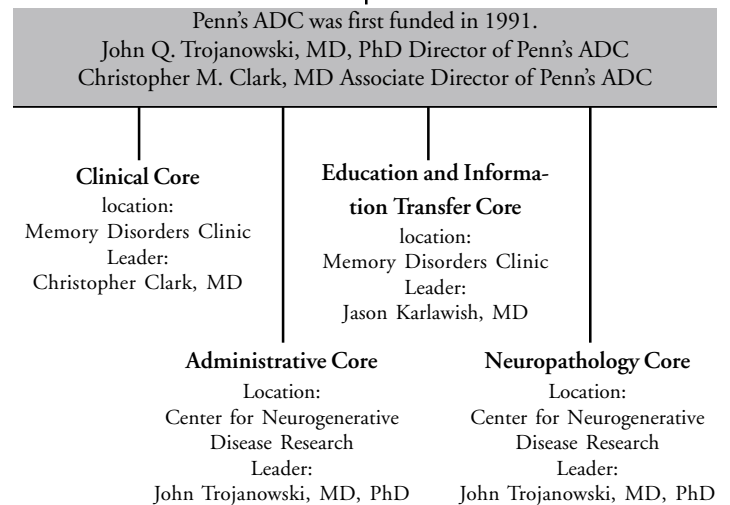
Established in 1930 under the Department of Health and Human Services it has since grown to include 27 Institutes or Centers

### NATIONAL INSTITUTE ON AGING

Established in 1974, its purpose is to lead the national effort in research on the biological, social and behavioral aspects of aging

### ALZHEIMER’S DISEASE CENTERS

First created in 1984 by the NIA. They now number 29 plus 3 affiliates.



support for individuals with AD and related disorders and their families. As the home of the ADC’s clinical core it is responsible for carefully collecting data on the course of AD and related disorders in patients and to provide an environment for the conduct of research to improve the standard of care for patients and

*Continued on next page*



# Alphabet of Alzheimer's disease . . .

*Continued from previous page.*

caregivers. Because the education and information transfer core's purpose is to provide education to patients and their families; healthcare professionals and the wider community, the staff and work overlaps and at times appears seamless with the MDC and clinical core. Doctor Jason Karlawish is an example of these inter-related roles and activities. He not only provides clinical care to patients and families attending the MDC but also is the associate director of the ADC's clinical core and director of the ADC's education and information transfer core. His work not only involves providing expert care for persons with dementing illness but educating patients, families, healthcare professionals and the community about AD and related disorders and conducting research into the challenging social and bioethical challenges that patients and families face when making treatment decisions.

## **What is the CNDR?**

The CNDR is the Center for Neurodegenerative Disease Research. It is a 6,500 square ft. state-of-the-art research facility at the Hospital of the University of Pennsylvania and the home of the neuropathology core and administrative core. Doctors Trojanowski and Virginia M.-Y. Lee, PhD co-direct the CNDR. Together, they lead over 35 researchers and collaborate on research projects with experts around the world. As the home of the neuropathology core and a number of other clinical and basic science research activities supported by the NIH (see below), it maintains the Brain, Tissue and Biological Samples Bank, performs brain autopsies, analyzes other biological samples (e.g. blood, urine and cerebrospinal fluids as diagnostic markers of disease during life) and provides an environment conducive to multidisciplinary, collaborative research into the causes, mechanisms, diagnosis and treatments of AD and related disorders. The administrative core of the ADC works behind the scenes as well as with funding agencies, the public and other investigators by organizing conferences, facilitating interactions between researchers within as well as outside the University, and managing budgets.

## **Who creates and funds the ADCs? The National Institutes of Health (NIH) and the National Institute on Aging (NIA).**

The National Institute on Aging was established in

1974 to provide leadership in all aspects of aging research. In 1984, the NIA's Dementias of Aging Program established the structure for ADCs. Five were funded. Now, there are 29 centers and 3 affiliates. The NIA devised the four-core structure and other requirements for an ADC, reviews the proposals submitted by medical institutions to be awarded ADC funding, and is responsible for overseeing their work.

The National Institute of Health (NIH) was established in 1930 as one of the health agencies comprising the Department of Health and Human Services. Its purpose was to fund and conduct medical and biological research to improve the health of the nation. Over the years it has expanded into 27 Institutes or Center, the National Institute on Aging being one.

The network of ADCs around the country has played a vital role in our increasing understanding of neurodegenerative illnesses such as AD. Research conducted at ADCs has led to the development of new diagnostic tools; improvements in the care of patients; the discovery of treatments; and a greater understanding of the impact of these diseases on the social, financial, and physical well being of persons with these diseases, their families and friends.

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## **How to Donate to the MDC:**

Your gifts are gratefully accepted and help to fund new and innovative research, education and care. Your support can be given through donations to the University of Pennsylvania and specifically directed to the Memory Disorders clinic.

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:  
Memory Disorders Clinic  
Attention: Program Administrator  
University of Pennsylvania  
3615 Chestnut Street, Room 212  
Philadelphia, PA 19104

Contributions are tax deductible. To find out more about our program needs please visit our website at [www.uphs.upenn.edu/ADC](http://www.uphs.upenn.edu/ADC) or contact our main office at (215) 662-7810.



# May we look at your brain . . .

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These important results may have never come to light if it wasn't for these generous gifts from the Sisters of Notre Dame.

The Brain Tissue Research Program at the Alzheimer's Disease Center of the University of Pennsylvania is located in Penn's Center for Neurodegenerative Disease Research (CNDR). The CNDR is home to a team of over 35 University of Pennsylvania researchers who conduct basic science research on illnesses such as Alzheimer's disease. It also functions as a "virtual center without walls" through its collaboration with researchers from around the world.

## **Who is eligible to participate in the Normal Aging Study?**

We are in need of both elderly men and women who do not currently have a problem with their memory or thinking, and are committed that upon their death they will donate their brain to the Brain Tissue Research Program.

## **What does participation involve?**

Participants in our Normal Aging Study agree to have an annual neurological exam and test of their memory and thinking, and to permit a brain autopsy at the time of their death. Hence, one clear benefit to people who participate is an annual check up on brain health, in other words, an answer to the question "Am I still normal?"

Brain autopsy has no effect on funeral arrangements and does not delay the burial process. It also does not leave any visible marks and does not interfere with an open casket funeral or cremation. Most religions support brain autopsy and tissue donations. The Normal Aging Study is one way that individuals fortunate enough to be spared can help find a cure for this tragic disease. For more information on this beneficial program please contact Marianne Watson at 215.662.4373.

## **Some final thoughts.**

The request to donate your brain upon death is certainly odd, even disturbing. But upon our death, what legacy do we wish to leave: past memories for our

family and friends, a record of accomplishments, money? A contribution to the effort to cure Alzheimer's disease can be part of that legacy. A brain donation to science can be one of the truest expressions of altruism.

## **Conference: *Living for today and planning for tomorrow***

by Valerie T. Cotter, MSN, CRNP

The Alzheimer's Disease Center is pleased to announce our first caregiver conference "*Dementia Caregiving: Living for Today and Planning for Tomorrow.*" The conference will be held on Friday, October 18, 2002 at the School of Nursing on Penn's campus. This one-day event will offer attendees cutting edge information on dementia care, with a focus on providing day-to-day care for persons with dementia and planning for the future. The program will address the needs of persons with dementia and their caregivers, such as a research update, staging of dementia and what to expect in the future, strategies for recognizing delirium, palliative and hospice care approaches, behavioral symptoms, and much more. Speakers include Dr. John Q. Trojanowski, Director of Penn's ADC, and Wendy Campbell, President of the Delaware Valley Chapter of the Alzheimer's Association.

The conference is designed for care providers as well as person's with early stage dementia and is free of

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## *In Memory...*

*The Memory Disorders Clinic gratefully thanks family and friends for the generous contributions made in memory of:*

***Rita D. Boone  
&  
John Streeper***



# Meet the leaders of Penn's ADC: An interview with John Trojanowski

by Jennifer Klocinski, MA

In September, 2001 the grant that funds The Alzheimer's Disease Center (ADC) at the University of Pennsylvania was up for renewal. Penn's ADC competed with 14 other medical institutions around the country for one of these multimillion dollar five-year long grants. Our hard work paid off. We were one of the 7 institutions awarded this prestigious grant—to make a total of 27 ADC's in the country. Doctors John Q. Trojanowski, Program Director and Core Leaders, Christopher M. Clark and Jason H. T. Karlawish will guide our research efforts over the next five years so that we may improve the standard of care for people with AD and related illnesses. But who are these physician-researchers? What do they see as the future for Penn's ADC and of research into the causes, diagnosis and treatment of AD?

*This is the first in a three part series that will introduce you to each of the ADC's directors and core leaders. This first part features John Q. Trojanowski.*

.....

## **ADC Director, John Q. Trojanowski, MD PhD:**

Dr. Trojanowski is a neuropathologist. He received his MD and PhD from Tufts University in 1976. After beginning his internship at Harvard Medical School he completed his training at the University of Pennsylvania and then joined the faculty. At Penn he is the Director of Medical Pathology, Director of the Institute on Aging, Director of the Alzheimer's Disease Center and Leader of the Center's neuropathology core, and Co-Director of the Center for Neurodegenerative Disease Research with Virginia M.-Y. Lee, Ph.D. Dr. Lee is the John H. Ware 3<sup>rd</sup> Professor of Alzheimer's Research in the Department of Pathology and Laboratory Medicine and married to Dr. Trojanowski. Dr. Trojanowski has and continues to serve on numerous committees including, National Advisory Council on Aging of the NIA ('94-'98), the Program Committee of the World Alzheimer Congress 2000 ('98-'00), and the Medical and Scientific Advisory Board of the National Alzheimer's Association ('92-present). He is a member of the Association of American Physicians, was elected President of the American Association of Neuropathologists ('97-98), and is on the editorial board of numerous scientific journals. He has published over 400 papers, reviews and monographs and has received several awards for his research including a Merit Award ('86-94) from the NIH and the first Pioneer Award from the Alzheimer's Association ('98).

prominently during my medical training, although I was certainly aware of Alzheimer's disease (AD), but when I went to medical school in the '70s there wasn't a crisp distinction in my mind or in the minds of others about the differences between normal age related memory loss and dementia. AD and senility seemed blended together and the thinking then was that AD would be the fate that everyone, as a factor of aging, would succumb to. It was only in the early '80s when many people (e.g. scientists, policy makers, demographers) recognized that AD was going to be a serious problem with the expansion of the population over 60.

Thus, when Virginia Lee and I began to collaborate together in research during the early '80s and enjoyed it, we asked each other: "What could we do together for the rest of our careers that would make the best use of both of our skills and in a team effort to solve a problem?" It didn't take very long for AD to become our number one topic of shared research interest because we had skills that seemed to be suitable to solving the problems that were pressing in those days in AD research, i.e. what is the nature of the pathology, is it a biochemical lesion, is it a morphological lesion, how does the pathology lead to behavioral impairments, etc. And, we both felt that AD was an important problem, something that would have an impact on the health and well-being of people down the line in our lifetime hopefully. That was about 1981 or 1982 when we began to formulate plans that led to our current research program on neurodegenerative diseases.

### **Conversation with John Trojanowski, MD PhD:**

**JK: How did you become interested in neurodegenerative research?**

JQT: You know it wasn't on my radar screen very

Previously, there was no AD program at Penn. So we  
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# Adult Day Care: Delaying Nursing Home Placement

by Tanya Nagahawatte

Adult day care is an important care option for persons with dementia. Unlike senior centers, adult day care centers offer services to individuals with physical, cognitive or functional impairments. Some centers offer programs and services specifically designed for individuals with dementia. Programs vary but most centers encourage socialization through group activities, offer a safe environment, provide meals, and other specialized services suited to the individual's particular health needs. In addition to these benefits it provides respite for caregivers thereby enabling them to provide better care.

Adult day care offers so many important benefits but we often find caregivers reluctant to take advantage of this care option. Why? We have found three main reasons. First, some caregivers are reluctant because they believe that adult day care is the first step towards nursing home placement, which they want to delay or avoid. However, adult day care usually does just that, delay placement in a nursing home. It can allow family members to retain jobs, assist with the physical aspects of caregiving, provide respite and offer social interactions that may reduce difficult behaviors at home thereby provide a way for the person with dementia to remain at home for as long as possible.

Second, some caregivers are reluctant to try adult day care based on the likes and dislikes of the person with

dementia before they became ill. It is not seen as an option because it is not compatible with the person's previous interests. However, dementing illnesses affect our personalities; our likes and dislikes. Many caregivers are pleasantly surprised by their loved one's positive response to adult day care.

Third, the person with dementia is resistant. Change for someone with dementia can be frightening and with any new activity a period of adjustment should be expected. For a caregiver, dealing with the person's

initial resistance can be difficult. It may take two to three visits a week for three weeks for the person to become acquainted. One or two visits are not enough since the person is likely to forget between visits and never become accustomed. After an adjustment period, attending an adult day care center will likely become a favorite activity.

## Helpful Hints

- *Identify your relative's specific needs. A place for socialization? Assistance with activities of daily living (eating, personal care, medicines)? Mental stimulation?*
- *Consider your personal needs. Freeing up business hours? Is there a transportation limitation?*
- *Visit every center under consideration. Did you feel comfortable there? Did your relative feel comfortable? An adjustment period is to be expected, ask the staff how they accommodate the transition.*

Things to consider when selecting a center include the number of patients to trained staff, staff credentials, and the schedule of the center. Adult day care is one way to provide an enriching experience for your relative and peace of mind for you. If you have any questions regarding adult day care services, please call the clinic Social Worker, Mirna Negrón, at (215) 349-8768.

*Thank you to the families that shared their experience and wisdom on this topic.*

## Conference ... Continued from page 4

charge but registration will be required, space is limited and will be based on a first come first served policy. Registration brochures will be mailed to newsletter recipients in August. The conference is funded through generous grants from Natestch Pharmaceutical Company Inc., the John A. Hartford Center of

Geriatric Nursing Excellence and the University of Pennsylvania Health System's Board of Women Visitors. For more information, please visit [www.med.upenn.edu/ADC](http://www.med.upenn.edu/ADC) or contact Jennifer Klocinski by email at [Jennifer@mail.med.upenn.edu](mailto:Jennifer@mail.med.upenn.edu) or phone 215.573.4634.



## Meet our leaders. . . *Continued from page 5*

said, "That's what we will do. Let's build a multi-disciplinary neurodegenerative diseases research program." We felt that that was going to be absolutely necessary to do research that had an impact on AD. We felt it was going to be a complicated problem to solve and if we were going to have a go at solving it, not just finding out what caused it, but finding therapies too, we would need basic scientists and clinicians. So from the very beginning we planned to be where we are today with a multi-disciplinary approach to AD and related disorders.

### **JK: What do you see as the most important contribution that Penn's ADC's neuropathology core has made to neurodegenerative research?**

JQT: Definitely improving understanding of how to diagnose AD, working with the clinical core to acquire clinically well characterized brain samples, cerebral spinal fluid samples, blood samples, and DNA samples from clinically well characterized patients. Having clarity about the nature of the disease that a patient has is so important for understanding disease mechanisms. It is an essential, supporting piece of any important high impact research. So I think the neuropathology core has done an outstanding job supporting the research of others through better case definition and through a number of exercises in developing better criteria for the rational and reproducible diagnosis of AD.

### **JK: What do you see as the mission of Penn's ADC?**

JQT: Based on the mandate of the National Institutes of Health (NIH) and the National Institute on Aging (NIA), the major funder of AD research, we don't have a lot of choices since all grants have constraints within which you must work. But we actually have a lot of choices about how we implement the mission. Thus, I am passionate about the mission of our ADC that is mandated by the NIA for all ADCs, which is to increase the quality and quantity of research on AD and related disorders thereby leading to better therapies for these diseases, as well as to increase the educational level of all parties essential to solving AD therapeutically, that is clinicians, nurses, basic scientists, caregivers, etc. Everyone has got to be part of the solution to the problem of finding better treatments for AD and related disorders, and we all should be on the same page about where we are now in understanding

these diseases so that we can move forward together to hasten efforts to find meaningful therapies.

### **JK: What do you see as our future?**

JQT: I think we are at a very exciting stage. When we have all the cures and the story about AD is told I think this juncture in time will be thought of as the most exciting. Certainly up until now it's been exciting, i.e. with gene discovery and the discovery of the proteins that form the lesions in AD. This basic and very tedious work to find out how the brain is falling apart was and is absolutely essential to getting to the next stage which is drug discovery, and that is precisely where we are right now. There is enough information about basic mechanisms of brain degeneration in AD to ramp up drug discovery efforts and part of the success of that endeavor will not only be drug discovery but imaging and diagnosis; how to diagnose the disease earlier (including some of the research we are doing now to sort out the differences between mild cognitive impairment and AD); who will develop mild cognitive impairment, and who will go on to AD and who will not. All of these important issues and questions are critical because the answers to them will enable us to get to the earliest stages of disease onset where it is most likely that we will have the biggest therapeutic impact, and, not surprisingly, this is true in many other diseases.

Early disease detection is critical to early therapeutic intervention where one can expect the biggest bang for your buck, i.e. the greatest therapeutic effect of a treatment for AD. And so when I talk about drug discovery it is not just about getting the molecules that you give to people but it's also about finding the right people to treat at the earliest stages of the disease or finding out that drug A works better at prevention and drug B works better when you have the disease. In summary, I think the future has never been more exciting because we are at a point where we can take all the basic science discoveries and begin to translate them into therapies.

*For more on Jennifer's interview with Dr. Trojanowski, see our website [www.uphs.upenn.edu/ADC](http://www.uphs.upenn.edu/ADC).*

**Next issue: Dr. Christopher M. Clark, Associate Director of Penn's ADC and director of the clinical core and Memory Disorders Clinic.**



# ADC NEWSLETTER



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

## Current Research Opportunities:

### **A study of the ability of estrogen and progesterone to prevent AD in post-menopausal women:**

The purpose of this study is to see if estrogen and progesterone can prevent AD in post-menopausal women who are at risk for developing AD (i.e. have a 1<sup>st</sup> degree relative with AD). Participants must be 65 years or older and cognitively normal. The study will last 5 years and participants will be randomly assigned to take estrogen/progesterone or a placebo. The sponsor of this study is Columbia University and it is funded by the National Institute on Aging (NIA).

### **A study of the relationship between a stress hormone and genetic risk factor for AD:**

The purpose of this study is to discover if the increased risk of developing AD that is associated with the APOE-e4 genotype is due to its affect on the stress hormone cortisol and does the effect of APOE-e4 change as we age. Participants are needed with and without Alzheimer's disease and

between the age of 18 and 90 years. This study involves two visits. The sponsor of this study is the National Alzheimer's Coordinating Center.

### **A placebo-control clinical trial of simvastatin to slow the progression of Alzheimer's disease:**

This study is not yet available. We hope to be enrolling participants this fall. The purpose of this study is to see if the drug Simvastatin which reduces cholesterol can slow the progression of AD. Participants must have mild to moderate Alzheimer's disease. The study lasts 15 months and is sponsored by the Alzheimer's Disease Cooperative Study Group (ADCS).

For more information on these or any other study contact Kris Gravanda by email [krisg@mail.med.upenn.edu](mailto:krisg@mail.med.upenn.edu) or phone at 215.349.5903.

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