



ALZHEIMER'S DISEASE CENTER



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

QUARTERLY

Use of Antihypertensives Preserves Cognitive Function in Older African-Americans

In this issue we address ethnic and racial differences in the risk, treatment, and diagnosis of Alzheimer's disease. The following article is reprinted by permission from "Reflections" Volume 9 Issue 1 of the Indiana School of Medicine's Indiana Alzheimer Disease Center Newsletter.

Researchers at the Regenstrief Institute and the Indiana University School of Medicine report that the use of antihypertensive medication by older African Americans to reduce high blood pressure also reduced their odds of cognitive impairment by 38 percent. The study was published in the October 14th issue of the [Archives of Internal Medicine](#).

The researchers, who followed 1900 older African American men and women for five years, found that the continuous use of medications to lower blood pressure reduced the risk of memory loss by more than a third.

"We have a lot of medications that keep people alive longer, but few to maintain their memories," says Michael D. Murray, Pharm.D., M.P.H., a research scientist at the Regenstrief Institute, professor of pharmacy at Purdue University, adjunct professor of medicine at the IU School of Medicine and first author

of the study. "We have now shown that antihypertensive medications can decrease the risk of cognitive impairment as well as lower the risk of stroke, myocardial infraction, and end-stage renal disease."

This is the first study to find a relationship between medication taken to control high blood pressure and cognitive impairment in older African Americans, although previous studies suggest that the use of antihypertensive medication by older white adults with high blood pressure preserves cognition. Cognitive impairment is defined as a measurable change in cognitive function. "Our study provides older African Americans with

yet another reason, in addition to preventing stroke, heart attacks and kidney problems, to take their blood pressure pills," says Dr. Murray.

All the participants were free of cognitive impairment at the beginning of the study and two thirds had high blood pressure. This is the largest longitudinal study to date on the cognitive effects of drugs in older African Americans. According to the National Center for Health Statistics approximately one quarter of Americans between the ages of 20 to 74 years are hypertensive. More than three-quarters of women aged 75 and older in the U.S. have hypertension, as do 64 percent of men of the same age. The prevalence of hypertension is 60 percent higher in African Americans, and their risk of stroke is 80 percent higher than Caucasians.

"This analysis is part of the ongoing Indianapolis-Ibadan dementia project, a study which is designed to identify potentially modifiable risk factors for Alzheimer disease by comparing the disease in two difference countries, African Americans living in Indianapolis and Yoruba living in Ibadan, Nigeria", explains Dr. Hugh Hendrie, a research scientist at the Regenstrief

For a summary of recent research on racial differences in Alzheimer's Disease see [page 5](#).

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Staff Awards and Honors

Valerie Cotter Awarded Book of the Year:

Valerie Cotter, MSN, CRNP, Education Director of the Alzheimer's Disease Center and Nurse Practitioner at the Memory Disorders Clinic has received the Book of the Year Award for Advanced Practice Nursing from the *American Journal of Nursing* for her book, "[Advanced Practice Nursing with Older Adults: Clinical Guidelines](#)", which she edited with Dr. Neville Strumpf. A review by Denise Kresevic cited it as "a rich reservoir of information on geriatric standards of care for all clinicians and educators." (*The Gerontologist*, 42: 4, 2002). This comprehensive book provides expert guidelines on all aspects of care for the older adult, including important information on pain management, dementia care and fall prevention.

Jason Karlawish awarded Virginia Brown Fellowship:

Doctor Karlawish, Associate Director of the Memory Disorders Clinic and Director of the Education and Information Transfer Core of the Alzheimer's Disease Center, has been awarded the Virginia Brown Fellowship for Aging and Stroke Research. This fellowship will support Dr. Karlawish's work on three critical and controversial issues: research decision-making, informed consent, and outcomes assessment - specifically quality of life.

Karen Hirschman awarded 2nd place at Resesarch Retreat:

Dr. Hirschman, a Post Doctoral Fellow at the Center for Neurodegenerative Disease Reseach (CNDR) has been working with Dr. Karlawish to study decision-making and advance care planning for patients with age-related neurodegenerative diseases.

Her research, "*How does the dementia patients' role in decision making change over time?*" was awarded second place in the "best poster" competition at the 3rd Annual CNDR Research Retreat that was held in November of 2002. This research was made possible by data gathered in the "caregiver minimum data set," the pink booklet filled out by carers during visits to the Memory Disorders Clinic.

In addition to her research, Dr. Hirschman sits on the Geriatric Enrichment Task Force and teaches research methods at the School of Social Work at the University of Pennsylvania. She also runs a monthly support group for Children of Aging ParentS (CAPS).

Antihypertensives and Cognitive Function *continued from page 1*

Institute and professor of psychiatry at the IU School of Medicine.

Drs. Murray, Hendrie, and colleagues recently began a four-year study sponsored by the National Heart, Lung, Blood Institute to determine whether minority and low-income patients with high blood pressure take their medications better when they are helped by a pharmacist and provided with special medication information aimed at person with low literacy. The trial will last four years and will determine whether providing supportive information improves medication-taking and reduces blood pressure in these patients.

In addition to Drs. Murray and Hendrie, co-authors of the Archives of Internal Medicine study on antihypertensive medication and preservation of cognition in older African Americans are Kathleen A. Lane, M.S., Sujuan Gao, Ph.D., Rebecca M. Evans, M.D., Frederick W. Unverzagt, Ph.D., and Kathleen S. Hall, Ph.D.

This study was supported by a grant from the National Institute on Aging.

Check out the Alzheimer's Disease Education and Referral (ADEAR) Center

The National Institute on Aging (NIA) funded ADEAR Center provides a wealth of information. Through it's publications and website. One important service is the Clinical Trials Database. The database lists clinical trials on dementing illnesses that are occurring around the country. Two new trials are underway: *Cholesterol Lowering Agent to Slow Progression of AD (CLASP)* which will occur at Penn's ADC (*see page 8 for details*) and *Treatment of Agitation/Psychosis in Dementia and Parkinsonism (TAP/DAP)*. Sites for this study include several medical centers in New York and the University of Pittsburgh ADCRC. Visit ADEAR's website at www.alzheimers.org to learn more about these and other studies.

ADEAR has recently released an updated version of "Alzheimer's Disease: Unraveling the Mystery." This free publication provides the latest research findings on the causes, diagnosis and treatment of AD in non-technical, easy to understand language. To obtain a free copy call 1.800.438.4380 or email adear@alzheimers.org.



How hip protectors - *not a pill* - can reduce one of the most devastating complications of dementia.

by Jason H. Karlawish, MD and Jennifer Klocinski, MA

Hip fractures cause much pain and suffering in older adults. But they are especially devastating to persons with a dementing illness. Hip fractures in a person with dementia lead to lengthy hospital stays, nursing home placement and even death. Post-surgery recovery is more difficult for a person with moderate to severe dementia since they may have difficulty following and remembering physical therapy instructions.

Not only is recovery more difficult in persons with dementia compared to persons without it, but the chief cause of hip fracture is more common too. Individuals with dementia are at a higher risk of falling and fracturing a hip than individuals without cognitive impairment.

Older adults with dementia are up to three times more likely to sustain a hip fracture than non-demented elders. As dementia progresses a person's balance and ability to walk is affected. In addition, they may be taking medications to treat common neuropsychiatric complications. Together, these may explain the higher risk of fractures.

Preventing a fall may be the best way to avoid a hip fracture. Strategies exist to prevent falls (see Box 1), but no strategy is guaranteed. Falls still happen. Another way of preventing a hip fracture is to take a lesson from professional football: wear a hip protector.

Hip protectors usually consist of padding and/or plastic shields that are attached to special undergarments. The idea makes sense, but it raises a number of questions. Are there barriers to their use? How costly are hip protectors?

Do they work? A review of the medical literature suggests that hip protectors do prevent fractures. The Cochrane Collaboration, a non-profit organization that conducts systematic reviews of healthcare interventions, reviewed six studies. They were able to combine the data from 3 of the 6 studies and found that 2.2% (N = 29/1313) of those allocated to the group

wearing hip protectors experienced a hip fracture while 6.2% (N= 130/2099) of those allocated to not wear hip protectors experienced a fracture. The difference between 2% and 6% may not seem like a huge difference but this is greater than a 60% reduction in hip fractures and to the person who falls and does not break a hip it matters quite a bit.

A study by Kannus (2000) also found a 60% reduction in the number of hip fractures for those who were allocated to wear hip protectors. They estimated that if 1,000 people wore hip protectors over a one-year period 21 fractures would occur compared to 46

fractures if people did not wear the protectors.

Preventing Falls

- Make living areas safer – for example, remove tripping hazards and slippery rugs, improve lighting, and install grab bars and handrails.
- Ask your doctor to review your medications looking for side effects and interactions that may lead to falls
- Have your vision checked

taken from CDC, National Center for Injury Prevention and Control. Fact Sheet: Falls and Hip Fractures Among Older Adults. <http://www.cdc.gov/ncipc/factsheets/falls.htm>

Are there barriers to their use? These studies consistently show efficacy, but they also show a consistent problem: compliance. People were not wearing consistently the hip protectors. In the study by Kannus (2000) 9 of the 13 fractures in the protector allocated group occurred when the hip protector was not being worn. The percentage of study participants allocated to wearing hip protectors

who actually wore them in the six studies reviewed by the Cochrane Collaboration ranged from a low of 24% to 86%. In the study by Kannus (2000) 31% of people eligible to participate in the study declined and 71% of those who did participate stopped wearing the hip protectors during the study.

Why are people not wearing the hip protectors? Major reasons given were discomfort and poor fit. Some people reported skin irritation. Another issue may be vanity. Who wants their hips to look larger? Chan (2000) cited dementia as the major reason for non-compliance. If the undergarments are uncomfortable someone with dementia may become agitated and refuse to wear it especially if they cannot understand the importance of wearing the hip protector. A symp-

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Hip Protectors: Reducing a devastating complication of dementia... *continued from page 3*

tom of dementing illnesses is poor judgment. Chan's study (2000) also reported that patients' non-compliance was related to their perceived lack of risk for a hip fracture.

Another issue to consider is incontinence. The need to wear incontinence products under the hip protector undergarment may add to the discomfort and may



Did you know...?

- One third of adults 65 years and older fall each year
- In 1998, about 9,000 people over the age of 65 died from a fall-related injury
- 60% of fatal falls happen at home
- Half of all older adults hospitalized for hip fractures cannot return home after their injury

Taken from CDC, National Center for Injury Prevention and Control. Fact Sheet: Falls and Hip Fractures Among Older Adults. <http://www.cdc.gov/ncipc/factsheets/falls.htm>



make dressing someone more difficult. One study found that incontinent residents needed 5 hip protectors rather than the three thought to be needed, which increases the cost.

We spoke with Dr. Thomas Lawrence, a geriatrician who practices at Penn at Radnor, to hear what a practicing physician has to say about hip protectors. His experience with nursing home patients who use hip protectors echoed the barriers discussed in the studies. He found that to be effective the hip protectors need to be tight fitting and his patients complained about the discomfort as well as the unflattering appearance. He also mentioned that certified nurse's aides (CNAs) often forgot to put them on the patients they assisted in dressing. Finally, Nursing Homes are reluctant to use them since the cost is not trivial and it is unclear about who should pay for them.

Hip protectors can significantly reduce the risk of a hip fracture and all the subsequent consequences. But they won't do much good if the discomfort and hassle of wearing one keeps it in the dresser drawer. Robert R. Recker, MACP, director of the Osteoporosis Research Center at Creighton University in Omaha, Neb describes one creative method for encouraging people to wear them. He asks some of the nursing staff to

wear them and when patients find that they cannot pick out who is wearing a hip protector they tend to feel better about wearing one.

Key references for this article:

Buchner DM, Larson EB. 1987. Falls and fractures in patients with Alzheimer-type dementia. *JAMA*. 257(11):1492-5.

Chan DK, et al. 2000. Effectiveness and acceptability of a newly designed hip protector: a pilot study. *Archives of Gerontology and Geriatrics*. 30(1):25-34.

Clague JE, et al. 2002. Predictors of outcome following hip fractures. Admission time predicts length of stay and in-hospital mortality. *Injury*. 33(1): 1-6.

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Morris JC, et al. 1987. Senile dementia of the Alzheimer's type: an important risk factor for serious falls. *Journal of Gerontology*. 42(4):412-7.

Parker MJ, Gillespie LD, Gillespie WJ. 2002. Hip protectors for preventing hip fractures in the elderly [Cochrane review]. *The Cochrane Database of Syst Rev*. 4. (software).

van Steenburgh J. Jan. 2003. Three developments that could change how you treat osteoporosis. *ACP-ADIM Observer*.



Hip Protector Retailers and Prices

- How much do they cost and where can one purchase hip protectors? An Internet search using *Google.com* and the key words "hip protector" turned up 9 websites. Below are 3 randomly selected companies.
- HIProtector
• Phone: 1-800-930-9255
• website: www.hiprotector.com
• Sale price ranges from \$89.95 to \$174.95
- HipSavers
• Phone: 1-800-358-4477
• website: <http://hipsavers.com>
• Price ranges from \$29.99 to \$50.00
- Tytex Group
• Phone: 1-877-728-3447
• website: <http://www.tytex.com>
• Price on currently on sale for 50% of \$89.95



How can genes and your race affect your chance of developing AD?

by Jennifer Klocinski, MA

African Americans as well as other minority groups have been historically, underrepresented in research. Why does this matter? Several studies suggest that the prevalence, familial risk and genetic and environmental factors associated with AD may be different for African Americans. In other words, Alzheimers disease and the risk of getting it may not be the same for all people. The consequences for patients are potentially significant. The results of studies based upon Caucasian's may not apply to African Americans and perhaps other ethnic and racial minorities.

Is AD more common among African American?

The Alzheimer's Association's report "[African-Americans and Alzheimer's Disease: The Silent Epidemic](#)" has brought together results from various studies, and the February, 2003 issue of the journal [Archives of Neurology](#) reports recent research on the relationships among genes, race and Alzheimer's Disease.

AD is more common among African American's. Prevalence estimates, that is, how many people currently have the disease, range from 14% to almost 100% higher in African Americans than Caucasian Americans. A sensible explanation for this is that African Americans are more likely to get AD. In other words, their annual risk, or incidence, is higher.

But the data do not consistently show a higher risk when comparing African and Caucasian Americans. Studies that have found a difference (e.g. Green et al, 2002) looked at only people with a 1st degree relative with AD (e.g. a mother or father) and not the general population. Clearly, more research is needed.

Are the risk factors the same across races?

One of the key risk factors for developing AD is the APOE gene. This gene comes in three common forms, e2, e3 and e4. Apolipoprotein is involved in lipid (i.e. cholesterol) transport and metabolism. The APOE e4 variant has been associated with cardiovascular disease and now with AD. Research has found that the APOE e4 gene appears more often in people with AD (40% compared to 15-20%). Until now much of this research has not examined the affect of race and APOE type on the risk of developing AD.

Evans et al. (2003) looked at the relationship between race and type of APOE gene and the risk of developing

AD (i.e. incidence rate). The results were interesting. The risk of developing AD was higher for African Americans than Caucasian Americans who do not have the APOE e4 gene but the results were not statistically significant. The difference in risk may not be real, but due to chance alone. A close look at the data shows a paradox. African Americans are much more likely to have the APOE e4 gene than Caucasian Americans (42.1% to 27.1%) but having that version of the gene that increases the risk in Caucasians did not increase the risk in African Americans. Caucasian Americans with the APOE e4 version of the gene were 2.7 times more likely to develop AD than Caucasian Americans without the e4 version. However, it had no effect on African Americans. This means that African Americans with the APOE e4 gene had the same chance of developing AD as African Americans with the APOE e2 and e3 gene.

Putting it all together.

African Americans have a greater prevalence of AD, their risk of getting the disease may be higher, but the genes that are typically implicated in this risk do not explain it. Why? We don't know. Several suggestions have been made as to why the APOE gene affects races differently. One suggestion is that APOE may interact with an environmental or other genetic factor that is more common in one race than the other. Some have speculated the greater prevalence of AD in African American's is due to vascular disease factors. More research is needed to understand these differences.

If treatments are developed to prevent the disease we need to be able to distinguish who is at risk for developing AD so that treatments are targeted at those most likely to benefit. Treating someone unlikely to develop AD with medication that could have side effects and might be costly benefits no one.

Selected References:

- Alzheimer's Association. 2002. African-Americans and Alzheimer's Disease: The Silent Epidemic. Chicago:IL.
- D. Evans et al. 2003. Incidence of Alzheimer Disease in a Biracial Urban Community. Arch Neurol. 60(2): 185-189.
- Green et al. 2002. Rick of Dementia Among White and African American Relatives of Patients with Alzheimer Disease. JAMA 287(3): 329-336.



Meet the Leaders of Penn's ADC: An Interview with Jason Karlawish

by Jennifer Klocinski, MA

The Alzheimer's Disease Center (ADC) at the University of Pennsylvania is one of 29 ADC's and 3 affiliates in the country. Every five years we compete with other medical institutions around the country for one of these multimillion dollar AD center grants. This is the final interview in the three part series that introduced you to each of the ADC's core leaders and director.

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Education and Information Transfer Core Leader, Jason H. T. Karlawish, M.D.:

Dr. Karlawish is a board certified geriatrician. He received his MD from Northwestern University in 1991. He completed his training in internal medicine, geriatrics and bioethics at Johns Hopkins University and the University of Chicago. Dr. Karlawish joined the Memory Disorders Clinic and Alzheimer's Disease Center in 1999. He now serves as Associate Director of the Memory Disorders Clinic and Leader of the Education and Information Transfer Core of the Alzheimer's Disease Center. He is Assistant Professor in the Department of Medicine, Division of Geriatrics, Fellow of the Center for Bioethics and Senior Fellow of the Leonard Davis Institute of Health Economics at the University of Pennsylvania. Dr. Karlawish's research focuses on ethical issues surrounding research with human subjects.

Conversation with Jason H. T. Karlawish, MD:

JLK: Tell me, how did you become interested in dementia care and research?

JHK: When I was a fellow in geriatrics the FDA approved Aricept and overnight the approach to dementia was transformed from no disease specific treatment to suddenly having a drug for Alzheimer's disease. I went on a crash course of learning more about what is Alzheimer's Disease and how did we discover this drug called Aricept and what does it really do for people? That, combined with a longstanding interest in issues surrounding human subjects research, woke me up. I saw a wide open set of topics about how we develop drugs and decide that they're safe and effective. I wanted to know how do we get these drugs particularly when the subject population is one of the most vulnerable subject populations, and the notion of what is a benefit for treatment is indeterminate and indistinct. The rest has been a confluence of good luck and hard work and meeting good people.

JLK: If you had not entered your current profession, what would you have liked to do?

JHK: I think I would either be a journalist who is a failed novelist or novelist who is a failed journalist.

JLK: What is the best piece of advice you've received and from whom?

JHK: "Go where they're not," and that was from a self-described eccentric pulmonary care intensivist. It means find out where everyone else is, turn around and go the opposite way. My corollary to it is, go where they're not, but where they should be. You have to make a case for why you're going in the opposite direction of where everyone else is going.

JLK: What do you see as the most important finding in Alzheimer's Disease research over the last several years?

JHK: Better understanding of the molecular pathology that underlies what we think is the disease, both the pathology of the plaques and the tangles. These results can lead to substantial advances in drug discovery and diagnosis, and challenge us to rethink is there any distinction between normal aging and AD? The ethical and social implications are profound.

JLK: What do you see as the most important contribution of Penn's ADC Education Core?

JHK: We have pushed issues that are recognized as important but traditionally not been seized on. These issues ought to be part of the discussion of research and care that involves patients: informed consent, quality of life, and decisionmaking with someone whose brain is slowly failing. I think our Alzheimer's disease Quarterly, web page, and the support group for patients are three solid examples of efforts to fulfill our mission and I really want to build on that. I think they can all fit together into a Center for Excellence in Dementia Care.

Continued on next page



Meet Out Leaders... *continued*
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JLK: What part of your work gives you the most pleasure?

JHK: Talking to patients and their families both as a clinician, to make diagnoses and to identify problems in need of treatment, but also talking to them just as people. And writing papers, whether those are research papers or papers on theory or related scholarship. They're two very distinct activities and yet the one informs the other. In some sense I couldn't do the one without doing the other.

JLK: Finally, what is your favorite book and why?

I keep on going back to reading Cormac McCarthy's "Blood Meridian." I think its because it has wonderful action and drama with vivid writing. It's a great story,

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: **Two articles by Drs. Karlawish**
: **and Clark appear in the *Annals***
: ***of Internal Medicine***
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: The March 4th, 2003 issue of the *Annals of Internal*
: *Medicine* contains two articles by Jason
: Karlawish, MD and Christopher Clark, MD. The
: first article is an update on diagnosing and treating
: AD. The second article reviews the current
: standard for diagnosing mild memory problems.
: Copies of these articles can be obtained from the
: website of the *Annals of Internal Medicine*:
: (<http://www.annals.org>).
: *Alzheimer Disease: Current Concepts and*
: *Emerging Diagnostic and Therapeutic Strategies.*
: *Annals of Internal Medicine* 138(5): 400-410.
:
: *Diagnostic Evaluation of Elderly Patients with Mild*
: *Memory Problems. Annals of Internal Medicine.*
: 138(5):411-419.
:

well written and one of those books that every time you read it you get a new insight on something about the human condition, but mostly because it's just so much fun. The other book that I've read multiple times and really enjoyed is Graham Greene's "The Heart of the Matter." Every time you read it you learn a new thing about love, devotion and sacrifice.

Center for Neurodegenerative Disease Research News

Donze family raises \$6,000:

The Center for Neurodegenerative Disease Research (CNDR) is extremely fortunate to have the support of Lucy Donze and her very talented family. Lucy turned her grief into action after her husband Santo passed away from a four year battle with a rare neurological disease. As many people do, Lucy requested that memorial contributions be sent to the CNDR. But she has done so much more. She has used her talents as a fundraiser to advance research at the CNDR. Lucy entertained at area nursing homes sending her fee to the CNDR. Then on September 7th she hosted a cocktail party by the sea.

Sixty guests were entertained at the Island House condominium in Margate, New Jersey with the musical talents of the Donze family. Oldest son Robert, a former radio announcer, served as MC for the event. Middle son, Richard provided musical entertainment while granddaughters Elizabeth and Nina sang. Nina dedicated "Out Here On My Own", to Pop-Pop (Santo) whom she said "came to every one of my performances." Through Lucy Donze's efforts \$6,000.00 was raised to support research conducted at the CNDR.

Support 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. Opportunities exist to fund specific projects both small and large, such as this Quarterly. To find out more about our program needs please contact our main office at (215) 662-7810 or visit our website (www.ups.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. Contributions are tax deductible.

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



ADC QUARTERLY



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

Research Opportunities:

Cholesterol Lowering Agent to Slow Progression of AD (CLASP):

This study will test the effectiveness of a cholesterol-lowering drug, Simvastatin (trade name Zocor) in slowing the progression of Alzheimer's Disease. Epidemiological studies have suggested that statins, a class of cholesterol-lowering drugs, reduces the risk of developing AD. This study examines the ability of statins to slow the disease by comparing participants assigned to take Simvastatin to those participants assigned to take a placebo.

This is a national study sponsored by the Alzheimer's Disease Cooperative Study (ADCS) Group. Participants must be 50 years or older with mild to moderate Alzheimer's disease. Participants cannot have high cholesterol or be taking cholesterol lowering medication.

Can Dietary Supplements Slow Progression of Alzheimer's Disease?

Homocysteine is an amino acid normally produced by the body. Research suggests that high levels of homocysteine may speed the progression of AD. This study will evaluate whether large daily doses of folate, vitamin B₁₂, and vitamin B₆ will reduce homocysteine levels and slow the rate of decline in memory and cognitive performance in patients with Alzheimer's disease. This is a national, multi-site study sponsored by the Alzheimer's Disease Cooperative Study (ADCS) Group. Participants must be 65 years or older, speak English or Spanish, have mild to moderate Alzheimer's disease and cannot be taking vitamins.

To learn more about these and other studies at the ADC please contact Kris Gravanda by phone at 215.349.5903 or email at Krisg@mail.med.upenn.edu.

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THE UNIVERSITY OF PENNSYLVANIA

Jason H.T. Karlawish, MD, Publisher
Jennifer Klocinski, MA, Editor
University of Pennsylvania
Ralston House, Rm 201
3615 Chestnut St.
Philadelphia, PA 19104
phone: 215.662.7810
fax: 215.662.7812

email: jennifer@mail.med.upenn.edu
internet: www.uphs.upenn.edu/ADC

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