

About people and efforts that bring the knowledge we seek on Alzheimer's disease and healthy brain aging ever closer *in sight*

Working Through Mild Cognitive Impairment (MCI)

A story of a man and his tools

by Carol Edwards

Donald Nye has a professional woodworking shop. It's fully outfitted with saws, sanders, routers, and the other tools he uses to make his custom furniture creations possible. And in his pocket is an iPhone. It too, is fully outfitted, with an electronic notepad, to-do list, mapping software, and the other tools he uses to make living with his mild cognitive impairment manageable.

About Mild Cognitive Impairment

Mild cognitive impairment, or MCI, is a condition where a person's memory or certain other cognitive skills have dropped below what's considered normal for someone of their age and level of education, but without affecting their reasoning and judgment, or their ability to function satisfactorily in daily life. "With MCI, a person who was always fast with math may now need extra time and a calculator to add numbers they previously did in their head," said Steven Huege, M.D., of the Penn Memory Center. "But with a support tool like the calculator, they can still do the task. Someone with dementia, a major cognitive impairment, would not be able to understand how a calculator worked or how it could help them."

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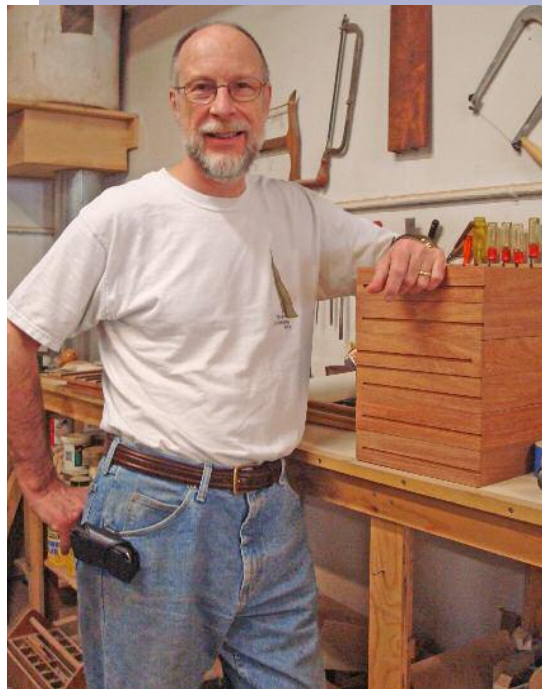


photo: Carol Edwards

Don Nye, in his shop with some of the woodworking tools he's skilled at using. He stands by a stack of rosewood drawer boxes he built for his latest project, a display chest for his collection of fountain pens. "I don't have any problems functioning in my shop," he said, "and the work is so satisfying." In day-to-day life, Don is learning to use the electronic tools in his iPhone — to-do lists, reminders, mapping, and more — to help work through the memory limitations of his mild cognitive impairment (MCI).

DRUG AND
DIAGNOSTIC
STUDIES



MCI
on the QT



on current
treatments



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link to AD?



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Don Nye, 63, is a friendly, well-spoken man with a warm, direct style. He has a Ph.D. in etymology, the study of insects. He spent a career in research and development of agricultural pesticides for a major international chemical company. A decade ago he left that world for new kinds of work, including making furniture.

Don is aware that there is dispute among researchers as to whether MCI is a condition distinct from Alzheimer's, or just symptoms of the disease in its very earliest stages. And while individuals with MCI have a much higher rate of developing Alzheimer's disease over time than the general population, about half never worsen significantly, remaining stable and functional for the duration of their lives.

On a splendid spring day in the Ralston House garden, Don talked with me about getting the diagnosis of MCI, and learning about living with its limitations.



I started to realize that, more and more, I had to write things down. Things I remembered easily in the past, I'd forget if I didn't make a note.

"It was affecting the way I interacted with people. I lost my outgoingness. If I was talking with someone, and I forgot part of what they said, I didn't ask them to repeat it; I just backed out of the conversation. I play squash a few times a week with guys I've known for years. It got to the point where the conversation on the court was them talking and me listening. I'd try to down-play it, but inside it had me really worried and frightened. And feeling depressed."

Getting past the fear, to an evaluation

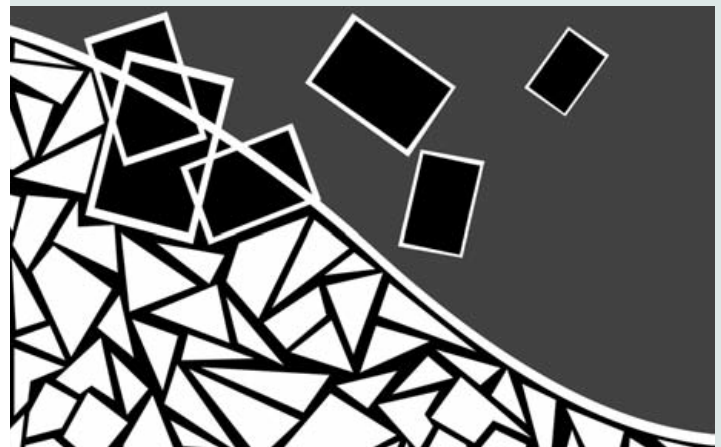
"One day last year, my wife Corrine asked, 'How would you feel about going to get tested for Alzheimer's disease?' and I said, 'I'm there.' I was terrified of the word 'Alzheimer's,' but I knew I needed to get some help for my memory, or at least find out what was going on. I'd been afraid to act. But Corrine opened a door for me. She brought up the idea of getting tested in a matter-of-fact way. I'm thankful she did.

"I had a Penn Memory Center evaluation with Dr. Jason Karlawish. Some of the memory tests were tough and I was very nervous about how I would do. When the diagnosis was not Alzheimer's, but mild cognitive impairment, I was so relieved. I learned that depression is common in people with memory problems, and I'd been feeling down because of my memory for a while. I was started on medications including

ABOUT MCI: Mild Cognitive Impairment



The term Mild Cognitive Impairment, or MCI, was first used in 1991 by Charles Flicker, PhD., and colleagues at New York University Medical Center's Aging and Dementia Research Center, to describe study participants functioning normally in daily life and living independently, but whose neuropsychological testing showed below normal scores. When researchers followed these subjects over 3 years, they found them more likely to decline into dementia than those who did not show such impairments in the initial examination.



Two decades after the term first appeared in the literature, MCI is still a concept under development. But by any definition, MCI means a markedly greater risk of developing dementia over time.

Two decades later, Mild Cognitive Impairment remains a concept under development. Most Alzheimer's researchers agree that MCI represents an array of changes and symptoms that are both distinct and common. But they debate whether MCI is a separate disorder, or simply the very earliest symptoms of Alzheimer's disease.

Currently, a diagnosis of MCI is generally given where tests of an individual's memory, attention, language, or other skills score below what is considered normal for someone of the same age and level of education, but when considered with other aspects, including their ability to maintain adequate day-to-day functioning, they do not meet the diagnostic criteria for Alzheimer's disease.

The disorder is usually sub-classified into one of two types: amnesic MCI (amnesic meaning "loss of memory") where problems with memory are the chief difficulty; and non-amnesic MCI, where problems with attention, concentration, or other cognitive functions are most prominent.

Studies reveal that people with the amnesic type of MCI are more likely to eventually develop dementia than age-matched persons who are cognitively normal. Among people with amnesic MCI, between 10 to 15% a year will develop dementia. This means that in a hypothetical group of 100 people with memory-related MCI, over a five year period, 40 to 60 of them will have developed dementia. Older adults who don't have MCI will typically develop dementia at a rate of 1 to 2% a year.

But not all persons diagnosed with MCI go on to develop dementia. About half will remain essentially stable and functional over their lifetimes.



MCI is common.



A National Institute on Aging study found that 1 in 5 people over age 70 have some type of cognitive impairment less severe than dementia. MCI is also increasingly seen in younger individuals.

Multiple clinical trials testing medications used to treat persons with Alzheimer's disease, in particular the cholinesterase inhibitors, have failed to show that these medications change the risk of conversion from MCI to dementia over time.

an antidepressant, which are effective. I feel much better overall, and about how I interact in the world."

Working through it

"I try to use the tools I need to make things easier. I make detailed notes during important conversations to refer to later. I have an iPhone, with scheduling, to-do lists, mapping, and more built right in. I use all that, and I should probably use it even more. But sometimes I get lazy. Maybe I won't write down what I know I should. Then I'll forget. If I try to just cover it up, my wife calls me on it. I appreciate her for that. Corrine has been wonderful with me in all of this.

"I'm open about my memory problems with my family and people who know me. It takes energy trying to hide it. I'd rather focus on trying to strengthen and support the memory ability I do have" . . . Don Nye

"If I get frustrated when I have trouble remembering, I try to stop, take a minute, then work through it. Driving to Ralston House for this interview today, some streets were closed for construction, and I had to go another way that wasn't familiar. I got confused whether I was heading east or west. I was anxious about getting lost and being late. So I pulled over, calmed down, and entered the address for Ralston House into the iPhone mapping application. I followed the route it showed, and got here fine after that.

"I'm open about my memory problems with my family and people who know me. It takes energy trying to hide it. I'd rather focus on trying to strengthen and support the memory abilities I do have. I play games and puzzles, I exercise, and I work on projects I like and do well. I've been building custom furniture in solid woods, for sale and for myself, for about 10 years. I don't have any problems functioning in my shop, and the work is very satisfying."

A role in research

"I didn't realize mild memory problems are common, or that there's research about it until I came to the Penn Memory Center. I've been in one study run by Dr. David Wolk and Katie Manning. It included an MRI and an EEG and a big battery of cognitive testing. The memory tests are a challenge for me, but the experience overall was kind of fun. It's a way

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to find out what's going on, for me, and for science in general. I spent most of my career in R&D; I know its value."

On living well now

"I'm relieved that my problem is not Alzheimer's disease. I know it could develop. But I try not to think about a negative future. My grandmother lived to 104, clear-thinking almost 'til the end. My mother is 93 and still handles her own meals, housekeeping, and finances. I hope Alzheimer's is not in my future, especially if I live as long as my family does, but if it happened, we would just have to cope with it.

"I'm so glad I got the tests and medicines I needed. I enjoy things and people again. We live in a neighborhood with lots of young people with kids. Now that the weather is better, it's

SUBJECTIVE (self-reported) MEMORY COMPLAINTS:

If you think you have memory problems . . .



Studies show that persons who sense persistent minor memory problems in themselves may be picking up on the earliest physiological changes seen in mild cognitive impairment. Worrying about or trying to hide your memory concerns may lead to depression, which makes memory and thinking difficulties worse.

If you are concerned about ongoing minor memory problems, contact the Penn Memory Center to schedule an appointment for an evaluation, 215-662-7810.

nice to stop on the street and talk for a minute. Corrine and I visit my family in Massachusetts, and we go out with our friends here. We both like to cook and eat, so we'll play in the kitchen. And I love riding my bike all over the city.

"This year is our 30th wedding anniversary. We've been talking about a trip through the countryside of Albania. Whatever we do, I know we'll enjoy it. As I said, I'm not thinking negatively about the future."

Another view:



has spent her career in elementary education. She's friendly and attractive and animated; you can sense that students would be at ease around her. She's a wife, a mother of grown chil-

dren, the family bookkeeper, helpful in the family business, involved with friends, and active at her church. She knows the bible verse that ends with "the truth shall set you free." And that's what she's worried about now. Being "set free," in her mid 50s, from a job she loves and a salary she relies on, because she has mild cognitive impairment, MCI.

About MCI

MCI describes a condition where test scores of an individual's memory, attention, language, or other skills have dropped below what is considered normal for someone of the same age and level of education, but not so low as to impair judgment or day-to-day functioning. A National Institute on Aging study reported 1 in 5 people over age 70 in the US has some cognitive impairment less severe than dementia, "and the condition is increasingly identified in younger individuals as well," said Dr. David Wolk, a neurologist at the Penn Memory Center.

It could be anyone's story

Donna is "happy to tell you everything about my situation," but "just can't risk the potential reactions," especially at work, if she were identified, so her last name is omitted here. Unlike many employees facing cognitive problems in their prime working years, Donna has confided her diagnosis to her boss, who is also a trusted friend. "She and I agreed that if a day comes when she feels I can no longer do the job she needs from me, she'll tell me, and I'll resign. I won't fight it. I love the kids and I would never shortchange them. But for now, [her boss] believes that, with some help in place, I can still be effective. And I believe that, too."

I was slipping . . .

About 3 years ago, Donna sensed "mental changes. I'd forget little things, or find it hard to concentrate. I would try to focus harder, or try to relax more, thinking it was just stress, but the problems didn't go away." She saw her family doctor and "tested out fine, but I just kept feeling like I was 'slipping.'"

At school, it took longer to complete work that "for years I did in a snap." She knew some co-workers had started to wonder — and comment — on these changes. "I was so worried that

Keeping her MCI on the QT



I would be seen as uncaring or burned out after almost 30 years in education, when I really love the job and the kids.” She shared her fears with her principal, who is also her dear friend. “We decided I should see a neurologist. I took some tests in his office. Ninety minutes later, he gave me a diagnosis of Alzheimer’s disease, a few prescriptions, and that was it.”

A more thorough approach

Donna, her family, and the friends in whom she confided “were shocked and scared and sad and determined” to get a more complete evaluation.

She learned the public was invited to view a one-hour documentary on Alzheimer’s at a local college, and that Penn Memory Center physicians would take questions afterward. She came to the event and met PMC neurologist Dr. David Wolk. “I called the next day to get an appointment with him for a full work-up.” After extensive testing including sophisticated diagnostic imaging studies, she was diagnosed with MCI.

MCI on the QT

Donna and her boss believe it’s best not to reveal her diagnosis at school. “If I had diabetes, or even cancer, I wouldn’t hesitate to let it be known. But this is a ‘brain thing’ most people don’t understand. Some people think you’re senile, or crazy. I don’t want to have to worry about coworkers or parents looking over my shoulder, just waiting to find something wrong.”

Donna believes that “adapting to the changes of this condition, not surrendering to it” is what’s called for. She’s left the after-school activities she once led to better manage her regular duties. “If I deal with one topic at a time, I’m more successful. One of my former students, who is currently a trainee at our school,

told me she remembers the way I taught her to break up assignments into sections, and work each one through. I’m taking that approach myself now.”



“If I had diabetes, or even cancer, I wouldn’t hesitate to let it be known at school. But this is a ‘brain thing’ that most people don’t understand. Some people think you’re senile, or crazy.

I don’t want to worry about co-workers or parents looking over my shoulder, just waiting to find something wrong.”

“At home, I did the bills recently, and found myself second-guessing what I paid. I asked my daughter to check them over. Everything was fine, and I realized that if just a little bit of help, like someone checking my work, makes me feel more comfortable, then I need to get used to asking for that.”

Looking ahead

Donna is aware there is dispute in science whether MCI is a condition separate from Alzheimer’s, or just symptoms of the disease in its very earliest stages. People with MCI do develop Alzheimer’s at a much greater rate than the general population. Yet, about half never worsen significantly, remaining stable and functional for the remainder of their lives.

But Donna “would not be surprised” if she someday develops the disease. “My mother has Alzheimer’s. I see a lot of myself in her. And I also see that sometimes she’s not very realistic about her condition. She pushes away the help she needs. I just hope that if I ever reach that point, I would have the grace to trust and rely on the people who love me.”

Donna is “concerned but not fearful” about her future. She’s looking forward to teaching a recreational class this summer and traveling with a friend. Her philosophy is to “stay positive and up. I’m not the type to wallow, and my friends won’t let me if I wanted to. I look at all the things I’ve

done and still do well, and I think ‘Just because I may not contribute 110% like I used to, what I can offer is still very worthwhile.’ Some people only give a 50% effort on their best days.”



Early-Onset Alzheimer's Disease now eligible for Social Security Disability

Early-onset Alzheimer's disease is among 38 new entries to Social Security's list of Compassionate Allowances, diagnoses eligible for review and likely approval of benefit claims "within days, rather than months and years," according to a recent statement from the agency. The Social Security Administration defines early-onset Alzheimer's disease (AD) as the diagnosis of AD for a person younger than age 65.

The list "quickly identifies diseases and medical conditions that clearly qualify for benefits, and allows the agency to electronically target and make speedy decisions for the most obviously disabled individuals." Changes were effective March 1, 2010.

Those with a diagnosis on the Compassionate Allowances list would not be expected to re-enter the workforce.

Social Security received a total of 3.3 million disability claims of all types in 2009.

The Compassionate Allowances list was initiated in 2008 with 50 conditions — 25 rare diseases and 25 cancers. Unlike many of the 38 newly-added diagnoses, which are quite rare and often affect children, early-onset AD,



For those forced from jobs in mid-life by Alzheimer's, an end to the added burden of delays and denials of disability benefit claims?

about 5% of Alzheimer's cases overall, affects as many as 250,000 people in the US today — most in their 40s or 50s, usually working, and in many cases supporting families — according to the Alzheimer's Association.

In expanding the list, Social Security heard testimony from early-onset AD patients and their families' whose claims for benefits had been denied or delayed through an appeals process lasting 18 months or more. Denials may reflect customary agency expectations that disability recipients who have worked will eventually return to work in some capacity, receiving vocational retraining if necessary or taking less demanding jobs. Individuals with a Compassionate Allowances diagnosis — conditions usually considered progressive and irreversible — would not be expected to re-enter the workforce.

"The diagnosis of Alzheimer's indicates significant cognitive impairment that interferes with daily living activities, including the ability to work," said Harry Johns, Alzheimer's Association President. "Now, individuals who are dealing with the enormous challenges of Alzheimer's won't also have to endure the financial and emotional toll of a long disability decision process."

While benefits may be awarded more quickly under these new guidelines, amounts paid still won't approach the former incomes of most of those who were forced from jobs by Alzheimer's in their prime earning years.

The average monthly social security disability payment in 2008 was \$1063.00.

www.socialsecurity.gov/compassionateallowances/

Having a parent with Alzheimer's means an increased risk of developing the disease yourself. But is that risk greater still if it was your mother who was affected?

More evidence of a maternal link to AD



That's the finding of much research over more than a decade, and is again in a PET scan study published online March 15, 2010 in the *Proceedings of the National Academy of Sciences*.

Lisa Mosconi, PhD, of NYU, and colleagues used PET scans with PiB, a radioactive tracer, to view amyloid in the brains of 42 normal individuals, aged 50 to 80. Fourteen participants had mothers with AD, 14 had fathers with the disease, and 14 had unaffected parents. Even after accounting for known risk factors (age, APOE4 gene status, etc.) AD-mother subjects averaged 15% more amyloid plaques than AD-father subjects, and about 20% more than subjects with no affected parent.

Mosconi speculates that genes transmitted particularly from mothers lead to amyloid depositions. Presence of amyloid plaques, however, does not necessarily mean an individual will develop AD. In fact, brain autopsy research reveals that about 30% of elderly individuals who are cognitively normal

You've got your mother's eyes . . . her smile . . . her Alzheimer's?

throughout life are found to have significant amyloid plaque pathology when their brains are examined after death.

These new results echo Marconi's previous findings on a maternal link to Alzheimer's. In an earlier PET study, adults with AD-mothers showed more early changes in glucose metabolism in their brain, similar to changes seen in persons with Alzheimer's, than subjects with a paternal link, and more still than subjects with no parental link at all to the disease.

<http://tinyurl.com/maternal-AD>

Elders who say their lives have a purpose are less likely to face cognitive decline, a new study suggests.

Purposeful life rebuffs Alzheimer's?



Findings are from the Rush University Medical Center Memory and Aging Project, an eight-year study of more than 1000 Chicago-area men and women, average age 81, all of whom had normal cognition when the study began.

In this new study, published in the March 2010 issue of *Archives of General Psychiatry*, Dr. Aron Buchman and colleagues sought "psychosocial factors associated with cognitive decline and dementia later in life." Participants assessed their "happiness, purposefulness in life, and well-being" by responding to statements such as: "I feel good when I think of what I have done in the past and what I hope to do in the future," and "I have a sense of direction and purpose in life."

Four years later, 16% of participants had developed Alzheimer's. People who most strongly related to positive statements about their lives were about 2.5 times less likely to

Shaping a life of purpose and direction may mean less cognitive decline

exhibit AD. Also, people who said they had more purposeful lives were less likely to have developed mild cognitive impairments, and had slower rates of general cognitive decline. The findings have implications for public health, Buchman said. "Social and physical activity, and purpose in life all seem linked with longer life, and decreased mortality, and disability. And now we have to find out what the biological basis is."

http://www.nlm.nih.gov/medlineplus/news/fullstory_95898.html



A report on the evening news said there are not yet any treatments against Alzheimer's.

But a commercial on the same program said Aricept is effective at all stages of the disease.

Which is correct?

Razadyne, medications classified as cholinesterase inhibitors, slow the breakdown of acetylcholine, a chemical in the brain that helps neurons transmit signals to one another. Memantine (Namenda), another medication used for Alzheimer's, helps regulate the activity of a different neurotransmitter chemical, glutamate.

The Alzheimer's Association website states that cholinesterase inhibitors "on average, delay worsening of symptoms for 6 to 12 months for about half the people who take them. Some experts believe a small percentage of people may benefit more dramatically." The site states that memantine "temporarily delays worsening of symptoms for some people. Many experts consider its degree of benefit is similar to the cholinesterase inhibitors."

"For many patients and families, the possibility of some treatment benefit, however modest or temporary, is better than nothing, and I can understand that," said Dr. Jason Karlawish of the Penn Memory Center. Payors may not agree. Citing lack of cost effectiveness in early and late stage patients, the UK's national health care system (NICE) pays for Aricept, Remyntyl, or Exelon only for moderate-stage AD, and does not pay for memantine at all.

What the medications now being tested are aiming for

There are now many Alzheimer's investigational drug trials underway at sites in the US, including the Penn Memory Center. These studies test new medications aimed at attacking the disease itself, by clearing or interfering with the production of plaque and tangle pathology that destroys brain cells.

The hope for such new treatments is that they would have a much more significant positive impact on the capability and functioning of far more patients than what currently available treatments provide.

Contact the Penn Memory to learn more about this vital research.

At present there are no approved treatments that can slow, stop, or reverse the progression of Alzheimer's disease in any person.

Current Alzheimer's medications, such as Aricept, or Namenda, may help temporarily slow the worsening of certain disease symptoms, such as problems with memory or thinking, in some patients, and are widely used. But these medicines have no effect on the underlying pathology that causes the disease. Here's a quick review of the facts.

Alzheimer's disease is "brain failure," resulting from the death of brain cells — called neurons — believed to be caused by a build up of two pathological proteins: beta-amyloid and tau. For rea-

sons not yet understood, these proteins collect in and around neurons to form the destructive plaques and tangles that characterize the disease.

There are presently no approved medications that can alter this Alzheimer's pathology and the ensuing neuron damage and death.

What current Alzheimer's medications do, and don't do

Brain cells communicate with each other through chemical interactions. In Alzheimer's disease, in addition to neuron death, changes in the normal chemistry of the brain may occur, hampering the way remaining brain cells relay and receive information. Aricept, Exelon, and



At present, there are no approved treatments that can slow, stop, or reverse the progression of Alzheimer's disease in any person



FDA calls Aricept TV ads "misleading," "deceptive," and "not supported by available research," and asks drug maker to pull the spots



a February 2010 letter to Eisai Co., Ltd and to Pfizer,

Inc., co-marketers of Aricept (donepezil hydrochloride), the Food and Drug Administration said two widely-shown television commercials for the product violate FDA standards by making "claims and presentations which misleadingly overstate the efficacy of Aricept, implying a greater benefit than has been supported by substantial evidence or substantial clinical experience." The FDA letter asks that these ads, and any promotional materials for Aricept that contain such violations be discontinued.

The TV spots, titled "Beach" and "Garden," for their respective settings, start by "presenting patients with Alzheimer's disease looking blank, confused, distant, and walking off apart from their family members," the letter states. "However, after talking to their doctors about treatment with Aricept, the patients are seen interacting and communicating with their family members, happily and actively involved in activities with them. These presentations imply that, as a result of Aricept treatment, patients' cognitive and daily functioning, specifically aspects of attention and focus, orientation, communication, and social interaction and engagement, will be restored to normal. The results from the Aricept efficacy trials in patients with mild to moderate and severe Alzheimer's disease do not support such improvement."

The fact that the ads superimpose the text 'Individual results may vary' "does not mitigate these misleading presentations," the FDA added.

Eisai, in a statement, said it would "weigh" the FDA's comments, and in the meantime would discontinue the commercials.

Aricept is the biggest seller among FDA approved drugs in its class (cholinesterase inhibitors) which also includes Exelon and Razadyne. Aricept sales generate about \$3 billion annually.

Download a .pdf file of the letter at www.fda.gov/downloads/.../EnforcementActivitiesbyFDA/.../UCM201238.pdf



Brain Donation

Brain donation is the logical conclusion to the extensive study PMC patients and normal controls received while alive. It is a priceless contribution to crucial knowledge, such as how biomarkers seen in living patients translate to findings in the brain, and the effects of trial medications.

● *To update your brain donor registration information, or to learn about becoming a donor, contact Marianne Watson, RN, at 215-662-4373.*



Classes for Caregivers of Relatives with Dementia

The Penn Memory Center offers a 6-week series of psychoeducational classes led by qualified mental health professionals open to anyone who cares for someone with dementia.

The classes emphasize skills related to patients earlier in the disease course, but caregivers of patients at any stage are welcome to join. You'll learn ways to better care for yourself and your loved one as you move through the changes of living with Alzheimer's or other dementias.

● *Take better care of yourself and all those you love with help from these classes. Day and evening sessions are offered. Call 215-662-7810 to learn more about the caregivers class.*

YOU

*You must be the change you want to see
in the world . . .*

Mahatma Gandhi

Penn Memory Center Director Steven Arnold wants to see more people join Alzheimer's Disease and Healthy Brain-Aging Research. So he volunteered for a study.

by Carol Edwards

THE C.V. OF STEVEN E. ARNOLD, M.D., DIRECTOR of the Penn Memory Center, lists 20 pages of educational and professional experiences that have made him the fine physician and scientific investigator he is. But there's one item not listed that adds a unique facet to his patient care and research approach. He's not only a brain-aging researcher. He's also a brain-aging research subject.



photo | Carol Edwards

Dr. Steven Arnold

Earlier this year, Dr. Arnold took part in an imaging study known as AV-45. It's a National Institute on Health-sponsored study of two methods of brain imaging to better understand brain pathology in a wide range of subjects. The principal investigator is Andrew Newberg, M.D., of the Department of Radiology and Psychiatry, who is also co-founder of the Center for Spirituality and Neurosciences at Penn.

I talked with Dr. Arnold about his experience in AV-45.

How did you decide to join a study?

"The Penn Memory Center is about advancing science through research. We ask our patients and normal controls to join studies all the time. I'm now old enough to qualify for a brain-aging study like this one, and I wanted to be able to describe research from first-hand experience. I have tremendous respect for the people who take part in our studies. When I recommend joining a study, and a patient or family asks me, 'Would you do it?' I want to be able to say, 'Yes I would, and more so, I did.'"

What's AV-45 about?

"For years, we've looked at metabolic rates in the brain using PET scans with FDG, a

radioactive tracer that shows glucose utilization. Brain cells at work use a lot of glucose, so you can see how particular areas of the brain are working, or not working, by how much glucose they use. But these tests are not highly specific for Alzheimer's.

"This study consists of an FDG PET scan, and a second scan using a new imaging compound known as AV-45, which binds to amyloid plaques, the major abnormal proteins in Alzheimer's disease. The idea is to allow any plaques present to be visualized. This approach may ultimately offer more specificity in identifying AD.

"So the study is about comparing two different ways to look at a brain for specific evidence of Alzheimer's disease."

Take us through the study step by step.

“First, the study is explained to you by our coordinator, Staci Hoops. You sign the consent form, and take a brief cognitive screening, the Mini-Mental Status Exam (MMSE). A broad range of MMSE scores (30-10) are eligible .

“If your MMSE and other eligibility criteria are OK, the two scans are scheduled. They need to be spaced a few days apart. They’re done over at HUP under the direction of our colleague Dr. Andrew Newberg.

“For the FDG scan, you have a finger stick to check blood glucose; if it’s too high it can affect the results. Then they start an IV in your arm and inject the tracer. You don’t “feel” the tracer in any way. You sit quietly in a comfortable lounge chair while the tracer moves through the bloodstream to the brain, about an hour. The lights are dimmed to reduce visual distractions. You’re

“On the scanning table, you have a soft pillow under your head. The scan takes about an hour. A PET scanner is open and quiet, not like an MRI, and some people drift off to sleep. When the scan is complete you get up and go back to work or home. There’s no recovery time needed. The tracer is fully excreted from the body in a few hours.

“The AV-45 procedure is identical, except you don’t need the finger stick, and trying to minimize thinking isn’t necessary, because this tracer doesn’t measure brain activity, it visualizes amyloid. So you can think all you like, or not think at all, and just use that hour to lie there and relax.”

What did you learn from being a study participant?

“I realized that no matter how healthy you believe you are, there’s still apprehension about any kind of experience like this. What if there was pathology or some other



photos | Carol Edwards

Left: Dr. Andrew Newberg, principal investigator of the AV-45 study, positions a study subject in the PET scanner. Unlike an MRI, a PET scanner is open and quiet, and participants sometimes drift off to sleep during the study. Right: Dr. Newberg reviews a scan obtained in the study on his office monitor.

anything else. Findings like those are made known to participants in any of our research studies.

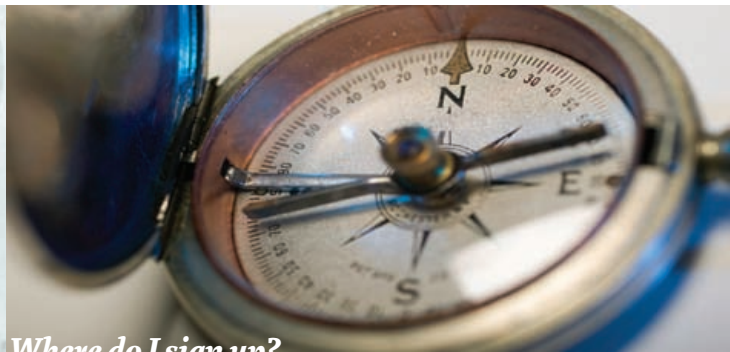
“But what if someday, this technology or some other approach now being tested is capable of forecasting that I will develop Alzheimer’s disease in 10 years, or 20?”

Even if I learned that, I don’t think I would change very much about my life, because I really like what I’m doing and how I’m living now.

Maybe I would even appreciate things more.

“I was a little surprised at the degree of satisfaction I felt from the experience. To know that I can talk with our normal controls, patients, and families about joining studies, from both a doctor’s and a subject’s point of view, makes me feel good. When we have a study with a lumbar puncture — spinal tap — that I’m eligible for, I plan to do that, too. I’m especially interested in gaining that perspective.”

“Such a tiny fraction of people who could join Alzheimer’s disease or heathy brain-aging research do so. Imagine if everyone who was eligible did even one study . . . Just think about where that could take us.” . . . *Dr. Steven Arnold*



Where do I sign up?

- The AV-45 study is open to men and women age 50 and older with normal memory and thinking, mild cognitive impairment, or Alzheimer’s disease (MMSE score 30-10).
- To learn more, call Penn Memory Center Research Coordinator Staci Hoops at 215-615-3082 or email staci.hoops@uphs.upenn.edu

asked to remain as ‘thoughtless’ as possible before and during the scan. Thinking — about work, or your kids, or sailing, or anything — activates the brain, and the object is to “keep the brain in neutral.”

abnormality discovered in my brain? What would it mean? Would I want to know?

“I learned there was nothing I needed to be made aware of, like a tumor or stroke or

As spring renews growth and hope . . .

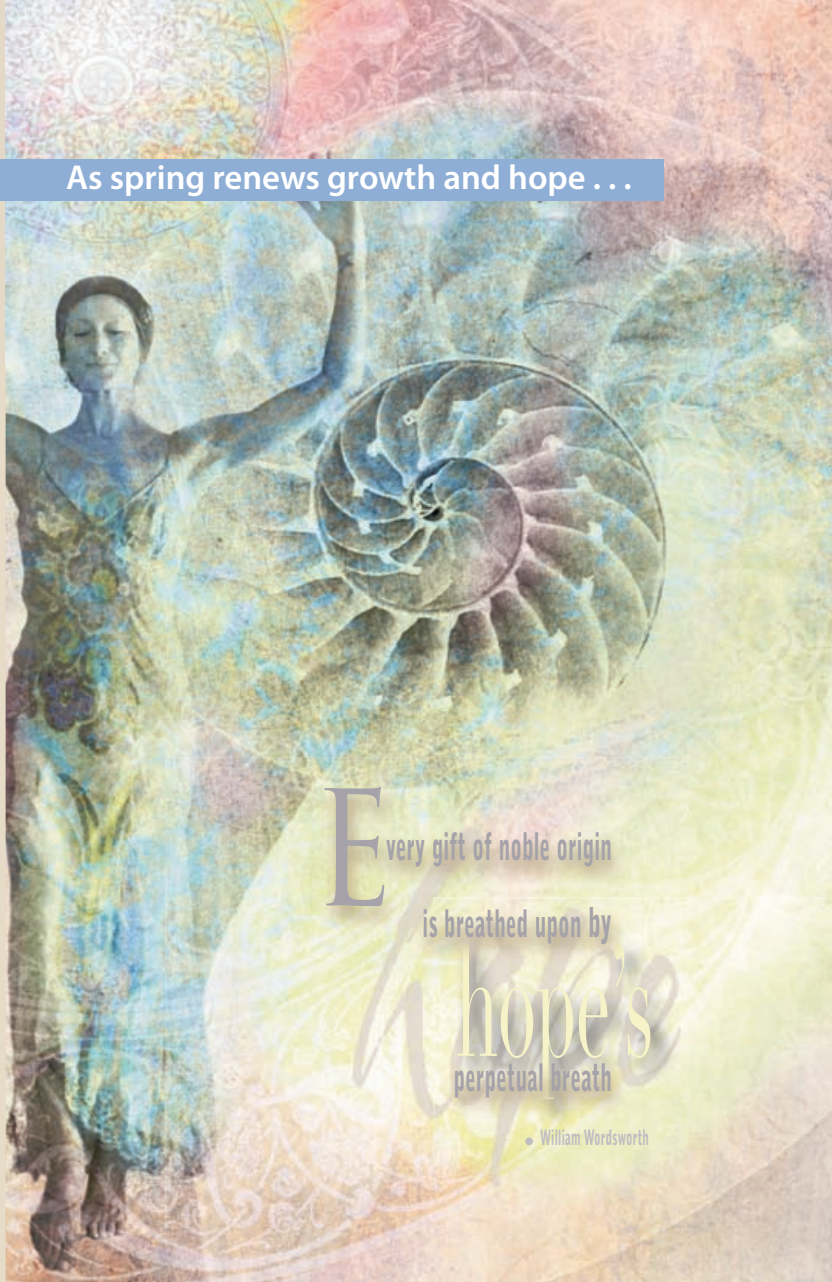


image: from 'Evolue' | elena ray | dreamstime.com

Please consider supporting the research and care of the Penn Memory Center. We rely on your gifts to ADVANCE.

Even as Alzheimer's disease threatens to grow into the largest public health crisis ever faced by our nation, federal and other funding for our efforts continues to be cut back. This hard reality makes your tax deductible gifts and bequests even more vital, to help support our research and nurture our advances.

We are especially grateful to those who have made gifts during these very trying

economic times. We recognize donors here and on our website. (To view, go to www.pennadc.org, click on "How to make a donation," then click on "Our List of Donors.")

Planned giving, matching gift programs, and a range of tax-advantageous structured giving approaches are also available. To learn about how your support can strengthen and advance the work of the Penn Memory Center, please call Irene Lukoff at 215-573-0187. Thank you.

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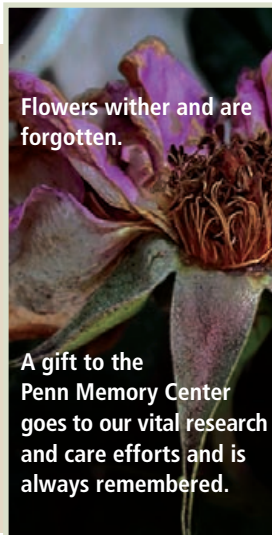
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donor list continued on page 14



Flowers wither and are forgotten.

A gift to the Penn Memory Center goes to our vital research and care efforts and is always remembered.



In lieu of flowers

In contemplating your own final arrangements, or those of a loved one, please consider an obituary request that, instead of flowers, donations for Alzheimer’s research at the Penn Memory Center be made to:

“Trustees of the University of Pennsylvania”
(write “ADC-PMC” on the memo line)

And mailed to Penn Memory Center (Attn: Faye Silag)
3615 Chestnut St.
Philadelphia, PA 19104

Questions? Call Faye at 215-615-0975

Make a gift on-line

You can make a gift easily, instantly, and securely on-line. At our website — www.pennadc.org — click on “How to Make a Donation.” You’ll be directed to the on-line donation form.

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PMC normal controls cited

A Penn Memory Center normal control since 2003, Clarissa Alleyne (r) is pictured with PMC Senior Research Nurse Marianne Watson, RN, who leads our normal control efforts, in a full-page photo and accompanying story on our normal control research in the recently released Penn Medicine publication entitled *Simply Because: A Community Benefit Report*.

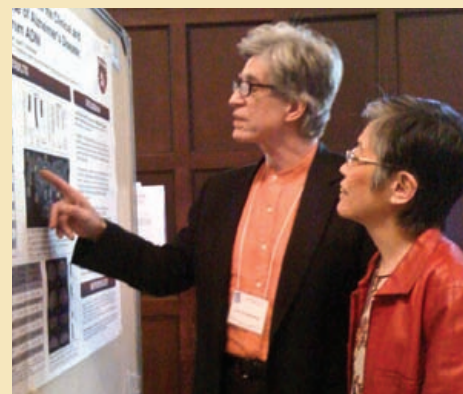
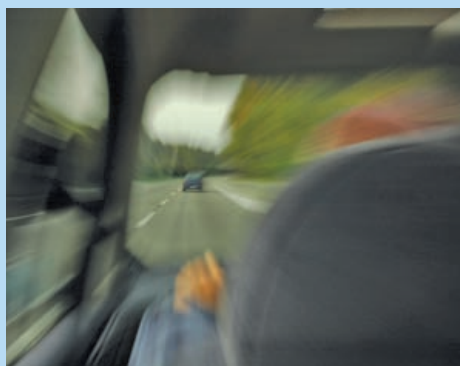


photo | Faye Silag

2010 Institute on Aging Retreat

John Trojanowski, M.D., Ph.D., Director of Penn's Institute on Aging (IOA) and Alzheimer's Disease Center, and, with Virginia Lee, Ph.D., MBA, co-directs Penn's Center for Neurodegenerative Disease Research (CNDR) is pictured with Dr. Lee reviewing the 1st prize poster in the clinical research category at the IOA retreat in May, 2010. Entitled *Apolipoprotein E Status Modulates the Clinical and Neuroanatomic Phenotype of Alzheimer's Disease*, the poster was submitted by David Wolk, M.D., neurologist and assistant director of the PMC.

Penn Medicine also announced a research agreement with AstraZeneca, to "find new therapies for Alzheimer's disease and bridge the transition from drug discovery to development." Trojanowski and Lee will lead this collaboration for CNDR.



Driving guidelines in the news

Jason Karlawish, M.D., associate director of the PMC, contributed to an ABC World News on-line story about guidelines for drivers with dementia from the American Academy of Neurology. He also spoke at the National Elder Law Foundation in Dallas, and the Martin Family Alzheimer Disease Symposium, sponsored by the Indiana Alzheimer Disease Center.

RESEARCH

MAJOR INVESTIGATIONAL DRUG TRIALS ARE OPEN AT THE PENN MEMORY CENTER.

Please call us to learn more



● I.G.I.V.

Immune Globulin Intravenous Study

Overview

Immune Globulin Intravenous (IgIV) has been approved and used successfully for over 20 years to treat autoimmune and immunodeficiency disorders. Increasing evidence suggests that immunotherapy targeting amyloid beta peptide can be used to treat Alzheimer's disease.

Because it contains anti-amyloid antibodies, IgIV is being investigated in a Phase III, double blind, randomized placebo controlled study as a treatment for Alzheimer's.

Key Study Elements

- Infusions 2 weeks apart over 14 months
- Infusions can be delivered at the patient's home by an RN
- you may be asked to participate in MRI, PET imaging, and cerebrospinal fluid sampling

Who may be eligible?

Those age 50-89 with mild to moderate Alzheimer's

● S-Connect: Overview

This study tests if a daily multi-nutrient drink containing Fortasyn™ Connect, proprietary nutrients, has a positive effect on cognitive performance in AD.



Key Study Elements • 4.2 ounces daily of a shake drink, vanilla or strawberry flavored • 6 study visits over 7 months

Who may be eligible? Those age 50 and above with mild to moderate AD who have not used omega-3 fish oil within 30 days.

Contact Patricia Martinez ■ 215-746-2557 ■ patricia.martinez@uphs.upenn.edu

● ELAN -- "ICARA"

Overview

This Phase III, double blind, placebo controlled randomized study tests the safety and effectiveness of Bapineuzumab, a humanized monoclonal antibody, in slowing the progression of Alzheimer's disease.

Bapineuzumab is designed to provide antibodies to amyloid beta directly to the patient, which would bind to and clear plaques characteristic of the disease.

Key Study Elements

- 6 infusions, 13 weeks apart over 18 months
- MRI exams
- you may be asked to participate in PET imaging and cerebrospinal fluid sampling

Who may be eligible?

Those age 50-89 with mild to moderate Alzheimer's

● L-ZAM

Overview

Because Alzheimer's disease is thought to be caused by pathological amyloid plaque, treatments to slow the build-up of amyloid beta, or increase its clearance from the brain might be expected to slow the progression of Alzheimer's disease.

This Phase III, double blind, randomized placebo controlled study tests if an anti-amyloid humanized monoclonal antibody can slow functional decline in persons with AD.

Key Study Elements

- 20 infusions, 4 weeks apart over 18 months
- you may be asked to participate in MRI, PET imaging, and cerebrospinal fluid sampling

Who may be eligible?

Those age 55 and above with mild to moderate Alzheimer's

For more information contact Felicia Greenfield ■ 215-614-1828
■ felicia.greenfield@uphs.upenn.edu

For more information contact
Staci Hoops ■ 215-615-3082
■ staci.hoops@uphs.upenn.edu



Penn Memory Center
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inSight

SPRING | SUMMER 2010

Newsletter of the Penn Memory Center

About people and efforts that bring the knowledge we seek on Alzheimer's disease and healthy brain-aging ever closer in sight

Jason H. Karlawish, Publisher
 jason.karlawish@uphs.upenn.edu

Carol Edwards,
 writer, designer, editor
 carol.edwards@uphs.upenn.edu
 voice: 215-573-4634

- inSight is produced by the Penn Memory Center, a part of Penn Medicine of the University of Pennsylvania.
- The Penn Memory Center is a National Institute on Aging-designated Alzheimer's Disease Center (ADC), one of only 30 such centers in the United States, and the only one in our tri-state region.
- Our staff and programs are dedicated to research in Alzheimer's disease and age-related cognitive problems, and improving the well-being and quality of life of our patients and their families.
- We welcome and encourage your questions, comments, suggestions, requests, and gifts.

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Good Golly, Miss Molly . . .

You may still be a kid at heart,
 but if you rocked to Little Richard like this crowd, you're the
 right age to join the Penn Memory Center as a Normal Control

Did you know that older adults with normal memory and thinking are vital to Alzheimer's research? Studying people in their 60s, 70s, and 80s with normal cognition helps science better understand exactly what goes wrong, and when, in the brains of those with age-related cognitive problems. These very important partners in brain-aging research are known as "normal controls."

- Please call Marianne Watson, RN, at 215-662-4373 to learn how you can advance Alzheimer's disease and healthy brain-aging research as a normal control.
- You won't be able to stay in your seat when you see Little Richard, age 60 at the time, perform "Good Golly, Miss Molly" in the 1991 film "King Ralph." Watch it on YouTube. <http://www.youtube.com/watch?v=kZ6hokyqSRk>