

R.I. READER

THE JOURNAL FOR PARTICIPANTS IN THE R.A.G.E. INHIBITOR STUDY

WINTER 2009



ALZHEIMER'S

UNFORTUNATELY

THERE ARE A LOT OF MYTHS ABOUT ALZHEIMER'S DISEASE, MYTHS THAT HAVE NO FOUNDATION OR SCIENTIFIC VALIDITY. TO HELP YOU BETTER UNDERSTAND THE DISEASE, WE OFFER SOME INSIGHTS. STORY PAGE 4

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DIRECTOR'S



MESSAGE

We welcome your input and look forward to hearing from you.

Welcome to the RI Study!



THIS IS OUR FIRST NEWSLETTER FOR THE RI STUDY so before I go any further let me express my great appreciation for your willingness to participate in this important Alzheimer's disease (AD) research study. We could not investigate new therapies for AD without people like you willing to take part in significant research studies.

Over the course of the study we will keep you informed through newsletters. We will provide you with important information going on in the Alzheimer's research field, articles of interest, and tips and tools such as brain teasers. In this first issue we explore recent advances in AD neurobiology, AD myths and whether memory loss is a normal part of aging. We hope you find these articles helpful and useful.

If you have any ideas or issues you would like to see addressed in a future newsletter please email us at Brainlink@ucsd.edu. We welcome your input and look forward to hearing from you.

Warmly,

Douglas Galasko, M.D.

RI Study Project Director,
Director – UCSD Shiley-Marcos Alzheimer's Disease Research Center

WHAT THE ALZHEIMER'S DISEASE COOPERATIVE STUDY *Is all about*

Do you know how the Alzheimer's Disease Cooperative Study (ADCS) functions? The ADCS, formed in 1991 as a cooperative agreement between the National Institute on Aging (NIA) and the University of California San Diego, is a consortium of over 70 sites in the United States and Canada. The ADCS is a major initiative for Alzheimer's disease (AD) clinical studies to facilitate the discovery, development and testing of new treatments for AD.

Check out our website at <http://www.adcs.org> and learn what the ADCS is all about. You will also find general information on AD and other dementias, AD research studies in progress, research news, and helpful links.

www.adcs.org



An exciting component of our new website is the Alzheimer's Disease Information Network. The goal of the Information Network is to register a significant portion of the 5 million people affected by AD, as well as people who have undiagnosed memory disorders or those who are interested in learning more about AD and dementia. The purpose of the Information Network is to educate the public with updates on AD research and treatment and upcoming clinical research studies.

The link to register for the Information Network is at <http://www.adcs.org/Research/registry.aspx>. Or, you can link to it from the home page.

Join the **ALZHEIMER'S DISEASE INFORMATION NETWORK**



Study Shows Vitamin B Supplements Did Not Slow the Rate of Cognitive Decline

A clinical trial led by Paul S. Aisen, M.D., professor of neurosciences at the University of California, San Diego School of Medicine, and director of the Alzheimer's Disease Cooperative Study, showed that high-dose vitamin B supplements did not slow the rate of cognitive decline in patients with mild to moderate Alzheimer disease (AD). The study was published in the October 15 issue of the *Journal of the American Medical Association (JAMA)*.

Aisen and other researchers had examined B vitamins as a possible way to reduce AD risk or slow its progression because the vitamin reduces homocysteine, an amino acid in the body, which has been found in high levels in the blood of people with AD.

"Prior studies using B vitamin supplementation to reduce homocysteine levels in patients with Alzheimer's weren't

large enough, or of long enough duration to effectively assess their impact on cognitive decline," said Aisen. "This study of several hundred individuals over the course of 18 months showed no impact on cognition, although it resulted in lower levels of homocysteine in these patients."

The study involved 409 people with AD at 40 sites throughout the United States. Some received daily doses of five milligrams of folic acid, one milligram of vitamin B12 and 25 milligrams of vitamin B6, doses well above the recommended daily allowance. The rest received daily placebo pills. The researchers also found that symptoms of depression were more common in the high-dose supplement group.

"Our study does not support the treatment of individuals with mild to moderate AD and normal vitamin levels with B vitamin supplements," the authors conclude.



CALCIUM OVERLOAD

by Michael Rafii, M.D., Ph.D.,
ADCS Associate Medical Director

Among the major uncertainties surrounding Alzheimer's disease (AD) is whether and how the amyloid plaques found in the brains of patients with the disorder actually damage neurons. One of the leading theories concerns calcium overload. Calcium ions play an essential role in transmitting signals from one neuron to another. Many studies have suggested that alterations in calcium regulation may be involved in the brain degeneration that characterizes AD. But scientists are not yet sure why.

A few major studies have recently looked at calcium in AD. First researchers verified that they could accurately show calcium levels in brain neurons. Then researchers showed that dendrites, the neuron branches, were almost six times more likely to have excessive levels of calcium in mice bred to exhibit AD pathology and symptoms with amyloid plaques, than in normal mice.

Finally they found how this calcium overload probably interferes with how neurons communicate with one another. Normally, specific signals being transmitted are reflected by distinct calcium levels in structures within the branches, called dendritic spines. But in the Alzheimer's mice, calcium levels were the same throughout a dendrite instead of changing at the locations of the spines. Those dendrites in which calcium levels were highest also had structural changes similar to those seen in the brains of patients who have died with AD.

In a related finding, abnormal calcium signaling was also linked to the more common late onset form of AD. In this study, researchers discovered a mutation associated with late onset that disrupted a brain calcium channel and led to accumulation of amyloid beta protein. This increased the risk of developing AD by 44%.

Cheung et al. Mechanism of Ca2 Disruption in Alzheimer's Disease by Presenilin Regulation of InsP3 Receptor Channel Gating. Neuron, Vol 58, 871-883, 26 June 2008
Dreses-Werringloer et al. A Polymorphism in CALHM1 Influences Ca2+ Homeostasis, Aβ Levels, and Alzheimer's Disease Risk. Cell, 133, 1149-1161, June 27, 2008



UNFORTUNATELY

THERE ARE A LOT OF MYTHS ABOUT ALZHEIMER'S DISEASE, MYTHS THAT HAVE NO FOUNDATION OR SCIENTIFIC VALIDITY. TO HELP YOU BETTER UNDERSTAND THE DISEASE, WE OFFER YOU THE FOLLOWING INSIGHTS.

Can drinking out of aluminum cans or cooking with aluminum pots and pans cause AD?

There is no proven evidence that shows a link between AD and aluminum. That does not stop rumors from running rampant over the Internet. Some claim that patients with AD have higher levels of aluminum in their brains than people without AD. There has been no conclusive evidence that affirms this opinion. In fact it was proven that the overall amount of aluminum in AD patients' brains is no different than the amount in the brains of people without AD. (Trapp et al 1978). Other studies of aluminum sources such as antacid medications and antiperspirants also failed to demonstrate a positive association with AD. (Flaten and Odegard 1988).

Can Aspartame Cause Memory Loss?

A popular email began circulating around the Web in the late 90s asserting that aspartame, the artificial sweetener that is marketed as NutraSweet and Equal, contributes to memory loss and AD. The email was erroneous, full of false allegations and contradictory statements. The FDA maintains that aspartame is safe.

"The FDA evaluates a sweetener's composition and properties, how

much of the substance is likely to be consumed, and various types of safety studies," says Laura Tarantino, Ph.D., director of the Office of Food Additive Safety in the FDA's Center for Food Safety and Applied Nutrition. "At this time, our position that aspartame is safe is based on the large body of information previously reviewed," Tarantino says. "Our conclusions are based on a detailed review of more than 100 toxicological and clinical studies on safety."

Can Vitamins Prevent or Stop AD?

Vitamin and supplement research is still ongoing. But to date, it has not been shown that B, C, and E vitamins or ginkgo biloba, selenium and folate have any effect on preventing or slowing AD from progressing. Nevertheless, researchers will continue to examine vitamins and supplements as a possible avenue for treatment. Vitamin E is a potent antioxidant that is believed to have a protective role and may help prevent free radical damage to the brain. Normal cell function produces a byproduct called a free radical. It is believed free radicals can damage cell structures and genetic material. The damage free radicals can produce is called oxidative stress and it is believed that it contributes

to the development of AD.

Vitamin E is not claimed to prevent or significantly slow the progress of AD. The main evidence that exists does suggest that high dose vitamin E may result in some mild functional improvement but not cognitive improvement.

Is AD Genetically Inherited?

Four major types of familial AD have been identified. Types 1, 3, and 4 are classified as early-onset AD because their signs and symptoms appear before age 65. Type 2 is classified as late-onset AD because its signs and symptoms appear after age 65. Other cases of AD are classified as sporadic or nonfamilial, which means they do not appear to run in families or have been inherited.

About 75 percent of AD cases are classified as sporadic. Although the cause of these cases is unknown, genetic changes may play a role. Virtually all sporadic AD begins after age 65, and the risk of developing this condition increases as a person gets older. The remaining cases of AD are familial, which means they are found in multiple members of a family. Familial AD can be divided into early-onset disease (symptoms begin before age 65) and late-onset disease (symptoms begin after age 65).

(Continued on Page 5)

WE ALL HAVE THOSE MOMENTS.

IS MEMORY LOSS A NORMAL PART OF AGING?

(Continued from Page 4)

The early-onset forms of AD are caused by gene mutations that can be passed from parent to child. Researchers have identified three genes that cause these forms of the disorder. Mutations in the APP gene cause AD type 1. Changes in the PSEN1 gene are responsible for AD type 3, while PSEN2 mutations lead to AD type 4.

The early-onset familial forms of AD (types 1, 3, and 4) are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the altered gene from one affected parent.

The inheritance pattern of late-onset (type 2) familial AD is uncertain. People who inherit one copy of the APOE e4 allele have an increased chance of developing the disease; those who inherit two copies of the allele are at even greater risk. It is important to note that people with the APOE e4 allele inherit an increased risk of developing AD, not the disease itself. Not all people with AD have the e4 allele, and not all people who have the e4 allele will develop the disease.

Will People with Head Injuries Develop AD?

Research has shown that not all brain injury patients will definitively develop AD, but it has been shown that brain injury patients are at an increased risk. Researchers do not yet understand exactly which brain injury patients will develop AD or when.

In 2002 University of Pennsylvania School of Medicine researchers found direct evidence that mild recurring head injuries, such as those suffered by professional sport players, can lead to the same type of biochemical effects that cause lesions in AD. Their evidence suggests that brain trauma accelerates Alzheimer's by escalating free radical damage and the formation of deposits of beta amyloid (Ab) proteins, the plaques found in the brains of AD patients. A 2001 study at the same institution suggested that brain injury can cause Boxer's Syndrome by activating mechanisms similar to those that cause tau lesions in the brain, one of the characteristic features of AD.

Will All AD Patients Eventually Become Aggressive?

AD affects each person differently. Not everyone with AD will become aggressive and hostile. But for those that do, it is often because they are frightened and frustrated by the changes occurring to themselves. One way to prevent or minimize this from occurring is for patients and their families to learn as much as possible about the disease, for families to learn new ways of communicating with an AD patient, to make the AD patient's surroundings as stable, comfortable and accessible as possible, and for family and friends to exercise great patience as everyone enters this new chapter of life.



The simple answer is yes.

Memory loss is natural as one ages. We all have those moments. At times, we may have trouble remembering where we placed our keys, can't recall the name of an author we are currently reading and can even have difficulty finding words. However, this doesn't mean that normal memory loss leads to a significant loss of function. It's not common for a person to wander away from home, forget how to bathe, or fail to remember the names of friends and loved ones.

As we get older, especially after the age of 65, we need to be aware that the risk for AD increases. We can struggle remembering phone numbers or forget the name of a popular television show, but we should be alarmed when we can't recognize a familiar place or lose the ability to drive a car. Thus, once memory loss interferes with everyday functions, it is important to seek treatment and support.

Easy Winter Recipes

So Velvety Sweet Potato Soup

Serves 4-6



- * 32 oz can of sweet potatoes
- * 2-1/2 cups of low sodium chicken stock
- * 1/4 teaspoon ground dried ginger
- * 2 tablespoons chopped pecans, toasted to light brown
- * 1/4 teaspoon ground cinnamon
- * 1/4 teaspoon ground nutmeg
- * 1 cup fat-free half-and half or low fat evaporated milk

Place sweet potatoes and a cup of chicken stock in a blender or food processor. Turn on and blend until very smooth. Transfer sweet potatoes to a pot on the stove and warm to medium heat. Whisk in the rest of the chicken stock, spices and half-and-half. Simmer until very hot. Spoon into bowl and sprinkle toasted pecan pieces onto each serving.

Artichoke and Sausage Frittata

Serves 4-6



Heat oven to 350 degrees.

- * 2 tablespoons olive oil
- * 1 pre-cooked sausage, sliced thin
- * 1 red bell pepper, diced
- * 1 8-1/2 oz can of artichoke hearts, drained and chopped
- * 1/2 onion, chopped
- * 2 minced garlic cloves
- * 1 teaspoon dried basil or 2 tablespoons fresh, minced
- * 1-1/4 cup egg substitute
- * 1/2 cup grated hard cheese such as Romano or Parmesan
- * 1 cup grated low-fat mozzarella cheese

Heat olive oil over medium-high in a medium sized pan. Sauté sausage, bell pepper, artichokes, onion and garlic in olive oil for five to seven minutes or until the onion turns clear. Set aside to cool.

In a bowl combine the basil and egg substitute; mix in the hard cheese only and the sautéed vegetables and sausage. Grease an 8-1/2 inch round quiche or pie pan. Pour in the egg mixture. Top with the mozzarella cheese. Bake for 40-45 minutes in the oven until lightly browned on top.

Winter Apple Crisp

Serves 4-6



Heat oven to 350 degrees.

- * 4 large tart apples, peeled and sliced
- * 1/4 cup water
- * 1 tablespoon lemon juice
- * 1/4 cup packed brown sugar
- * 3 tablespoons butter or margarine, melted or softened
- * 1/4 cup flour
- * 1/4 cup old-fashioned rolled oats
- * 1/2 teaspoon ground cinnamon
- * 1/4 teaspoon ground nutmeg

Place apples in an 8-inch square baking pan. Mix water and lemon juice and pour over apples. In a separate bowl, mix sugar, flour, oats, and spices. Add butter (or margarine) and mix until crumbly. Sprinkle mixture over apples. Bake for 40 minutes until the topping is light brown.

WEB WEB EVERYWHERE

Websites with advice, care-giving tips and resources continue to abound on the Web.



CAREGIVING

<http://www.sharethecare.org/> *Share caregiving advice and stories, and learn how to organize a group for a loved one.*

<http://www.ces.purdue.edu/extmedia/CFS/CFS-455.html> *Coping with Caregiving, How to Manage Stress When Caring for Elderly Relatives.*

http://www.ahaf.org/pubs/CaringCaregiver_Stress.pdf *"Care for the Caregiver: Managing Stress," from the American Health Assistance Foundation: This publication discusses the signs of stress and how to reduce it.*

<http://www.nia.nih.gov/Alzheimers/Publications/caregiverguide.htm> *Tips for Caregivers of People with Alzheimer's Disease from the National Institute on Aging.*

<http://www.aoa.gov/prof/aoaprogram/caregiver/caregiver.asp> *The Resource Room on the National Family Caregiver Support Program website offers a wide array of information from state facts on family caregiver support to a caregiver immunization toolkit to financial steps for caregivers and more.*

ELDERCARE AND ALZHEIMERS DISEASE RESOURCES

<http://www.eldercare.gov/Eldercare/Public/Home.asp> *Locate services and resources for older adults in any U.S. community. This site links older adults and their caregivers with state, local, and community agencies on aging (800-677-1116).*

<http://www.lotsahelpinghands.com/> *Coordinate rides and other services for your loved one using a group calendar that only family, friends, and volunteers can access.*

http://www.alz.org/living_with_alzheimers_respite_care.asp *Respite Care: The Alzheimer's Association has created a very informative brochure for caregivers on respite care. This brochure reviews the respite care services offered through community organizations, agencies or residential care facilities.*

<http://www.respitelocator.org/> *National Respite Care Locator.*

http://www.alz.org/living_with_alzheimers_respite_care.asp *The Adult Day Center information sheet created by the Alzheimer's Association provides useful information for caregivers. This sheet reviews such topics as selecting a center and services provided.*

ALZHEIMERS DISEASE INFORMATION

http://www.alz.org/living_with_alzheimers_african_americans.asp *African-Americans and Alzheimer's disease*

<http://www.nia.nih.gov/Alzheimers/Publications/managing.htm> *Resource List: Managing Communication and Behavioral Problems in People with Alzheimer's Disease from The Alzheimer's Disease Education and Referral Center (ADEAR). This list reviews some of the many books, manuals, reference guides, and information packages that may assist family members with communication and behavior issues.*

BRAIN EXERCISE

Mind Games are a really fun way to exercise the mind. Check out the mind games on the AARP website — good for both caregivers who want to stay sharp and study participants with mild dementia.

http://www.aarpmagazine.org/games/printandplay_brain_teasers.html

BRAIN TEASERS Guess the meaning of...

1 LONG
DO

2 WEAR
LONG

3 MIND
MATTER

4 T
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5 T
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C
H

ANSWERS
1. Long Overdue 2. Long Underwear 3. Mind Over Matter 4. Downtown 5. Touchdown

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University of California, San Diego

9500 Gilman Drive
La Jolla, CA 92093-0948
<http://www.adcs.org>

ADCS Director:
Paul Aisen, MD

Project Director:
Doug Galasko, MD

Editor:
Jeffrey Itrich

Contributing Editor:
Peggy Chambers

Layout and Graphics:
Larry Janus

