ALZHEIMER'S
RESEARCH REVIEW

A publication for friends and donors of Alzheimer's Disease Research **Fall 2008**

Getting the Tangles Out

New therapy may slow disease progression, improve cognition

A treatment that targets neurofibrillary tangles may slow disease progression and heighten cognitive function in people with mild to moderate Alzheimer's disease, according to a study presented at an international conference on Alzheimer's disease.

The study focuses on a drug called methylthioninium chloride, which inhibits the aggregation of tau, the main protein in neurofibrillary tangles. The results mark the first time a tau-based therapy has been shown to alter Alzheimer's pathology.

"The data from this study strongly suggest that this kind of treatment could halt disease progression at an early Braak stage – in other words, when the pathology is just beginning to kill neurons," says principal investigator Claude Wischik, M.B., Ch.B., from Aberdeen University, and chair of TauRx Therapeutics, which developed the drug.

Wischik says tau-based therapies offer an alternative to the amyloid hypothesis, which attributes Alzheimer's disease largely to the buildup of beta-amyloid proteins in the brain.

Other scientists, however, emphasize the importance of researching both hypotheses. Sam Gandy, MD, Ph.D., associate director of the Mount Sinai Alzheimer's Disease Research Center, suggested that a double-pronged research approach could pave the way for "hit[ting] the AD pathway at multiple steps and maybe shut it down completely, sort of like combination chemotherapy for cancer."

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Cohabitation Could Lower Alzheimer's Risk

Studies reinforce importance of social stimulation

Swedish researchers have learned that living with a spouse or partner can significantly reduce the risk of developing Alzheimer's disease and other forms of dementia.

The findings, presented at an international Alzheimer's conference, show that people living with a spouse or partner around the age of 50 are about half as likely to develop the disease as people living alone.

Those who live alone their entire adult life run twice the Alzheimer's risk of partnered people, while people who are divorced in midlife and remain single run three times the risk. At greatest risk are widows and widowers, who are six times more likely to develop the disease than married couples.

The findings suggest that the social and intellectual stimulation provided by a partner can help ward off the disease's onset. According to researcher Krister Hakansson, the study also underscores "how important it is to put resources into helping people who have undergone a crisis. Such an intervention strategy could also be profitable for society considering the costs of

President's Corner

Hitting Alzheimer's from every side

What is the main driver behind Alzheimer's disease? Is it the insoluble twisted fibers within the neurons of the brain? Or is it the beta-amyloid plaque that builds up around those neurons? As you'll see from this issue of ***Alzheimer's Research Review***, there is a mounting body of evidence to support both theories. The good news is that we don't have to choose one theory over another.

In fact, by moving forward on *both* research fronts, we will learn more and more about the stages of Alzheimer's pathology, and in the process, secure more and more windows for intervention. The result, as one scientist suggested, may one day be a suite of therapies that attack Alzheimer's on every possible front.

Through your help, ADR has long focused on promoting research that attacks Alzheimer's disease from every angle. Recently, ADR committed $1,000,000 to Dr. Donald Weaver's research team at Dalhousie University to develop single drugs that attack both pathways. Funding from ADR donors, "has been instrumental to the success and progress of this international multi-site, multidisciplinary research program," says Dr. Weaver in a recent ADR press release.

For all you've done to take us closer to that possibility, you have our deepest gratitude.

Brian K. Regan, Ph.D.

Please share this newsletter with someone you know who might be interested in learning about some of the latest advancements in research to prevent, treat and cure Alzheimer's disease. The *Alzheimer's Research Review* is published by Alzheimer's Disease Research, a program of the American Health Assistance Foundation, a nonprofit organization located at 22512 Gateway Center Drive, Clarksburg, Maryland 20871, 301-948-3244, 800-437-2423, www.ahaf.org.

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Alzheimer's May Reveal Itself Decades Before Diagnosis

Studies suggest disease has adverse educational impacts early in life

People who develop Alzheimer's disease may exhibit symptoms of the disease, including educational impairment, several decades before it has been diagnosed, says a study published in the journal *Alzheimer's Disease and Associated Disorders*.

The study found that, among a group of nuns who developed Alzheimer's disease, those with small head size had significantly lower educational achievement in their early years. The findings are significant because previous research has found that people with smaller heads are more likely to show Alzheimer's symptoms. Larger brains appear to provide a greater reserve against the disease.

"If brain damage related to Alzheimer's disease begins earlier in adult life, then having less reserve due to a small brain could compromise intellectual ability in those destined to get Alzheimer's and lead to them getting less education," said the study's lead author, James Mortimer, Ph.D., professor of epidemiology at University of South Florida. "Although it has been known for many years that individuals with lower education have a greater risk of getting Alzheimer's, this is the first report showing that reduced educational attainment may actually be an early sign of the underlying disease."

The latest study adds to mounting evidence that people who ultimately develop Alzheimer's show marked differences early in life – including impaired memory and thinking. Researchers say these findings may be useful in predicting who is at greatest risk from the disease and developing earlier interventions.

Acknowledge the Special People in Your Life

Honor gifts to ADR give twice over

Looking for a special way to acknowledge the important people in your life? Consider an honor gift to Alzheimer's Disease Research.

Honor gifts can be given on special occasions – a friend's or relative's birthday, graduation or anniversary – or they can be given on holidays like Christmas, Hanukkah, Mother's Day or Father's Day. Or they can be given at any time of the year to show appreciation for someone's kindness or to recognize someone's impact on your life.

Alzheimer's Disease Research's honor gift program can help you to thank others for their unselfish acts of kindness – while advancing memory-giving and life-enhancing research and educational efforts.

For more information on this unique way of giving, contact Katherine Jimenez of Alzheimer's Disease Research at 1-800-437-2423.

Thank you for thinking of Alzheimer's Disease Research!

Learn More Online at www.ahaf.org

Simply click on the Alzheimer's Disease Research link to learn more about what's new in the world of research. You'll also find practical tips on diet and lifestyle and how caregivers can minimize damage to their own health.

Research Roundup

No sign of Alzheimer's in world's oldest woman

The brain of a Dutch woman who died at 115 exhibited little to no sign of Alzheimer's disease, suggesting that dementia may not be an inevitable result of aging.

"Our observations suggest that, in contrast to general belief, the limits of human cognitive function may extend far beyond the range that is currently enjoyed by most individuals, and that improvements in preventing brain disorders of aging may yield substantial long-term benefits," concludes a study led by Prof. dr. Gert Holstege of University Medical Centre Groningen, The Netherlands.

Previous studies have found at least some cognitive impairment in elderly brains. However, as the number of centenarians continues to grow, new findings suggest that brains do not necessarily deteriorate even in extreme old age.

Cholesterol levels may be tied to dementia

Low levels of "good cholesterol," or high-density lipoproteins (HDL), in middle-aged patients may leave them at heightened risk of memory loss and dementia later in life, says a study published in *Arteriosclerosis, Thrombosis and Vascular Biology*.

The study, undertaken by French and English researchers, followed thousands of patients and found that those with decreased levels of HDL cholesterol were more likely to suffer impaired memory by age 60.

The reasons for the linkage remain unclear, but HDL cholesterol, in addition to lowering the risk of heart attacks, helps control the growth of beta-amyloid, the major component in the brain plaque found in people with Alzheimer's. "HDL could also affect memory through its influence on atherosclerotic disease and stroke, or vascular injury," says study author Archana Singh-Manoux, Ph.D. "Finally, HDL cholesterol may influence memory through its anti-inflammatory and antioxidant effects."

The American Heart Association recommends raising HDL cholesterol and lowering LDL cholesterol through a combination of exercise and a diet low in trans fats and saturated fats and high in monounsaturated fats.

Exercise may slow brain shrinkage in Alzheimer's patients

Among patients with mild Alzheimer's disease, those who are more physically fit show four times less brain shrinkage than those who are less fit, according to findings published in the medical journal of the American Academy of Neurology.

"People with early Alzheimer's disease may be able to preserve their brain function for a longer period of time by exercising regularly and potentially reducing the amount of brain volume lost," suggests study author Jeffrey M. Burns, M.D., of the University of Kansas School of Medicine in Kansas City. "Evidence shows decreasing brain volume is tied to poorer cognitive performance, so preserving more brain volume may translate into better cognitive performance."