The Shiley Gift: Bringing Discovery and Hope to the ADRC

Donald and Darlene Shiley are no strangers to the University of California, San Diego. Longtime supporters of UCSD healthcare and neuroscience initiatives, the couple has generously given to Leon J. Thal, M.D.’s Alzheimer’s disease research, experimental Alzheimer’s brain cell therapy research, and to the world-renowned Shiley Eye Center at UCSD. This past fall, the Shileys’ benevolence touched UCSD yet again. In November 2004, UCSD announced a $4 million pledge from Donald and Darlene Shiley to support the UCSD Alzheimer’s Disease Research Center (ADRC), bringing their commitment to the university to more than $8 million. In recognition of their gift, and in honor of Darlene’s mother Dee Marcos, UCSD has renamed the ADRC the Shiley-Marcos Alzheimer’s Disease Research Center.

Donald and Darlene Shiley are personally invested in Alzheimer’s disease research and treatment. Explaining this commitment, Darlene

“...it is difficult to draw firm conclusions or make recommendations.”

Vitamin E and Alzheimer's Disease by Leon Thal, M.D.

A recent publication (Ann Intern Med 2004; 142:1-10) examined the number of deaths in 19 clinical trials of vitamin E, including a total of 136,000 subjects. These trials varied in the characteristics of the subjects enrolled, the dose of vitamin E used, the duration of treatment, and the outcome measures studied. Many of the subjects enrolled in these trials had coronary artery disease or risk factors for cardiovascular disease. In about half of the studies, the active treatment under investigation was a combination of vitamin E plus other vitamins or minerals.

None of the individual studies showed an increase in risk of death for subjects on vitamin E alone. Similarly, when all 19 studies were examined together, there was no increase in the risk of death. However, when the studies were arranged by dose of vitamin E (above or below the 400 IU/day median dose), it was noted that the combination of vitamin E with other vitamins or minerals was associated with a lower risk of death.
The Shiley Gift: Bringing Discovery and Hope to the ADRC

This gift will help give families hope in caring for their loved ones afflicted with this disease.

Roulla Drego Receives 2004 Diversity Award

Roulla Drego, one of our UCSD work-study employees, has been an integral part of our team since 2001. She was recently selected as one of the 14 campus-wide recipients of the Equal Opportunity/Affirmative Action and Diversity Award for 2004. Frances Martinez-Goodrich, MSW, coordinator of our Hispanic Component at the ADRC, nominated Roulla for this award in gratitude for the essential contributions that have made her an asset at the Center.

In 2004 she effectively handled with minimal supervision the responsibility of coordinating the Hispanic Caregiver Conference, an event that caters to the needs of monolingual Spanish-speaking caregivers. She helped obtain $56,214.00 in funding from pharmaceutical companies and community agencies, which enabled us to offer this event for free. Utilizing her sharp computer skills, she organized a resource binder for participants and caregivers that assisted the conference.

Advocating on behalf of patients with Alzheimer’s disease seems to come naturally to her. Her many skills enable her to be an effective and compassionate communicator, recently making a strong impact on hundreds of high school students she spoke to at a health fair in South Bay.

This young lady is beyond her 22 years of age; she is a phenomenal human being and outstanding worker gifted with the winning combination of skills, ethics and talent.

Vitamin E and Alzheimer's Disease

A cautious interpretation of the risk reported in the new publication would be that cognitively normal individuals and those with MCI should limit their intake of vitamin E. For individuals with AD, the results are much less clear.

Based on the pooled data in the recent publication, it is difficult to draw firm conclusions or make recommendations. The benefits of vitamin E supplements for AD prevention are unproven, and individuals with MCI have not shown benefit from vitamin E. A cautious interpretation of the risk reported in the new publication would be that cognitively normal individuals and those with MCI should limit their intake of vitamin E. For individuals with AD, the results are much less clear.

Research studies will continue to investigate vitamin E at various doses, as well as combinations of antioxidants, and will take appropriate precautions to monitor the well being of research participants.

Leon Thal, MD
Mary Sano, PhD
Paul Aisen, MD
Ronald Petersen, MD, PhD
Douglas Galasko, PhD
Fred Schmidt, PhD
Pierre Tarlow, MD
High levels of beta-amyloid (protein that accumulates and plaques) may be responsible for starting the disease. Some scientists believe the key to slowing down the progression of AD may lie in regulating levels of this protein.

Despite these adverse events, an autopsy case suggested disappearance of amyloid plaques. Furthermore, patients who developed antibodies showed a slower decline in the course of the illness than those who did not develop antibodies. Based on these findings, scientists believed immunization therapy deserved further exploration. They have since been working on developing a new vaccine, one that would induce clearance of amyloid plaques without inciting the immune response of their previous attempt. For years they experimented with "passive" vaccines on lab mice in the hopes of eventually reducing or halting the progression of AD in humans.

These new passive immunizations consist of directly injecting beta amyloid antibodies into the brain. Peripheral injection of moderate levels of antibodies showed these antibodies were able to enter the central nervous system, surround plaques, and induce clearance of preexisting amyloid. These studies also show an increase in synaptophysin, a chemical that indicates proper synaptic function (enabled cell communication). Lab results seem promising: that which was intended was accomplished without the need to stimulate an immune response, and thus less likely to actuate adverse events such as encephalitis.

We at the UCSD Shiley-Marcos ADRC will be part of the upcoming Elan Pharmaceuticals multi-center recruitment of human subjects to participate in Phase II clinical trials of AAB-001, a newly developed passive vaccine aimed at reducing beta-amyloid and amyloid plaque formation. For more information with regards to this clinical trial, please contact Karen Wetzel MPAS, PA-C at 858-622-5800 or via e-mail kwetzel@ucsd.edu.
If you are interested in participating or would like more information, please contact the Study Coordinator listed with each trial.

- They may all be reached at the Shiley-Marcos ADRC.
- There is no cost to participate in any of these research protocols

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Director</th>
<th>Time Involved</th>
<th>Description</th>
<th>Study Duration</th>
<th>Compensation</th>
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<tr>
<td><strong>CLASP Study</strong> Cholesterol Lowering Agent to Slow Progression of Alzheimer's Disease**</td>
<td>Gang Tong, M.D., Ph.D.</td>
<td>This study involves 8-9 visits over 20 months</td>
<td>The study aims to investigate the safety and effectiveness of simvastatin or an inactive placebo.</td>
<td>Up to 26 months</td>
<td>There will be no payment for participation in the study; however, all tests, examinations, and medical care required as part of the study will be provided.</td>
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<td><strong>Huperzine A</strong> **</td>
<td>Jody Corey-Bloom, M.D., Ph.D.</td>
<td>Study participation will be 24 weeks</td>
<td>This study is to determine whether huperzine A is beneficial in the treatment of mild to moderate Alzheimer's disease. Huperzine A is a natural cholinesterase inhibitor, derived from the Chinese herb huperzia serrata, used in China to treat AD. Individuals 55 years of age or older who are not currently taking cholinesterase inhibitors and have mild to moderate Alzheimer’s disease are eligible for screening. Treatment with memantine (Namenda) and vitamin E is allowed. Two-thirds of participants will randomize assigned to receive huperzine A throughout the study; the other third will receive placebo for 8 weeks. An open-label extension study providing huperzine A to all participants for at least 6 months is anticipated. There is no payment for participation in this study; however, all tests, examinations, and medical care required as part of the study will be provided.</td>
<td>Up to 26 months</td>
<td>There will be no payment for participation in the study; however, all tests, examinations, and medical care required as part of the study will be provided at no cost.</td>
</tr>
<tr>
<td><strong>VALID Study</strong> Valproate in Dementia **</td>
<td>Jody Corey-Bloom, M.D., Ph.D.</td>
<td>Study participation will be 26 months</td>
<td>This study is to determine whether valproate not only delay the time until such behavioral symptoms as agitation or psychosis emerge, but also slow the expected cognitive and functional decline of AD. This is a randomized, placebo-controlled, double-blind trial of outpatients 55 or older with AD (MMSE 10-20 inclusive) who lack agitation and psychosis and do not require treatment with psychotropic medications. Participants will be randomly assigned to receive placebo or placebo (an inactive substance). Treatment with Aricept (Donepezil), memantine (Namenda), oxcarbazepine (Trileptal), or vitamin E is allowed. Participants will be randomly assigned to receive one of two doses of the experimental drug ONO-2506 or a placebo.</td>
<td>Up to 26 months</td>
<td>There will be no payment for participation in this study; however, all tests, examinations, and medical care required as part of the study will be provided at no cost.</td>
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<tr>
<td><strong>ONO-2506 Study</strong> **</td>
<td>Jody Corey-Bloom, M.D., Ph.D.</td>
<td>Study participation will be 26 months</td>
<td>This is a study to find out whether an experimental drug, ONO-2506, is beneficial in the treatment of patients with mild to moderate AD. This study is sponsored by ONO Pharma, Inc. We are seeking participating in the study; however, all tests, examinations, and medical care required as part of the study will be provided at no cost.</td>
<td>Up to 26 months</td>
<td>There will be no payment for participation in this study; however, all tests, examinations, and medical care required as part of the study will be provided at no cost.</td>
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<tr>
<td><strong>Antioxidants Study</strong> **</td>
<td>Jody Corey-Bloom, M.D., Ph.D.</td>
<td>Study participation will be 26 months</td>
<td>This study is to find out whether an antioxidant treatment regimen in patients with mild to moderate AD. We are seeking men and women who are 40-90 years of age and have mild to moderate AD. We are looking for male and female volunteers:</td>
<td>Up to 26 months</td>
<td>There will be no payment for participation in this study; however, all tests, examinations, and medical care required as part of the study will be provided at no cost.</td>
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<tr>
<td><strong>Biomarkers Study</strong> **</td>
<td>Douglas Galasko, M.D.</td>
<td>Study participation will be 26 months</td>
<td>This is a study to find out whether an experimental drug, ONO-2506, is beneficial in the treatment of patients with mild to moderate AD. We are seeking men and women who are 40-90 years of age and have mild to moderate AD. We are looking for male and female volunteers:</td>
<td>Up to 26 months</td>
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COULD OMEGA-3 FATTY ACIDS HELP THE FIGHT AGAINST ALZHEIMER’S?

Fatty acids are one of the components of phospholipids, a type of fat that is a building block of cell membranes. They serve as energy for muscles, heart, organs, and as energy storage for the body as a whole. Essential fatty acids are those the body needs for metabolic functioning but cannot produce and therefore must be acquired from food. Docosahexaenoic acid (DHA), a major component of fish oil, is a fatty acid of the omega-3 type that is synthesized from essential fatty acids (such as ALA) or obtained in the diet. DHA is a vital component of the phospholipids in human cell membranes, particularly those in the brain and retina. It is needed for regulation of all bodily functions and the breakdown of dietary fats within the body, as well as necessary for optimal neural development and visual acuity. DHA-containing phospholipids in nerve cells are believed to be critical for cell signaling (communication), and are the prominent structural fatty acid in the gray matter of the brain. Deficient levels of DHA have been associated with cystic fibrosis, some congenital metabolic diseases, attention deficit disorder, and may be a risk factor for Alzheimer’s disease (AD).

A number of studies have implicated high DHA intake as a preventative measure and/or possible therapeutic approach for several illnesses. A large body of scientific research suggests that increased dietary omega-3 fatty acid intakes are associated with significantly reduced risks of cardiovascular diseases, prompting the American Heart Association to recommend all adults eat fish at least twice weekly. Some studies have suggested that increasing DHA intake may be beneficial to diabetic individuals, especially those with high triglyceride levels, as DHA supplementation reduces triglyceride levels. Fish oil supplementation for at least 12 weeks has consistently decreased the number of tender joints and reduced morning stiffness in individuals with rheumatoid arthritis. Various observational studies have also documented correlations between high DHA intake and lower incidence of Alzheimer’s and other dementias. Researchers at the Lipid Metabolic Lab in Tufts University found diets rich in DHA reduced risk of developing dementia by 48% compared to those diets containing low amounts of DHA. Neuron published an article on a UCLA study where high DHA intake was observed to help prevent memory loss and brain damage in mice genetically engineered to get AD-like disease. Furthermore, the British Medical Journal published an article last year which reported elderly people who consumed fish at least once weekly were at lower risk of developing dementia, including AD.

Preheat oven to 375 degrees. Spray muffin pan with non-stick spray.

In a medium bowl mix canola oil, milk, egg, honey, and vanilla. Add sugar, flour, wheat germ, flaxseed, salt, cinnamon, and chopped walnuts; mix until just blended. Fold in blueberries and baking powder (do not overmix - this makes the muffins harder and less fluffy). Spoon mixture into muffin pan. Sprinkle a little wheat germ over the top of the muffins. Bake for 15-20 minutes or until toothpick comes out clean after inserted in the middle of one of the muffins. Would you like this column to become a regular feature? Tell us what you think! Call (858-622-5800), write (8950 Villa La Jolla Dr. Suite C-129; La Jolla, CA 92037), or e-mail us (padilla@ucsd.edu) with your input or suggestions.
A muchos de nosotros se nos ha olvidado en ocasiones donde hemos estacionado el carro o donde hemos dejado las llaves. A veces hasta olvidamos lo que estamos diciendo a mitad de oración. Mientras que un poco de olvido es normal y aumenta con la vejez, otros cambios de memoria pueden ser más serios y requieren atención médica.

La gente que sufre de cambios en la memoria, capacidad mental y/o comportamiento puede que estén padeciendo de algún tipo de mal cerebral conocido como “demencia”. Los pacientes con demencia no sólo olvidan dónde han puesto las llaves, puede que ni se acuerden cómo utilizarlas. Solo en repetir preguntas, perderse en lugares conocidos, olvidar nombres de personas allegadas o perder noción del tiempo y/o lugar.

Existen muchos tipos de demencia. Algunas formas de demencia son reversibles; tales como aquellas causadas por deficiencias nutricionales, enfermedades metabólicas, deshidratación o leves lesiones de cabeza. Otros tipos de demencia son causados por cambios cerebrales y no son reversibles. Uno de dicho tipo y la causa más común de demencia es la enfermedad Alzheimer.

En la enfermedad de Alzheimer, cambios en las células afecan distinta partes del cerebro. Los síntomas aparecen lentamente y crean dificultad en la ejecución de tareas comunes. Pueden presentar dificultad con el idioma y causar que las personas olviden palabras simples. Otros síntomas comunes incluyen cambios drásticos de personalidad, falta de juicio, pérdida de tiempo y/o lugar. Ellos pueden repetir preguntas, perderse en lugares conocidos, olvidar nombres de personas allegadas o perder noción del tiempo y/o lugar.

Mientras que no existe cura para la enfermedad de Alzheimer, es posible aliviar algunos de los síntomas que acompañan este mal. Mientras más pronto se le diagnostique, mejor la probabilidad de que sus síntomas respondan a tratamiento. Su médico puede recetar una de varias medicinas existentes. La reacción a cualquiera de estos medicamentos varía entre personas.

En la actualidad se están desarrollando otros medicamentos para disminuir los síntomas de la enfermedad de Alzheimer. Estos medicamentos por lo regular se consiguen a través de pruebas clínicas en centros de investigación. Su habilidad de participar varía de acuerdo a la prueba clínica y sus requisitos de participación. Los centros de investigación mantienen su información en confidencia y únicamente comparten sus datos con su doctor si usted lo autoriza.

La participación en pruebas clínicas tiene en sí mismas recompensas. Se pueden probar medicamentos que aún no se recetan, seguimiento de su condición, e histórico médico bien documentado que pudiera beneficiar a otros miembros de su familia. Estas investigaciones ayudan a los científicos a comprender mejor esta enfermedad e identificar los factores de riesgo que contribuyen al desarrollo de la misma. La información obtenida a través de su participación voluntaria pudiera ayudar a descubrir la causa de esta enfermedad y algún día encontrar la cura. Cada granito de información cuenta. Considere participar en investigaciones científicas si usted o algún ser querido está mostrando síntomas o tiene diagnóstico de Alzheimer, o si no tiene síntomas y está dispuesto(a) a participar como sujeto normal (para comparar resultados con aquellos de personas afectadas).

Mientras que no existe prueba diagnóstica específica para determinar si una persona padece de Alzheimer, es posible que su médico le pueda referir a un neurólogo para que le hagan una evaluación extensa. Se le diagnosticaría como “posiblemente padeciendo de Alzheimer” tras una evaluación minuciosa de su historial médico y varias otras pruebas. Algunas de estas pruebas pueden ser un examen físico y neurológico completo, pruebas de laboratorio, y evaluaciones de memoria y otras capacidades mentales. Este proceso toma más de un día como paciente ambulatorio.

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There are at least 55 ongoing ADRC affiliated AD research studies within UCSD’s School of Medicine. The goal of these research studies is to enhance medical knowledge of the disease, its progression and impact on patients, families and caregivers. Like the ADRC, their ultimate goal is preventing and someday curing the disease. The ADRC longitudinal study is the backbone and primary source of volunteers for these studies. Those of you enrolled in the ADRC are asked at each annual exam if you are willing to be contacted about additional studies you may be eligible to participate in. Sue Johnson refers contact information of willing volunteers to pertinent study coordinators, ensuring each individual is referred to only one study at a time. The particular study coordinators contact potential participants to present information about their study and ask whether or not the individual would like to be involved. Please know you are selected and referred to these studies because you meet the study criteria while many other willing volunteers may not.

There have been times when the availability of research volunteers runs short of studies’ needs. If you would consider participation in these affiliated UCSD AD research studies or have a friend who is, please call us to discuss your options. Don’t hesitate to contact Susan Johnson, ADRC Program Representative, at (858) 622-5850 for information or answers to questions about other UCSD affiliated AD research studies. Thank you for your continued support.