Biomarkers are biochemical or other measurements that relate to a disease process. They can provide objective and sometimes quantitative measurements that can help to screen, diagnose, or follow treatment responses of diseases. Some biomarkers are currently widely used as diagnostic aids in clinical practice, for example serum prostate specific antigen (PSA) for prostate cancer, troponin levels to diagnose a heart attack, or bone densitometry for osteoporosis. Interest in biomarkers for dementia, particularly Alzheimer's Disease (AD), has burgeoned in the past decade. Research studies have identified some promising leads, but a clear role has not yet emerged for biomarkers in clinical practice.

There are two main areas of attention:

First, neuroimaging techniques provide indices of the structure, metabolism and function of specific brain regions, and have been widely investigated as potential biomarkers for dementia. By manipulating detailed MRI images on a computer workstation, researchers can identify specific regions in the brain or outline the whole brain and calculate how large these structures are with great accuracy. This line of research has yielded interesting data showing that areas of the brain that are vulnerable to AD show early loss of volume (atrophy), which can be detected even at the stage of early memory decline which has not yet progressed to AD (called Mild Cognitive Impairment [MCI]). Atrophy also increases over time as AD progresses.

The next steps will include doing larger studies that include patients from different centers, to make quality control of imaging as rigorous as possible. Also, because it is time and labor intensive for a research assistant to manipulate the MRI images and obtain volumes, automated methods for tracing structures and defining volumes are being tested.

(Continued on Page 2)
Second, biochemical changes are being sought in the cerebrospinal fluid (CSF) and blood. CSF bathes the brain, and can be obtained by lumbar puncture. Because CSF is closer to the brain than blood, many researchers feel that biochemical clues about changes in AD are more likely to show in the CSF. The brain in AD is littered with molecular clues, and it is challenging to decipher which of the many possible markers are important as early or initiating events in AD and which are secondary, representing later or "downstream" parts of a cascade of degeneration. At present, there is evidence from many research studies (some of the earliest of which were carried out at UCSD) for increased CSF levels of tau (a molecule found in tangles in the brain) and decreased levels of Aβ42 (a long form of the Aβ protein, which is deposited in plaques in AD) in patients with AD compared to controls. Other biomarkers, for example related to inflammation or oxidative damage, can also be found in the CSF.

At the ADRC, we are now interested in searching for novel biomarkers. At present there are two ongoing studies that collect CSF and blood for this research:

- The stress/APO-E study is looking at whether hormones such as cortisol (a main choreographer of stress responses) is altered in the CSF or blood of patients with AD compared to controls. Surplus CSF is also collected in this study to support further biomarker research.

- We are also working with Elan Pharmaceuticals, Inc., to obtain blood and urine samples from patients with AD, MCI and controls. These will be used for large scale studies in which thousands of proteins are identified and compared between the groups of patients, using state-of-the-art biochemical techniques, which fall under the category of proteomics.

Casting such a broad net may help to identify novel proteins which could help us to understand mechanisms involved in AD, and potentially could have an impact on diagnosis or treatment.

New Vaccine Trials May Be On the Horizon

In January of 2002, Elan Pharmaceuticals put a halt on their clinical trials for a vaccine against Alzheimer's disease (AD). The drug triggered life-threatening brain swelling in a few of their volunteers. Now researchers are currently working on the development of a new vaccine, one that will not lead to the brain inflammation of the previous attempt.

The first vaccine contained a synthetic form of beta-amyloid, the protein fragment that accumulates and clumps together killing brain cells and developing into the plaques believed to be the hallmark feature of AD. Researchers were hopeful the AN-1792 inoculations would spur an immune reaction in the body, producing antibodies that would target and destroy the brain plaque.

Despite the unexpected turn of events following AN-1792 injections, researchers have not given up on the concept of developing a vaccine that would halt the neurodegeneration (nerve damage) produced by AD. Two pharmaceutical companies are currently working on a new vaccine using a slightly different approach. Both companies are working on developing injections of lab-made antibodies instead of a vaccine. They are hoping to eradicate brain plaque through a process unlikely to produce the brain inflammation of the prior attempt.
**DID YOU KNOW?**

Huperzine A is a moss that grows in China. Huperzia tea has been used in traditional herbalism to treat fever, blood loss, irregular menstruation, and as a diuretic. Huperzine A is a chemical derived from huperzia. It is medicinally active and, like caffeine and cocaine, belongs to a class of chemicals known as alkaloids. More of a drug than an herb, it is sold over the counter as a dietary supplement to treat memory loss and mental impairment.

Much like current available medications used to treat Alzheimer's disease, huperzine A inhibits the enzyme acetylcholinesterase. Acetylcholinesterase is the protein that breaks down the neurotransmitter acetylcholine, which plays an important role in memory. The higher levels of acetylcholine achieved through inhibition of acetylcholinesterase improve memory and mental functioning in people with Alzheimer’s. Clinical trials performed in China show huperzine A to be as effective in improving such cognitive abilities.

Medications that prevent acetylcholine breakdown often produce side effects including nausea, vomiting, excess saliva and tear production, and sweating. Other than dizziness, no severe side effects were reported in clinical trials investigating huperzine A. Further clinical trials need to be performed to test its efficacy and safety.

If you choose to use huperzine A, we recommend you do so only under physician supervision. High doses of huperzine may be toxic and produce a cholinergic reaction. Although it seems to be a promising, more economic treatment for Alzheimer’s disease, more studies are needed to investigate possible drug interactions and long-term safety of huperzine A use. The Alzheimer's Disease Cooperative Study is planning on launching a clinical trial next Spring investigating the effectiveness of huperzine A in treating Alzheimer’s disease.

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**Declining Glutamine Synthetase (GS) in AD Patients**

Glutamine synthetase (GS) is an enzyme present throughout the body and is found in particularly high concentrations in the liver, muscle, kidney, and brain. This protein is involved in the metabolic process that detoxifies ammonia (a protein byproduct) and glutamine (a protein building block). Brain-specific GS is mainly located in the astrocytes (cells in the brain that aid neuronal function) which support neurons that use glutamate as a neurotransmitter. It participates in the control of glutamate transmission by regulating glutamate conversion into glutamine.

Studies show brain GS levels decline with age, yet particularly so in the brains of Alzheimer's disease (AD) patients. It is hypothesized that the increase in brain glutamate resulting from decreased GS may be involved in the origin of some neuropathologies such as Alzheimer's disease.

Given such correlation, some studies are investigating the possibility of measuring blood and urine levels of GS to aid the diagnosis of AD. Multiple centers across the nation are recruiting for clinical trials to develop a test that may accurately measure GS levels in blood and urine and ultimately aid the diagnostic process of AD.
Clinical Trials

VITAL Vitamins to slow Alzheimer's Disease

STUDY DIRECTOR
Adam Fleisher, M.D.

TIME INVOLVED
Study participation will be about 8 weeks

DESCRIPTION
A new study is seeking 400 individuals to participate in a clinical trial to see whether reducing homocysteine levels in patients with AD will slow the rate of cognitive decline. People with AD have elevated levels of this protein in their blood and researchers want to find out if high-dose supplements of folate and vitamins B6 and B12 can lower homocysteine levels and slow down the devastating effects of AD.

The VITAL study is seeking volunteers who:
- Have mild or moderate AD
- Are age 55 or older
- Are fluent in English or Spanish
- Are on stable medications for at least 4 weeks prior to screening
- Have a study partner - a friend or relative who can accompany the volunteer to all clinical visits and answer questions about him/her

CONTACT
Mary Margaret Pay, N.P., and Judith Rivera, F.N.P., and ask for the “Vital Study”

Glutamate Synthesase (GS) Analyzing Levels of GS as Potential Biomarker for AD

STUDY DIRECTOR
Jody Corey-Bloom, M.D., Ph.D.

TIME INVOLVED
A one-time visit to the ADRC of 2-3 hours in duration

DESCRIPTION
Sponsored by SYN X Pharma, Inc. to evaluate the effectiveness of a blood test for the clinical diagnosis of Alzheimer’s disease. This study will be aimed at detecting levels of GS in blood and urine. GS (Glutamate synthetase) is a protein in the blood that may be a sensitive and specific marker for Alzheimer’s disease. No genetic testing will be performed and this is not a treatment study.

We are looking for individuals between 40 and 90 years of age who have Alzheimer’s disease or memory complaints and no dementia. Individual participation will involve a one-time visit to the ADRC of 2-3 hours in duration. This one-time visit will include clinical and psychometric evaluations. Blood and urine specimens will be collected for testing.

CONTACT
Karen Wetzel, PA-C, M.P.A.S., and ask for the “GS Study”

TAP/DAP: Treatment of Agitation/Psychois in Dementia and Parkinsonism

STUDY DIRECTORS
John Wu, M.D.
Adam Fleisher, M.D.

TIME INVOLVED
Study participation will be about 8 weeks

DESCRIPTION
A new study is seeking 400 individuals to participate in a clinical trial to see whether reducing homocysteine levels in patients with AD will slow the rate of cognitive decline. People with AD have elevated levels of this protein in their blood and researchers want to find out if high-dose supplements of folate and vitamins B6 and B12 can lower homocysteine levels and slow down the devastating effects of AD.

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CONTACT
Mary Margaret Pay, N.P., and Judith Rivera, F.N.P., and ask for the “Vital Study”

R-Flurbi, a Non-Steroidal Anti-Inflammatory Drug (NSAID) and its Effect on Beta Amyloid Protein

STUDY DIRECTORS
Douglas Galasko, M.D.
Edward Koo, M.D.

TIME INVOLVED
5 visits over a 2 month period

DESCRIPTION
A new study is now recruiting subjects between the ages of 55-80, in general good health, not taking NSAIDs, with no significant memory problems, and willing to undergo 2 spinal taps. The spinal taps are done to measure the amount of Beta amyloid protein in the spinal fluid prior to and at the end of taking study medication. We hope to see a reduction in the amount of Beta amyloid proteins, especially the AB42 protein.

The study will involve taking study medication for 3 weeks and 2 spinal taps. One spinal tap will be performed the day you receive your study medication and the second spinal tap will be performed at the end of 3 weeks. You will be asked to return one month after completion of study for a follow-up visit.

COMPENSATION
You will be compensated $200.00 for your participation.

CONTACT
Helen Vanderswag, B.A., and ask for the “Flurbi Study”

Cerebral Spinal Fluid (CSF) Studies

STUDY DIRECTOR
Douglas Galasko, M.D.

DESCRIPTION
We are currently looking for participants for a group of CSF studies, some of which involve using CSF (Cerebral Spinal Fluid) to monitor a response to an experimental procedure and others involve looking for novel diagnostic biomarkers for AD.

Both normal controls and early to moderate AD participants are needed. These studies will involve lumbar puncture for the withdrawal of cerebrospinal fluid.

COMPENSATION
You will be compensated $300.00 for your participation.

CONTACT
Helen Vanderswag, B.A., and ask for the “CSF Study”

CLASP Study: Cholesterol Lowering Agent to Slow Progression of Alzheimer’s Disease

STUDY DIRECTOR
Gang Tong, M.D., Ph.D.

TIME INVOLVED
This study involves 8-9 visits over 15 months

DESCRIPTION
Statins are drugs that are used to lower cholesterol to reduce the risk of heart disease. This study will investigate the safety and effectiveness of simvastatin (Zocor) in slowing the progression of AD.

Studies in animals have shown a link between lowering cholesterol and decreased severity and risk of AD.

Participants will take a study drug for 12 months, and this drug may be simvastatin or it may be an inactive placebo.

All participants must be accompanied by someone who can answer questions about them and who can make sure they are taking the study drug.

If you or a family member have AD, and are not currently taking a cholesterol drug, you may be eligible to participate.

CONTACT
Susan Johnson, G.N.P., or Ingrid Paclita at (858) 622-5800 and ask for the “Statin Study”

Glutamate Synthesase (GS) Analyzing Levels of GS as Potential Biomarker for AD

STUDY DIRECTOR
Jody Corey-Bloom, M.D., Ph.D.

TIME INVOLVED
A one-time visit to the ADRC of 2-3 hours in duration

DESCRIPTION
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CONTACT
Karen Wetzel, PA-C, M.P.A.S., and ask for the “GS Study”

VITAL Vitamins to slow Alzheimer’s Disease

STUDY DIRECTOR
Adam Fleisher, M.D.

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Study participation will be about 8 weeks

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Mary Margaret Pay, N.P., and Judith Rivera, F.N.P., and ask for the “Vital Study”

R-Flurbi, a Non-Steroidal Anti-Inflammatory Drug (NSAID) and its Effect on Beta Amyloid Protein

STUDY DIRECTORS
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TIME INVOLVED
5 visits over a 2 month period

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Helen Vanderswag, B.A., and ask for the “Flurbi Study”

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Both normal controls and early to moderate AD participants are needed. These studies will involve lumbar puncture for the withdrawal of cerebrospinal fluid.

COMPENSATION
You will be compensated $300.00 for your participation.

CONTACT
Helen Vanderswag, B.A., and ask for the “CSF Study”

Clinical Trials Registry

Are you interested in clinical trials but don’t find one that suits you? You can now join our ADRC Registry to be placed on a list for future studies.

PARTICIPANTS CAN BE:
- Normal Controls
- Have a slight memory problem
- Be diagnosed with early to moderate AD

Call the ADRC at (858) 622-5800
Our team from the Hispanic Component of the ADRC outdid itself once more coordinating the annual Hispanic Caregiver Conference. It was held August 14th at the National City Holiday Inn. This conference is free of charge to attendees in an effort to reach out to members of our community that might otherwise not have access to resources and information addressing issues affecting those who care for Alzheimer’s patients in our Latino community.

Conference speakers addressed topics ranging from information about our program, to general overview of the physiology and symptomatology of Alzheimer’s disease; information on getting a diagnosis, durable power of attorney, adult daycare, management of difficult behaviors, and community groups that offer help and support.

We are thankful to those who helped and contributed to the success of this event. It truly has been a cooperative effort. Your support and hard work have been instrumental in spreading the word about Alzheimer’s disease and providing much needed assistance to caregivers in our Latino community. We thank you from the bottom of our hearts.

By Ingrid Padilla

Nuestro equipo del Componente Hispano se ha lucido una vez más coordinando la Conferencia para quien presta cuidado (a pacientes que padecen de Alzheimer’s) llevada a cabo anualmente. Tomó lugar el 14 de agosto en el Holiday Inn de National City. Esta conferencia es gratuita a los asistentes como esfuerzo a extender la mano a aquellos miembros de nuestra comunidad quienes de otra manera pudieran no tener acceso a recursos e información tratando asuntos que afectan aquellos quienes cuidan de pacientes que padecen de la enfermedad de Alzheimer (EA) en nuestra comunidad latina.

Los conferenciantes discutieron temas variados incluyendo información acerca de nuestro programa, un vistazo general de la fisiología y sintomatología de la EA; información acerca de cómo obtener un diagnóstico, directivas anticipadas para el cuidado de la salud, cuidado diurno para adultos, manejo de comportamientos difíciles, y grupos comunitarios que ofrecen ayuda y apoyo.

Le estamos agradecidos a aquellos quienes ayudaron y contribuyeron al éxito de este evento. Verdaderamente ha sido un esfuerzo cooperativo. Su apoyo y trabajo arduo han sido instrumental regando la voz acerca de la EA y proveyendo muy necesitada asistencia a quienes cuidan de pacientes en nuestra comunidad latina. Le damos las gracias desde lo más profundo de nuestros corazones.
Eileen DaPena, BA, PsyD

Although we have mentioned Eileen in past articles, we had yet to formally introduce her. Eileen is a native of Panama who arrived in the States in 1991. She graduated from UCSB earning a B.A. in Psychology in 1994. In 2002 she obtained her PsyD degree at CSPP. Bilingual and bicultural, Eileen joins us as a part-time psychometrist for the Hispanic Component.

Rosa Montoya, BA

Rosa was born in Mexicali and has been in the States since she was two years old. She is a UCSD graduate, earning her B.A. in Human Development in 2002. Rosa utilizes her excellent Spanish language skills as part-time psychometrist for the Hispanic Component. Rosa hopes her experience with us will be helpful in future application to graduate school.

Helen Vanderswag, BA

Helen is a native Californian who earned her Associate Degree at Palomar College and subsequently her B.A. from the University of Phoenix. In her 22 years of nursing experience she has worked in psychiatric inpatient and home care, and clinical research. She comes to us from the Geropsychiatry Unit at the VA and will be working with Drs. Galasko and Koo on a number of clinical trials.

Jenny Reibenspies, BA, MA

Jenny comes to us from the Lone Star state. A varsity athlete at Notre Dame, she earned her B.A. double majoring in Pre-Med and Psychology. She pursued further studies at Loyola University where she finished her M.A. in clinical Psychology. She comes to us after spending three years teaching at an all-boys Catholic high school in Texas, and joins the team as a full-time psychometrist.

The George G. Glenner Alzheimer’s Family Centers, Inc.

CONVERSATIONS WITH CAREGIVERS

"Conversations with Caregivers", is a NO COST course designed to educate and train family caregivers of Alzheimer’s/dementia patients on how to provide quality care and deal with the stress associated with caring for a loved one with dementia.

- "Conversations with Caregivers" offers bilingual (English/Spanish) Alzheimer’s care education/training to families throughout San Diego county.
- Courses consist of 6 two-hour sessions.
- The George G. Glenner Alzheimer’s Family Center, Inc. is now enrolling caregivers for fall sessions.
- Free adult day care available during classes (subject to availability).

Pre-registration required.
For more information please contact Rachel Farias, Program Director at (800) 736-6674.

Hillcrest Center
Tuesday and Thursdays
October 28 - November 13, 2003
2 - 4 PM

Chula Vista Center (Spanish ONLY)
Tuesday and Thursdays
October 28 - November 13, 2003
2 - 4 PM

Escondido Center
Tuesday and Thursdays
October 28 - November 13, 2003
9:30 AM - 11:30 AM
ANNUAL OPEN HOUSE

Everyone at the
UCSD Alzheimer's Disease Research Center
would like to cordially invite you
to our annual Open House

Please join us at the La Jolla Radisson Hotel
Thursday, December 4, 2003
10:00am ~ 11:30 am

We will be providing light refreshments and presenting research updates

RSVP (858) 622-5800