GOVERNOR SIGNS ADRC-INITIATED BILL SUPPORTING ALZHEIMER’S RESEARCH

by Mary Sundsmo, M.B.A.

It all began more than two years ago...

When Leon Thal, M.D., Doug Galasko, M.D., David Salmon, Ph.D. and Mary Sundsmo, M.B.A. met with local Assembly member, Howard Wayne (D-San Diego) to discuss an existing law in the state of California that affected clinical research. We told him that the law, as written, impeded the progress of research into Alzheimer’s disease (AD) because it limited participation to those who had the ability to understand a research protocol and give their own consent to participate. The participant’s family was not permitted to act on their behalf.

According to the law, the only allowable surrogates were 1) a legally named conservator or guardian for healthcare or 2) an individual named in an advance healthcare directive, that specifies research. Neither of these conditions is common among our participants. The law effectively threatened to limit participation to those in the earliest stages of the disease or the very few who met the criteria just mentioned.

Our goal was to change the law to allow a family member to act as a surrogate decision maker for those individuals who no longer had the capacity to make the decision to participate themselves. We wanted to establish a list of potential surrogate decision makers, similar to what currently existed in State law to obtain consent for medical treatment.

(Cont’d on Page 2)
First, we had to find a sponsor and the University of California Office of the President (UCOP) agreed to sponsor our legislation. In the fall of 2001, UCOP began to draft the language of our bill. Next, an author had to be selected to shepherd our bill through the legislature. On February 21, 2002, our bill, AB 2328, was introduced to the State Assembly with Howard Wayne as the primary author. We were now a part of the legislative process.

Our bill was assigned to two Assembly committees for review: Health and Judiciary. The Health Committee’s task was to look at the impact of the bill upon health. Given our aging population, they couldn’t argue against the fact that we have a disease that affects a large number of Californians. Following their approval, we moved past this committee’s consideration and on to Judiciary review.

The Judiciary Committee’s main concern is to preserve the rights of the individual. Would affected individuals be taken advantage of by their families and asked to participate in studies that they would not agree to do if they were able to give consent themselves? This committee was tougher, but we argued that families know the wishes of the individual best and that they should be allowed to act as a surrogate decision maker. [See the hierarchical list in the box.]

We passed the Judiciary committee and moved to the floor of the Assembly. Our bill was approved by the Assembly, and it moved on to the Senate in May. Here our bill was assigned to the Health and Human Services Committee. Lola Crosswhite, one of our participants with Alzheimer’s, and her daughter, Diana Shaw, flew up to Sacramento to testify before this committee. Their testimony was very powerful. Hearing the words, “My name is Lola and I have Alzheimer’s disease” had a profound impact and set the tone for all the testimony heard about our bill that day. We passed through this committee and through the Senate floor. After the Senate, our bill went back to the Assembly floor for concurrence, which came easily. It finally went on to the Governor for signature and became law on January 1, 2003.

I would like to personally thank all of you who took the time to write, e-mail or fax letters to Sacramento in support of our bill. It was a team effort. We couldn’t have accomplished this alone. I have asked Mr. Wayne to obtain a copy of our bill for us, bearing the signature of the Governor. It will be displayed in our waiting room.
One of the features of Alzheimer’s disease is the accumulation of “senile plaques” in brain that are composed of amyloid \(\beta\)-protein. It is believed that in particular, the longer 42 amino acid form of amyloid \(\beta\)-protein (A\(\beta\)42) represents an initiating factor. Thus, reducing the production of A\(\beta\)42 could be an effective way to reduce amyloid \(\beta\)-protein in brain.

Dr. Edward Koo at UCSD recently found that some nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen (Advil) lower the production of A\(\beta\)42 in the brain of laboratory animals. Among the NSAIDs tested, ibuprofen, sulindac, indomethacin, and flurbiprofen appear to have the most potent A\(\beta\)42 lowering effects. Flurbiprofen (Ansaid) is an FDA approved drug and has been used for many years.

Dr. Koo and Dr. Douglas Galasko, another UCSD investigator, have found that a near chemical equivalent of flurbiprofen (R-enantiomer to be exact), which does not have the same gastrointestinal complications found with current NSAIDs, is effective in lowering A\(\beta\)42 production in laboratory experiments.

Under a grant from NIA and funding from Myriad Pharmaceuticals, Dr. Galasko and Dr. Koo will be conducting a study on

- **Normal control subjects**
- **55-80 years old**

Myriad Pharmaceuticals will be supplying this compound called R-flurbiprofen (MPC-7869). FDA approval has been obtained to test R-flurbiprofen in healthy individuals.

Please contact Sharon Krubel, R.N. for more information
(858) 622-5805
In cell cultures, increasing cholesterol levels result in more of the abnormal cuts, and therefore more A-beta. Studies with animals have shown that increasing cholesterol in the diet increases A-beta in the brain. Mice that have a gene for increased amyloid show much greater levels of A-beta in their cerebrospinal fluid when they have a high cholesterol diet. Similar mice fed a low cholesterol diet had lower levels of A-beta. The mice with the high cholesterol diet also showed more amyloid plaques in the brain.
Another study has shown that increasing cholesterol in the diet of mice that have a gene for AD results in less secretion of all forms of amyloid, probably because the amyloid is trapped in the cell. The cholesterol may be making the cell walls more rigid, impeding enzymatic break down of APP. As APP increases within the cell, there may be a greater chance of developing A-beta and the plaques that result.

There is growing evidence that humans who take STATIN drugs to lower cholesterol have a reduced risk of developing Alzheimer’s disease. Epidemiological studies use existing information to compare groups of people in an attempt to identify effective therapies. One such study looked at the computerized records of three hospitals and found that people taking statins had less than half of the prevalence of AD than the population as a whole. The problem with this kind of study is that we cannot rule out the possibility of there being some other explanation for the difference. It may be that people taking statins had higher risk factors for heart disease and didn’t live long enough to get AD.

A couple of cross-sectional studies have compared test scores of people taking statins with people not taking them. Even when the different groups were matched in age, education, and occupation, the groups taking statins did slightly better on the tests than the groups not taking statins.

In order to test whether statin drugs actually have a delaying effect on AD, scientists need to conduct studies where they choose two groups of people who are similar in age, education, health status, and so on, and give one group statin drugs and the other group a placebo. This is called a prospective (i.e., looking forward, not back at already existing data) double-blind placebo controlled study (i.e., some people will get an inactive placebo, but no one will know who is getting which pill).

One such study on patients with high cholesterol levels found that brain cholesterol was lowered by use of statin drugs. Another study looked at patients with mild AD and normal cholesterol levels. They were given the statin drug Simvastatin for six weeks, which decreased the levels of A-beta in the cerebrospinal fluid. We look forward to additional clinical trials to investigate whether people with AD can show improvement or slower decline if they take cholesterol-lowering medicines.
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 and we will mail you a brief questionnaire to fill out.

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. See the article on pages 4-5 for more information about statins and 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 lowering drug, you may be eligible to participate.

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

Higher Dose Donepezil (Aricept®) Pfizer Pharmaceuticals

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

TIME INVOLVED: Study participation will last about 6 months

DESCRIPTION: Although donepezil is already marketed for Alzheimer’s disease (AD) at doses of 5-10mg/day, doses above 10mg/day have not been studied and are considered investigational.

This study will investigate the safety and effectiveness of 15mg/day and 20mg/day of donepezil in patients with mild to moderate AD.

Everyone in the study will receive at least 10mg/day of donepezil.

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

Mild Cognitive Impairment (MCI) Cortex Pharmaceuticals

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

TIME INVOLVED: Study participation will be about 8 weeks

DESCRIPTION: The reason for this study is to determine whether an investigational drug, CX516 (Amagixx®), is safe, well tolerated, and effective for use in patients with mild cognitive impairment.

This study will evaluate one dose level of CX516 administered by mouth for 4 weeks compared to a placebo (an inactive substance).

COMPENSATION: All tests, examinations, and medical care required as part of this study will be provided at no cost to the participant.

Participants will be paid compensation for travel expenses incurred if they complete the study.

CONTACT: Sharon Krubel, R.N., and ask for the “R-3 Study”

Cerebral Spinal Fluid (CSF) Studies

STUDY DIRECTOR: Douglas Galasko, M.D.

TIME INVOLVED: It includes only 2 visits, a screening visit, and a testing visit

DESCRIPTION: We are currently looking for participants for a group of CSF studies, some of which involve using CSF to monitor a response to an experimental procedure and others involve looking for novel diagnostic markers for AD.

Both normal controls and early to moderate AD participants are needed.

These studies all involve lumbar puncture for the withdrawal of cerebrospinal fluid.

CONTACT: Sharon Krubel, R.N., and ask for the “CSF Study”
The Hispanic Component of the ADRC continues to grow, maintaining approximately one hundred participants. The strong support, enthusiasm and commitment of the participants to scientific research is evidenced by their continued annual participation in the program. We at the ADRC are extremely grateful to all the participants for their continued support throughout the years.

We are happy to report that clinical drug studies now have forms available in both English and Spanish. As a result, we hope to recruit a greater number of Latinos in future clinical drug trials. We would like to thank all who have enrolled in the “Healthy Aging and Memory”, “AIT”, and vaccine studies.

Ingrid Padilla is now in charge of recruitment and may contact you for future studies. We will continue to provide you with updates on clinical drug trials and information about future studies during your yearly evaluations. Of course, we are always available to answer questions and/or provide information (619-691-1264 in Chula Vista, 858-622-5800 in La Jolla).

Thanks again for your contributions throughout the years to the Hispanic Component of the ADRC.

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El Componente Hispano del ADRC (Centro de Investigación de la Enfermedad de Alzheimer) continúa creciendo, manteniendo aproximadamente cien participantes. El fuerte apoyo, entusiasmo y compromiso de los participantes a la investigación cientifica es evidente a través de su continua participación anual en el programa. Nosotros en el ADRC estamos extremadamente agradecidos a todos los participantes por su continuo apoyo a través de los años.

Estamos contentos de reportar que las pruebas clínicas de medicamentos ahora tienen a su disposición formularios en ambos inglés y español. Como resultado, esperamos reclutar un número más grande de latinos en pruebas clínicas de medicamentos en el futuro. Queremos darle las gracias a quienes se han inscrito en los estudios de Envejecimiento saludable y la memoria, AIT, y de vacuna.

Ingrid Padilla está ahora a cargo de reclutamiento y puede que se comunique con usted con respecto a estudios en el futuro. Nosotros continuaremos proveyéndoles información al día acerca de las pruebas clínicas, tanto como información acerca de estudios en el futuro durante sus evaluaciones anuales. Por supuesto, siempre estamos disponibles para contestar preguntas y/o proveer información (619-691-1264 en Chula Vista, 858-622-5800 en La Jolla).

Gracias una vez más por sus contribuciones a través de los años al Componente Hispano del ADRC.
Congratulations, Dr. Thal!

On September 4th of this year Dr. Leon Thal received a letter from Tommy Thompson, Secretary of Health and Human Services, inviting him to serve on the National Advisory Council on Aging of the National Institutes of Health.

The National Advisory Council on Aging advises on the conduct and support of biomedical, social, and behavioral research; training, dissemination of health information, and other programs involving aging and the diseases and needs of the aged. Two-thirds of the 18 member council are from health and scientific disciplines and one-third are from the general public.

*Congratulations on your appointment Dr. Thal. Your accomplishments bring great pride to our center!*
Karen Wetzel, PA-C, M.P.A.S.

Karen joins our staff working with Dr. Jody Corey-Bloom in AD and MS research and as a clinician at the MS Center. She is originally from Pennsylvania and received her Bachelor’s degree as a Physician Assistant from the University of Nebraska. She further pursued her studies earning Master degrees in both Psychology and PA Studies and Neurosciences. She spent 23 and a half years as a PA in the Air Force, and has been working in research for the last eight years. She has a 15 year-old son of whom she is very proud for being quite the computer whiz.

Adam Fleisher, M.D.

Dr. Fleisher was born in North Carolina and raised in Phoenix, Arizona. He started his undergraduate studies at the University of Pennsylvania and completed his B.A. in Philosophy, minor in Biochemistry at the University of Arizona. He attended medical school at the University of Rochester and did his neurology residence at Johns Hopkins Hospital in Baltimore, Maryland. He joins our staff as a neurology fellow under Dr. Thal’s mentorship. His area of interest is functional imaging of cognitive disorders.

Sharon Krubel, R.N.

Sharon graduated with a B.S. in Nursing from San Diego State University. She did clinical work for the first ten years of her career, providing primary nursing and outpatient care in various clinical environments. In 1994 she switched gears and has since worked as a clinical trials coordinator in research. She joins our staff coordinating clinical trials with Dr. Galasko and Dr. Koo.

Al Symer

by Aida Masliah

Please hurry up honey, we’ll be late for our ADRC appointment.

Well, I just want to pass the “smell” test.
The UCSD Alzheimer’s Disease Research Center Would Like to Thank and Recognize Our Major Supporters in the Community

Through Contributions, the Following Individuals and Companies Support the Center’s Mission to Investigate the Diagnosis, Causes, Treatment, and Prevention of Alzheimer’s Disease:

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There are many ways to support Alzheimer’s disease research through your gift to UCSD’s Alzheimer’s Disease Research Center.

You can make an outright or commemorative gift.

For more information about making a gift, please contact Pamela Bell at the ADRC
(858) 622-5800
You're Invited!

January 14, 2003
10:30 AM

ADRC Open House

Radisson Hotel
3299 Holiday Court
La Jolla, CA 92039

(Across the street from the ADRC, behind the gas station as you're coming up the hill)

Currents

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