News for the VA research community

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VA Research Currents

Update from the Cooperative Studies Program...

CSP proactively testing therapies for diseases affecting the brain

By John R. Feussner, MD, MPH, director; Steve Berkowitz, PhD, asst. dir.; and Joe Gough, MA, program mngr.

Historically, the Cooperative Studies Program (CSP) has rigorously evaluated existing or novel treatments for major chronic illnesses that are prevalent among veterans. One of the designated research areas for the Office of Research and Development is "diseases of the brain." CSP has addressed this research goal through several recently completed and active trials focused on diseases that affect cerebral functioning.

Since 1990, CSP has collaborated with the National Institute on Drug Abuse (NIDA) to evaluate emerging pharmaceuticals and the effectiveness of health care delivery models for substance abusers. Notably, one study led to FDA approval of a new drug, levomethadyl acetate hydrochloride, to treat opiate dependence. VA/NIDA studies will continue to assess treatment options for addictive brain disorders related to substance abuse.

A recently completed CSP trial provided empirical evidence that naltrexone, an FDA-approved and widely prescribed medication, was no more effective than placebo for treating alcoholism (*New England Journal of Medicine,* Dec. 13, 2001). Study findings may alter treatment options in and beyond the VA health care system.

One study presently in the data analysis phase will determine the clinical effectiveness, side effects, and economic impact of the antipsychotic drug olanzapine versus a less expensive drug, halperidol, for the treatment of schizophrenia.

Last year, CSP completed a study comparing two group-based behavioral interventions for PTSD in Vietnam veterans. Also last year, CSP initiated a similar individual-based behavioral treatment trial among women veterans with PTSD. In 2003, CSP will complete a trial comparing a high-intensity, protocol-directed intervention, the Bipolar Disease Treatment Program, to the current standard of care for manic depression in veterans.

A recently completed trial among

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Study shows benefits for 'opportunistic' diabetes screening

A VA cooperative study published in the Jan. 2002 J*ournal of General Internal Medicine* shows that performing diabetes tests on patients visiting the doctor for other concerns may be a cost-effective screening strategy. This "opportunistic" screening, say the authors, can be easily incorporated into a patient's care and offers several benefits, including a better chance for follow-up care.

Researchers at the VA Medical Center in Durham found that of 1,253 VA outpatients without recognized diabetes, 4.5 percent were found to have the disease through opportunistic screening. Of these, 61 percent required a change in treatment for conditions other than diabetes, such as high blood pressure or cholesterol, based on their newly discovered diabetic status.

"Theoretically, the screening methods studied could be adopted by VA medical centers all over the country almost immediately," said lead author David Edelman, MD. "What we have here is a very practical way of discovering previously undiagnosed cases of diabetes."

Dr. Edelman noted that opportunistic screening relies on a non-fasting test, where patients are not required to refrain from eating prior to screening. This in itself carries an advantage, he said. "The downside to fasting tests, while more direct with a better

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Recent publications and presentations

Below is a sampling of recent publications and presentations by VA investigators. Due to space constraints, only VA authors and affiliations are noted. Notification of upcoming publications and presentations can be faxed to (410) 962-0084 or e-mailed to researchinfo@ vard.org.

"The Accuracy of Medical Record Documentation in Schizophrenia." Julie Cradock, PhD; Alexander S. Young, MD, MSHS; Greer Sullivan, MD, MSPH. **West Los Angeles** and **Central Arkansas** (GS). *Journal for Behavioral Health Services and Research,* Nov. 2001.

"Analyzing the Cost of Pain Management." Bonnie Wakefield, PhD., RN. **Iowa City.** *Home Health Care Consultant,* Dec. 2001.

"At the Interface: Convergence of Neural Regeneration and Neural Prostheses for Restoration of Function." P. Hunter Peckham, PhD; Jeffrey Kocsis, PhD. **Cleveland** (PHP) and **West Haven,** Conn. *VA Journal of Rehabilitation Research and Development,* Nov./Dec. 2001.

"Comparison of Cefuroxime Axetil with or without Intranasal Fluticasone for the Treatment of Rhinosinusitis." Rowena J. Dolor, MD, MHS; David L. Witsell, MD, MHS; John W. Williams Jr., MD, MHS; David L. Simel, MD, MHS; et al, for the Ceftin and Flonase for Sinusitis (CAFFS) Investigators. **Durham** and **South Texas** (JWW). *Journal of the American Medical Association,* Dec. 26, 2001.

"Distribution of Intraventricularly Administered Antiamyloid-Beta Peptide Antibody in the Mouse Brain." Neelima B. Chauhan, PhD; George J. Siegel, MD. **North Chicago.** *Journal of Neuroscience Research,* Oct. 15, 2001.

"The Effect of Tax-Exempt Out-of – Pocket Premiums on Health Plan Choice." Matthew L. Maciejewski, PhD. **Seattle.** *National Tax Journal,* Dec. 2001.

"Formation and Implications of a Ternary Complex of Profilin, Thymosin Beta 4, and Actin." Michael R. Bubb, MD. **Gainesville** (Fla.). *Journal of Biological Chemistry,* Dec. 7, 2001.

"Helicobacter Pylori and Iron Deficiency Anemia: Guilty as Charged?" Edmund J. Bini, MD. **New York.** *American Journal of Medicine,* Oct. 15, 2001.

"Long-term Outcome Study of Growth-Factor-Treated Pressure Ulcers." Wyatt G. Payne, MD; Diane E. Ochs, RN; Rudy J. Mannari, PA-C; Martin C. Robson, MD. **Bay Pines** (Fla.). *American Journal of Surgery,* Jan. 2001.

"Medical Students' Attitudes Toward Patient-Centered Care and Standardized Patients' Perceptions of Humanism: A Link Between Attitudes and Outcomes." Paul M. Haidet, MD, MPH. **Houston.** *Academic Medicine,* Oct. 2001.

"Mesalamine Induces Manganese Superoxide Dismutase in Rat Intestinal Epithelial Cell Lines and In Vivo." John F. Valentine, MD. **Gainesville** (Fla.). *American Journal of Physiology: Gastrointestinal and Liver Physiology,* Oct. 2001.

"Personality Disorders in Veterans with PTSD and Depression." Nancy Jo Dunn, PhD; Jeanne Schillaci, PhD; Elisia Yanasak, MA; Sofia Simotas, PhD; Lynn Rehm, PhD; Julianne Souchek, PhD; Terri Menke, PhD; Carol Ashton, MD, MPH; Joseph D. Hamilton, MD. **Houston.** Annual meeting of the International Society for Traumatic Stress Studies, Dec. 2001.

"Predictors of Quality of Life Following Acute Coronary Syndromes." John S. Rumsfeld, MD, PhD; Maureen M. O'Brien, PhD, RPh; John A. Spertus, MD; Nathan R. Every, MD, MPH; Anne E. Sales, PhD, MSN. **Denver** (JSR, MMO) and **Seattle.** *American Journal of Cardiology,* Oct. 2001.

"A Program for Teaching Psychiatric Residents to Provide Integrated Psychiatric and Primary Medical Care." Steven Dobscha, MD; Linda K. Ganzini, MD. **Portland (**Ore.). *Psychiatric Services,* Dec. 2001.

"Racial Differences in Physician Recommendation of Hormone Replacement Therapy." Colleen McBride, PhD; Hayden B. Bosworth, PhD; Lori A. Bastian, MD, MPH. **Durham.** *Preventive Medicine,* Dec. 2001.

"Transforming Growth Factor Beta-2 Lowers the Incidence of Incisional Hernias." Michael G. Franz, MD; M.A. Kuhn; K. Nguyen; Xue Wang, PhD; Francis Ko; Terry E. Wright, MD; Martin C. Robson, MD. **Bay Pines** (Fla.). *Journal of Surgical Research,* May 2001.

"Treating the Cognitively Impaired Older Adult with Cognitive-Behavioral Therapy." A. Lynn Snow, PhD; David Powers, PhD; L. Siskin, PhD; Suzann M. Ogland-Hand, PhD. **Houston.** Geron. Soc. of America, Nov. 2001. ■

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VA presents Magnuson Award to prosthetics pioneer

Dudley S. Childress, PhD, a VA research engineer whose groundbreaking work in prosthetics and rehabilitation technology has helped thousands of people with severe disabilities, received VA's Magnuson Award on Feb. 11 at the agency's national meeting for rehabilitation investigators in Arlington, Va. The annual award is VA's highest honor for rehabilitation investigators.

Dr. Childress is a prosthetics and orthotics researcher at the VA Chicago Healthcare System and professor of biomedical engineering and physical medicine and rehabilitation at Northwestern University. In the 1960s he was among the pioneers of myoelectric control, which applies electrical signals from muscles to prosthetic limbs. A decade later his team developed the "sip and puff" wheelchair—the type used by actor Christopher Reeve—to enable quadriplegics to perform certain activities by breathing in or out.

The focus of Dr. Childress' research shifted in the 1980s to the development of CAD/CAM (Computer-Aided Design and Manufacture) systems to speed and improve the production of prosthetic components. His lab invented the "Squirt Shape" method to quickly and accurately produce sockets for artificial legs.

Today, Dr. Childress and his graduate students are studying the biomechanics of human walking, and using this knowledge to improve the design of prosthetic feet and legs. Among their projects is the development of a relatively inexpensive prosthetic foot that may be especially helpful to amputees in poor nations.

The Magnuson Award was established in 1998 in honor of Paul B. Magnuson, MD, a bone and joint surgeon and Chief Medical Director for VA in the years after World War II. He initiated VA's university-affiliation model and was known for his dedication to finding innovative and individualized solutions for patients with disabilities. Magnuson Award winners receive a $5,000 cash award and a plaque, along with an additional $50,000 per year for three years to support a currently funded, nationally peer-reviewed research project. ■

Ed. note—Our next issue will feature more coverage from the annual national meetings of Rehabilitation Research and Development and Health Services Research and Development, both held this month in the Washington, D.C., area.

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Gulf War veterans with physical symptoms of fatigue, memory loss, and muscle and joint pain evaluated the effectiveness of cognitive behavioral therapy, alone and in combination with physical exercise, for the relief of symptoms.

In 2002, a new CSP study for cardiac bypass surgery will compare two open-heart surgical procedures: one relying on cardiovascular bypass, the other on the beating heart. Among other outcome measures, the study will assess how cognitive function is affected by these two surgical techniques. Similarly, the VA CSP Type II Diabetes treatment trial will assess the neuropsychological effects of intensive glycemic control as a secondary outcome measure.

Another ongoing CSP trial is comparing the current standard treatment for epileptic seizures, carbamazepine, to two newly approved drugs, gabapentin and lamotrigine.

In Feb. 2002, CSP initiated a landmark trial to evaluate a promising neurosurgical treatment for Parkinson's disease in collaboration with the National Institutes of Neurological Diseases and Stroke (NINDS). The trial aims to determine if surgical electrode implantation and stimulation in specific regions of the brain provide relief from the disabling symptoms of Parkinson's disease in patients for whom medical treatment is no longer effective.

CSP will continue its proactive evaluation of novel therapies designed to enhance the quality of care for veterans with illnesses affecting the brain. Inquiries on any of these studies may be directed to Joe Gough, MA, CSP program manager, by e-mail at joe.gough@hq.med.va.gov or by telephone at (202) 273-8248. ■

Clinical Research Career Development Program

Letters of intent to apply for the Cooperative Studies Program Clinical Research Career Development Program are due **May 1** and **Nov. 1** of each funding year. For full details on the program, log onto http://www.va.gov/resdev/fr/csp_crcdp.cfm or call Joe Gough at (202) 273-8248.

Upcoming events

Sleep researchers to meet

The first National VA Sleep Research Conference will be held March 8 – 9, 2002, at the Philadelphia VA Medical Center. According to conference co-organizer Samuel T. Kuna, MD, a sleep researcher with VA and the University of Pennsylvania, a major goal of the meeting is to expand the abilities of VA physicians to evaluate their patients' sleep disorders.

"Many VA physicians who are knowledgeable about, and interested in, sleep disorders do not have access to sleep laboratories to evaluate their patients," said Dr. Kuna. "We want to start a dialogue to determine what opportunities are available to address this and other challenges."

Dr. Kuna said that advances in the development of inexpensive, portable sleep monitors and related technologies may enable patients with obstructive sleep apnea and other disorders to sleep at home, rather than at a hospital-based sleep lab, and send diagnostic data electronically to a lab for analysis. He said VA could take the lead in developing an innovative, cost-efficient way to diagnose and treat sleep disorders.

For details on the conference, sponsored by VISN 4 of the Veterans Healthcare Administration, e-mail Sam Kuna at skuna@mail.med.upenn.edu or Dr. Charles Atwood, of the Pittsburgh VA Medical Center, at Charles.Atwood@med.va.gov.

National VA Research Week will take place March 31 – April 6, 2002. Research offices have received instructions and will be receiving packets containing posters, fact sheets and other materials. For more information contact Christine Amereihn, R&D Communications, at (410) 962-1800, ext. 273, or chris@vard.org.

The Fourth Annual Summer Epidemiology Session, hosted by VA's Epidemiologic and Information Centers (ERICs), will take place June 24 – 28, 2002, at the University of Washington in Seattle. To receive more details or a registration packet, send e-mail to carrie.mccloud@med.va.gov. or log on to the Seattle ERIC website at www.eric.seattle.med.va.gov.

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sensitivity and specificity than any non-fasting tests, is that patients don't always fast," said Dr. Edelman. "There are significant benefits in not having to worry about that."

He added, "The non-fasting test also gives us important information on how severe the diabetes is, so you know right from the beginning what the urgency of intervention is."

R&D Hotline Conference Calls: 12 – 12:50 p.m. (EST), on March 11, May 13, July 8, Sept. 9 and Nov. 18. Dial (877) 230-4050, access code 17323.

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Reflections of a VA Nobel laureate

An interview with Dr. Andrew Schally on the occasion of the Nobel Centennial

Twenty-five years after his Nobel Prize and 40 years after joining VA, Andrew Schally, PhD, MD, shows no signs of slowing down. The New Orleans researcher—who swims a mile a day and follows an exercise regimen that would shame most college students—published some 25 papers in the last year alone. Career total? About 2,200.

Dr. Schally may not yet have found the fabled "cure for cancer," but he's come about as close as any medical researcher. Nowadays, he's hot on the trail of compounds he believes will revolutionize cancer treatment. While he is careful to distinguish between effective treatments and "cures," he brims with excitement when describing this latest work—combining cancer-cell-killing drugs with hormone analogs, and then targeting tumors that have receptors for those hormones. The result is "smart" chemotherapy that zaps cancer cells with far fewer side effects.

"The beauty of these methods is that they are targeted," says Dr. Schally, a Distinguished Medical Research Scientist at the New Orleans VA Medical Center and professor of medicine at Tulane University. "They go to the tumor and they can destroy malignant cells. If you repeat it two, three times, you can perhaps totally destroy the tumor. In such a case, you have a treatment that comes very close to being a cure."

Discovery of 'releasing hormones' leads to new treatments

The methods mentioned above are but one example of an ever-expanding web of therapeutic applications for Dr. Schally's work. In the 1960s and '70s he discovered and synthesized three hormones—all peptides, or chains of amino acids—produced in the hypothalamus region of the brain. The hormones are dubbed "releasing hormones" because they travel to the pituitary gland and release other hormones. They affect a myriad of health conditions, from infertility and obesity to ulcers and tumors. The road from Dr. Schally's initial discoveries to his research today has been filled with milestones, all of which contribute to saving lives and figure prominently in the everyday work of oncologists, gynecologists, gastroenterologists and endocrinologists.

Drs. Schally and Comaru-Schally in front of the Swedish Parliament during their recent visit to Stockholm for the Nobel Centennial .

Two examples from his work on cancer: The current treatment for testosterone-dependent prostate cancer—used successfully in hundreds of thousands of men—is derived from a brain hormone called luteinizing-hormone releasing hormone (LH-RH) that he discovered. More recently, his team reported on a promising new therapy for renal cell carcinoma—one of the most lethal forms of cancer— using a cytotoxic (cell-killing) analog of somatostatin, another hormone secreted by the hypothalamus, discovered by later research teams building on Dr. Schally's findings. Dr. Schally is now exploring methods similar to the above for treating breast, ovarian, pancreatic, lung and other tumors.

His early discoveries earned him the 1977 Nobel Prize for medicine, which he shared with fellow hormone researcher Roger Guillemin and Rosalyn Yalow, a friend and VA colleague who pioneered the field of radioimmunoassay.

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"Dr. Yalow's work greatly helped us," notes Dr. Schally. "Radioimmunoassay is a modern, very fast method for measuring hormone levels."

In December, Dr. Schally, along with his wife and research partner, endocrinologist Ana Maria Comaru-Schally, MD, attended the gala Nobel Centennial celebrations in Stockholm. Prior to the ceremonies they delivered lectures at Sweden's prestigious Karolinska Institute. As their limousine approached one of the Institute hospitals, they saw a huge American flag waving proudly outside the building—a rare sight in Europe—alongside the Swedish flag. The flag had been placed there in honor of Dr. Schally. For Polish-born Dr. Schally and his Brazilian-born wife, both longtime naturalized Americans, it was a proud, emotional moment.

"To go overseas and see an American flag displayed in this way was very special. It brought tears to my eyes," recalls Dr. Comaru-Schally. She adds that Karolinska officials heaped praise upon her husband for his remarkable longevity and productivity.

After a half century of medical research and international accolades, what is it that keeps Dr. Schally coming to the lab before 7 a.m. every day?

"The main reason for my success is scientific curiosity," he says. "This is a trait I still have. I want to know how nature controls these mechanisms."

Focus of research shifts from reproductive health to oncology

It was this curiosity—along with a strong sense of ethical responsibility as a scientist—that in the 1970s caused Dr. Schally to shift the focus of his hormone research from reproductive health to oncology.

"I began to see that the role of hormones in breast and prostate cancer was much greater than originally demonstrated," he remembers. "We had patients with various tumors. We could inject our hormones and show inhibition of the tumor. So I realized I would be a fool—even scientifically criminal—to not use some of the hormones from the brain, which I discovered, in oncology.

Today, his team is involved in several clinical trials of hormone-based treatments. "I believe we are very, very close to new methods for cancer treatment," says Dr. Schally.

Among other trials, Dr. Comaru-Schally is leading a new study of a treatment for advanced renal cell carcinoma using an LH-RH antagonist (an agent that blocks the hormone's action).

"The main reason for my success is scientific curiosity. ... I want to know how nature controls these mechanisms."

"I've already received calls from veterans, even from Alaska," she says. "They want to participate in this trial, because they have this malignancy and there is no other treatment available."

The Schallys' lab at the New Orleans VA Medical Center attracts visiting fellows from around the globe. Drs. Schally and Comaru-Schally speak seven or eight languages between them, and the atmosphere at work is not unlike the United Nations. "We're an international family," says Dr. Comaru-Schally. European colleagues sometimes bring videotapes of big soccer games for Dr. Schally to watch on weekends. He was an avid soccer player in his youth.

At 75, Dr. Schally works as hard as ever but knows how to relax. He abides by the maxim "a healthy mind in a healthy body," and carves out ample time in his pressing schedule for exercise. "At home," asserts his wife and colleague, "we don't talk about research."

Dr. Schally confides he has begun working on his memoirs—but only occasionally. He doesn't want to take time away from his VA and Tulane responsibilities. There are critical experiments to be conducted, treatments to be refined—perhaps even cures to be found.

"I am in good health," says Dr. Schally, "and Nobelists never retire." ■