



VA Research Currents

Update from Rehabilitation Research and Development...

New REAPs focus on tissue engineering, patient safety

By Mindy Aisen, MD, *Director*

Over the last four years, the Rehabilitation Research and Development Service has successfully broadened its programs and increased the depth of its expertise to shape new discoveries in technology and medicine into optimal rehabilitative health care for veterans. As part of this capacity-building effort, the Service was recently pleased to issue its first Research Enhancement Award Program (REAP) solicitation. REAPs allow funded VA investigators with different backgrounds, skills, and training to focus their varied expertise on fostering new ideas and approaches to solve serious medical problems.

With this first solicitation, Rehab R&D has dedicated nearly \$2.5 million over the next five years to fund two

new REAPs in two very different, yet equally important areas: tissue engineering and safety for the “at-risk” patient. The new REAPs will be based at the VA New England Healthcare System and the VA Sunshine Healthcare Network (in Florida) and will be operational this July.

Tissue-engineering-based rehabilitation builds on tissue culture, molecular biology, and proteoglycan biochemistry research, with the ultimate goal of replacing prosthetic and orthotic devices to aid veterans affected by traumatic injury, disease, or aging. The Boston VA Medical Center will house the Tissue Engineering-Based Rehabilitation REAP. Because engineered tissue can be exposed to mechanical stress, it promises to revolutionize

rehabilitation and provide opportunities for more complete recovery.

This is an example of research with strong implications for the future of rehabilitation, but which falls in a gap between traditional bench research and applied clinical research. We are very pleased to fund this exciting new research. The REAP team will be led by Myron Spector, PhD, and will benefit from Dr. Spector’s affiliation with Harvard University.

The Tampa VA Medical Center will also host a newly formed REAP. Directed by Gail Powel-Cope, PhD, RN, the Technology to Prevent Adverse Events in Rehabilitation REAP will study patient safety, focusing on

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Innovative St. Louis program takes extra step in assuring research quality

Like so many clinical trials today, a research subcommittee at the St. Louis VA Medical Center is known by a clever acronym—ODEAR (Organization, Documentation, Evaluation and Review). The group, part of the center’s Human Studies Subcommittee, is an innovative effort that helps clinical investigators with the administration of their studies and guides them in meeting the strict standards for human-subjects protection set by VA and outside funding agencies, such as the National Institutes of Health.

“We’re trying to find errors and correct them, in a non-threatening way,” said ODEAR chair Sharon Carmody.

The group is currently made up of seven study coordinators who volunteer their time for the extra role. They meet monthly to randomly choose three studies to audit—two that are under way, and one that is newly approved. With the new studies, said Carmody, “If any problems are occurring, we can catch them very early.”

One or two ODEAR members spend about two hours with the principal investigator (PI), looking at consent forms and other documentation, discussing safety and confidentiality procedures, and checking other organizational aspects of the study. Any problems are reported to

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technology to manage patient falls, pressure ulcers and pain.

Research on falls will focus on developing new technology to prevent falls and fall-related injuries, including patient-care equipment and tele-health systems. It will also explore related issues such as therapeutic interior design and the biomechanics of falls. Pressure ulcer studies will evaluate technology to prevent pressure ulcers in persons with impaired sensation or mobility. Risk-assessment tools for pressure ulcers, targeting specific disabilities, will be developed and validated. Pain research will evaluate, develop, and test pain-management approaches in specific disabilities.

Data derived from this REAP could identify low- and high-technology solutions to significantly reduce adverse events in rehabilitation, speed patient recovery and decrease health-care costs.

These two diverse, yet critical areas add a new dimension to our rehabilitation research. Through funding a core of investigators in these areas, we hope to continue to foster an atmosphere of collaboration and lead an effort that will bring new discoveries into rehabilitative health care. Plans are already under way for a second REAP solicitation in 2003. ■

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103 S. Gay St., Rm. 517
Baltimore, MD 21202
(410) 962-1800, ext. 223
researchinfo@vard.org

**Recent publications
and presentations**

Below is a representative sampling of recent publications and presentations by VA investigators. Due to space constraints, only VA authors and affiliations are noted.

“Anticonvulsant Activity of a Nonpeptide Galanin Receptor Agonist.” Claude Wasterlain, MD. **Greater Los Angeles.** *Proceedings of the National Academy of Sciences*, May 14, 2002.

“Association Between Inhaled Beta-Agonists and the Risk of Unstable Angina and Myocardial Infarction.” David H. Au, MD, MS; J. Randall Curtis, MD, MPH; Nathan R. Every, MD, MPH; Mary B. McDonnell, MS; Stephan D. Fihn, MD, MPH. **Puget Sound.** *Chest*, April 2002.

“Comparing Performance of Multinomial Logistic Regression and Discriminant Analysis for Monitoring Access to Care for Acute Myocardial Infarction.” Monir Hossain, MS; Steven Wright, PhD; Laura A. Petersen, MD, MPH. **Boston and Houston (LAP).** *Journal of Clinical Epidemiology*, April 2002.

“Do Neuropsychological Tests Detect Preclinical Alzheimer’s Disease: Individual-Test Versus Cognitive-Discrepancy Score Analyses.” Mark W. Jacobson, PhD; Dean C. Delis, PhD; Mark W. Bondi, PhD. **San Diego.** *Neuropsychology*, April 2002.

“Epidemiologic Differences Between Adenocarcinoma of the Oesophagus and Adenocarcinoma of the Gastric Cardia in the USA.” Hashem B. El-Serag, MD; Nancy J. Petersen, PhD. **Houston.** *Gut*, March 2002.

“Inhibition of KIT Tyrosine Kinase Activity: A Novel Molecular Approach to the Treatment of KIT-Positive Malignancies.” Michael C. Heinrich, MD; Charles D. Blanke, MD; Christopher L. Corless, MD, PhD. **Portland.** *Journal of Clinical Oncology*, April 2002.

“Interventions That Increase Use of Adult Immunization and Cancer Screening Services: A Meta-Analysis.” Brian S. Mittman, PhD; Lisa V. Rubenstein, MD; Laurence Z. Rubenstein, MD; Paul G. Shekelle, MD, PhD. **Greater Los Angeles.** *Annals of Internal Medicine*, May 7, 2002.

“P53, Proto-Oncogene and Rheumatoid Arthritis.” Herman S. Cheung, PhD. **Miami.** *Seminars in Arthritis and Rheumatism*, April 26, 2002.

“Pain in Multiple Sclerosis: A Biopsychosocial Perspective.” Robert D. Kerns, PhD; Marilyn Kassirer, MD; John Otis, PhD. **West Haven (Conn.) and Boston (MK).** *VA Journal of Rehabilitation Research and Development*, March/April 2002.

“Prognostic Value of Immunologic and Virologic Markers in Late-Stage HIV-1 Disease: Data from HAVACS (HIV Atlanta Veterans Affairs Cohort Study).” Jodie L. Guest, PhD, MPH; David Rimland, MD. **Atlanta.** Ninth Conference on Retroviruses and Opportunistic Infections, Feb. 2002.

“Tamoxifen Decreases Fibroblast Function and Downregulates TGF(beta 2) in Dupuytren’s Affected Palmar Fascia.” Wyatt G. Payne, MD; Martin Robson, MD. **Bay Pines (Fla.).** *Journal of Surgical Research*, April 2002.

“Validation of Case-Mix Measures Derived from Self-Reports of Diagnoses and Health.” Vincent S. Fan, MD, MPH; David Au, MD, MS; Mary B. McDonnell, MS; Stephan D. Fihn, MD, MPH. **Puget Sound.** *Journal of Clinical Epidemiology*, April 2002. ■

'Hunger hormone' may be key in weight loss

Thousands of obese Americans know firsthand that gastric bypass surgery can achieve long-term weight loss when dieting, exercise and medications have failed. The reason for the difference may hinge on a recently discovered appetite-stimulating hormone, according to VA research published in the May 23 *New England Journal of Medicine*.

A study led by a team at the VA **Puget Sound** Health Care System and the University of Washington compared blood samples from dieters and gastric-bypass patients and found dramatic differences in the levels of "ghrelin," a hormone secreted by the stomach. The hormone was first identified by Japanese researchers in 1999, and was shown by British scientists last year to trigger appetite in humans—the first known hormone to do this.

The new findings may explain why keeping off excess weight through dieting, exercise or even medication is often a constant uphill battle, whereas obese patients who lose up to 200 pounds or more through gastric bypass surgery tend to keep off the pounds permanently. The study shows that dieting raises ghrelin, while gastric bypass surgery sharply reduces it, almost to undetectable levels. The research is the first to document the effects of low-calorie dieting versus gastric bypass surgery on ghrelin levels.

According to lead author David E. Cummings, MD, the findings not only shed light on what may be an underlying reason for the success of gastric bypass surgery, but raise the possibility of a new generation of safer, more effective weight-loss drugs. ■

Testosterone helps older men's brains

Older men with higher testosterone levels performed better on cognition tests in a recent study led by a VA researcher. The study, which appeared in the April *Journal of the American Geriatrics Society*, suggests that older men who are prescribed testosterone supplements may reduce their risk of cognitive decline.

Men's bodies tend to produce less testosterone as they age, and some doctors have begun prescribing supplements of the hormone to boost libido and treat other age-related problems in men.

"The men in the study with higher levels of bioavailable testosterone—the testosterone that can reach the brain—did significantly better on these cognitive tests than men with lower levels," said lead author Kristine Yaffe, MD, chief of geriatric psychiatry at the **San Francisco** VA Medical Center.

However, Yaffe does not recommend that men begin taking testosterone to improve cognition. "Our study only looked at natural testosterone levels and so it doesn't prove that testosterone supplements can prevent cognitive decline," she said. "We will need results of large randomized clinical trials in older men before we can confidently say that testosterone supplements are beneficial and safe."

R&D Hotline Conference Calls

July 8 and Sept. 9, noon – 12:50 p.m. (EST). Dial (800) 767-1750, #17323

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the center's institutional review board, and the PI must respond with a plan to address the issue.

The initiative has been well-received by investigators, said ODEAR member Elizabeth Clark, RN. "We have a post-audit questionnaire that gives the PIs an opportunity to respond on how they thought it went. We've had very positive comments. All the investigators have been very responsive to any suggestions we've made. They seem to be very glad to have someone helping them out and making things a little clearer for them."

Mentoring is a critical feature of ODEAR. The group's members have several years' combined experience managing clinical trials, and look to share their wisdom with newcomers.

"One of our main goals is to have people with some background and expertise help new people," said Clark. "Frequently in the VA system, new research staff is hired for each project. This group is an opportunity to offer training and guidance to new personnel at the onset of each study."

Surveyors from the National Committee for Quality Assurance, an independent organization that conducts rigorous on-site reviews of research at VA medical centers and provides accreditation, expressed strong approval of ODEAR's role in quality management.

"They were very impressed with what we were doing," said Carmody. She added that ODEAR may be a good model for other VA medical centers to adopt, both to boost regulatory compliance and supplement the training of research staff.

For more information, contact Elizabeth Clark at (314) 289-7690 or Elizabeth.Clark3@med.va.gov. ■

Career milestones

Stephen G. Waxman, MD, PhD, director of the VA Rehabilitation Research and Development Center for Spinal Cord Injury and Multiple Sclerosis (MS) in West Haven, Conn., and chair of neurology at Yale University, received the Dystel Prize from the National Multiple Sclerosis Society for his work on disease and recovery in MS. His research on sodium channels—tiny pores along the axon that help enable nerve conduction—has shed light on the origin of neurological problems in MS and stimulated interest in developing treatments to improve nerve function.

Denise M. Hynes, PhD, RN, was recognized alongside winners of this year's Secretary's Awards for Excellence in Nursing and the Advancement of Nursing Programs. Hynes, a nurse researcher who directs VA's Information Resource Center in Hines, Ill., led a recent study showing that subcutaneous administration of the drug erythropoietin for end-stage renal disease could save Medicare as much as \$142 million each year. ■

Eisenberg Award to VA research chief Feussner

John R. Feussner, MD, MPH, chief research and development officer for VA, received the John Eisenberg National Award for Career Achievement in Research in General Medicine at the 25th annual meeting of the Society of General Internal Medicine, held in May in Atlanta. The award recognizes members of the society whose work has had an important impact on research methodology, patient care or health policy.

Feussner has directed VA's health research program since 1996, and conducted research for VA for more than 20 years. He has authored or co-authored nearly 120 publications in the medical literature, with a focus on health-care delivery, systemic quality improvement, primary-care screening and risk assessment, geriatrics, and cardiovascular health. Prior to his role at VA's Central Office, Feussner was based in Durham, N.C., where he directed VA's Center for Health Services Research in Primary Care.

The John Eisenberg Award is named for the former director of the Agency for Healthcare Research and Quality, who passed away earlier this year after a long illness.

CSP sabbatical program

VA's Cooperative Studies Program, through the Career Development Enhancement Award program, is providing funding for established clinician scientists to train in clinical research methodology for one year at one of three sites: the CSP Coordinating Center in West Haven, Conn; the Epidemiologic Research and Information Center (ERIC) in Boston; or the ERIC in Durham, N.C. CSP provides salary and benefits for six months, to be matched by the applicant's VA medical center. Applications are due Nov. 1.

For an information packet contact Joe Gough at (202) 565-8274 or joe.gough@hq.med.va.gov.

VA Research and Development Communications
Department of Veterans Affairs
103 S. Gay St., Rm. 517
Baltimore, MD 21202