



VA Research Currents

Abstracts sought for first ORD-wide scientific meeting

The first national scientific meeting encompassing all areas of VA research will be held March 9 – 12, 2004, in Washington, DC. The event is designed to encourage the sharing of research ideas and collaboration across the spectrum of VA research, from bench to bedside. Applicants are asked to submit abstracts for posters, workshops, oral presentations and panels by Oct. 17, 2003.

The theme of the meeting—”From Bench to Bedside: Today’s VA Research Leading Tomorrow’s Health

Care”—is based on the new vision statement for VA research.

“This is one of many activities planned to implement the vision,” said Dr. Shirley Meehan, VA’s deputy director for Health Services Research and co-coordinator of the event with Bob Potts, director of Technology Transfer.

According to Potts, the meeting represents an important new direction for VA research that emphasizes innovative collaborations among basic, clinical and health services investigators.

“This event will cut across all the different aspects of our research enterprise,” said Potts. “It will bring together people who normally don’t have the opportunity to meet, and expose investigators to new areas of potential collaboration.”

Guidelines for submission and other details, including contact people from each of the four Office of Research and Development services, are in the Hot Topics area of the VA Research website (www.va.gov/resdev). ■

Vision Update

Minority programs, clinical centers of excellence among new initiatives

Each month, VA Research Currents will highlight key issues relating to the implementation of VA’s new vision: “Today’s VA Research Leading Tomorrow’s Health Care.” You are invited to e-mail questions or comments to researchinfo@vard.org.

VA’s Office of Research and Development (ORD) recently announced funding for two new training programs: Mentored-Minority Research Training programs, which will create partnerships between VA and minority-serving institutions to increase scientific career opportunities for underrepresented minorities; and Clinical Research Centers of Excellence, which will create a national network of research facilities to train young investigators for leadership roles in clinical research.

Expanding research opportunities for minorities and increasing cooperation with minority-serving institutions (MSIs) are major strategic priorities for ORD and the national VA research community. To accomplish those

objectives, ORD developed three new Mentored-Minority Research Training programs. The programs will be coupled with a national campaign to reach out to leadership at MSIs and increase VA’s participation at professional and educational meetings and conferences.

The three new mentoring programs will provide research training for individuals at the high school through mid-career level.

- The Mentored-Minority Research Enhancement Coordinating Center supports institutional collaborations between VA and MSIs. These include Historically Black Colleges & Universities (HBCUs), Hispanic-Serving Institutions (HSIs), Tribal Colleges & Universities (TCUs), and institutions of higher learning with sizeable concentrations of Asian Americans, Pacific Islanders, Native Hawaiians, Native Americans, and Alaskan Natives. Students and

Study shows benefits of extended therapy for stroke survivors

Stroke survivors who received therapist-supervised, progressive therapy after completing in-hospital rehabilitation significantly improved their endurance, balance and walking ability, according to a small study reported in the Aug. 15 online issue of the journal *Stroke*.

“This study goes beyond the commonly held therapy paradigm that stroke patients achieve their most dramatic recovery within the first 30 days after stroke,” said lead

author Pamela W. Duncan, Ph.D., director of the VA Rehabilitation Outcomes Research Center at the Gainesville VA Medical Center and a physical therapist professor at the University of Florida, Gainesville. “We demonstrated that by providing a home-based exercise program that’s much more aggressive than what is typically prescribed, stroke survivors can improve their walking

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faculty from these institutions will partner with VA mentors.

- The Mentored-Minority Supplemental Program provides one-to-one training in research on VA-funded research projects. Eligible program participants include high school, undergraduate, graduate, and pre-doctoral students currently enrolled in good academic standing, or those who have graduated within the last two years.

- The Mentored-Minority Early Career Enhancement Program offers a supportive career path for mentored research in VA. Eligible participants are those who have completed (within the last two years) their clinical fellowship or PhD doctoral training in health services or biological sciences. Upon completion of the Mentored-Minority Early Career Enhancement

Program, awardees are expected to remain in VA and pursue additional training opportunities offered through the Research Career Scientist and Career Development programs.

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Clinical Research Centers of Excellence (CRCoEs) are designed to advance VA’s capacity for integrating state-of-the-art science with clinical practice. Clinical research has been defined as patient-oriented investigations focusing on mechanisms of human disease, therapeutic interventions, clinical trials, epidemiologic and behavioral studies, outcomes and health services research, and the development of new medical technologies. While a growing number of academic generalists have pursued careers in outcomes research, there is still a need for sub-specialists with a solid foundation in key clinical research disciplines— statistics, epidemiology, study design, qualitative methods. Therefore, CRCoE awards will primarily support the training and development of junior faculty in the scientific disciplines that form the basis for clinical research, and facilitate the integration of clinical research with clinical care for patients.

Despite large investments in bench research, resulting discoveries are not being efficiently converted into clinical practice that improves health care for

veterans and all Americans. By the same token, much of clinical practice is not based on rigorous clinical research. Enhancing evidence-based clinical practice is a major strategic priority for VA. Through CRCoEs, VA aims to increase training opportunities for clinician-investigators and promote the progression of important bench-research findings to clinical trials.

Initially, CRCoE awards will focus on the development of a national network of research facilities to support training for the next generation of leaders in clinical research. To that end, CRCoEs will receive up to \$400,000 of funding to create a core facility of methodologists to facilitate mentoring and grant development. CRCoEs also will receive salary support for junior faculty. In addition to providing mentoring services at their local VA facility, CRCoEs will work together to support the mentoring and development of clinical researchers throughout VA. CRCoEs also will provide a national clinical research “consultation resource” to support VA investigator-initiated research ideas. Finally, once established, CRCoEs will be responsible for developing and maintaining a clinical-research portfolio in their chosen areas of excellence.

Drafts of the program announcements discussed above are available on ORD’s website: www.va.gov/resdev. ■

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New oral drugs halt cytomegalovirus in mice

Two new oral drugs developed by VA scientists and colleagues at the University of California, San Diego (UCSD), show powerful activity against cytomegalovirus, a common and sometimes dangerous herpesvirus. The research was presented Sept. 14 in Chicago at the 43rd annual Interscience Conference on Antimicrobial Agents by Earl Kern, PhD, of the University of Alabama at Birmingham, whose team successfully tested the drugs in virus-infected mice.

The new compounds are modified forms of cidofovir, an intravenous drug used primarily to treat cytomegalovirus eye infections in AIDS patients. The compounds have also proved effective against smallpox and cowpox in recent mouse and tissue-culture studies. Since they can be taken orally, the new drugs may be especially useful in a bioterrorist attack.

“Cidofovir’s drawback is poor bioavailability. It can only be given intravenously,” said Karl Y. Hostetler, MD, an endocrinologist with the San Diego VA Healthcare System and UCSD who developed the cidofovir derivatives with James Beadle, PhD, of VA and UCSD. “If you’ve got thousands of people exposed to smallpox, a drug that needs to be injected would be difficult to use widely.”

Hostetler’s group created the new compounds, called HDP-CDV (hexadecyloxypropyl-cidofovir) and ODE-CDV (octadecyloxyethyl-cidofovir), by “disguising” cidofovir in partially degraded fat molecules. These molecules are rapidly absorbed through cell membranes. Inside the cell, enzymes remove the fatty part of the molecule and the cidofovir binds to the virus and stops it from replicating.

Though HDP-CDV and ODE-CDV are being developed mainly for use as a smallpox treatment, the compounds may play a valuable role in treating cytomegalovirus infection. This virus, while often harmless, can result in deadly infections in AIDS patients, transplant patients and others with suppressed immune systems. Currently, few safe treatment options exist.

“It is exciting that these compounds appear to have another possible use,” said Hostetler.

In experiments by Kern’s group, oral treatment with HDP-CDV or ODE-CDV significantly reduced virus replication in mice infected with cytomegalovirus. In one group of mice, human retinal tissue was implanted into the eyes of the mice and later infected. Drug treatment was begun 24 hours after infection and continued for four weeks. HDP-CDV outperformed regular cidofovir by 90 percent in reducing viral load. In another group of mice, into which human thymus and liver tissue was implanted and later infected, HDP-CDV and some doses of ODE-CDV resulted in no detectable virus at all, starkly outperforming regular cidofovir.

Besides showing the effectiveness of the new drugs, the experiments represented a key advance on another front: Human cytomegalovirus does not infect animal cells; Kern’s team bypassed the problem by developing mouse models into which human tissue could be implanted and then infected.

According to Hostetler, HDP-CDV and ODE-CDV may be associated with side effects, and formal toxicity testing will determine whether the compounds are safe enough for human use. ■

STROKE (cont. from page 2)

ability, balance and cardiovascular endurance.

Duncan said the study was the first to incorporate multiple components—strength, balance, endurance and upper extremity function—into a comprehensive stroke recovery program. Stroke is the leading cause of disability in older Americans, and falls are a major problem for stroke survivors.

The researchers studied 92 stroke survivors from the Kansas City Stroke Registry. Each had mild to moderate stroke deficits and had completed in-hospital rehabilitation. One group received the new comprehensive, progressive exercise program. The other group received “usual care”—varied levels of therapy, ranging from no additional therapy to limited physical or occupational therapy.

The intervention group received physical therapy focusing on their strength, balance, cardiovascular endurance and use of their arms and hands in 36 supervised sessions during the 12-week study. Among the usual care patients, 46 percent received no therapy during this period, while the remainder received an average of about 9 physical therapy visits and 10 occupational therapy visits.

Both groups showed improvement after three months, but the intervention group improved significantly more in balance, endurance and mobility. The intervention group bicycled during stress tests an average of 1.39 minutes longer than they could at enrollment, while the usual care group bicycled an average of 0.16 minutes longer. Patients in the intervention group walked about 200 feet farther in six minutes compared to their baseline, while usual-care participants walked an average of 110 feet farther. ■

Career milestones

Christine Elnitsky, PhD, RN, was named chief of research policy management. A nurse researcher with a background in community health and epidemiology, Elnitsky will help develop Office of Research and Development policy, guide its implementation in the field, and act as a liaison between ORD's scientific function and regulatory bodies. Her past health-services research at the VA San Diego Healthcare System focused on health delivery systems, program evaluation and outcomes, older populations with chronic illness, health policy, community needs assessment, and population health. She can be reached at (202) 254-0199.

Marvella E. Ford, PhD, associate director of VA's Houston Center for Quality of Care and Utilization Studies, was invited to serve on the National Institutes of Health Risk Prevention and Health Behavior 3 Study Section, Center for Scientific Review, for a four-year term.

Statins may help against macular degeneration

According to a VA and University of Alabama at Birmingham study published in the September *British Journal of Ophthalmology*, elderly men who take cholesterol-lowering drugs known as statins are less likely to develop age-related macular degeneration (ARMD). ARMD occurs when light sensitive cells at the back of the eye, or macula, break down. The condition is the leading cause of blindness in older adults in the United States.

Using anonymous VA databases, the researchers evaluated 6,000 elderly male patients, including 550 who had recently been diagnosed with macular degeneration. Researchers found a significantly lower occurrence of macular degeneration in men who were taking statins. For every three cases of the disease found in men taking statins, researchers found 10 cases in men not taking statins.

According to senior author Robert J. Crain, MD, chief of ophthalmology at the Birmingham VA Medical Center, the study suggests the need for a clinical trial to test the effectiveness of statins in curbing the incidence and progression of the disease. In explaining how statins may work against ARMD, Crain pointed to recent research showing that cholesterol deposits are present in the Bruch's membrane of aging eyes.

Though there is currently no medical treatment that arrests the development of ARMD, especially in the early stages before vision loss occurs, the naturally occurring carotenoid known as lutein—found in corn, squash, red grapes and many other fruits and vegetables—has been shown to help prevent the condition. A yearlong study led by Stuart Richer, OD, PhD, of the Chicago VA Healthcare System, recently tested whether lutein, along with other antioxidants, vitamins and minerals, could improve vision in 90 veterans with ARMD. The results are pending publication. ■

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