



VA Research Currents

Genomics plan will help VA 'personalize' care

VA is moving to a model of care in which care is tailored specifically to the needs and challenges of individual patients. Genomic medicine will help us move from providing medicine that is preventative to medicine that is predictive.”

Those are the words of Dr. Jonathan Perlin, VA’s undersecretary for health, regarding VA’s new genomic medicine initiative. The initiative was formally launched in mid-March with the naming of an advisory panel by Secretary James Nicholson. The group includes leading scientific and medical experts in the field, as well as ethicists and a Veterans Services Organization representative.

The centerpiece of the program will be pharmacogenomics, which involves

analyzing a patient’s DNA and customizing drug treatment accordingly. Researchers have learned that variations in a person’s DNA can affect response to a particular drug. For example, a University of Washington team showed last year that variations in a gene called VKORC1 can predict, to a significant extent, how a patient will respond to the anti-clotting drug warfarin. Too little of the drug can result in clots, and too much can cause bleeding. It can sometimes take months for a doctor to determine the ideal dose for a patient. With DNA testing, information obtained in a single office visit could play a key role in setting the right dose from the outset, thus achieving maximal benefit and

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Middleton award to Seattle neurologist

Thomas D. Bird, MD, a neurologist at the Geriatric Research, Education and Clinical Center at the VA Puget Sound Healthcare System, has received the 2005 Middleton Award, VA’s highest honor for achievements in biomedical or behavioral research.

Bird, who has been with VA nearly three decades and was formerly chief of neurology at the Puget Sound VA, is recognized as a pioneer in the field of neurogenetics. His work since the 1970s in analyzing patient cohorts for genetic links to neurodegenerative diseases has helped lay the groundwork for a number of

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Update from Rehabilitation Research and Development (RR&D)

Neurotrauma and burn rehabilitation research are priorities for RR&D

By Robert Ruff, MD, PhD, director

Improvised explosive devices and rocket-propelled grenades cause the majority of troop injuries in Iraq. Although Kevlar helmets and other advances in body armor have saved the lives of many soldiers, they do not protect the head, face and cervical spinal cord against blast wave force or penetrating fragments. As a result, traumatic brain injury (TBI) and cervical spinal cord injury (SCI) account for 28 percent of the injuries among troops serving in operations Iraqi Freedom and Enduring Freedom.

In addition to these injuries, many soldiers are left with complex burns. Whereas *survival* used to be the culmination of a burn “success story,” today more and more individuals are surviving burns over 80 percent or more of

their body, making successful reintegration into society the new milestone.

To advance our knowledge of the molecular and physiologic underpinnings of these conditions, and to advance rehabilitation treatments and technologies, VA is expanding its research portfolio in brain, spinal-cord and burn injury. Letters of intent in response to our recent program announcement on neurotrauma indicate that VA investigators are interested in probing areas such as protection of neural cells from secondary effects of brain trauma; identification of biomarkers to assess functional

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Study finds ‘mantram’ repetition helpful for veterans, VA staff

A simple spiritually-based focusing and relaxation technique taught to 30 veterans and 36 hospital employees at the VA San Diego Healthcare System was used effectively by most of them to deal with stress and other negative emotions, according to a study published in the *Journal of Advanced Nursing* last month.

In five-week training sessions held in 2001 and 2002, a team led by nurse-researcher Jill Bormann, PhD, RN, taught the volunteers to silently repeat a word or phrase with spiritual meaning—a “mantram”—when confronted with stressful situations, such as traffic jams, arguments or pain. The mantram could also be practiced simply to relax. (Bormann points out there are differences between “mantram” and the more familiar “mantra,” which in its colloquial use has lost some of its original meaning.)

In phone interviews conducted about three months after the volunteers had completed their training, 55 of them—83 percent—reported successfully using the technique and cited 147 incidents where it was helpful. The researchers used the respondents’ own words to categorize the responses. The most frequently reported use was for managing negative emotions other than “stress,”

such as anxiety, impatience, anger or frustration. Other reported uses were for handling stress, or dealing with insomnia or unwanted thoughts.

“These findings suggest that spiritually inspired psychosocial interventions that are properly and sensitively adapted to the healthcare system might fill gaps in current health care, as well as [provide] additional options for enhancing mental health,” wrote the authors.

In December of last year, Bormann and colleagues reported on a related pilot study in the *Journal of Holistic Nursing*. Sixty-two veterans learned the mantram method and were given wrist-worn counters to track their practice. They used their respective mantrams—which ranged from traditional spiritual words such as Jesus or shalom, to more secular words such as “one”—an average of nearly eight times per day over the five-week study period, and reported significant reductions in stress and anxiety, as well as

improvements in quality of life and spiritual well-being.

According to Bormann, the technique used in her studies differs from most other relaxation or meditation techniques in that it can be used anywhere, anytime—even while driving, for example, or standing in line at the supermarket.

“It’s personal, portable and invisible,” she said in an interview with WebMD, a medical-news website. “It’s immediately available, inexpensive, nonpharmacological and non-toxic. [It can be a] stress-reduction technique for our modern day and age, when people say they don’t have time for stress-management techniques.”

Bormann’s research, which has explored mantram effects on study populations including veterans with posttraumatic stress disorder, family caregivers, and VA employees, is supported in part by VA and the National Institutes of Health. ■

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important discoveries. Most notably, his research contributed to the discovery of presenilin and tau genes involved in Alzheimer’s disease and frontal temporal dementia. The genes have become important targets for drug development. Scientists have also used this knowledge to develop animal models that have been instrumental in dementia research, such as those used in studying the pathology of the tangles found in the brain cells of Alzheimer’s patients.

In 1974, Bird established the nation’s first neurogenetics clinic for adults, at the University of Washington, and remains its director. Each year, the clinic offers evaluation, diagnosis and counseling for more than 300 clients with genetic diseases of the nervous system, such as Huntington’s disease, Charcot-Marie-Tooth neuropathy, muscular dystrophy, and familial dementia.

A professor in the departments of neurology, medicine and psychiatry at the UW School of Medicine, Bird was interviewed for a 2000 article in a university publication about the opening of the school’s division of neurogenetics. He offered this perspective on neurodegenerative disease: “The brain is what makes us human. You’re dealing with diseases that really impact the humaneness of people. ... To be able to do something about them is very important.” ■

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Career milestones

Thomas Bowman, MD, PhD, of the Massachusetts Veterans Epidemiology and Information Center (MAVERIC) received the Robert G. Siekert New Investigator Award at last month's International Stroke Conference for his report titled "A Comparison of Blood Pressure Parameters in Assessing Risk of Total, Ischemic and Hemorrhagic Stroke in Apparently Healthy Men." The conference and the award are sponsored by the American Stroke Association, part of the American Heart Association.

Myron Spector, PhD, director of tissue engineering at the VA Boston Healthcare System, was elected a fellow of the American Institute for Medical and Biological Engineering. Spector's current work focuses on the potential use of collagen scaffolds for spinal cord regeneration and other applications.

Alan M. Garber, MD, PhD, Palo Alto, received the Clinician-Investigator Award from the California Region of the Society for General Internal Medicine. The award recognizes investigative, teaching and leadership skills. Garber's research focuses on the demography and economics of health and aging.

Dawn Vogt, PhD, a Boston-based psychologist with VA's National Center for PTSD, is co-winner of the 2005 Walter G. Klopfer Award from the Society for Personality Assessment for her recent article "Assessment of Accurate Self-Knowledge."

Raymond F. Schinazi, PhD, a researcher at the Atlanta VAMC since 1982, received the Distinguished Scientist Award from the Hepatitis B Foundation for his contributions to developing drugs to treat the disease. According to the foundation, as many as 7 in 10 people treated for HIV and Hepatitis B have received a drug that Schinazi helped develop.

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outcomes; and clinical diagnosis of mild TBI versus posttraumatic stress disorder. We look forward to funding the most promising of these proposals.

In the area of burn injury, VA and the United States Institute for Surgical Research, part of the Department of Defense, have jointly authored an executive summary outlining a research agenda. This will serve as the framework for a future program announcement. Priority areas will include managing burn scar contractures; fostering successful psychosocial adjustment; and establishing reliable outcome measures to guide clinical care. An example of a burn-rehabilitation project on which VA and DoD may collaborate is finger prostheses. The inability of burned fingers to remain vascularized and receive adequate oxygenation often results in the loss of those fingers. To date, no commercial device exists that adequately restores function for individuals who have lost fingers from burn. RR&D currently supports the development of a metacarpal (five-finger) prosthesis at the VA Chicago Healthcare System, and we hope to see further research in this area.

Severe burn injury alone results in devastating and debilitating chronic pain. When additional pain occurs—for example, as the result of exercises required to prevent contractures and modify scars—soldiers may find it almost impossible to continue therapy. In March 2006, we reviewed more than 70 research proposals focused on pain as a secondary consequence to primary impairments such

as burn, spinal-cord or brain injury. VA researchers will soon begin exploring new approaches to pain treatment, and various pharmacological and biological treatments to ameliorate pain to manageable levels, with the goal of helping soldiers continue with rehabilitation and achieve maximum functionality.

These areas are top priorities for VA, and we are committed to funding cutting-edge research to help our injured troops attain the highest possible levels of recovery, function and overall health status. ■

JRRD features work on SCI, prosthetics

The current issue of VA's *Journal of Rehabilitation Research and Development (JRRD)* (Vol. 45, No.5) focuses on spinal cord injury and prosthetics. Full-text articles are available free at www.rehab.research.va.gov.

Supplement features VA research on women's health

A supplement in the March issue of the *Journal of General Internal Medicine* highlights VA research on women's health. Articles cover topics such as the health status of women veterans; why women choose or do not choose VA healthcare; contraceptive availability at VA medical centers; and television-viewing and obesity among women veterans. Abstracts can be viewed at www.blackwell-synergy.com/toc/jgi/21/s3.

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avoiding complications.

According to Joel Kupersmith, MD, VA's chief research and development officer, genomic data will be integrated into VA's electronic medical records, thus enhancing the benefits of both aspects of VA healthcare. "Starting a genomic medicine program may be the most significant initiative for VA healthcare since the computerized medical record," he said. "And this can build on the success of VA's computerized medical record, so this is a very exciting project."

Kupersmith noted that discussions of ethics and privacy issues will be an important focus in the early stages of the project.

ORD has already issued a request-for-proposals for a pharmacogenomics analysis laboratory to spearhead the "systematic examination of pharmacogenomic data in therapeutic decision-making." According to the announcement—available at www.research.va.gov/funding/solicitations/default.cfm—VA will develop the use of genetic information for diagnosis as well as treatment. A related solicitation, also recently issued and available on the ORD website, will fund research into combinations of diagnostic tests and treatments—for example, the use of a set of genomic markers to determine the dose of an antipsychotic drug, or the use of gene-amplification or immunohistochemical tests to match cancer patients with the best therapy.

Timothy O'Leary, MD, PhD, director of Biomedical Laboratory R&D and Clinical Science R&D for VA, said other requests-for-proposals are forthcoming that will provide additional underpinnings for VA's genomics program. "The pharmacogenomics analysis lab and some other solicitations planned for the near future will provide some of the baselines for this effort," he said. "This is being done in tight cooperation with [VA] Patient Care Services. We're working on a translational front, and involvement on both sides is going to be absolutely critical." ■

VA scientist honored for Alzheimer's work

Karen H. Ashe, MD, PhD, a physician and neuroscientist at the Minneapolis Veterans Affairs Medical Center and the University of Minnesota, is one of three recipients of the 2006 Potamkin Prize from the American Academy of Neurology. The award, given for outstanding advances in the understanding of Alzheimer's disease and related disorders, carries a cash award of \$100,000, to be shared among the winners. Ashe, an investigator at the Geriatric Research, Education and Clinical Center (GRECC) at the Minneapolis VA, has conducted extensive animal studies on factors in the brain that cause memory loss.

In a March 2006 article in *Nature*, Ashe's team reported on a newly identified protein derivative—called A-beta *56—that appears to disrupt memory, independent of the loss of neurons or the buildup of amyloid-beta protein in the brain. It has been found in human brains and could become the target of early-detection tests or drugs that would block its action.

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