



# VA ResearchCurrents

## Columbia disaster held special meaning for this VA scientist and former astronaut

When the space shuttle Columbia disintegrated over Texas on Feb. 1—resulting, above all, in a tragic loss of human life—there were more than 80 scientific experiments aboard. One of them belonged in part to VA investigator Millie Hughes-Fulford, PhD, a cell biologist and former astronaut who herself flew on the Columbia in 1991.

Hughes-Fulford, director of the Laboratory of Cell Growth at the San Francisco VA Medical Center,

was collaborating with Zurich-based principal investigator Dr. Augusto Cogoli on an experiment to test the effects of microgravity on human T cells. These white blood cells are a critical component in the body's immune response. They destroy antigens such as fungi, parasites, viruses, some cancer cells, and foreign tissue. Past studies have shown that T cells in space fail to respond normally to antigens. As a

see **SPACE** on pg. 2

## Federal study yields more answers on ephedra

A meta-analysis of the efficacy and safety of the controversial compound ephedra by a team from VA, RAND and Cedars-Sinai Medical Center concluded that the substance helps promote limited short-term weight loss but carries important health risks. The analysis, commissioned by the Department of Health and Human Services (HHS), showed that ephedra, especially when used with caffeine, is associated with an increased risk of heart palpitations, nervous-system hyperactivity, gastrointestinal problems and psychiatric symptoms.

The study findings, announced by the Food and Drug Administration (FDA) on Feb. 28, prompted the FDA and HHS to take immediate steps toward establishing new restrictions on ephedra-containing products.

Ephedra is derived from the Chinese herb *ma huang*. Its main active ingredient is ephedrine. While natural forms of ephedra have long been used in Chinese medicine to treat respiratory symptoms, ephedra-containing products have in recent years been promoted and used extensively in the United States to enhance weight loss and sports performance.

The meta-analysis, led by Paul G. Shekelle, MD, PhD, of the Greater Los Angeles Healthcare System and RAND, included data from 20 controlled trials. It did not cover two recent studies, published in *Neurology* and the *Annals of Internal Medicine*, that raise additional concerns about ephedra's safety. ■

Update from the Medical Research Program...

## Dr. Hoffman leaving legacy of achievement in biomedical research

By Douglas K. Anderson, PhD, acting director

In Feb. 2003, Medical Research Service (MRS) bid farewell to Paul M. Hoffman, MD, who had served as director since 1996. Dr. Hoffman came to VA Central Office following a long career as a VA intramural scientist, which began with a career development award in 1978. At a recent annual meeting of the Medical Research Advisory Group (MRAG) held in New Orleans, Dr. Hoffman was lauded for making significant contributions to the VA biomedical research program.

Dr. Hoffman's accomplishments stemmed from his constant solicitation of views and opinions from the field regarding MRS programs. He formed the MRAG, a group of VA senior scientific advisors representing different research areas, to review and evaluate MRS programs and funding each year. He also conducted formal reviews of MRS programs using field representatives.

Dr. Hoffman initiated new programs, such as the Research Enhancement Award Program (REAP), to support groups of collaborating investigators work-

see **HOFFMAN** on pg. 3

**SPACE** (continued from pg. 1)

result, astronauts suffer decreased immunity, along with other effects such as bone loss, muscle loss, and anemia.

The T cell experiment was being carried out by pilot William McCool. He was trained for the experiment by a team from the European Space Agency, which funded the research along with NASA's Office of Biological and Physical Research.

"Astronauts are 'equal opportunity perfectionists,' said Hughes-Fulford. "When they get an experiment, they learn everything about it, and why they're doing it. They really pay attention. They know what they're doing is important."

Specifically, the experiment focused on whether microgravity inhibits the expression of interleukin 2, a protein that acts as a growth factor for T cells, enabling them to proliferate and do their job.

"We were looking at the first steps required for the immune cells to work," said Hughes-Fulford. "This is important for all of us here on the ground. If anything happens that impedes that early activation, the later activation doesn't happen."

Along with immunity studies, bone loss has been an ongoing focus for Hughes-Fulford, including the work

she conducted as a payload specialist on the 1991 flight.

"Bone loss is one of the major physiological 'show stoppers' in sending humans to Mars," she writes on her website ([www.spacedu.com](http://www.spacedu.com)). "Astronauts lose about one percent of their bone per month while in zero-gravity. If a Mars mission would take 30 months to complete, that's about 30 percent of our bone—so no one could return to Earth without the possibility of bone fracture."

It is not clear whether NASA plans to repeat the T cell experiment—along with others from the ill-fated Columbia flight—on a future space shuttle mission. Asked if she would fly again given the chance, Hughes-Fulford said "sure." And the Columbia disaster has not dimmed her vision of humans venturing further into space.

Said Hughes-Fulford, "I would still like to see a Mars mission." ■

### AMSUS awards

The Association of Military Surgeons of the United States (AMSUS), a group of more than 12,000 military and federal health professionals from all disciplines, recognizes outstanding achievements through its annual awards program. All VHA employees are eligible to be nominated. The deadline for submitting nominations is June 30. For more information, visit [www.amsus.org](http://www.amsus.org).

For details on submitting a nomination and sharing your program- or employee-focused nomination letter with VA's Virtual Learning Center, for educational purposes, contact Dot Brady, Management Support Office, VA Central Office, at (202) 273-8873 or [dot.brady@hq.med.va.gov](mailto:dot.brady@hq.med.va.gov).

### Wanted: Authors for history of VA research

Authors are being sought to write chapters on geriatrics, substance dependence, basic sciences and surgery for a book chronicling VA research. The project is being led by Dr. Marguerite Hays, former head of VA research nationwide and today a consultant at the Palo Alto VA Medical Center.

Hays has completed the book's first volume, which chronicles VA research from its inception in 1925 through 1980. The second volume will contain chapters written by various authors and edited by Hays, detailing the history of specific subject areas in VA research, or the history of research programs at individual medical centers. If you are interested in contributing a chapter about your field of research or medical center, or would like more information, contact Hays at [Ritahays19@yahoo.com](mailto:Ritahays19@yahoo.com) or [Marguerite.Hays2@med.va.gov](mailto:Marguerite.Hays2@med.va.gov).

VA personnel who have committed so far to write chapters include: Jay Schneider, MD, PhD, cardiology; Kenneth James, PhD, cooperative studies; Timothy Takaro, MD, coronary artery surgery studies; Clark Sawin, MD, endocrinology; John Farrer, MD, gastroenterology; Shirley Meehan, PhD, and Geraldine McGlynn, health services research; Richard Streiff, MD, hematology; Richard P. Wedeen, MD, nephrology; Shri Mishra, MD, neurology; Andrew Gage, MD, pacemakers; Robert Freedman, MD, psychiatry; Walter Penk, PhD, psychology; Gordon Snider, MD, pulmonary medicine; Neil McAleer, rehabilitation research; and Thomas Benedek, MD, rheumatology.

National Hotline Conference Call schedule:  
[http://vawww.va.gov/resdev/fr/call\\_calendar.cfm](http://vawww.va.gov/resdev/fr/call_calendar.cfm)

#### VA Research Currents

*is published monthly for the*

Office of Research and Development  
of the Dept. of Veterans Affairs  
by VAR&D Communications

103 S. Gay St., Rm. 517

Baltimore, MD 21202

(410) 962-1800, ext. 223

[researchinfo@vard.org](mailto:researchinfo@vard.org)

## 21st HSR&D national meeting

### Dr. Wray, new CRADO, emphasizes translation of findings into practice

**N**elda P. Wray, MD, MPH, the new chief research and development officer (CRADO) for VA, urged those attending the 21<sup>st</sup> national meeting of VA Health Services Research and Development (HSR&D), held Feb. 12 – 14 in Washington, DC, to visualize a health system in which conclusive research findings are almost immediately adopted into practice. Wray's remarks were summarized by the new vision statement for VA research that she projected on a huge screen for the meeting's more than 600 attendees: "Today's VA Research Leading Tomorrow's Health Care."

Wray outlined three main goals for VA research, revolving around the new vision. She said her office would work to:

- Expand clinical research to generate the hard evidence on which evidence-based medicine should be practiced;
- expand translational research to ensure that when a treatment is proven effective, it is quickly adopted into clinical practice; and
- strengthen programs to measure the quality of VA research and interventions.

Wray, herself an accomplished health services researcher, said she would increase efforts to identify barriers to the translation of research findings into clinical practice, and encourage the adoption of new organizational structures to eliminate those barriers.

"We at VA have done more than anyone else [in this area]," said Wray, "but what we need to do now is really figure out how to partner with the clinical side of the house, how to put in place systems which will rapidly translate the knowledge we develop into clinical practice."

Wray recalled the first national meeting of VA health services research she attended, in the late 1980s, with fewer than 40 attendees, and cited the bustling 2003 meeting as a sign of the remarkable growth of the program, both in scope and quality.

"Today, there is no question that [this is] the leading national meeting for the most scientifically rigorous health services research," she said.

Wray also emphasized her desire to boost VA training programs, especially for clinician researchers, through

see **MEETING** on other side

---

### Under Secretary's Award to Dr. Morris Weinberger of Durham

"The VA has been instrumental in any success I've achieved in my career," said Morris Weinberger, PhD, on receiving VA's 2003 Under Secretary's Award for Outstanding Achievement in Health Services Research at the HSR&D meeting.

Weinberger is an investigator with VA's Durham-based Center for Health Services Research in Primary Care and is the Vergil N. Slee Distinguished Professor of Healthcare Quality Management in the Department of Health Policy and Administration at the University of North Carolina. A medical sociologist, he is noted for his innovative studies aimed at improving

care for chronic health conditions, especially those prevalent among veterans and older adults.

In a refreshingly candid and often amusing talk, Weinberger traced the evolution of his career as a health services researcher: "I entered graduate school with one career goal: to teach at a small liberal arts college," said Weinberger. "My dissertation was simply a means to that end. If all went according to plan, my dissertation would be my first and last foray into research."

He thanked VA for the opportunity to explore different roles, at different sites, and for promoting his achieve-

ments as an investigator, mentor, center director and journal coeditor. He recently completed a five-year term as coeditor of *Medical Care*, a leading forum for the publication of health services research.

Weinberger praised the work of numerous colleagues and students in Durham. "I've had outstanding and creative colleagues—investigators from different disciplines coming together for a common project. It's not only that these folks are extraordinarily bright and creative; but I've been blessed to work with incredibly nice people, who simply make it easy and fun to work hard." ■

**WRAY** (continued)

initiatives such as increased salary support for both trainees and mentors. “I believe there is nothing more important than the next generation,” she said.

In keeping with the theme of the meeting—“Diverse Veteran Populations: Challenges and Opportunities”—Wray voiced her commitment to increasing the number of minority researchers in all branches of VA research. “Those of you who know me know that I’m passionate about every individual in this country having equal opportunity,” said Wray.

**Keynote talk on ‘Complexity of Diversity’**

In other highlights of the meeting, hosted by HSR&D’s Center for Mental Healthcare and Outcomes Research in Little Rock, AR, keynote speaker Junius Gonzales, MD, of the National Institute of Mental Health addressed the “complexity of diversity.” The son of South American immigrants, Gonzales discussed cultural competence—the ability of health professionals to understand and work with patients with different values, attitudes, beliefs and backgrounds. He also pointed out the importance of being aware of additional levels of diversity in health-care settings. For example, he said, cultural differences among physicians or organizations should be factored in when designing effective interventions, and translating them across various settings.

“Diversity is quite complex,” said Gonzales. “We may want to think about it as a mosaic of conditions. In order to improve health care services and health services research, [an understanding of] the dynamism of diversity ... is going to be critical.”

In a moving presentation, mental health advocate Moe Armstrong, MBA, MA, spoke about his own battle with schizophrenia and homelessness. A Vietnam veteran, Armstrong thanked VA researchers and clinicians for their help in “putting the pieces of his life back together.”

In one of six plenary paper sessions, a team from the VA San Diego Healthcare System presented findings from a randomized trial of an innovative alternative model for inpatient psychiatric care, called the Short-Term Acute Residential Treatment (START) model. The study found that START, which relies on attractive community-based housing facilities, is more cost-effective than hospital-based care and produces greater satisfaction among veterans.

In another plenary session, Said Ibrahim, MD, MPH, of VA’s Pittsburgh-based Center for Health Equity Research

and Promotion, discussed the results of a study of whether physician recommendations for cardiac revascularization vary depending on patients’ race. The study found some differences among three VA hospitals, and suggested the need for further research to understand the reasons for the variations.

**Homelessness as health-care problem**

Robert Rosenheck, MD, of the Northeast Program Evaluation Center at the VA Connecticut Healthcare System, delivered a plenary talk on the cost effectiveness of supported housing for homeless veterans. His study found that supported housing through a partnership of VA and the Department of Housing and Urban Development yields superior housing outcomes (better conditions and more nights housed) but no improvements in clinical outcomes. Rosenheck prefaced his remarks by providing compelling statistics to illustrate why the VA health care system has an important stake in the problem of homelessness.

Two-thirds of homeless veterans have psychiatric or addiction problems. Sixty percent have chronic medical problems.

“Why should a health care system be focusing on homelessness? Isn’t that a social welfare or housing problem? Well in fact, two-thirds of homeless veterans have psychiatric or addiction problems. Sixty percent have chronic medical problems, and 28 percent of all VA psychiatric inpatients are homeless at admission—a very large number, distinguishing us from the vast majority of other health care systems. And the risk of mortality among homeless veterans is two to three times that of other VA psychiatric patients.”

Poster presentations, workshops and additional plenary sessions focused on a wide range of other pressing issues in VA health care, from ethnic and racial health care disparities to outpatient pharmacy expenditures and management issues. Workshops also covered research methodology and administrative issues, such as grant proposals, interviewing techniques, the extraction of cost data from federal-agency databases, and the recruitment of study participants. ■

## Dr. Aisen of Rehabilitation R&D appointed deputy CRADO

**M**indy Aisen, MD, director of VA Rehabilitation Research and Development (RR&D), was promoted in February to deputy chief research and development officer (CRADO). Along with her duties as deputy CRADO, Aisen will continue as director of VA's Rehabilitation Research and Technology Transfer programs, and serve as acting director of the Medical Research Service.

During Aisen's four-year tenure as RR&D director, the program's funding grew from about \$27 million to more than \$40 million. This expansion of VA's rehabilitation-research portfolio included the establishment of eight additional centers of excellence and the Research Enhancement Award Program (REAP). RR&D centers and REAPs today address an increasingly diverse range of areas, including spinal cord injury, sensory loss and biomedical engineering.

A staunch supporter of nurturing investigators' careers, Aisen increased the number of rehabilitation scientists and engineers with long-term funding and helped qualified investigators with disabilities to participate in rehabilitation

research. She also increased the percentage of statistically-significant, evidence-based rehabilitation research proposals. This transition is reflected in the growing emphasis by VA's *Journal of Rehabilitation Research and Development*, of which Aisen is editor in chief, on the publication of larger, more statistically meaningful studies.

"My vision as director of Rehab Research and Development was to redefine rehabilitation research as a scientific discipline to include all the rigor of other medical disciplines," said Aisen. "I also broadened the scope of our research portfolio, so our resources would benefit veterans with impairments of all organ systems."

A board-certified neurologist with a focus on neurologic disorders such as multiple sclerosis and spinal cord injury, Aisen is president of the American Society of Neurorehabilitation. She is also a fellow in the American Academy of Neurology, and chair of the Technology Transfer subcommittee of the Interagency Committee on Disability Research. ■

### HOFFMAN (cont. from pg. 1)

ing on a common research theme. Since the inception of the program, 34 REAPs have been funded by MRS, spanning research in aging, psychiatry, neurobiology, cardiology, endocrinology, oncology, infectious diseases, pulmonology, and gastroenterology.

Additionally, Dr. Hoffman was a proponent of developing career tracks to train scientists, especially clinicians, and retain them within VA. Under his guidance, capacity-building programs were designed to attract junior investigators dedicated to research careers in VA. The Associate Investigator program was formulated to attract potential scientists as their clinical or graduate work ended. The Merit Review Entry Program was developed to provide mentored training for both clinician and non-clinician scientists. Enhancements to the Career Development program have been significant in

attracting clinician researchers to careers in VA. In light of the amount of research training needed to achieve independence as a funded investigator, the Career Development program now offers the possibility of six continuous years of salary and research support. In order to ensure the retention of a rich resource of senior non-clinician scientists for collaborating, training and mentoring clinicians, Dr. Hoffman revitalized the Research Career Scientist program.

In addition, Dr. Hoffman was a proponent of improving research laboratory infrastructure. Together with former chief research and development officer (CRADO) Dr. John Feussner, Dr. Hoffman instituted the Research Evaluation project to assess the state of research infrastructure at local VAMCs and recommend improvements. In some cases, funding was provided to drastically improve the state of research laboratories.

Dr. Hoffman succeeded in developing partnerships outside VA to enhance our scientific efforts in several key areas. These partners include the Eastern Paralyzed Veterans Association, American Thoracic Society, and other government agencies such as NIH and DoD.

We wish Dr. Hoffman continued success as he begins his new career as VA's assistant CRADO for Neuroscience Research, and director of the Clinical Neuroscience Research Program, a joint venture between the Baltimore VA Medical Center and the University of Maryland. ■

#### Deployment research

For VA's newest solicitation for studies on the health effects of military deployment, see [www.va.gov/resdev/fr/ProgramAnnouncementDeploymentHealthIssues.pdf](http://www.va.gov/resdev/fr/ProgramAnnouncementDeploymentHealthIssues.pdf).

# New VA study: HIV drugs not causing rise in vascular disease

**A**mid concern over the impact of potent HIV drugs on patients’ cardiovascular and cerebrovascular health, a study of 36,766 patients treated for HIV in the VA health-care system from 1993 to 2001 found a steady drop in the rate of deaths and hospital stays due to these vascular problems, even as use of highly active antiretroviral therapy (HAART) increased. The findings appeared in the Feb. 20 issue of the *New England Journal of Medicine*.

The study also found a 75 percent drop in the overall death rate among VA’s HIV patients between 1993 and 2001, consistent with other evidence that HAART—which became available in 1996 and was quickly adopted by VA practitioners—may prolong survival. “Fears about vascular disease as a side effect of these drugs shouldn’t keep patients and their doctors from using the best treatments available, consistent with guidelines,” said study leader Samuel A. Bozzette, MD, PhD, an infectious disease specialist with the VA San Diego Health Care System.

Though the study is the largest of its kind to date, it analyzed data only from an eight-year span—1993 to 2001—and may not reflect the rate of serious vascular disease with longer-term use of HAART.

“It’s reasonable to expect that metabolic abnormalities will be harmful to people with HIV over a longer time frame,” said Bozzette, who is also affiliated with the University of California, San Diego, and RAND. He said HIV patients must be monitored carefully for vascular disease and other side effects, and treated accordingly.

The increased use of potent combinations of anti-HIV drugs has led to a sharp decline in the number of AIDS-related death since 1996. Today, patients infected with HIV are leading longer, healthier lives. However, the drugs helping to keep them alive—usually a combination of reverse transcriptase inhibitors and protease inhibitors—can also cause serious side effects, affecting the heart, blood, kidneys, liver and nervous system.

Protease inhibitors, in particular, have been associated with metabolic abnormalities such as blood-sugar imbalances and diabetes, redistribution of body fat, or “protease paunch,” and defects in how the body metabolizes fat. Over time this could damage the vessels that supply blood to the heart or brain, resulting in angina, heart attack, stroke or other life-threatening conditions.

On the other hand, there is some evidence that HIV itself can cause vascular disease, and HAART may protect against this damage by suppressing the virus. Research is ongoing to better understand how HIV, HAART and vascular disease are interrelated.

Of the 36,766 patients included in the study, only 21,659 were still alive at the end of the eight-year study period, reflecting the deadly toll of HIV and AIDS. However, the rate of death from any cause dropped sharply from 1993—when 2,273 of 16,763 patients died—to 2001, when 410 of 17,891 patients died. ■

Inside this issue...

- Coverage of HSR&D national meeting
- Ephedra analysis prompts federal action
- Aisen appointed as deputy CRADO