



VA Research Currents

Research at Hines aims to prevent outbreaks due to increasingly resistant hospital germ

For decades, hospitals have contended with a potentially nasty germ called *Clostridium difficile*. The bacterium tends to proliferate and cause disease in hospital patients who acquire it after having been on antibiotics, which disrupt protective normal bowel flora. Infection with *C. difficile* is one of the most common hospital-acquired infections worldwide, and in the United States alone it causes some 400,000 cases of diarrhea and colitis each year in hospital patients.

In a Dec. 8, 2005, *New England Journal of Medicine* article, a team of researchers including Dale Gerding,

MD, and Stuart Johnson, MD, from the Hines VA Medical Center reported on a previously uncommon strain of *C. difficile*—known as the BI/NAP1 isolate—that appears to be the culprit in an emerging epidemic of *C. difficile*-associated disease, or CDAD. The strain is a particularly toxic form of *C. difficile*, and now appears the most likely suspect in a string of increasingly deadly CDAD outbreaks that has plagued Canadian and U.S. hospitals in recent years.

Gerding and colleagues collected 187 isolates from eight U.S. hospitals see **OUTBREAKS** on page 2

Career Development program ‘harmonized’

A new initiative intended to “clarify, simplify and enhance” VA’s Career Development program has been announced and is described in full detail on the ORD website at www.research.va.gov/funding/CDP.cfm.

Previously, each of ORD’s four services had its own program for recruiting, developing and retaining promising early-career researchers. Now, opportunities for clinician and non-clinician researchers will be integrated into one ORD-wide program, with three levels of mentored awards and a non-mentored career-enhancement award for senior scientists. ■

Update from the Office of Research and Development...

Site visits are valuable opportunity for ‘face time’ with field

By Joel Kupersmith, MD, chief research and development officer

Last month, I had the pleasure of visiting our Chicago and Hines facilities. Next month, I plan to meet with members of the VA research community in Atlanta and the Bronx.

These visits, along with earlier visits to Boston, Philadelphia and Baltimore, are part of a series of informal site visits I’ll be conducting over the next year or two. My goal is to see firsthand what is going on in the field and get a better sense of our needs for the future.

At each site, my plan is to meet with the following individuals: the medical center director and associate director; chief of staff; chair of the R&D committee; administrative officer and associate chief of staff for Research; VISN representative; dean of the affiliated medical school; and director of the nonprofit research foundation. Equally important, I hope to tour each facility,

including the labs, and hold a “town meeting” where I present an overview of our nationwide research program and answer investigators’ questions.

This kind of face-to-face interaction is very important to me. Much of my time in Washington is spent advocating for the needs of our researchers in the field, and shaping goals and plans for the future. The more firsthand knowledge I have about the work of VA researchers and their administrative colleagues, the more effective I can be in these roles.

Future visits planned for later in 2006 will take me to Seattle, San Francisco, Portland and several other sites, some of which are not yet confirmed. I look forward to meeting in person with many of you, and expect that I will continue to be as deeply impressed as I have been until now. ■

OUTBREAKS (cont. from pg. 1)

where outbreaks occurred between 2000 and 2003, and analyzed them against his database of more than 6,000 historical strains of *C. difficile*. The isolates were also tested for toxicity and antibiotic resistance.

“We were able to identify the outbreak strain within our library of typed strains and document that these strains were found in the 1980s and 1990s, but did not cause epidemics then, as they were not yet resistant to the new fluoroquinolone antibiotics,” said Gerding.

The newly obtained samples of BI/NAP1, however, showed universal resistance to fluoroquinolones—a large family of broad-spectrum antibiotics that have been used by hospitals since the late 1980s to treat a wide range of infections.

“The new strains have acquired this resistance,” noted Gerding, “and it may be an important reason why they are now disseminating widely.”

Better infection-control methods in hospitals may be one part of the solution. Another may be more prudent use of fluoroquinolones.

“Inappropriate use of antibiotics is at the heart of the CDAD problem in my view,” said Gerding. He points out the need for “careful studies of antibiotic restriction when specific

antibiotics are identified as associated with CDAD cases.” He says past studies have shown success in restricting the use of clindamycin and other antibiotics, but restricting use of the widely used fluoroquinolones may prove a tougher challenge.

That’s why Gerding is especially hopeful about his research with “friendly” strains of *C. difficile*, which has been supported through VA Merit Review grants. The theory is that by intentionally colonizing the colon with non-toxic strains of *C. difficile*, doctors will be able to prevent the toxic types—including the now notorious BI/NAP1—from thriving.

Based on very successful hamster studies, in which CDAD mortality dropped from 100 percent to less than 3 percent, Gerding says, “We think that the non-toxigenic strains obtained from asymptomatic hospitalized patients are able to colonize the GI tract following antibiotic use, and once established, will keep out toxigenic strains.” He holds patents for his methods in the United States, Canada and Europe, and is licensing them to a pharmaceutical company for development. He hopes to be conducting clinical trials within two years.

“If non-toxigenic *C. difficile* works in humans like it does in hamsters, I believe we will be able to significantly reduce, if not eliminate, CDAD as a significant hospital infection problem,” said Gerding. “This will fulfill my ultimate dream after 25 years of doing research on *C. difficile*.” ■

Field conference calls

ORD Field Conference calls are scheduled for the following dates in 2006: Feb. 27, March 20, April 17, May 15, June 19, July 17, Aug. 21, Sept. 18, Oct. 16, Nov. 20 and Dec. 18. Dial 1-800-767-1750, access code 17323.

Cleveland researcher feted by VA, United Spinal Assoc.

Chester Ho, MD, a researcher at the Cleveland FES Center, received the James J. Peters Scholar Award at ORD headquarters last month. The award, sponsored by the United Spinal Association, is presented annually by VA’s Rehabilitation Research and Development (RR&D) Service to cite outstanding achievements on behalf of veterans with spinal cord injury.

Ho’s research focuses on skin and bladder problems related to SCI. In addition to his role as a principal investigator at the Cleveland FES Center, a leading site for studies on functional electrical stimulation, Ho is a staff physician at the Cleveland VA Medical Center and an associate professor at Case Western Reserve University. The Cleveland FES Center is a consortium of VA, Case Western Reserve University and MetroHealth Medical Center.

Among Ho’s current projects is a study on the use of BIONs—tiny, implantable devices that use electrical signals from an external controller to stimulate nerves. The aim is to improve tissue health and prevent pressure sores. Pressure sores, a common complication in medical conditions involving immobility, are a leading cause of recurrent hospitalization among those with SCI.

Ho is also investigating whether pressure sores can be helped by pulsatile lavage, a type of hydrotherapy; and whether digital photos taken by patients, visiting nurses or family caregivers can be used to help physicians assess pressure wounds.

The award included \$75,000 from United Spinal in support of Ho’s Career Development funding from RR&D. ■

VA Research Currents

is published monthly for the

Office of Research and Development

of the Dept. of Veterans Affairs

by VA R&D Communications

103 S. Gay St., Rm. 517

Baltimore, MD 21202

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Study: Prostate-cancer screenings may not curb mortality

A VA study of about 1,000 men found no survival advantage for those who had been screened for prostate cancer. The findings appeared in the Jan. 9 *Archives of Internal Medicine*.

Led by John Concato, MD, MPH, and a team at Yale University and the Clinical Epidemiology Research Center and Cooperative Studies Coordinating Center at the West Haven VA Medical Center, the researchers sought to determine the effect on survival of the most common method for prostate-cancer screening: the blood test for prostate-specific antigen (PSA), with or without a digital rectal exam. Even though the PSA test can detect prostate cancer at an early stage, it has a high “false positive” rate: As many as 7 in 10 men with abnormal results find out only after further testing that they have no detectable cancer. And even for those who do receive a cancer diagnosis, the benefits conferred by early detection are questionable, say many experts.

Other than skin cancer, prostate cancer is the most common cancer among American men, and a leading cause of cancer deaths. However, prostate cancer usually grows slowly, and many older men with the disease die of other causes before they experience any troubling symptoms from the cancer. In fact, most men develop prostate cancer if they live long enough, but fewer than 3 in 100 actually die from it. Moreover, treatment can cause serious

problems, such as urinary incontinence and erectile dysfunction. H. Gilbert Welch, MD, a VA physician and health-outcomes researcher and professor at Dartmouth Medical School, wrote in the *Washington Post* in 2004:

“While screening probably has helped a few men live longer, it has also clearly hurt others. Millions have been biopsied who otherwise wouldn’t have been. Many with non-progressive disease have been turned into cancer patients unnecessarily. Most have been treated, and many have suffered ill effects. A few have even had their lives shortened by treatment.”

From nearly 72,000 older men who had received care at 10 VAMCs in New England, Concato and colleagues identified 501 men who received a diagnosis of prostate cancer between 1991 and 1995 and died by 1999. For comparison, they then selected a control group of 501 living men, with or without prostate cancer and matched to the deceased men for age and VAMC.

No benefit for screening was found, in that 14 percent of the men who died of prostate cancer and 13 percent of those in the control group had been screened with the PSA test. The authors reason that if the test reduced mortality, the rate of screening among the deceased men would have been lower. Screening was also not found to reduce mortality among younger or healthier men, or when the digital rectal exam was factored in.

The authors concluded: “Optimal clinical strategies for diagnosing and treating prostate cancer remain uncertain and in need of additional investigation. Based on available evidence, including the present study, recommendations regarding screening for prostate cancer should not endorse routine testing of asymptomatic men to reduce mortality. Rather, the uncertainty of screening should be explained to patients in a process of ‘verbal informed consent,’ promoting informed decision making.”

Concato noted in an email, “The findings are consistent with existing VA clinical recommendations regarding screening for prostate cancer.”

Other VA research in this area has focused on improving current methods of prostate-cancer detection, such as by enabling physicians to more accurately interpret screening results and risk factors; or finding new biomarkers that can be tested along with PSA to identify patients with more aggressive tumors, who would undeniably benefit from treatment. ■

Journal supplement showcases VA’s implementation research

The Feb. 2006 issue of the *Journal of General Internal Medicine* contains a supplement produced by VA’s Health Services Research and Development Service and titled “Implementing Evidence into Practice: Proceedings from the State of the Art VA Conference.”

Among the articles featured in the supplement, which grew out of national state-of-the-art conference held by HSR&D in 2004, are an assessment of financial incentives and other quality-improvement incentives; a look at how organizational structure affects implementation; and an overview of “lessons learned” by investigators with VA’s Quality Enhancement Research Initiative (QUERI).

Career milestones

Andrea Behrman, PhD, a research scientist and coordinator of the Locomotor Treatment Research Initiative at VA's Brain Rehabilitation Research Center at the Gainesville, Fla., VA Medical Center, received the Award for Research Excellence from the Neurology Section of the American Physical Therapy Association.

Jeremiah Silbert, MD, senior medical investigator emeritus at the Bedford VAMC and a professor of medicine at Harvard Medical School, lectured at a Nov. 2005 event held in Jerusalem by the Israel Academy of Sciences and Humanities to honor the 80th birthday of Israeli researcher Dr. Nathan Sharon. Silbert's talk, titled "Glycoproteins and Lectins in Biology and Medicine," highlighted Sharon's achievements.

Christopher Bever Jr., MD, was named associate chief of staff for research at the Baltimore VAMC. Bever is also chief of neurology at the medical center and director of the

Baltimore-based VA Multiple Sclerosis Center of Excellence.

Kazem Azadzoï, MD, director of urology research at the VA Boston Healthcare System, was named to the Hall of Fame of the International Continence Society during their recent 35th annual meeting, in recognition of his presentation on "The Role of Ischemia and Oxidative Stress in Bladder Neurodegeneration."

Seattle Summer Session

The next Summer Session of the Seattle Epidemiology, Research and Information Center will take place June 26 – 30, 2006, featuring courses in epidemiology, biostatistics and clinical research methods. Tuition is waived for VA employees. For details visit www.eric.seattle.med.va.gov or call John Messina at 206-277-4376.

New URL for VA research website

VA's main research website can now be found at www.research.va.gov. The old URL was www.va.gov/resdev.

Publication notifications

VA investigators or their local research offices should notify VA Research Communications of all scientific publications or presentations, upon acceptance, in accordance with VHA Handbook 1200.19 (available at www.va.gov/vhapublications). To email the notification, search the Global Address List in VA's Outlook System for **VHA Co 12 Publication/Presentation Notifications**. If emailing from outside the VA system, send to **research.publications@va.gov**. Include the article or abstract title, along with an electronic copy of the abstract, manuscript or poster; VA investigators' full names and degrees; and the journal or meeting title and date. A brief lay summary of the findings should be included as well.

The Health Services Research and Development Service has established additional requirements regarding notification of pending publications and presentations. Visit www.hsrdr.research.va.gov/for_researchers/pub_notice.cfm for more information. ■

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