

Health Services R&D director named

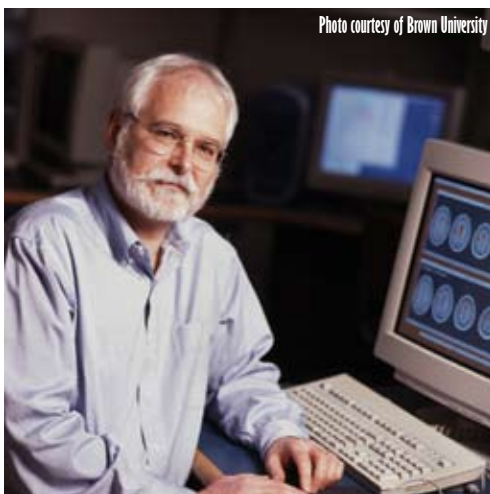
Seth A. Eisen, MD, MSc, whose research over more than three decades with VA has centered on war-related illness and pain, and on substance abuse among veterans, has been named director of VA's Health Services Research and Development Service. With Eisen's appointment, acting director Shirley Meehan, MBA, PhD, will resume her post as deputy director of HSR&D.

An investigator and director of ambulatory care at the St. Louis VA Medical Center, Eisen holds a medical degree from Washington University, where he is a professor of medicine and psychiatry. He also holds a master's of science in epidemiology from the Harvard School of Public Health. Eisen is recognized for his role as a mentor and teacher to young health-services

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Brown/VA scientist profiled in *Discover*

John Donoghue, PhD, a Brown University neuroscientist who became affiliated with VA when the agency established its Providence-based Center for Restorative and Regenerative Medicine in 2004, was profiled in the Dec. 2006 issue of *Discover* as one of two runners-up for the magazine's Scientist of the Year Award. The article, which describes the researcher's work on BrainGate, is available at <http://www.discover.com>.



John Donoghue, PhD, has been developing technology called BrainGate that allows movement signals from the brain to be picked up by a tiny implanted sensor and decoded into commands for electronic or robotic devices, such as prosthetic limbs.



Study to probe risk factors, outcomes of violence against servicewomen

According to a Dec. 2006 Associated Press story, "Women warriors are writing a new chapter in military history, serving by the tens of thousands, fending off enemy fire and taking on—and succeeding in—high-profile roles in the battlefield and the skies as never before."

But even as American servicewomen in many cases are proving to be heroes, they are sometimes victims: In 2005, the Department of Defense reported 2,374 cases of sexual assault in the military—an increase of 40 percent over 2004. DoD has launched programs to combat the trend. But how is the situation affecting the physical and emotional health of the women in today's military? And what factors put them at risk?

These questions are at the core of a new VA-funded study led by Anne G. Sadler, RN, PhD, acting chief of psychology at the Iowa City VA and an investigator with VA's Center for Research in the Implementation of Innovative Strategies in Practice. The research will include interviews with about 500 active-duty women and female veterans from five Midwestern states, all currently or formerly with the reserves or National Guard, which account for the majority of U.S. troops in Iraq and Afghanistan.

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Career milestones

Jonathan Cohn, MD, Durham, presented the keynote Frank Brooks Memorial Lecture at the recent annual joint meeting of the American Pancreatic Association and the International Association of Pancreatology. Cohn, whose research is funded by VA, the National Institutes of Health and the Cystic Fibrosis Foundation, described how the gene mutation that makes people carriers of cystic fibrosis also increases their risk for pancreatitis, a potentially life-threatening condition.

Barry Massie, MD, chief of cardiology at the San Francisco VA and clinical coordinator of VA's Heart Failure Quality Enhancement Research Initiative (QUERI), is one of 13 heart-failure experts from North America and Europe who will lead the ASCEND-HF trial (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure). A news release from the trial sponsor, Scios, Inc., called it the "largest trial ever planned in the acute heart failure field."

Gregory Boivin, MS, DVM, Cincinnati VA, is part of a University of Cincinnati team awarded the 2007 Ann Doner Vaughan Award from the American Academy of Orthopaedic Surgeons, for a study and paper titled "Functional Tissue Engineering for Tendon Repair: A Multidisciplinary Strategy Using Mesenchymal Stem Cells, Bioscaffolds and Mechanical Stimulation."

Palo Alto alcoholism researcher cited for findings on natural vs. treated remission

Rudolf H. Moos, PhD, senior research career scientist at the Palo Alto VA and professor at Stanford University, has won the 2006 Dan Anderson Research Award from the Butler Center for Research at the Hazelden Foundation, a nonprofit group that helps people coping with addictions.



Rudolf H. Moos, PhD,

Moos earned the award for his study "Rates and predictors of relapse after natural and treated remission from alcohol use disorders," published in 2006 in the journal *Addiction*. The study found that people with alcohol-use disorders who participated in treatment or Alcoholics Anonymous within the first year of recognizing their problem were much more likely to stay sober than individuals who didn't receive help via treatment or AA.

In his study, Moos compared three-year remission rates and subsequent 16-year relapse rates for a group of individuals who entered treatment or AA within the first year of seeking help and for a group of individuals that similarly recognized their alcohol problem but did not get help from treatment or AA. Study participants were contacted by phone at 1, 3, 8 and 16 years after entering the study.

Two key findings: (1) After the three-year follow-up, 62.4 percent of participants who received help within the first year remitted (or stayed sober), while only 43.4 percent of the group that got no help remitted. (2) At the 16-year follow-up, among the group that had put their alcohol problems into remission, 60.5 percent of the no-help group relapsed, while 42.9 percent of the remitters who got help relapsed.

"A difference of 15 to 20 percent is very significant," said Moos. "Our study indi-

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researchers, and has been leading a VISN 15 HSR&D core group focused on musculoskeletal disease since Nov. 2004.

Eisen played a key role in developing a registry of 7,400 twins who served in the military during the Vietnam War. He and several colleagues continue to conduct research based on the registry. More recently, he was lead author on a major VA study that found that 10 years after the Gulf War, the physical health of deployed and non-deployed veterans was similar, although Gulf War deployment was associated with a higher risk for fibromyalgia, chronic fatigue syndrome, skin conditions, dyspepsia, and a clinically insignificant decrease in the physical component of the SF-36, a questionnaire used to measure health.

Among the areas he plans to focus on in his new role are developing the next generation of health-services researchers and furthering collaborations across VA's four research services.



Seth Eisen, MD, MSc

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research.publications@va.gov
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Stopping cancer in its tracks: Lab seeks compounds to halt metastasis

Using a unique video microscopy setup, a VA team in Columbia, Mo., has been testing compounds and antibodies that halt metastasis—the spread of cancer—by preventing the bond between cancer cells and blood vessel walls. Learning how to block this adhesion, says lead investigator Vladislav V. Glinsky, MD, could dramatically shrink cancer mortality.

“Metastasis is basically what kills cancer patients, because a primary tumor can usually be treated or removed by different modalities,” says Glinsky, a research health scientist at the Harry S. Truman Memorial Veterans Hospital and research assistant professor of biochemistry at the University of Missouri, Columbia.

A study featured on the cover of the Nov. 2006 issue of *Neoplasia*, on which Glinsky collaborated with a team at the University of Buffalo, found that a monoclonal antibody called JAA-F11 could reduce lung metastasis by more than 50 percent in mice implanted with human breast cancer cells. An earlier study by Glinsky and colleagues at other sites, published in the same journal in 2005, used a variety of antibodies and carbohydrate-based compounds to achieve even more striking results. Each of four agents used in the experiments was able to decrease by more than 90 percent the spread of breast and prostate tumors to mouse lung and bone.

Glinsky’s approach centers on breaking up the “marriage” between tumors and endothelial cells, the flat cells that line blood vessels. When a primary tumor grows, some cells escape and enter the bloodstream. If they adhere successfully to the blood vessel and form clumps with each other, they can thrive and spread to bone or other organs.

“Blood-borne tumor cells need to find their home in blood vessels,” explains the researcher. “It’s a necessary step. If they don’t attach to the vessel wall, they will be eliminated by the body—they’ll die out. There will be no metastasis.”

Glinsky’s team relies on innovative methods for imaging blood vessels and cancer cells, and for analyzing the interactions



The orange orbs are three cancer cells, migrating through a porcine blood vessel. The cells were genetically modified to express a fluorescent protein that allows them to be seen via video microscopy.



Vladislav Glinsky, MD, uses video microscopy to track the interaction of cancer cells and the blood vessels that enable them to spread in the body.

between them in a variety of settings: in vitro, ex vivo, and in vivo. “In some terms, our video microscopy system is unique,” he says. “We have designed a stage that allows us to literally follow each individual cancer cell as it moves through the vasculature of a target organ. This way, we can observe dynamic changes in metastatic cell adhesive behavior over an extended period of time.”

Some of the potential therapeutic agents he has studied, such as JAA-F11, work by blocking TF antigen, a carbohydrate structure commonly expressed by tumor cells. Another important target molecule is TF antigen’s partner in the deadly dance of metastasis: galectin-3, found in both endothelial and cancer cells. “Adhesion requires interaction of two molecules,” notes Glinsky. “On the side of the cancer cell, it’s TF antigen, and on the side of the endothelial cell, it’s galectin-3.”

Glinsky, whose work has been supported by both VA and the National Cancer Institute, is especially hopeful about a compound developed by his lab that consists simply of a sugar and an amino acid: lactose and leucine. Called Lac-L-Leu, it tricks blood-vessel cells into thinking it is TF antigen.

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Recent publications and presentations by VA investigators

Below is a brief sampling of recent publications and presentations by VA investigators, based on notifications received by R&D Communications (see reporting requirements at www.research.va.gov/resources/policies/pub_notice.cfm). Every attempt is made to present a cross section of investigators, topics and medical centers. Only VA-affiliated authors are listed here, due to space constraints.

“Aortic Pseudoaneurysm Associated With Posterior Spinal Instrumentation: A Case Report.” Vidya Jayawardena, MD. **Richmond**. International Congress of Behavioral Medicine, Nov. 2006.

“A Distressed Heart: A Prospective Study of Posttraumatic Stress Disorder Symptoms and Coronary Heart Disease in the Normative Aging Study.” Karestan C. Koenen, PhD; Avron Spiro III, PhD; Pantel S. Vokonas, MD; David Sparrow, DSc. **Boston**. *Archives of General Psychiatry*, Jan. 2007.

“Effect of Iron and Ascorbate on Uroporphyrin in Ascorbate-Requiring Mice as a Model for Porphyria Cutanea Tarda.” Judith M. Jacobs, PhD; Jacqueline F. Sinclair, PhD; Peter R. Sinclair, PhD. **White River Junction**, *Hepatology*, Jan. 2007.

“How Do Patients with HIV/AIDS Understand and Respond to Health Value Questions?” Susan N. Sherman, DPA; Joseph M. Mrus, MD, MSc; Joel Tsevat, MD, MPH. **Cincinnati**. *Journal of General Internal Medicine*, Dec. 2006.

“Impact of Guideline-Concordant Empiric Antibiotic Therapy in Community-Acquired Pneumonia.” Marcos I. Restrepo, MD, MSc; Eric M. Mortensen, MD, MSc. **San Antonio**. *American Journal of Medicine*, Oct. 2006.

“Intranasal Administration With NAD⁺ Profoundly Decreases Brain Injury in a Rat Model of Transient Focal Ischemia.” Weihai Ying, PhD. **San Francisco**. *Frontiers in Bioscience*, Jan. 2007.

“Mantram Repetition for Stress, Coping, and Spiritual Well-Being in HIV-Infected Adults: A Mixed Method Analysis.” Jill Bormann, PhD; Jeanne Kempainen, PhD. **San Diego**. International Congress of Behavioral Medicine, Nov. 28-Dec. 2, 2006.

Prevalence and Trends of Selected Urologic Conditions for VA Healthcare Users.” Min-Woong Sohn, PhD; Huiyuan Zhang, BS, MS; Brent C. Taylor, MD; Michael J. Fischer, MD; Timothy J. Wilt, MD, MPH. **Hines, Minneapolis**. *BMC Urology*, Nov. 2006.

“Prospective Evaluation of the Use and Outcome of Admission Stool Guaiac Testing: The Digital Rectal Examination on Admission to the Medical Service (DREAMS) Study.” Edmund J. Bini, MD, MPH; Jean-Pierre Reinhold, MD; Elizabeth H. Weinschel, MD. **New York**. *Journal of Clinical Gastroenterology*, Oct. 2006.

“RelA is Required for IL-1B Stimulation of Matrix Metalloproteinase-1 Expression In Chondrocytes.” Matthew Vincenti, PhD. **White River Junction**. *Osteoarthritis and Cartilage*, Nov. 7, 2006.

“Risk of New-Onset Atrial Fibrillation in Relation to Body Mass Index.” Sascha Dublin, MD, PhD. **Seattle**. *Archives of Internal Medicine*, Nov. 27, 2006.

“Should Patients with Anemia and Low Normal or Normal Serum Ferritin Undergo Colonoscopy?” Mandeep P. Sawhney, MBBS, MS; Douglas B. Nelson, MD; Frank A. Lederle, MD; Thomas Rector, PhD; John H. Bond, MD. **Minneapolis**. *American Journal of Gastroenterology*, Oct. 13, 2006.

“Specific High Affinity Interactions of Monomeric Endotoxin: Protein Complexes With Toll-Like Receptor 4 Ectodomain.” Jerrold P. Weiss, PhD; Theresa L. Gioanini, PhD. **Iowa City**. *Journal of Biological Chemistry*, Nov. 22, 2006.

“The Association between Number of Pap Smears Performed and Self-Reported Confidence in an Internal Medicine Residency.” Ryan B. Chew, MD; Lisa D. Chew, MD, MPH; Katharine Bradley, MD, MPH. **Seattle**. *Journal of Women's Health*, Oct. 2006.

“The Impact of Unstable Angina Guidelines in the Triage of Emergency Department Patients with Possible Acute Coronary Syndrome.” David A. Katz, MD, MSc. **Iowa City**. *Medical Decision Making*, Nov./Dec. 2006.

“Uric Acid Decreases Nitric Oxide Production in Pulmonary Artery Endothelial Cells Through Activation of the L-Arginine/Arginase Pathway.” Jawaharlal M. Patel, PhD; Edward R. Block, MD. **Gainesville**. Evolution of Pulmonary Hypertension Meeting, Dec. 7-8, 2006.

“Voluntary Modulation of Motor Cortical Activity by a Person with Amyotrophic Lateral Sclerosis: Initial BrainGate Experience.” Leigh R. Hochberg, MD, PhD. **Providence**. Society for Neuroscience Annual Meeting, Oct. 14-18, 2006.

“Younger Stroke Survivors Have Reduced Access to Physician Care and Medications: National Health Interview Survey From Years 1998 to 2002.” Deborah A. Levine, MD, MPH; Catarina I. Kiefe, MD, PhD; Thomas K. Houston, MD. **Birmingham**. *Archives of Neurology*, Nov. 13, 2006. ■

Who's at risk for falls?

Interventions such as CBST or tai chi may be effective in preventing falls among older adults (*see story at right*), but which patients should be targeted?

A review study led by researchers with the GRECC at the VA Greater Los Angeles Health System analyzed data from 18 studies looking at risk factors for falls among community-dwelling seniors. Their results, published Jan. 3 in the *Journal of the American Medical Association*, show that seniors who have fallen in the past year or who have clinically detected problems with gait or balance are at highest risk.

Other factors, such as visual impairment, medication variables, decreased activities of daily living, or impaired cognition, did not consistently predict falls. Orthostatic hypertension—a sudden drop in blood pressure upon standing—also did not independently predict falls.

“We evaluated risk factors identifiable during the routine clinical examination. The risk factors we identified can be considered screening tests for future falls,” wrote the authors, led by David A. Ganz, MD, MPH, of the Greater LA VA and the UCLA Multi-campus Program in Geriatric Medicine and Gerontology. They continued: “Screening for falls is as easy as asking, ‘Have you had any falls in the past year?’ and then inquiring about gait or balance problems if the patient has not had a fall.”

Ganz's coauthors included Yeran Bao, MD, now at the Palo Alto VA; Paul Shekelle, MD, PhD, of VA and RAND Health; and Laurence Z. Rubinstein, MD, MPH, of VA and UCLA.



Tai chi classes such as this one, sponsored by the University of Texas Southwestern Medical Center, have been shown to help prevent falls in seniors, but a VA study in Ann Arbor suggests a special balance-training program may be even more effective.

Balance training may top tai chi for fall prevention

In a study involving 213 older adults, researchers at the Ann Arbor VA and University of Michigan found that training focused on increasing step length and speed was more effective than tai chi for improving mobility and balance. The results appear in the Dec. 2006 *Journal of the American Geriatrics Society*.

Tai chi, a Chinese martial art based on slow, rotating movements and weight-shifting, has been shown to help reduce falls among seniors, but its value relative to other fall-prevention programs has remained open to debate.

According to senior author Neil B. Alexander, MD, and lead author Joseph O. Nnodim, MD, PhD, of the Geriatric Research, Education and Clinical Center (GRECC) at the VA Ann Arbor Healthcare System and the University of Michigan Health System, the new findings carry an important message for seniors at risk for falls: “What this tells us is that if you want to improve your ability to balance and walk, try a program that focuses on improving balance while moving and on the ability to step quickly and further,” said Alexander, acting director of the GRECC. He added

that the balance-training program—known as Combined Balance and Step Training (CBST)—requires no specialized equipment or advanced training for the instructor, and is “very easy to implement.”

The 10-week study included three one-hour sessions per week with an instructor, with half the participants doing CBST and the other half doing tai chi. CBST activities included turning the upper body while bouncing and catching a ball; walking on a plank; and stepping on and off curbs or over obstacles, and other tasks. The tai chi classes focused on body alignment, weight shifts, hip and ankle rotations, various stepping motions, and relaxation.

After 10 weeks, overall performance had improved more with CBST than with tai chi. Compared with the tai chi group, CBST participants did from 5 to 10 percent better in two stepping tests, and 9 percent better in the “Timed Up and Go” measure, in which they had to quickly rise from a seated position, walk three meters, turn, and go back to their chair. The CBST seniors also showed greater improvements in tests in which they had to stand with one foot forward, or on one leg. ■

REMISSION (from pg. 2)

cates that if an individual recognizes an alcohol problem and gets into treatment or AA relatively soon after that, then they are much more likely to be remitted after three years and to stay remitted after 16 years.”

Moos said his findings help prove that “natural remission,” a term used to denote the recovery of those who get sober without help, “may be less stable than remission that is associated with obtaining help. Our findings on the benefits of relatively rapid entry into treatment and/or AA support the value of strengthening the referral process for individuals who recognize their alcohol problems and initiate help-seeking,” he said.

Moos added, “Those gatekeepers or first-responders who do the initial assessments of people with alcohol problems need to be aware of the important role they can play up front. Assessing help-seekers’ readiness for change may help target high-risk individuals for interventions. Motivational Interviewing techniques could help guide those individuals to treatment or AA.”

Substance abuse, including alcoholism, is among the top three diagnoses in VA’s healthcare system, affecting some 215,000 veteran patients each year. VA counselors typically recommend that patients become involved in community-based self-help groups, though such participation is not mandated.

Moos will accept the award and a \$2,000 honorarium in May at the National Association of Addiction Treatment Providers conference in San Diego. The award is named for the late Dan Anderson, PhD, the former president of Hazelden. ■

Next ORD field conference call:

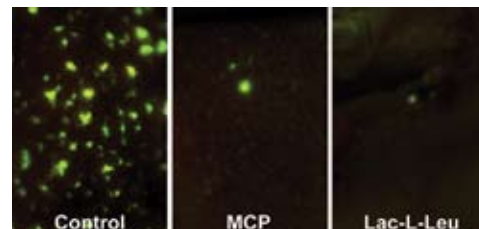
Monday, Feb. 26, 2007 • 1:30 pm EST

Dial 1-800-767-1750
(access code: 17323)

CANCER (from pg. 3)

“It binds to galectin-3 even better than TF antigen, and blocks it so it can’t mediate adhesion anymore,” says Glinsky.

Another promising compound he has tested, Modified Citrus Pectin, was developed by his collaborators at Wayne State University and the University of Michigan. According to Glinsky, “Both compounds are completely non-toxic and show great promise as potential anti-metastatic drugs.” ■



This image from the VA lab of Vladislav Glinsky, MD, shows the effects of two carbohydrate-based metastasis inhibitors, Modified Citrus Pectin (MCP) and Lactulosyl-L-leucine (Lac-L-Leu), on the proliferation of malignant cancer cells within the microvasculature of mouse lungs. The green shapes are fluorescently labeled cancer cells.

Hill happenings

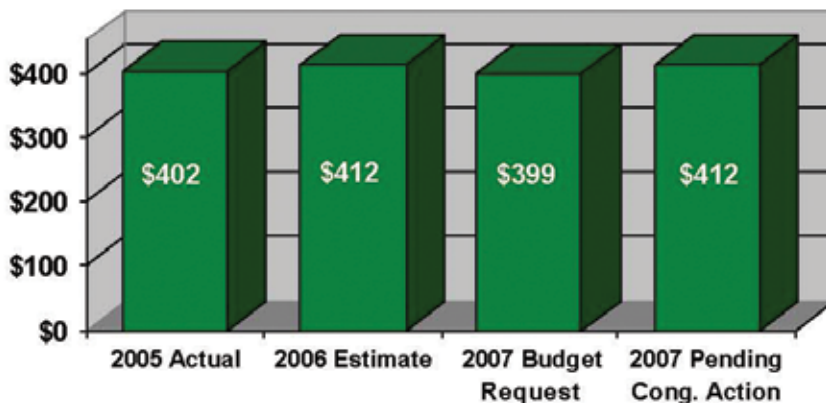
FY '07 funding bill for VA pending approval

Editor’s note: Three times per year, VA Research Currents provides an update on congressional action affecting funding for VA research.

Congress has passed two of the 11 fiscal year 2007 appropriations bills to date—Defense and Homeland Security. Until Congress passes the remaining nine spending bills, agencies funded by them, including VA, will operate under a Continuing Resolution, a stop-gap funding measure. The latest Continuing Resolution provides funding through Feb. 15, and allows VA to transfer up to \$683,970,000 from other accounts to Medical Services during this period. Discussions are under way on Capitol Hill to enact a Continuing Resolution covering the remainder of the fiscal year.

To view and track the appropriations bills, visit: <http://thomas.loc.gov/home/approp/app07.html>.

**VA Medical and Prosthetic Research
Direct Appropriations**
(dollars in millions)



WOMEN (from pg. 1)

“We know very little about risk factors for gender-based violence in the Reserve and National Guard, and we know very little about these risk factors in deployed populations,” says Sadler. “So this is a unique opportunity.”

Besides identifying risk factors for sexual assault and physical violence against women, the new study will look at health outcomes for the study participants and any barriers to VA care. Another study by Sadler, already under way, is examining gynecological health outcomes for women who have experienced sexual violence. One of the questions her team is asking is how the women view VA healthcare.

Sadler: “The VA has changed a lot over the past two decades, which is verified in the common expression ‘It’s not your father’s VA anymore.’ Of the 500 interviews we’ve done so far in the current study, on reproductive health, the vast majority of



Some 500 Reserve and National Guard women, active duty and veterans, will be interviewed in a VA study focused on risk factors and health outcomes related to gender-based violence in the military.

women view the VA as a good place for women’s healthcare. We will continue to ask about women’s perceptions of VA in the new study, so that we can understand their needs and work to provide them with the best care possible.”

The new effort will include interviews with three groups—women deployed to

combat regions, those deployed elsewhere, such as Germany, and those who have not been deployed.

One major concern, particularly with respect to women serving in Iraq and Afghanistan, is posttraumatic stress disorder. Among the general population, says Sadler, rape survivors are thought to be the largest single group suffering from PTSD, with up to 58 percent of female victims developing PTSD afterward. And studies of Persian Gulf War veterans in the late 1990s found that both female gender and Guard or Reserve status were associated with higher PTSD rates. In one study, women who had been exposed to combat and sexual trauma had twice the rate of PTSD as men who had experienced combat alone—16 vs. 8 percent.

While VA has been expanding mental health care, as well as women’s care, over the past few years, Sadler says there’s a critical need for more research to guide care for victims of sexual assault.

“We want to provide evidence-based care,” says Sadler. “If we characterize the deployment experiences of these women and their health outcomes, we can improve

Past research found high rate of rape, other assaults

Four in 10 women veterans who took part in an earlier study led by Sadler said they had been raped or assaulted during their service. The study, published in the Sept. 2004 *Journal of Women’s Health*, also found that women who reported repeated violence had more outpatient visits and poorer health than women who had been victimized only once, or who had never been attacked. These same women were also more likely to report a history of childhood violence and post-military violence.

Sadler and her colleagues said the study suggested that repeated violence—as opposed to a single episode—may have a particularly strong adverse effect on women’s health. “Our findings indicate that it is necessary to include the concept of repeated violence in any future research studies of the health effects of violence,” they wrote.

The study included 520 women veterans from six cities who had served during the Vietnam or subsequent eras. The women were selected from a registry made up mainly of women who had used VA health care or sought a disability rating. Rape was reported by 29 percent of the participants, and physical assault by 36 percent.

More than half the women reported some form of physical or sexual violence before their military service. Almost half of this subgroup of women said they joined the military to escape an abusive or distressing home life.

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 U.S. Department of Veterans Affairs
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WOMEN (from pg. 7)

the care we give them. We might identify women who need a different type of trauma screening, for example, or different types of interventions.”

Meanwhile, Sadler remains deeply impressed by the servicewomen and female veterans she has met, and hopes her new

‘They participate with our research because they want to help other women.’

study will contribute significantly to their healthcare and well-being.

“The women I see clinically, and those who are participating in our current study, are very bright and patriotic,” she says. “They participate with our research because they want to help other women. They want to make a difference. They are forthright and they tell it like it is. They’re patriots who are dedicated to the mission, and we feel very pleased to be doing good research on their behalf.” ■



Peggy Druar staffs a booth during last year's Research Week activities at the VA Western New York Healthcare System.

VA Research Week 2007: May 13 – 19

Holding tours of your research facility, inviting congressional representatives to visit, organizing a lecture or poster session, sponsoring a luncheon for research volunteers—these will be just some of the many projects being undertaken by VA medical centers across the country in honor of VA Research Week 2007, to be held May 13 – 19.

The VA research website contains a toolkit to help research offices plan, coordinate and report on their Research Week activities. Among the items on the website, for example, are samples of letters to members of Congress, press releases and Research Day agendas. For more details, visit www.research.va.gov/resources/ORD_Admin/research_week/default.cfm.