

Discovery and Collaboration for Exceptional Health Care

VA RESEARCH TODAY

SPRING 2011 — Published in commemoration of National VA Research Week 2011

- Taking brain imaging to the next level
- Targeting homelessness among Veterans
- MVP: Building a genomics database
- Probing blasts' auditory effects
- Making the most of electronic health records
- Nature's answers to cancer



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Research & Development
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VA-ACADEMIC PARTNERSHIPS: A CORNERSTONE OF MEDICAL RESEARCH AND CARE IN THE U.S.



As you read through the feature stories in this year's *VA Research Today*—our second annual edition of the magazine—you'll see a consistent theme: **VA and its university partners working together to foster advances in research and patient care.**

The collaboration between VA's health care system and the nation's medical schools began in 1946, with an historic agreement known as Memorandum Number Two. Today, VA has affiliations with nearly 130 of the nation's medical schools, and in essence has become the largest provider of health care training in the nation. Some 30,000 medical residents and 20,000 medical students rotate through VA facilities each year.

Over the past 65 years, this public-private partnership has enriched the learning environment in VA facilities as well as university medical schools and teaching hospitals; spurred remarkable progress in medical research; and notably improved health care for Veterans and all Americans.

Another facet of this partnership is that most VA investigators also teach at an affiliated university medical school, and in many cases provide patient care at the university's hospital. Open the pages of any leading journal, such as the *New England Journal of Medicine* or the *Journal of the American Medical Association*, and you'll see studies by authors with dual affiliations—the VA Connecticut Healthcare System and Yale University School of Medicine, for example, or the VA San Diego Healthcare System and the University of California, San Diego.

Another legacy of Memorandum Number Two is the many research centers of excellence nationwide that are under the joint auspices of VA and an affiliated university. Examples include the Cleveland Functional Electrical Stimulation (FES) Center, which involves VA and Case Western Reserve University, along with other partners; and the Human Engineering Research Laboratories, a project of VA and the University of Pittsburgh.

It should be noted that some of the nation's leading research centers that involve VA researchers are collaborations among VA, its university partners and the Department of Defense. One example, featured on the cover of this magazine, is the Center for Imaging of Neurodegenerative Diseases, in San Francisco. Another is the McKnight Brain Institute in Gainesville, Fla., which is under the auspices of the University of Florida but has relied on critical input from VA and DoD.

Other federal agencies, too—namely the National Institutes of Health—play a critical role in helping to fund much of the vital work that VA- and university-affiliated researchers conduct nationwide.

In today's economic climate, such partnerships are invaluable. They enable researchers to share and leverage resources—from equipment to expertise—in ways that vastly improve efficiency and productivity.

In the pages that follow, you'll read about some of the results of this work, and about some exciting new projects under way. Along with our partners, we look forward to continuing to serve Veterans and find innovative ways to improve their lives.

Sincerely,

A handwritten signature in black ink that reads "Joel Kupersmith". The signature is written in a cursive, slightly slanted style.

Joel Kupersmith, MD
Chief Research and Development Officer
Veterans Health Administration

DISCOVERY AND COLLABORATION FOR EXCEPTIONAL HEALTH CARE

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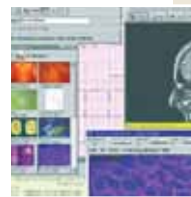
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Cover: *With imaging technicians Katherine Wu at the monitor and Stephen Kriger at the “magnet,” a study participant prepares to undergo an MRI scan at the Center for Imaging of Neurodegenerative Diseases at the San Francisco VA Medical Center. See feature on page 2.*



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HIGH-TECH IMAGING CENTER HUNTS FOR CLUES ON VETERANS' BRAIN AILMENTS

The Center for Imaging of Neurodegenerative Diseases is a leading site for studies on Alzheimer's, PTSD, Gulf War illness and numerous other disorders

In 1980, as a nephrologist and the new chief of hemodialysis at the San Francisco VA Medical Center, Michael Weiner, MD, performed basic experiments using the earliest form of a technology that had just been developed—magnetic resonance imaging (MRI).

He says he never dreamed he would one day direct a high-tech research facility such as the Center for Imaging of Neurodegenerative Diseases. Today, CIND is the only imaging center in VA exclusively devoted to MRI of the human brain. As such, it plays a key role in clinical research on Alzheimer's disease, posttraumatic stress disorder, Gulf War illness, traumatic brain injury, Parkinson's disease, and other maladies affecting the brain and central nervous system.

[In the vanguard of medical imaging from its earliest days](#)

Even in those early days of MRI, Weiner foresaw the potential impact on research and health care.

"My work with rats, when I created techniques for using NMR [nuclear magnetic resonance—an earlier form of MRI] to study whole animals, happened to be one of the first biological applications of NMR," he says. "Because I was a physician with a broad clinical background, I could see that once they made magnets big enough to hold people, the potential diagnostic applications of this new technology were going to be huge. But nobody in

their wildest dreams predicted the speed at which the field would grow."

When he first began his experiments, Weiner found a total of 60 papers on biological applications of NMR in the scientific literature. "Today, there are hundreds of papers published every day on MRI. I had the extreme good fortune to become involved in the field at its very beginning."

In growing his MRI program from a basement laboratory to an internationally renowned center with a staff of more than 70, Weiner has never hesitated to think big.

In 2005, he was named lead investigator for the Alzheimer's Disease Neuroimaging Initiative (ADNI), a \$140-million, 10-year clinical trial involving more than 1,000 patients at 55 centers in the U.S. and Canada.

Supported by a consortium that includes the National Institutes of Health, private industry and the Canadian government, ADNI is designed to validate biomarkers for detecting and monitoring progression of Alzheimer's.

"Currently, we use subjective clinical measures such as memory tests or activities of daily living, which have a lot of variability from one day to the next," explains Weiner. "The beauty of a biomarker is that it doesn't have that variability. This objective consistency will become extremely important in identifying Alzheimer's at an early stage and



Brain power—Dr. Norbert Schuff and imaging technician Monica Camacho review MRI brain scans from a recent study. Schuff is the lead physicist at VA's Center for Imaging of Neurodegenerative Diseases and a professor of radiology at the University of California, San Francisco.

State-of-the-art MRI: Zooming in on the brain

A new high-powered MRI system soon to be installed at the Center for Imaging of Neurodegenerative Diseases will dramatically improve imaging of brain anatomy, blood vessels, blood flow, white matter and brain metabolites, says CIND senior scientist Norbert Schuff, PhD.

In fact, the powerful 7 Tesla MRI, which is used only for research and not routine clinical diagnosis, will enable scientists to view brain anatomy that was previously unseen. Schuff offers three examples of how the new magnet will further research:

- Improved spatial resolution will help researchers measure changes in the hippocampus, which loses volume in both

Alzheimer's disease and PTSD. "Different hippocampal subfields are affected in each condition," notes Schuff. "This will help us distinguish between the two."

- Increased signal-to-noise ratio will result in much more accurate measures of brain metabolites—chemicals important for brain function—through proton MR spectroscopy. "We can spread the signal out and see metabolite levels in much greater detail," according to Schuff.
- Nerve fiber bundles, or white matter, which are damaged in traumatic brain injury, appear in much greater detail in diffusion tensor imaging—a form of MRI—performed on a 7 T machine.



Imaging pioneer—In 1980, Dr. Michael Weiner was one of the first investigators in the nation to use nuclear magnetic resonance—which later evolved into magnetic resonance spectroscopy, a technique related to MRI—to study metabolism of organs inside a living animal.

Center director cited for long, fruitful career in brain imaging

Michael Weiner, MD, director of VA's Center for Imaging of Neurodegenerative Diseases and a professor at the University of California, San Francisco, accepted the Ronald and Nancy Reagan Research Award from the Alzheimer's Association in April 2011 on behalf of the nationwide Alzheimer's Disease Neuroimaging Initiative, which Weiner leads.

In 2006, Weiner received the William S. Middleton Award, VA's highest scientific honor, in recognition of his contributions to the field of magnetic resonance imaging and his exemplary service to VA.

Weiner says the VA honor was especially meaningful to him because at the outset of his VA career, four decades ago, he had the opportunity to know Middleton. "He was instrumental in implementing the system of affiliations between VA medical centers and medical schools, such as the affiliation between the San Francisco VA and the University of California, San Francisco. This collaboration has been of incredible mutual benefit to the VA and to doctors around the United States."

Looking back on his career, Weiner says: "I've been very lucky. I was lucky to be in the right place at the right time in the development of the field of MRI, and I've been equally lucky in my colleagues and collaborators. Most importantly, I've been extremely fortunate to spend my entire career in the VA system, which has been a hugely supportive environment for medical research."

measuring both the progression of the disease and the success of new treatments as they are developed."

To date, ADNI researchers have published more than 170 peer-reviewed papers and are, according to Weiner, "zeroing in" on biomarkers based on brain imaging, cerebrospinal fluid and blood. "I'm very optimistic that we will succeed," he says.

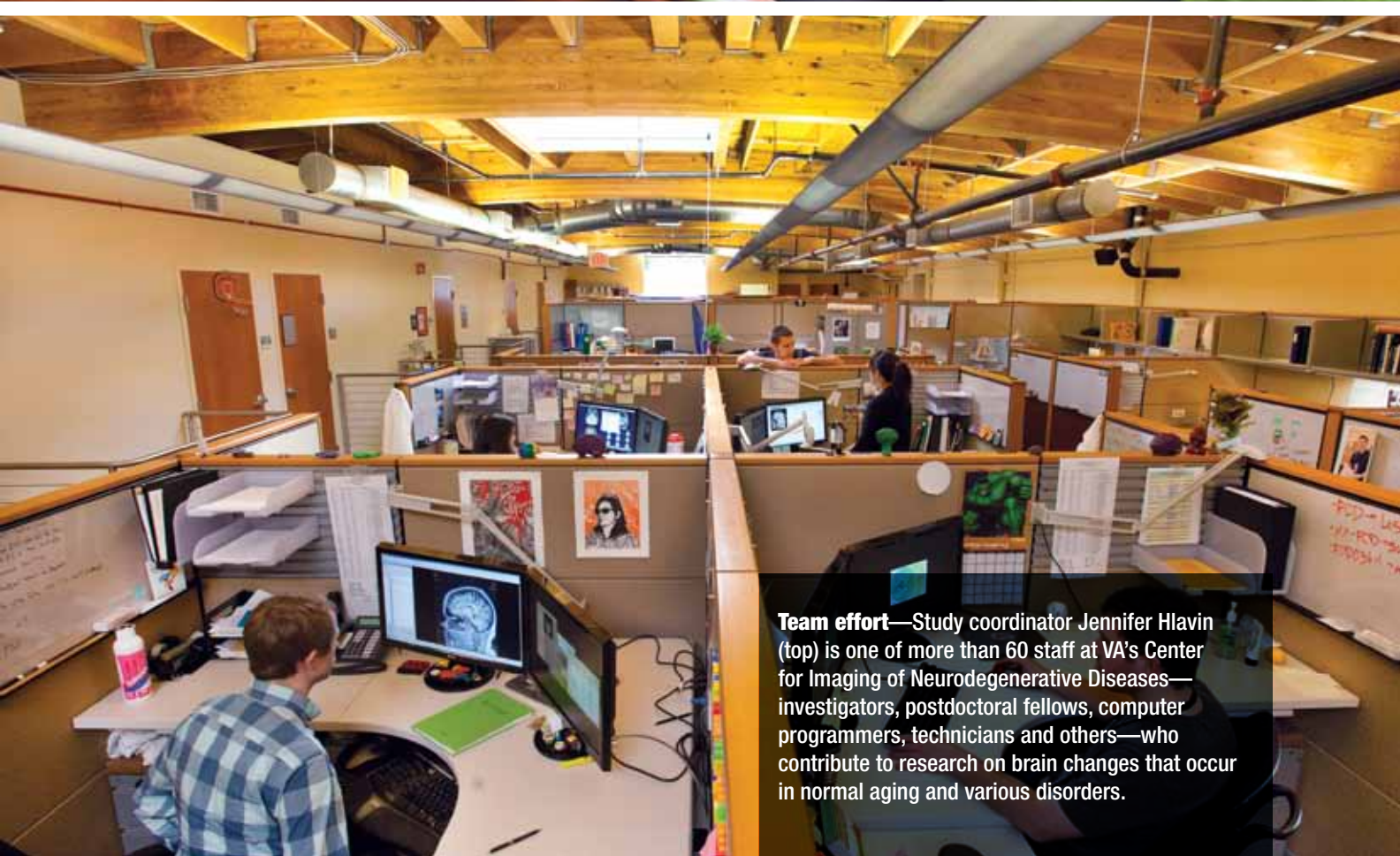
At Weiner's direction, ADNI investigators share all their raw data on the Internet without embargo (adni-info.org and adni.loni.ucla.edu). The success of this strategy has led Weiner to become a passionate advocate for the widespread sharing of scientific data (scientificdatasharing.com). "Imagine a time when all published papers include raw data at the time of publication," he says. "This will become a huge resource that will transform the scientific community, create new types of research, lead to accelerated discovery and improve treatments. It may even stimulate the economy by creating new value and new businesses."

Working with the Department of Defense

CIND is also home to a very different research partnership: the Neuroscience Center of Excellence, a collaboration among the Department of Defense (DoD), VA, and NCIRE-The Veterans Health Research Institute, the nonprofit institute that supports biomedical research at the San Francisco VA. Since 2004, with Weiner as principal investigator, DoD has supported more than \$35 million in research projects in PTSD, traumatic brain injury (TBI) and other neurotraumas, Parkinson's disease and basic neuroscience.

Weiner, an Air Force Veteran who served during the war in Vietnam, emphasizes the relevance of the Neuroscience Center to the mission of VA. "Today's active service members are tomorrow's Veterans. The hazards they are exposed to today, such as TBI and PTSD, will increase their risk for neurodegenerative diseases as they age. I'd love to see many more research collaborations between the VA and DoD."

Thomas Neylan MD, director of the PTSD Program at the San Francisco VA, says the Neuroscience Center has been a huge help to his team's work. "Mike and his team have had many PTSD-related grants, projects



Team effort—Study coordinator Jennifer Hlavin (top) is one of more than 60 staff at VA's Center for Imaging of Neurodegenerative Diseases—investigators, postdoctoral fellows, computer programmers, technicians and others—who contribute to research on brain changes that occur in normal aging and various disorders.



MRI Central—CIND investigators and technicians are among the nation's top experts in advanced MRI research techniques such as susceptibility-weighted MRI and MR spectroscopy.

and publications over the last 14 years. And CIND is a key component of the Sierra Pacific VA Mental Illness Research and Education Clinical Center.”

Weiner notes that a unique strength of CIND is the diversity and expertise of its staff. “Our research group is composed not just of medical people, but physicists and computer scientists who are largely focused on developing new techniques and improving the ability of our machines to acquire and process data. That’s made our productivity greater. We rarely repeat the work of others, thanks to our enhanced capabilities.”

Ramping up the ‘toolkit’ with mighty new magnets

Currently, CIND uses two magnets for its MRI studies: a 1.5 Tesla unit for large-scale clinical studies, and a 4 Tesla machine for research involving highly detailed brain images (Tesla is a measure of magnetic strength; the higher the number, the more powerful the magnet). Soon, that toolkit will be upgraded significantly with the arrival of a new 3 T unit for clinical studies and an advanced, state-of-the-art 7 T instrument for specialized research. Both magnets are funded by VA.

The new 3 Tesla machine “will lead to huge increases in speed, image quality, flexibility, and efficiency,” according to CIND senior scientist Norbert Schuff,

PhD. Researchers will be able to combine imaging modalities, he says, analyzing not only brain structure but perfusion (blood flow) and diffusion (water) simultaneously in one session. Finally, says Schuff, “Because there are so many other 3 T systems in use throughout the world, we will have a better chance to compare our results with data from other sites, which will improve the power of our studies.”

The 7 Tesla unit will enable highly detailed imaging of brain structure, function and physiology. “With a stronger magnet, we will have increased signal-to-noise ratio,” says Schuff. “Then there’s spatial resolution—we will be able to probe smaller brain structures in a more detailed way, and at higher contrast. The 7 T will give us two to three times the spatial resolution of the 4 T. We will go from millimeter scale to submillimeter scale.”

Gulf War Veteran and wife among many study volunteers

For their imaging studies, CIND researchers depend not only on patients who have been referred to them, but also on healthy volunteers who serve as controls. Many are Veterans. Retired Navy Captain Mike Pivonka has volunteered for two imaging studies at CIND, one on Gulf War illness and one on memory and risk of cognitive decline. Pivonka, who is without cognitive difficulties, volunteered for the Gulf War study on the thought that “if it could help people who had problems, especially Veterans who had problems after the Gulf War, that would be a good thing to do. That appealed to me.” He found the experience of being scanned “kind of relaxing. It took about 45 minutes, and I took a nap every time.” He would volunteer again, he says: “I have recommended the experience to others, including my wife, who has volunteered herself.”

At any given time, says CIND study coordinator Jennifer Hlavin, there are 10 to 15 imaging studies under way at CIND. “I really enjoy working with our Veteran volunteers,” says Hlavin. “Not only do they know their way around the VA, but they are really happy to help, and very interested in being involved. Many healthy volunteers come here because a family member or friend is affected by Alzheimer’s or another serious condition. Many are repeat volunteers, and we are happy to have them.” —

RESEARCHERS LOOK TO NATURE FOR POTENT CANCER FIGHTERS



Turmeric and green tea may not sound like the stuff of cancer treatment, but many tumor-thwarting drugs in use today derive from natural compounds

Is it possible to treat cancer with compounds made from nature? A better question may be: Is it possible to treat cancer *without* them?

Many common cancer drugs are based on natural sources, including paclitaxel (from yew leaves), daunorubicin and doxorubicin (from bacteria), and vincristine and vinblastine (from the periwinkle plant). In fact, natural products have been the basis for more than half of all drugs in use today, including penicillin (mold) and aspirin (willow bark).

According to a 2007 published review, 100 drugs were approved as anticancer agents between 1981 and 2006. Of those, 63 were natural products or based on natural products. A recent example: In January 2011, the Food and Drug Administration approved Halaven for the treatment of breast cancer. The drug is a synthetic form of a compound found in a sea sponge.

Natural products are “alive and well in cancer research,” says David J. Newman, DPhil, chief of the Natural Products Branch at the National Cancer Institute and coauthor of the review. Newman spent nearly 20 years involved in research on halichondrin B, the sea-sponge compound that eventually resulted in Halaven.

To capitalize on this noteworthy track record, VA funds several investigators studying the promise of natural products to prevent or treat cancer.

Spices as sources

Adhip Majumdar, PhD, DSc, is a professor at Wayne State University’s School of Medicine and an investigator with the John D. Dingell VA Medical Center in Detroit. Some of his work focuses on the potential of curcumin, a potent anti-inflammatory compound found in the spice turmeric, against colorectal cancer.

About half of those diagnosed with colorectal cancer will experience a recurrence—the cancer comes back after treatment appears to have destroyed it. Some research suggests that recurrence is due to cancer stem cells. Normal stem cells are like factories that can churn out multiple types of daughter cells. Cancer stem cells are similar, with a deadly exception: They produce more cancer cells.

“They are a small population of cells, and highly resistant to chemotherapy,” Majumdar says. “We want to find something that would destroy them.”

His lab may have found an answer in curcumin. It appears to stop cancer cells or cancer stem cells from growing in animal models. Moreover, an initial clinical trial found that curcumin had no side effects. “It’s very nontoxic,” he says. “You can take up to eight grams a day.”

Majumdar has also studied curcumin in combination with FOLFOX, a three-drug regimen used to treat

The science of saffron—Dr. Sushanta Banerjee and his team at the Kansas City VA Medical Center have studied crocetin, among other natural products, as a potential anti-cancer agent. Crocetin is a compound found in the spice saffron.



colorectal cancer, and with resveratrol, an antioxidant found in grape skins. Both strategies appear promising, says the researcher. Recent experiments in his lab have also yielded strong results from standard chemotherapy combined with a curcumin analog—a synthetic molecule that mimics the natural compound.

Notwithstanding Majumdar's successes, one hurdle to curcumin studies is that the body doesn't easily absorb the compound. A team with VA and the Jonsson Comprehensive Cancer Center at the University of California, Los Angeles, created an injectable form of curcumin. In October 2010, that group reported that this form of curcumin made the anticancer drug cisplatin more effective in destroying head and neck cancer cells.

Saffron and green tea also show promise

Sushanta Banerjee, PhD, director of the Cancer Research Unit at the Kansas City (Mo.) VA Medical Center and a professor at Kansas University Medical Center, is studying another spice. His group has found that crocetin, a compound in saffron, has anticancer properties. But his work highlights the fact that not all compounds will work well together. "We found that if we give crocetin with gemcitabine"—first-line chemotherapy for pancreatic cancer—"that crocetin blocks that drug's action," he says.

Banerjee's group is now looking into combining gemcitabine with other natural products. He has found a compound from the bitter orange tree that makes gemcitabine up to five times more active against pancreatic cells in the laboratory. If the results hold, adding the bitter-orange molecule to treatment could reduce the necessary doses of gemcitabine to levels that cause no toxic effects.

“If we can establish that this [combination] works and go to clinical trials, I’m optimistic that we can change the treatment profile for pancreatic cancer,” says Banerjee.

Banerjee’s group also has discovered a breast cancer gene called CCN5 that appears to be a marker for noninvasive tumors. If the gene could be activated in all breast cancer cells, it would theoretically stop them from spreading, or metastasizing. Interestingly, Banerjee’s lab discovered that a compound in green tea, epigallocatechin-3-gallate (EGCG), seems to activate CCN5.

Green tea is one of several tumor-fighting compounds that Santosh Katiyar, PhD, has studied over the past two decades. His work at the Birmingham VA and the University of Alabama has also highlighted the anti-cancer potential of grapeseed extract, silymarin from milk thistle, and honokiol, a compound derived from magnolia bark.

Katiyar also studies EGCG by itself. He has shown that applying this green tea compound to the skin in mice and humans will inhibit photo-damage caused by ultraviolet (UV) radiation. Sunlight overexposure is a

major factor in skin cancer, which affects more than one million Americans each year.

“The polyphenols in green tea have strong antioxidant and anti-inflammatory properties,” explains Katiyar. His research shows that these compounds promote DNA repair by boosting the production of interleukin-12, an immune-system protein.

His work also has shown the preventive effect of consuming green tea: Mice given green tea polyphenols in their drinking water had a lower risk of UV-induced cancerous changes in the skin, compared with mice not given the green tea polyphenols. Katiyar notes that the concentration of green tea extracts is low enough that if people drink the beverage regularly, they should garner the same benefits. “Four to five cups a day can prevent UV-induced damage at the same level as in animal models,” he says.

Though other research suggests that drinking green tea may have wide-reaching health benefits, the jury is still out. In September 2010, the FDA warned the makers of two products with green tea as an ingredient that they could



Food as medicine—Curcumin, from the spice turmeric (left), and resveratrol, an antioxidant found in grape skins, are among many nature-based compounds being studied by VA investigators and others for their cancer-fighting properties.



Loss of mother to breast cancer fuels scientist's quest for natural cures

A native of India who became a U.S. citizen in the 1990s, Santosh Katiyar, PhD, drinks two cups a day of green tea. The VA and University of Alabama researcher says people with fairer skin, who are at higher risk for skin cancer, may need to drink up to six cups per day to derive benefit. For the perfect cup of tea, he advises that people boil water, remove it from the heat, and then steep the leaves, covered, for four or five minutes. "In that time, most of the polyphenols will dissolve in the warm water. If you boil it with the leaves in it, the polyphenols may get oxidized and polymerized and reduce their activity."

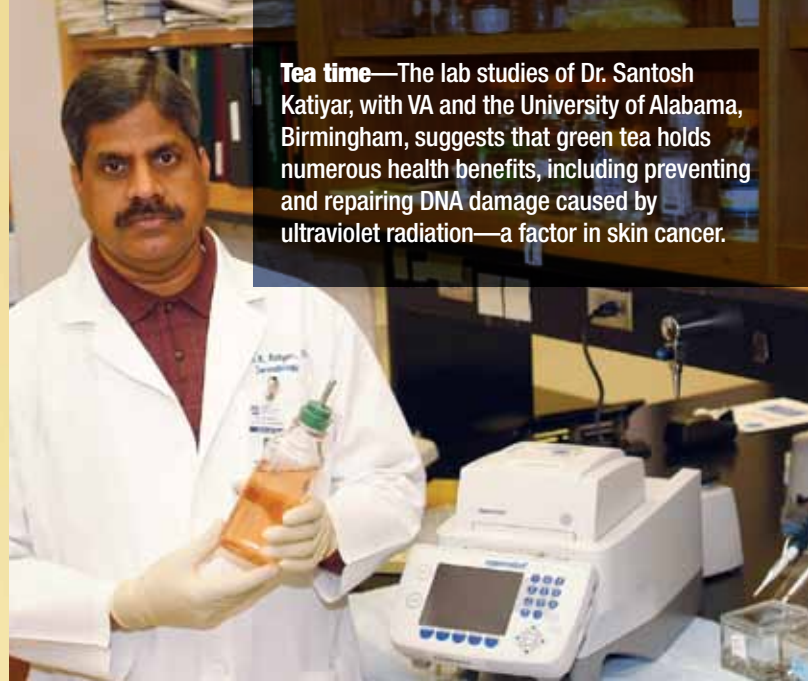
The researcher, who has been funded by VA as well as the National Center for Complimentary and Alternative Medicine and National Cancer Institute, believes military personnel may be at special risk for skin cancer, given their increased exposure to sunlight. That is part of what motivated him to join VA in 2003 and conduct research on behalf of Veterans. More than a decade earlier, his initial passion for exploring natural cancer therapies centered on quite a different population: mothers.

not make unsubstantiated claims about its health benefits.

Promoting green tea as a health beverage, however, is different than showing anticancer activity for a specific compound, which many labs—including the VA groups mentioned above—have done through numerous rigorous studies. Admittedly, the notion of a food or whole herb having therapeutic value still meets with skepticism in the scientific world.

Part of this attitude may stem from the Western idea of one drug, one effect. "One roadblock in natural products research is the mindset that we have to have a drug to affect only one small aspect, one pathway," says Majumdar. He contrasts this with the approach of Ayurvedic medicine, the traditional healing system in India, which he says "deals with a concoction of natural products. There are active ingredients but they have supporting elements. In allopathic medicine, it has to be a drug."

This debate aside, isolating the active compound in a plant or other natural substance and developing it



Tea time—The lab studies of Dr. Santosh Katiyar, with VA and the University of Alabama, Birmingham, suggests that green tea holds numerous health benefits, including preventing and repairing DNA damage caused by ultraviolet radiation—a factor in skin cancer.

"I lost my mother to breast cancer," shares Katiyar. "I had done my PhD in nutrition, and I realized that my parents had devoted a lot of time and energy to my education. Yet, I could not help my mother. So I resolved to do something to help all the other mothers who are still here. I decided I would work on cancer—how it can be prevented, particularly by dietary supplements and nutrients."

as a drug makes sense in many cases because it would be impossible for a patient to get a therapeutic dose otherwise. Similarly, coming up with synthetic analogs of these compounds in the lab—rather than attempting to harvest the natural product on a large scale—often seems to make economic and practical sense.

In any case, in the face of what continues to be one of mankind's most dreaded diseases, scientists like VA's Majumdar, Banerjee and Katiyar—and their dedicated teams—are determined to continue pursuing nature's potential cures. —



Award-winning research

To read about VA investigators recognized during National VA Research Week for their groundbreaking work, visit www.research.va.gov/researchweek.

NEUROSTEROIDS—THE ‘FORGOTTEN MOLECULES’— MAY YIELD NEW HOPE FOR ILLNESSES FROM SCHIZOPHRENIA TO PTSD

Brain substances such as pregnenolone, studied long ago by researchers, have come to the fore once more

Pilots and factory workers seemed to perk up from a substance called pregnenolone in studies of stress and fatigue done as long ago as the 1940s. But then a half-century went by with little attention paid to the compound, which occurs naturally in the brain and is believed to play an important role in stress, memory and other vital mental functions.

Pregnenolone, which belongs to a class of compounds called neurosteroids, caught the attention of Durham VA Medical Center and Duke University psychiatrist Christine Marx, MD, MA, for its auspicious preliminary research—and the dearth of follow-up clinical studies.

“I thought, ‘This can’t possibly be. My literature search must have been done incorrectly. I have to be missing something,’” says Marx, co-director for research at VA’s Mid-Atlantic Mental Illness Research, Education and Clinical Center. Seizing the opportunity to make strides in this wide-open area of study, Marx first focused on neurosteroids such as pregnenolone to treat some of the most onerous symptoms of schizophrenia. Based on promising results, her research has mushroomed into other areas that are particularly relevant for combat Veterans, including posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI).

“While I first became interested in neurosteroids for their possible relevance to schizophrenia,” Marx says, “I saw compelling characteristics that made them logical candidates for study in various psychiatric and neurological disorders.” The potential uses of these long-overlooked molecules for brain disorders are several-fold, Marx says. They could be biomarkers for various disorders, either identifying those at risk or hinting at the earliest stages of illness. They could also serve as the basis for new therapies where current treatments are falling short. Additionally, they could indicate how well a therapy is working.

Starting with schizophrenia

Currently, schizophrenia is treated mainly with antipsychotic medications. By and large, they are helpful for hallucinations and delusions, but less so for “negative” symptoms such as lack of emotion and motivation, or cognitive earmarks of the disease such as trouble with attention and memory. But a Marx-led, VA- and National Institutes of Health-supported pilot study in 21 people with schizophrenia has provided hope that neurosteroids may be effective against the negative and cognitive symptoms of this frequently disabling disease.



Healing for Heroes—Soldiers from the Fourth Infantry Division operate in Kandahar Province, Afghanistan, earlier this year. Research on neurosteroids could lead to new therapeutic tools for deployment-related conditions such as PTSD and TBI.

Neurosteroids may eventually figure in PTSD, TBI treatment

In a recent study, VA and Duke University psychiatrist-researcher Christine Marx, MD, MA, and her colleagues linked reductions in a neurosteroid called allopregnanolone with various symptoms of posttraumatic stress disorder. Allopregnanolone is a substance produced when pregnenolone—the substance Marx has been studying in schizophrenia—is metabolized. Based on the finding that allopregnanolone levels spiked substantially in those patients who received pregnenolone, researchers are hopeful that pregnenolone will prove useful as a PTSD therapy.

Marx's work on traumatic brain injury points to therapeutic possibility for neurosteroids in this condition, as well. A small study in Veterans signaled possible improvement from pregnenolone in certain PTSD symptoms common after TBI,

such as irritability, sleep problems and trouble concentrating. Marx has another, larger study in the works to clarify the substance's potential in mild TBI in particular.

In the Durham VA researcher's most recent study, levels of some neurosteroids were found to be significantly reduced in returning Veterans who had sustained a blast-related TBI, compared with those who had not. Marx believes neurosteroids may not only lessen PTSD symptoms following brain injury but also represent useful biomarkers for identifying TBI. Look at a Veteran's post-injury levels of neurosteroids, Marx theorizes, and you may be able to foretell TBI symptoms and PTSD symptoms, and perhaps predict whether neurosteroid treatment could promote recovery.

The clinical trial built on Marx's prior animal studies showing that blood levels of neurosteroids correlated with brain levels—meaning researchers could potentially get a virtual peek inside the brain by simply studying the blood. It was also based on work by other researchers showing that rodents' learning and memory improved on pregnenolone. (She notes that while pregnenolone is available over the counter, her team tested a carefully controlled and purified formulation that could be a far cry from versions sold as dietary supplements.)

In Marx's research, reported in 2009 in the journal *Neuropsychopharmacology*, people who received pregnenolone reported a significant lessening of negative symptoms, compared with the placebo group. Marx's research team—representing not only Duke and VA, but also four other universities—found clues, too, that measuring steroids in the blood may help predict the effectiveness of neurosteroid treatment for cognitive symptoms.

While stressing that additional study is needed, Marx and her coauthors concluded that “pregnenolone may represent a novel therapeutic advance for the treatment of cognitive and negative symptoms in schizophrenia.” In Marx's words, the findings are “very promising, especially given the lack of options currently for negative symptoms and cognitive symptoms in those with schizophrenia.”

The psychiatrist-researcher, who is a co-applicant on a U.S. patent for the use of neurosteroids in central nervous system disorders, is pursuing larger studies of neurosteroids for schizophrenia. She is also exploring their usefulness in other conditions such as PTSD and TBI. “All of these disorders are impacting very large numbers of today's Veterans,” she says of the spectrum of brain-associated conditions she is studying (added most recently to the list: Alzheimer's disease).

Says PTSD expert Jonathan Davidson, MD, “If we can find something to help people with the toughest-to-treat symptoms of schizophrenia, then it makes sense it would have a fighting chance of being useful in PTSD.” Davidson, a Duke University emeritus professor and collaborator on Marx's PTSD research, says about Marx herself: “She has become a world authority in the field of neurosteroids. With the integrity and precision she brings to her research, you know the work she does is of the absolute best quality.”

Will Marx's findings translate into improved patient care? She expresses guarded hope, now that the research spotlight has been refocused on these long-neglected neurosteroids: “Our studies are at a very early stage, but support is continuing to accrue for the theory that neurosteroids may in time serve as effective interventions.” —

Cautiously optimistic—Dr. Christine Marx, with VA and Duke University, is hopeful that neurosteroids—hormone-like substances produced in the brain—will emerge as an effective treatment for conditions ranging from schizophrenia and Alzheimer's disease to PTSD and TBI.



INFECTIOUS DISEASE STUDIES SEEK TO PROTECT TROOPS ABROAD

VA researchers are helping to build a new understanding of infectious diseases that are common in areas where U.S. troops are deployed

Given the threats they face each day, troops in Iraq and Afghanistan likely don't worry much about bug bites. But two diseases—leishmaniasis and malaria—can infect them through insect bites, and both diseases carry the potential for serious consequences. Another infectious disease common in areas of the world where U.S. troops are deployed, tuberculosis, is spread directly from human to human. With no effective vaccines yet available for any of these diseases, VA researchers are among those seeking better ways to prevent, diagnose and treat the illnesses. Part of the work involves studying the human immune system's reaction to these invisible dangers.

Sand fly bites: More than a nuisance

Worldwide, about 350 million people are at risk for leishmaniasis, which has multiple forms. All are caused by one-celled *Leishmania* parasites of the that are spread by sand fly bites.

U.S. troops in recent years have sustained only a handful of cases of visceral leishmaniasis—the most serious form of the disease, which is usually fatal without treatment. A far more common—and milder—form of the disease is cutaneous leishmaniasis, which produces sores around the bite. Some patients develop only an insignificant sore that disappears on its own. Others develop deeper

sores. Without treatment, the sores usually disappear over time, though they can last for months and form scars, or become chronic, non-healing lesions.

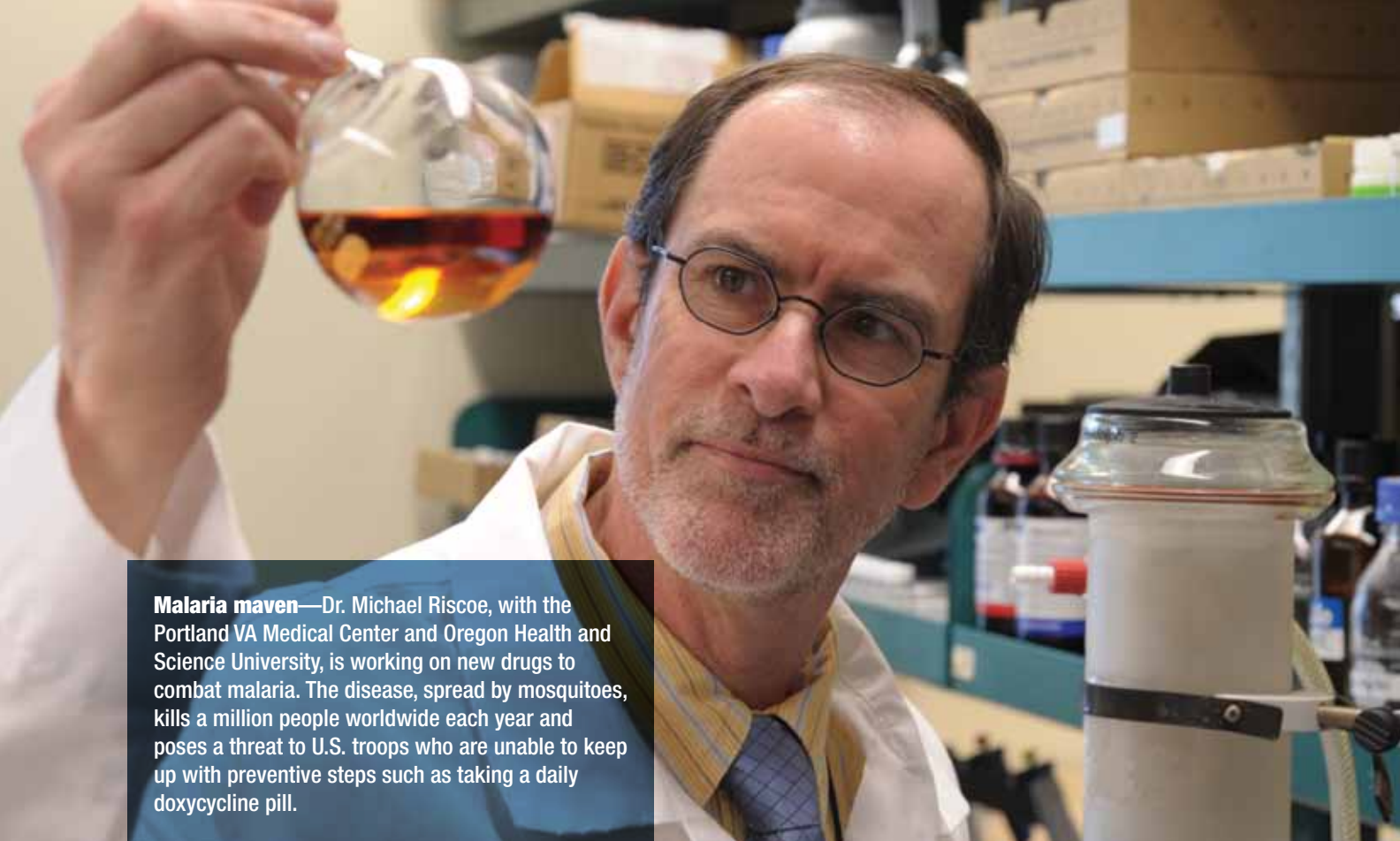
Cutaneous leishmaniasis is rare in the U.S.—cases have been found in Texas, near the border with Mexico—but it is much more common in the Middle East. Afghanistan's capital, Kabul, is a high-risk site for leishmaniasis. According to the World Health Organization, about 200,000 cases occur there each year. A 2003 study found that about three percent of Kabul residents had active leishmaniasis, and another 22 percent had scarring from past infections.

Since 2003, there have been about 3,000 documented cases of leishmaniasis in U.S. troops, with almost all of them being the cutaneous form, says Col. Alan Magill, MD, former division director of experimental therapeutics at the Walter Reed Army Institute of Research and attending physician with the infectious disease service at Walter Reed Army Medical Center.

In 2003 and 2004, nearly 1,400 U.S. personnel in Iraq and Afghanistan were diagnosed with cutaneous leishmaniasis, in the largest recorded outbreak of the disease. Magill says that now, cases stand at about 100 per year. "Protective clothing, DEET [an Army-developed chemical that today is used in most insect repellents], bed nets, they all

Immunity booster—Dr. Laurence Buxbaum, an infectious-disease specialist at the Philadelphia VA Medical Center and University of Pennsylvania, is studying how to bolster the body's immune response to the parasite that causes leishmaniasis.





Malaria maven—Dr. Michael Riscoe, with the Portland VA Medical Center and Oregon Health and Science University, is working on new drugs to combat malaria. The disease, spread by mosquitoes, kills a million people worldwide each year and poses a threat to U.S. troops who are unable to keep up with preventive steps such as taking a daily doxycycline pill.

work well as prevention,” he says. “The vast majority of cases occurred in the first year or so, when many people were sleeping out in the desert. Now it’s a more mature environment, and cases have dropped dramatically.”

But Magill estimates that for every diagnosed case of leishmaniasis, there are three to five others that are never seen because the lesions aren’t serious enough for troops to seek medical treatment, or because they do not want to leave their units.

Laurence Buxbaum, MD, PhD, a physician-scientist at the Philadelphia VA Medical Center and University of Pennsylvania, studies the body’s immune response to the *Leishmania* parasite. In general, there are two types of immunity: innate immunity, a general response by the body that’s required to fight off pathogens; and adaptive immunity, a specific response in which the body creates antibodies and mounts cell-mediated responses against an invader.

Buxbaum has discovered that the antibodies created by the adaptive immune system in response to the parasite

might be doing more harm than good. They induce the body to make a protein called interleukin-10, which in turn suppresses the cell-mediated phase of the adaptive immune response.

“IL-10 normally prevents an immune response to infection from getting out of hand,” he says. “But in leishmaniasis, you don’t want that to happen; the immune system response is dampened when you actually want it strengthened.”

He’s now studying what part of the parasite attracts the antibodies. If he can pinpoint that part, “We could block the antibody response by creating a drug that looks like the target,” he notes. “The antibody would bind to the drug instead of the parasite, no IL-10 would be produced and your body could fight off the parasite more strongly.”

A vaccine for this disease is not an immediate possibility, he says. “Vaccines work by using protective antibodies, and in leishmaniasis it’s likely that any antibody response you’d get would make things worse.”

Mary Wilson, MD, of the Iowa City VA Medical Center and the University of Iowa, studies the genetics of

outcomes to leishmaniasis infection. She and colleagues have collected information on more than 1,400 people who live where leishmaniasis is endemic. They hope to determine whether certain genes are associated with risk of infection, and whether others are linked with better or worse outcomes after infection. Wilson's research could lead to gene-based treatment or prevention strategies.

Malaria: Common to Afghanistan's river valleys

Each year, malaria strikes about 250 million people worldwide, killing 1 million. Like leishmaniasis, there are multiple types of malaria. All result from infection by *Plasmodium* parasites, carried from person to person by mosquitoes.

While there is no malaria in Iraq, both *P. vivax* and *P. falciparum* forms have infected troops in Afghanistan, says Magill. "It's seasonal there, and not urban," he says. "But there is malaria in the river valleys."

Military personnel are prescribed a daily preventive pill for malaria. "If they take it daily, they're unlikely to get malaria," according to Magill. "But like anything you have to do every day, it doesn't always happen." In addition to taking the pill, troops are advised to use DEET products and cover their skin to help ward off mosquito bites in the first place.

Magill recalls only a few severe, complicated cases of malaria since 2003, with service members being treated in Germany or at Walter Reed Army Medical Center. He's also seen cases of vivax malaria in Veterans who have been back in the U.S. for weeks or months. The vivax parasite can lie dormant in the liver for months and then cause a relapse, making it complex to diagnose.

"We've had relapsed vivax cases in which someone shows up with a bad fever, a headache," he says. Under those conditions, "We assume that if they were in Afghanistan within the year, they have malaria until proven otherwise." But most hospitals in the U.S. are not going to diagnose malaria, he says, because it's not on the radar: Basically, the disease doesn't exist here.

Battling drug-resistant malaria

Drug treatment options for malaria are few; all strains of the disease are now resistant to quinine and

chloroquine, which used to be standard treatments. Michael Riscoe, PhD, at the Portland VA Medical Center has several projects under way to find new drugs.

Supported by VA, the National Institutes of Health and the Medicines for Malaria Venture, Riscoe's team and colleagues at the University of South Florida are designing and testing drugs that will block the function of parasite mitochondria while leaving human cells untouched. Mitochondria are the energy-creation centers of cells; without them, cells die. The potential drugs, in a class called quinolones, could be tested in humans within the next two to three years, Riscoe says.

He is also working on synthesizing a "chemical cousin" of chloroquine that works without the problem of drug resistance. Riscoe says that drug, which he is very optimistic about, is three or four years from clinical testing.

One roadblock to discovering malaria drugs is that the parasite takes on several forms. After infection by a mosquito, the parasite hides in the liver, replicating for a week or two. Then a different form is released into the bloodstream, causing a high, spiking fever. The bloodstream form invades red blood cells and replicates there. A third form can be picked up by a feeding mosquito and transmitted to another person.

The chloroquine-like drug that Riscoe envisions would work against the bloodstream parasites, but not the other two forms. The quinolone drugs—which block parasite mitochondria—appear active against all three forms of the parasite. "The great hope," says Riscoe, "is that we could use these drugs to both treat and prevent malaria."




Tuberculosis test, vaccine in the works

Tuberculosis (TB) is endemic in both Iraq and Afghanistan, putting U.S. troops at risk for infection, says Suman Laal, PhD, a research career scientist with VA and an associate professor of pathology and microbiology at New York University.

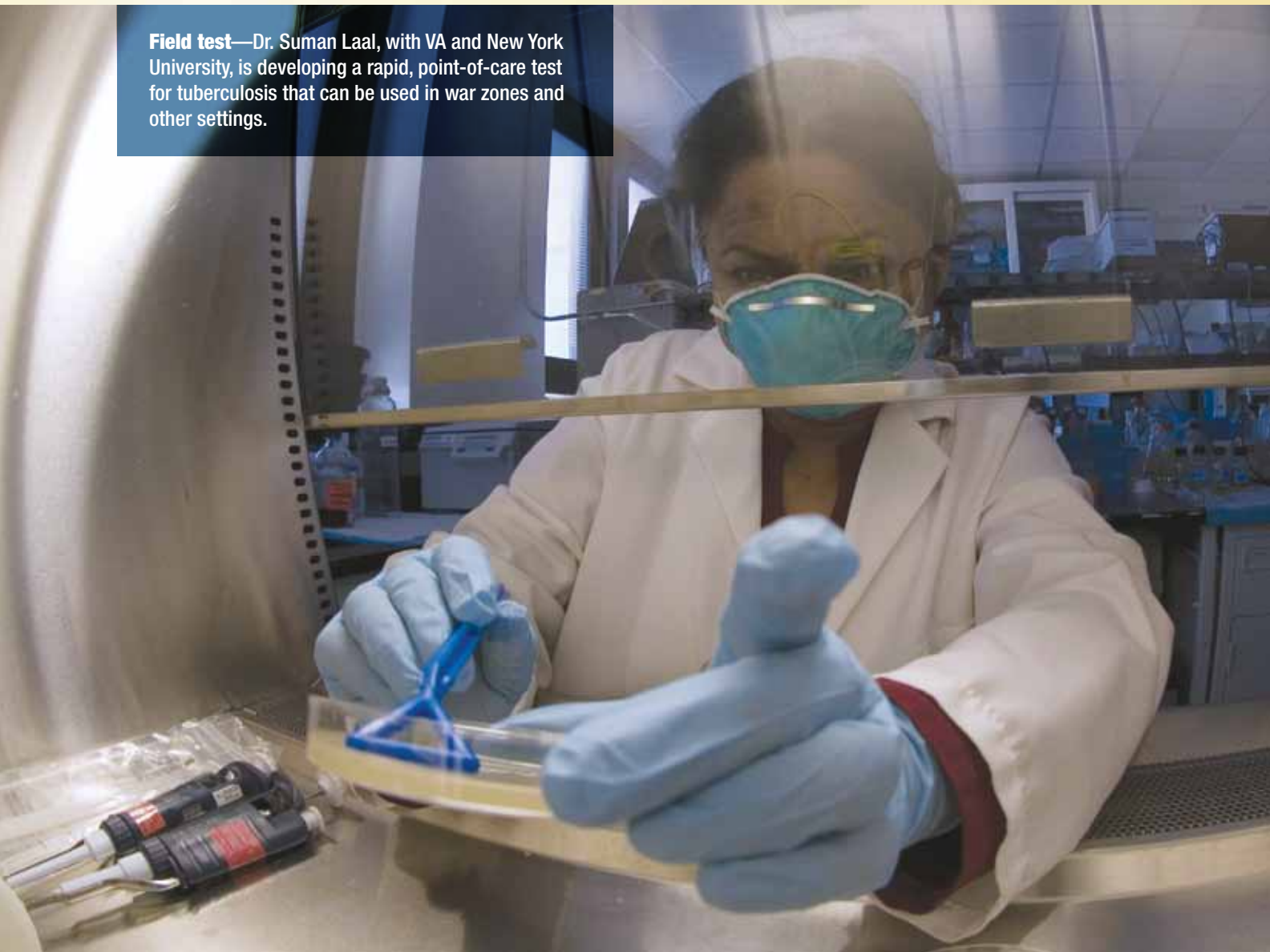
The bacterium that causes the infection—*Mycobacterium tuberculosis*—usually attacks the lung and is spread through coughing. When a TB patient coughs, droplets carrying bacteria are released into the environment. Any person who breathes in these droplets can get infected. Treatment involves multiple drugs and lasts at least six months.

M. tuberculosis grows slowly, so it can be months or years between infection and symptoms developing. So military

personnel infected in Afghanistan or Iraq may develop TB several months or years after returning stateside. There is no effective prevention for TB, and there are no simple tests to diagnose it in the field. Moreover, says Laal, the tests that are available work only after symptoms are present, not before.

Laal's research focuses on developing a rapid, point-of-care test for this disease. Her group has found several candidate antigens—bacterial proteins—that could be used in such a test. They also have identified antigens that appear to play roles in the initial infection by the bacteria. These antigens could be used to design a TB vaccine to prevent infection altogether, she says. 

Field test—Dr. Suman Laal, with VA and New York University, is developing a rapid, point-of-care test for tuberculosis that can be used in war zones and other settings.



RESHAPING PRIMARY CARE TO TARGET HOMELESSNESS AMONG VETERANS

Offering many services under one roof—including mental health care and housing support—is one of the keys to success

Stefan Kertesz, MD, MSc, today a physician-researcher at the Birmingham VA Medical Center and the University of Alabama, recalls a patient he saw at a homeless shelter in the 1990s. The man had high blood pressure and a mood disorder. Clinical guidelines and performance measures called for aggressively managing the blood pressure. But Kertesz sensed that if he were to go that route during their initial meetings, it would drive the man away and stifle their budding patient-doctor relationship.

“I felt if I pushed my agenda—treating his blood pressure—I would have to not focus on the problems that he was presenting to me,” says Kertesz. “I would have to minimize the time and energy we put into his mood issues and the concerns he was having about his ability to reside in that shelter.”

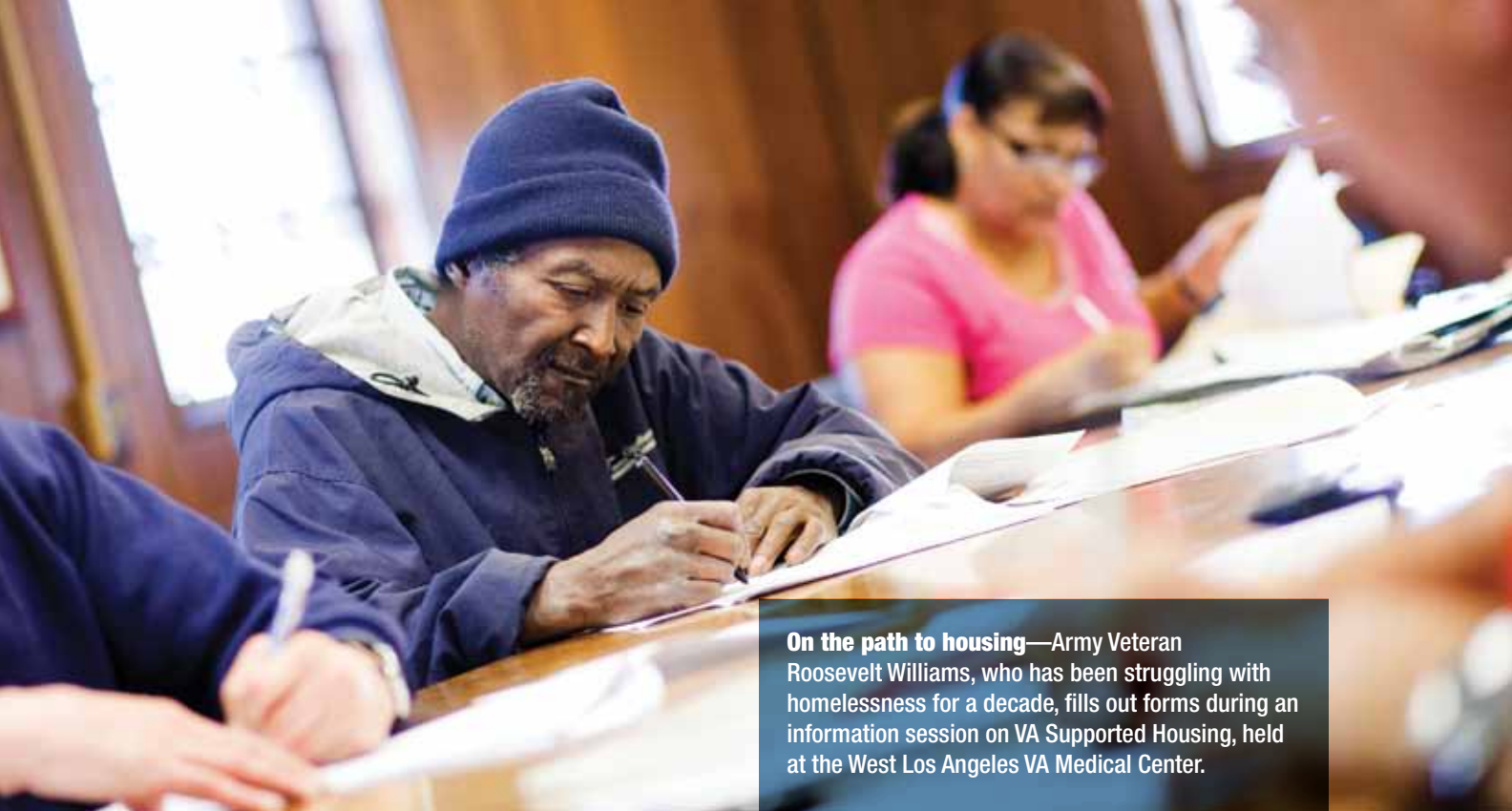
Kertesz followed his instincts: He held off on treating the high blood pressure. As a result, he was gently reproached by his medical director. Looking back, though, he doesn’t regret his action. In fact, he sees the episode as a cautionary tale about why standard approaches to primary care may not work for those who are homeless. He was inspired by the encounter—and many similar ones—to study what primary care for the homeless should look like. What do patients need and want most? What will draw them into a VA clinic,

keep them coming back, and improve their health and social outcomes? Do standard guidelines and quality measures—which often focus narrowly on managing a single disease—work for this population?

His findings—from interviews with homeless Veterans and clinicians and managers involved in their care, both in and outside VA—confirm that one critical factor is trust. Without it, he says, primary care for the homeless is a non-starter.

Kertesz: “Homeless patients are very experienced with stigma, and they are accustomed to finding that doctors, social workers and other authority figures tend to discount their concerns and agenda in favor of what the expert clinician judges to be the problem that merits attention. This fosters distrust. We stand a better chance of achieving our clinical goals over the long term if we can first establish a durable and sustainable relationship.”

His research has a “heavy emphasis,” he says, on enlisting patients who are homeless to help define quality. In addition to surveying homeless Veterans about their experiences with VA primary care, Kertesz plans to compare existing models within the VA system and learn which features work best.



On the path to housing—Army Veteran Roosevelt Williams, who has been struggling with homelessness for a decade, fills out forms during an information session on VA Supported Housing, held at the West Los Angeles VA Medical Center.

Lack of chronic-disease care shortens lives

As many as 400,000 Veterans experience homelessness each year. Many are coping with mental illness or substance abuse, although Robert Rosenheck, MD, who has studied homeless programs for VA for more than two decades, asserts that “homelessness is clearly a function of two things: low incomes and high rents.” Rosenheck is with Yale University and VA’s Northeast Program Evaluation Center.

VA has been a national leader in homeless programs overall since the 1980s, including efforts spanning housing, work rehabilitation, substance abuse treatment, and mental health. But the agency has been less successful at engaging homeless Veterans in primary care.

That is crucial, because chronic diseases typically managed in primary care—diabetes, hypertension, heart disease—are widespread among the homeless. And they account, in large part, for a sharp rise in mortality. Life expectancy for people living on the streets is 30 years less than for Americans on average.

The VA health system is working to brighten that picture. As of today, most VA medical centers still deliver primary care to homeless Veterans through

mainstream clinics. Veterans are usually referred from other VA homeless programs—such as one of VA’s 43 Comprehensive Homeless Centers. These programs do outreach on the street and in shelters—and even sometimes in county jails—to find Veterans who are homeless and link them with the VA services they need, including housing.

Some VA sites have added primary care providers to their mental health clinics, to speed up access to primary care. Conversely, with the changeover now under way in VA nationwide to a new model of primary care called patient-aligned care teams (PACT), standard primary care clinics will increasingly have mental health therapists and social workers on staff. This shift to a more comprehensive primary care model may hold some benefits for Veterans who are homeless, but services will still need to be tailored substantially to meet their needs. That’s the view of most experts, including Lillian Gelberg, MD, MSPH, a family physician and health services researcher who is studying how the PACT model can serve homeless Veterans.

“If people don’t have a home, and they’re coping with mental illness or substance abuse, and housing and food

instability, and they're having a lot of trauma and violence in their life, there is definitely some tailoring that needs to be done," says Gelberg, a professor with the University of California, Los Angeles, who consults for VA.

She says that in standard primary care, providers might not even know who among their patients is homeless. And those who are homeless will often not volunteer the information, because of the stigma. So a doctor, for instance, could prescribe a drug that needs refrigeration without realizing the patient doesn't have a refrigerator.

Primary care tailored to the homeless

Several VA medical centers around the country have recognized the need for tailored care and moved in this direction. The goal at these sites is to blend primary care with a full array of homeless services. Rather than having to navigate through a maze of various services at different locations on different days, Veterans can see an internist, psychologist and vocational rehabilitation counselor, for example, all in one morning. Missed appointments—a common problem with homeless patients—are minimized. Primary care becomes the hub of treatment, rather than one element to be coordinated with others.

One of the best-known examples of this approach is the Mental Health Outpatient Treatment Center on the VA campus in West Los Angeles—a city sometimes called the homeless capital of America. The center was funded by VA in 2002 as a demonstration project. An 18-month study published in 2009 by a team including Rosenheck, Gelberg and James McGuire, PhD, a social work researcher at the Los Angeles VA, showed the clinic had boosted access to primary care and curbed reliance on emergency rooms.

Today, the clinic, part of the larger Comprehensive Homeless Center at the West LA VA, has about 30 staff members. They do medical assessments for Veterans who have been living on the street or in shelters and provide primary and mental health care. They also help determine if patients are eligible for VA benefits and offer assistance with vocational rehabilitation. They can also help with placements in residential drug treatment, transitional housing or permanent housing, as appropriate. Significantly, all these services occur under one roof: one-stop service for people with multiple, complex health and social needs.

Andre Guyton, age 50, was living on the street four years ago. He needed pain medication because of a hip



Getting back on his feet—Former Marine Ray Stromoski (left), 49, is now in transitional housing in Santa Monica. During his recent visit to the West Los Angeles VA he was helped by registered nurse David Yentes.

Giving back—After living on the streets for 10 years, Army Veteran Michelle O’Neil turned her life around: She now goes to school and works as a medical support assistant with the VA Greater Los Angeles Healthcare System. She has also done outreach for Veterans struggling with homelessness. O’Neil: “My experiences here motivated me to want to help Vets on a higher level, especially female Vets.”



Greetings and gratitude—Kenny Wasson, 50, is a reception clerk in a primary care clinic at the West Los Angeles VA that tailors care to Veterans who are homeless. Wasson, who himself was homeless in 2006, says he loves his VA role: “This job was made for me. I get to help people.”



problem, and he found his way to the clinic at the West LA VA. One thing led to another, and the broad-chested Army Veteran landed a job with VA in the recycling crew. “A lot of people on the street don’t have anywhere to go and don’t know where to go,” he says. “But if you’re a Vet, this place here is the best place to help you get on your feet, if you’re serious about it.”

Another success story—one that is still in progress—is that of patient Juanita Chapman, who served in the Army in the late 1970s. Not long ago, she was sleeping in her car. Today, she is at a family shelter in North Hollywood. “I find myself moving forward,” she says. “I’ve gotten the medical attention I needed. Just having the fundamental things—sanctuary, medical attention, a plan—makes all the difference in the world in wanting to go on. Even though I would never kill myself, sometimes you just don’t want to go on. I’m so thankful. This was a lifesaver.”

Chapman adds: “I’ve been through a lot of services. This VA at West LA is a well-oiled machine. Ninety-nine percent of the time they’ve been on-point.”

Recent additions to the West LA clinic include a fast-track system to get patients to dentists, and home telehealth services for formerly homeless Veterans who now live in their own apartments. The model’s success

has inspired a similar, though not as extensive, VA clinic in nearby southern Nevada.

Gelberg, of UCLA and VA, says telehealth figures in other outreach efforts at the Los Angeles VA. As part of her group’s implementation research, social workers with the Housing and Urban Development-Veterans Affairs Supported Housing (HUD-VASH) program—a long-standing partnership between federal agencies that places homeless Veterans in their own apartments—are identifying Veterans who are eligible for home telehealth because of medical, mental health or substance abuse issues. A related effort relies on peer counselors in the Vet to Vet program (<http://vet2vetusa.org>) to help enroll and retain homeless Veterans in primary care and home telehealth, and assist them with keeping appointments and following prescribed treatments.

“This is community-oriented primary care,” says Gelberg. “We’re going out to this community of homeless Veterans and helping them access the system and stay connected. We want to identify barriers and find solutions.”

Motivating Veterans to seek care

Another program focused on linking homeless Veterans with primary care is led by physician-researcher Thomas O’Toole, MD, at the Providence VA Medical Center

in Rhode Island. Walk-ins are welcome at his clinic. Patients can see primary care doctors as well as mental health providers, social workers, and benefits and housing counselors. Referrals to VA substance abuse programs are made as necessary. “We try to have open access and sensitive care,” says O’Toole.

Part of his research is on how to motivate Veterans to visit the clinic in the first place. “They are a treatment-resistant population,” he says. “But if we can somehow increase their motivation, they will seek out care.” One approach the group has tried is sending a nurse along with a social worker to do outreach at local shelters and soup kitchens. The nurse does personalized health assessments and uses motivational interviewing to try to engage the Veterans in taking steps toward accessing medical care at the clinic.

O’Toole’s team has also studied patient outcomes. In a study published in December 2010 in the *American Journal of Public Health*, the researchers found that “tailoring primary care to homeless Veterans can decrease unnecessary emergency department use and medical admissions and improve chronic disease management.” The study involved 177 homeless Veterans who received care throughout one year at either the special clinic or a general primary care clinic. Those who received the tailored care had more favorable outcomes in terms of blood pressure, blood sugar and

cholesterol. And when they relied on the emergency room, it was more likely to be for true emergencies.


Measuring results based on health *and* housing

O’Toole, Kertesz and other experts have little doubt at this point that primary care for Veterans who are homeless works best when it’s integrated with the other homeless services that VA offers—housing, work, mental health, addiction treatment. “These are crucial pieces for the homeless, and they are obvious strengths of VA,” notes Kertesz. But how exactly all the pieces should fit together remains to be determined. The Los Angeles and Providence VA models seem fairly successful, but researchers are still working to nail down the optimal approach and replicate it across the entire VA system.

Most critical is the housing piece. O’Toole measures outcomes at his clinic based not only on how many Veterans come in for primary care, and how their health metrics change, but also on how many eventually end up with housing. “We’re trying to connect people to resources so they’re able to go, say, from an emergency shelter into per diem housing or a domiciliary. Those environments are going to be more conducive to better chronic disease management.”

Another key element, perhaps less tangible, is the attitude with which care is provided. Through his research, Kertesz is learning to craft questionnaires for homeless patients that will enable providers to gauge how well they are doing in this regard.

O’Toole echoes Kertesz on the importance of building relationships and respecting these Veterans’ concerns and needs—even when they seem to compete with medical goals per se. “Unless we spend time understanding what the patient’s priorities are and meet them halfway,” he asserts, “our agenda will be dead in the water.”

“We need to convey expectations about high quality and patient engagement—the same humanity and dignity that would be afforded any other patients. Patients who are homeless clearly respond to that.” 

Veterans and homelessness

- Roughly a third of U.S. adults who are homeless are Veterans. Some 131,000 Veterans, about 97 percent male, are estimated to be homeless on any given night.
- Many other Veterans are considered at risk for homelessness because of poverty, lack of social support, and dismal living conditions in cheap hotels or substandard or overcrowded housing.
- About 45 percent of Veterans who are homeless have mental illness, and more than 70 percent suffer from drug or alcohol abuse. There is considerable overlap between the two groups.

For more information on VA’s current programs for Veterans experiencing homelessness, visit www.va.gov/homeless.

VA-ACADEMIC PARTNERSHIP: AN HISTORICAL TIMELINE

On the following pages, a snapshot of milestones in the partnership between VA and the nation's medical schools, now celebrating its 65th anniversary

Continuing the legacy—Dr. Theresa Pape studies brain injury at the Hines (Ill.) VA Medical Center and Northwestern University. In 1946, the two sites signed the nation's first VA-academic affiliation agreement.



1946

Public Law 293 is passed by the 79th Congress and signed into law by President Harry S. Truman, establishing the Department of Medicine and Surgery within the Veterans Administration (later to become the Department of Veterans Affairs). The law allows VA to greatly expand and enhance its physician workforce, enabling it to care more effectively for millions of returning World War II Veterans. Within six months, some 4,000 physicians are recruited into the VA system.

In follow-up to Public Law 293, VA issues Policy Memorandum No. 2, providing the legal basis for affiliations between VA and the nation's medical schools and embarking upon "a program that is without precedent in the history of Federal hospitalization." The move not only improves VA care and bolsters U.S. physicians' training, but sets the stage for significant growth in VA's medical research program.

Northwestern University Medical School and the University of Illinois College of Medicine become the first medical schools to enter into partnerships with VA hospitals, followed soon after by the University of Minnesota Medical School.

1947

By early 1947, VA medical centers—which had no resident physicians in training before 1946—now had some 1,000 residents. The influx of physicians comes to play an important role in VA's ability to conduct groundbreaking studies, including large multisite clinical trials—an effort that would later evolve into VA's Cooperative Studies Program. According to one journalist at the time, "VA medicine has undergone a revolution," and the changes have "infused the whole hospital program with a spirit of modern, scientific medicine."

1951

By this year, VA researchers—most with dual VA-university appointments—are publishing more than 800 articles per year in medical journals, compared to fewer than 100 per year in the mid-1940s.

1966

Public Law 785 is enacted by the 89th Congress, establishing medical training as a formal component of VA's medical care mission and authorizing VA to enter into agreements with medical schools to share resources such as equipment, personnel and lab space. The measure is referred to by some as the "Magna Carta" of the partnership between VA and the nation's medical schools.

1972

The VA Medical School Assistance and Health Manpower Training Act expands existing medical education programs and facilities and establishes several new medical schools near existing VA hospitals. One example is East Tennessee State University's James H. Quillen College of Medicine, affiliated with the Mountain Home VA Medical Center.

1976

The Veterans Omnibus Health Care Act of 1976 is signed into law by President Gerald Ford. Among other provisions, the bill provides statutory authority for VA's research mission. The goal is to protect the VA research program from potential reductions in funding that could jeopardize VA affiliations with medical schools and adversely affect patient care and physician recruitment.



L-R: >Dr. Melina Kibbe, with the Jesse Brown VA Medical Center in Chicago and Northwestern University, reviews lab results from a study on vascular disease with research fellow Dr. Nick Tsihlis; >Dr. Dustin Tyler (right), of Case Western Reserve University and VA's Advanced Platform Technology Center in Cleveland, instructs graduate students Erik Peterson and Smruta Koppaka on a prosthetics project; >Dr. Robert Gailey, a prosthetics researcher with VA and the University of Miami, watches Army Veteran Henry Diaz as he tries out a computerized artificial knee; >A bioengineering student from the University of Washington places reflective markers on a foot model at VA's Seattle-based Center of Excellence for Limb Loss and Prosthetic Engineering; >Drs. Paul Hamilton (left) and Nathan Ravi, with the St. Louis VA Medical Center and Washington University, use a robotic "lens stretcher" they built as part of an optics project; >Dr. Leonard Egede conducts health-disparities research at the Charleston VA Medical Center and Medical University of South Carolina.

1988

Public Law 100-322 authorizes VA to establish nonprofit research institutes to facilitate the flow of non-VA funds—for example, from federal agencies such as the National Institutes of Health, or from private industry sponsors—to support VA research. Today, there are 82 such institutes. The largest is NCIRE-The Veterans Health Research Institute, supporting research at the San Francisco VA Medical Center.

1990

The Friends of VA Medical Research (FOVA) is founded to advocate for appropriate funding for research and other health programs serving Veterans. Today, FOVA is a diverse coalition of more than 80 member organizations, including academic, medical and scientific societies; voluntary health and patient advocacy associations; and industry partners.

1998

The Association of American Medical Colleges holds the first meeting of what comes to be known as the Group on Research Advancement and Development (GRAND). The mission of GRAND, formalized in 2002, is to "provide a national forum for the promotion, support, development, and conduct of biomedical research in medical schools and teaching hospitals [including VA medical centers] through the exchange of information and the examination of issues critical to the research enterprise."

2006

The 60th anniversary of VA Policy Memorandum No. 2 is commemorated at the 117th annual meeting of the Association of American Medical Colleges. At the meeting, VA's Office of Academic Affiliations debuts a video titled "Still Going Strong: The History of Academic Affiliations."

2009

The Blue Ribbon Panel on VA-Medical School Affiliations, established by VA in 2006 to advise the agency on enhancing partnerships with medical schools, issues a report titled "Transforming an Historical Partnership for the 21st Century." The report recommends that "VA and its academic partners redouble their efforts to develop new knowledge through collaborative research."

2010

An Association of American Medical Colleges working group, comprising experts from VA, the National Institutes of Health, and medical schools and teaching hospitals, issues a report on information technology security and privacy in medical research. The report contains a series of recommendations, building on existing federal and VA-specific safeguards and regulations, intended to fulfill the group's charge to "examine and develop standard practices and processes that assure data security, yet allow appropriate use of data in research."


2011

The 65th anniversary of VA Policy Memorandum No. 2 is commemorated during National VA Research Week, both at VA headquarters in Washington, DC, and at VA facilities nationwide.



THE VA RESEARCH AND DEVELOPMENT PROGRAM: IMPROVING VETERANS' LIVES THROUGH HEALTH CARE RESEARCH

VA Research — Discovery, Innovation, Advancement

 For more than 85 years, the Veterans Affairs (VA) Research and Development program has been improving the lives of Veterans and all Americans through health care discovery and innovation. ■ The VA Research program is unique because of its focus on medical issues that affect Veterans. It is part of an integrated health care system with a state-of-the-art electronic health record and has come to be viewed as a model for superior bench-to-bedside research. ■ The groundbreaking achievements of VA investigators—most of whom also provide direct patient care—have resulted in three Nobel prizes, six Lasker awards, and numerous other distinctions. ■ While realizing the advantages of an intramural program and embracing its close ties to academic affiliates, the VA Research and Development program fosters dynamic collaborations with other federal agencies, nonprofit organizations, and private industry—thus furthering the program's impact on the health of Veterans and the nation.



“By spearheading research that directly advances the medical care of Veterans, the VA Research and Development program has become an acclaimed model for conducting superior bench-to-bedside research.”

— Joel Kupersmith, MD, Chief Research and Development Officer, Veterans Health Administration



VA's Research and Development program is an essential part of our mission to provide cutting-edge health care to our nation's Veterans.

— Eric K. Shinseki, Secretary, Department of Veterans Affairs

INTRAMURAL PROGRAM, COLLABORATIVE SPIRIT: FOUR MAIN RESEARCH SERVICES WORKING TOGETHER

The VA Research program works to address the full spectrum of Veterans' health needs

BIOMEDICAL LABORATORY

Research and Development

This division conducts preclinical research to understand life processes from the molecular, genomic, and physiological level in regard to diseases affecting Veterans. It includes research on animal models and investigations of tissues, blood, or other biologic specimens from humans, but does not include studies with people.

CLINICAL SCIENCE

Research and Development

This division focuses on clinical trials and other research involving human volunteers to study new treatments, compare existing therapies, and improve clinical practice and care.

The *Cooperative Studies Program* within this division is responsible for planning and conducting VA's large multicenter clinical trials and epidemiological studies on health issues vital to our nation's Veterans.

HEALTH SERVICES

Research and Development

This division supports research to improve the delivery of health care to Veterans. Among the areas studied are quality and organization of care; patient access and outcomes; and cost-effectiveness.

The division's *Quality Enhancement Research Initiative* (QUERI) is designed to translate research findings into advancements in Veterans' care.

REHABILITATION

Research and Development

This division conducts research to discover knowledge and create innovations that restore Veterans who have become disabled due to injury or disease to their greatest possible functional capacity in their families, communities, and workplaces.

CROSS-CUTTING COMPONENTS

Other programs are cross-cutting. The *Program for Research Integrity Development and Education* (PRIDE), for example, is responsible for policy development, guidance, training, and education in relation to the protection of human research participants throughout VA. And the *Technology Transfer Program* is dedicated to translating discoveries and inventions by VA researchers into practice.

PRODUCTIVE PARTNERSHIPS

While embracing its status as an intramural program with close ties to its academic affiliates, the VA Research program also fosters and develops dynamic collaborations with other federal agencies, nonprofit organizations, and private industry. Such teamwork promotes the leveraging of resources, speeds the translation of study results into clinical practice, and maximizes the overall impact of VA Research.

RESEARCH FUNDING: VA R&D BY THE NUMBERS

An overview of the resources that fuel VA's innovative medical and rehabilitation studies

In fiscal year 2010, VA Research and Development supported more than 2,100 research projects at VA medical centers nationwide, ranging from preclinical studies to health services research to multisite clinical trials. Of VA's 153 medical centers, 116 have the capacity to conduct research. VA's vibrant nationwide community of bright, talented investigators publishes some 7,500 articles each year in the medical and scientific literature. VA researchers are frequent contributors to leading journals such as the *New England Journal of Medicine*, the *Journal of the American Medical Association*, and *Science*.

VA funding for research can take several forms:

- Investigator-initiated research (Merit Review)
- Mentored research (Career Development)
- Large-scale, multisite clinical trials (Cooperative Studies Program)
- Centers of Excellence
- Service-directed research (*sponsored by one of the four services that make up VA Research; see page 29*)

VA Research is an intramural program, meaning that only VA employees can conduct research under VA's auspices. Typically, though, VA researchers collaborate with academic colleagues and others outside VA.

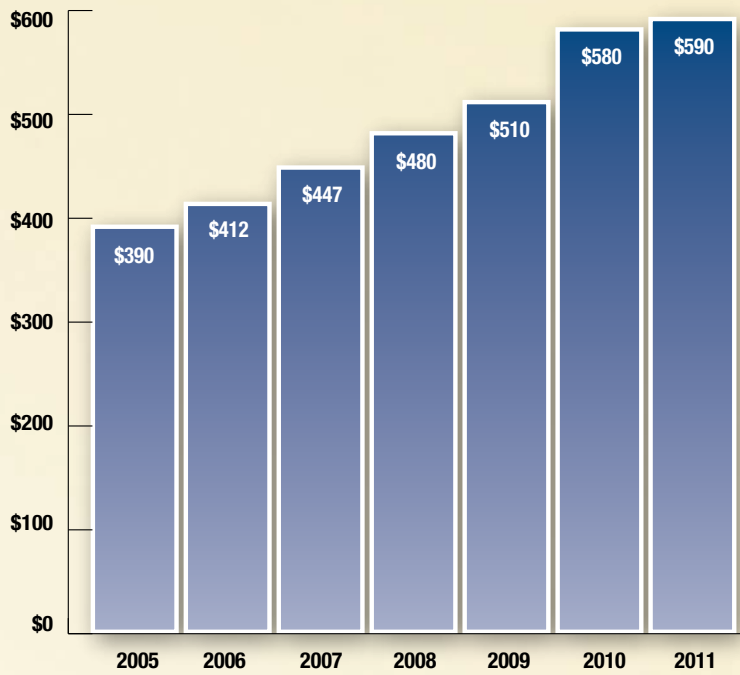
Investigators must compete for funding. They submit

proposals, which are then peer-reviewed. Only the most meritorious projects are funded. To meet the needs of the entire Veteran population, VA Research invests in a balanced portfolio of studies.

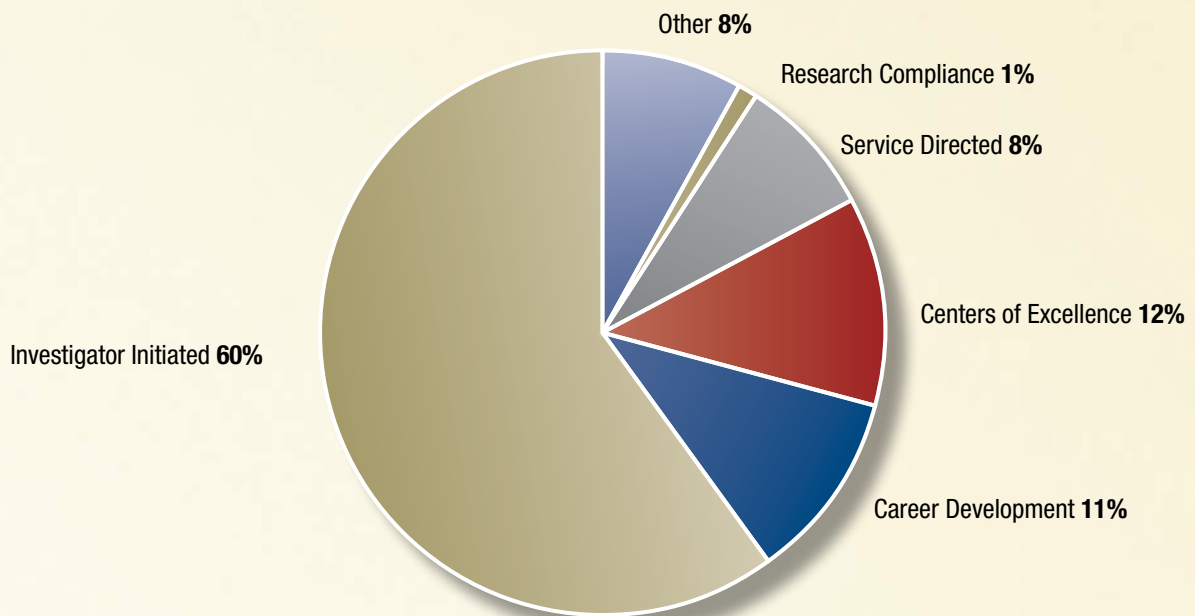
The congressional appropriation for VA Research for fiscal year 2011 is \$590 million. VA studies are also supported in part by VA medical care dollars, as well as funding from non-VA sources, such as other federal agencies, nonprofit associations and industry partners. In fact, VA researchers are expected to leverage their VA funding whenever possible—that is, seek additional support for non-VA sources—to maximize the scope, quality and impact of their research and the resulting gains for Veterans. The National Institutes of Health is the most prominent source of such funding for VA investigators. Another benefit of NIH funding is that it assures the public that VA and NIH research projects are of equal quality.

Funding from industry comes mainly from drug companies and is typically administered through nonprofit corporations. In 1988, Congress passed legislation that empowered VA medical centers to establish VA-affiliated nonprofit research corporations. These entities provide flexible funding mechanisms for the administration of non-VA funds for the conduct of VA-approved research.

Congressional allocation for VA Research (in millions)



VA research funds spent in fiscal year 2010



VETS HELPING VETS: PEER SUPPORT PROVES POPULAR AND EFFECTIVE FOR THOSE COPING WITH CHRONIC DISEASE

For illnesses such as diabetes and hypertension, peer support can be just what the doctor ordered

In the Milwaukee area, members of Veterans of Foreign Wars posts volunteered as peer health leaders and helped other VFW members stay on track with managing their high blood pressure.

In Philadelphia, African American Veterans with diabetes served as peer mentors to others in their community to help them keep their blood sugar in check.

In Ann Arbor, Veterans with diabetes who took part in a mutual peer support program did as well as—or even better than—Veterans who were assigned nurse care managers.

These examples, all from recent VA research, show the benefits of an approach that is gaining increasing traction nationwide among doctors and health policy experts. Peer support, for one thing, is a smart way to leverage resources in strained health care systems. The arrangement also taps into a powerful social force—the ability of peers to motivate one another—that no medical system can replicate on its own.

“Patients know a lot about living with their condition and the strategies they have developed,” says Michele Heisler, MD, MPA. “They have a lot to share with others who are also struggling.”

Heisler is a physician-investigator with the Center for Clinical Management Research at the VA Ann Arbor Healthcare System. She’s also an associate professor

at the University of Michigan’s Medical School and School of Public Health.

She observed firsthand the positive effects of peer support in a recent trial that involved 244 Veterans with diabetes. Some of the patients took part in mutual peer support, while others worked with a nurse care manager instead.

In the peer group, Veterans were trained in communication skills and asked to talk with their partners by telephone at least once a week. They were encouraged to both give and receive support, focusing on self-care areas they and their partners were working on to boost their diabetes control. They also took part in nurse-run group sessions to exchange experiences with other patients.

After six months, those on the peer program had achieved, on average, a small reduction in their blood sugar levels, compared with a slight increase in blood sugar among the nurse management group. Those in the peer group were also more likely to have started on an insulin regimen. That’s not necessarily a worse outcome, though. The researchers say peer support—especially from partners who were themselves already on insulin—may have helped Veterans overcome their resistance to an intensive therapy that was tough to adapt to but medically necessary. Those working with nurse managers may have been less able to adjust to the idea.



Peer pressure—Nurse manager Kelly Johnston of the Ann Arbor VA checks the blood pressure of Allen Shuh, who took part in a study of peer support for Veterans with diabetes.

Veterans in the peer group, not surprisingly, also reported more diabetes-specific social support. Importantly, each peer who received support also gave it, and this aspect of the interaction yielded its own benefits.

“The Veterans in our study were very motivated when they felt they were helping someone else,” says Heisler. “Our model was testing the hypothesis that a good way to activate patients was to give them some skills and encouragement to both help and be helped. Just as in education, they say that the best way to learn something is to try to teach it.”

Training is essential

Martha Mitchell Funnell, MS, RN, CDE, a colleague of Heisler’s at the University of Michigan, says peer support is an effective way to deliver tried-and-true behavioral strategies such as problem-solving and goal-setting. One challenge, though, is ensuring that peers receive proper training. Researchers still need to better understand this area, says Funnell. “Very little is known about the training required for peers to successfully implement behavioral strategies and even less is

known about the supervision needed or the qualities or qualifications that enable a person to become an effective peer partner,” she wrote in a recent review article in the journal *Family Practice*.

She, Heisler and other researchers in Ann Arbor are working toward creating and disseminating best practices to address this point. Earlier this year in the journal *Diabetes Educator*, they shared an approach they believe can be effective, even if it entails a serious commitment on the part of prospective peers. Their training program, developed over a year by a multidisciplinary team, involves 46 hours of training over 12 weeks. It covers both diabetes knowledge and communication and behavior-change skills. The training sessions are designed to be lively and interactive, featuring role plays, brainstorming and practice support groups. The materials are now available for use in similar programs at other VA medical centers.

Other work at the Ann Arbor VA is exploring the role of peer support in depression. According to Marcia Valenstein, MD, a mental health researcher at the site, “Peer support interventions have been recommended by

Flying high, even with diabetes

Until recently a pilot, and now a crew member, with the Civil Air Patrol, Glenn Cuff remembers when his military flying career was cut short because of his weight.

“I went into the Air Force the first time for six years,” he says. “When I went to re-up they said I was too fat to fly. I had gained too much weight and had unhealthy habits.”

Cuff would go on to join the Army Reserve, then the Air Force Reserve. Later, he went to work for US Airways and worked his way up through various jobs with the company, eventually going back to school and getting his wings as a commuter pilot.

Still, he struggled with health problems related to his weight—even to the point where he found himself homeless for a stretch. At his heaviest, Cuff, 5 feet 10 inches tall, weighed 365.

“Back when I got so sick because of my weight and the complications, I became homeless, even though I had a college degree and a pilot’s license, and I had owned houses and cars,” recalls the Philadelphia resident.

Through lots of hard work over several years, he managed to turn his life back around. He lost 125 pounds. Getting his diabetes under control was also part of the effort.

“When I was first diagnosed with diabetes I was in bad shape and my [hemoglobin] A1C was up near 10. My primary care physician was really mad. Getting healthy was a team effort with my doctor,

trial and error with exercise, diet and different medications.”

Helping young people to soar

Nowadays, aviation is a big part of his life, both in and outside of work. He’s proud of the search and rescue missions he takes part in for the Civil Air Patrol, and equally passionate about his service in the community. He volunteers at a middle school where he teaches young people to fly.

“We teach them navigation and other basics at the school, and use aircraft at the Northeast Philadelphia Airport jet center for their pilot training. We’re not there to push the military, but they can start as a senior airman if they complete our program.”

Cuff also volunteers at a Vet Center, the Philadelphia VA Medical Center, and a local Veterans of Foreign Wars post. He says he wants to “give back to my brother and sister Vets,” and remembers all too easily where he was a few short years ago.

“At that time I made myself a promise that if I got back on my feet I would give back and now that’s what I do every day. You never know about people’s situations. At the Vet Center, I recently helped someone who is a lawyer and another who is a registered nurse, and they’re homeless right now because of circumstances.”

The peer-mentor research at the Philadelphia VA was a natural fit for him.

“Participating in this study was great for me because I already was talking with my peers to find out how I could help them,” says Cuff. “If we start on common ground, we can help each other. I’m not there to preach to them. We really became friends.”

He recounts some of the ways in which he helped other Veterans in the study: “I told them to call me anytime. If they were at a family party and there was a peach pie on the table and they wanted to have it, they could call me and be honest about it. I’d tell them to have just a small slice of pie and next time whittle it down to a smaller slice.”

‘Sometimes, we would just talk’

Cuff says shared medically sound advice that had paid off for him. “Don’t try to stick to unreasonable diets. When a person has been eating like that for years, you cannot cut them off cold turkey.”

Reducing sugar intake was another strategy. “I’ve been sugar-free for three years. For some of these guys, if you can cut out sugar, that’s half the battle.”

Often, the conversations would extend to other areas. “Sometimes we would just talk, not just about diabetic things. I’d ask if they’ve been getting to their VA appointments.”

Though the study has ended, Cuff has no intention of closing out the relationships with the Veterans he helped. “As long as they want me to, I’ll be there for them.”



Smart choices—Glenn Cuff, who has served as a mentor to fellow minority Veterans with diabetes through a study at the Philadelphia VA Medical Center, says he tries to share practical strategies on eating that have worked for him. (See sidebar on facing page)

prestigious national task forces and incorporated into the VA Comprehensive Mental Health Strategic Plan.”

Mentors lead the way

Unlike Heisler’s diabetes study, some peer research involves mentor, not reciprocal, relationships. This form of peer support appears equally effective.

A team led by Judith Long, MD, of the Center for Health Equity Research and Promotion at the Philadelphia VA Medical Center, tested peer mentoring along with another strategy—financial incentives—to help minority Veterans manage their diabetes.

The pilot study included 118 Veterans, all of whom were struggling to control their diabetes. One group received usual care, a second received counseling from trained peer mentors, and a third became eligible for payments of up to \$200 if they succeeded in significantly lowering their hemoglobin A1C levels—a measure of blood sugar—over six months.

The peer mentors were Veterans who had overcome their own challenges in managing diabetes. After a brief training session, they earned a modest reward—\$20 per month— if they contacted the person they were counseling at least four times a month during the study.

The results, presented in February at a national VA meeting, were very favorable for peer mentoring. Financial incentives failed to show the same benefit. Long is now doing further research on the peer model used in the study.

Glenn Cuff, who took part in the Philadelphia research as a peer mentor (see sidebar), says he found the study worthwhile on several counts. “Although it’s not for everyone, peer support is an extremely beneficial supplement to the clinical experience. Additionally, the experience gave me the chance to establish friendships with other Veterans that I am still in contact with today.” —

AT THE HEART OF VA HEALTH CARE: RESEARCH EFFORT BOOSTS QUALITY IN CARDIAC CATH LABS NATIONWIDE

An innovative system for collecting and monitoring data from cath labs has helped raise VA heart care to new heights

David Taft gives new meaning to the phrase “cool under pressure.”

A Navy surgeon who volunteered to serve in Vietnam and again in the Persian Gulf and Somalia, Taft was awarded the Navy Cross for saving a Marine’s life in 1967. It was no ordinary surgery, even by military-medicine standards—the young Marine had a live rocket embedded in his leg.

Taft saw what needed to be done and cleared the operating room, except for a Navy corpsman who would stay nearby to assist. Taft carefully performed the surgery; the Marine’s leg had to be amputated, as all the nerves and blood vessels were destroyed. He then carried the limb outside, gently placing it in a hole that some troops had dug.

When he returned to the operating room to finish up with the patient, he heard a loud boom—the 2.75-inch rocket had spontaneously detonated.

Today, at 77, Taft is fighting health battles of his own, but he says he’s getting good care at the VA Puget Sound Healthcare System. In 2007, he had three stents placed in a blocked coronary

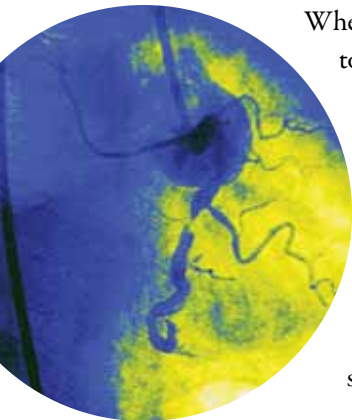
artery. Last year, another angioplasty was needed for a different artery. Earlier this year, he had a pacemaker implanted to keep his heart beating steady.

Taft is one of many thousands of Veterans each year who are benefiting from continual improvements in VA cardiac care over the past decade. Ischemic heart disease—reduced blood flow to the heart—is a top cause of hospitalization and death in the U.S. and among Veterans who use VA health care. The diagnosis affects half a million VA patients. So the area has been a prime target for quality improvement, and VA research has helped drive progress. One initiative, in particular, has focused on cardiac cath labs—the fast-paced areas in hospitals where doctors visualize the heart and blood vessels and diagnose and treat a wide range of heart problems (see sidebar).

Past studies spark cardiac initiative

A few years ago, VA got a warning signal about the quality and availability of its cardiac care—especially procedures requiring catheterization.

In 2003, an article in the *New England Journal of Medicine* reported that VA patients were less likely than Medicare patients to undergo cardiac catheterization procedures at the time of their heart attack when such procedures were called for by existing health care guidelines.





Monitoring makes for good medicine—VA cardiac catheterization labs like this one at the VA Pittsburgh Healthcare System feed data on every procedure into a national computer system that tracks quality and outcomes and identifies best practices.

A Harvard study published the following year compared VA patients and Medicare patients who had suffered heart attacks in the late 1990s. It found that VA patients traveled farther than Medicare patients to reach the hospital; that they were less likely to be admitted to a hospital capable of cardiac catheterization; and that nearly 35 percent of these men and women under VA care died within a year, compared to about 31 percent of Medicare patients.

Though some of the research was controversial because of concerns over methodology, VA nonetheless responded quickly and decisively. The agency created what became known as the Cardiac Care Initiative to boost Veterans' access to top-notch heart care. Through the initiative, new state-of-the-art cath labs were built so more VA hospitals could perform the heart procedures that Veterans needed. Performance measures were set to track how individual hospitals were doing in cardiac care. And patient case histories were studied in-depth to learn how quality could be further improved.

“This was a very ambitious and focused effort to improve cardiac care, on a very large scale, and it’s really paid off in a big way over the years,” says Stephan Fihn, MD, MPH, a Seattle-based physician with VA who is widely recognized for his research and policy leadership.

Part of the overall cardiac initiative addressed catheterization. Among other problems, VA leadership lacked an accurate picture of the types of procedures taking place in the system’s hospitals. Nor did they know the characteristics of the patients undergoing procedures—how sick they were, for example, or what other medical conditions they had. They also were uncertain as to how many patients experienced complications as a result of their cardiac procedures, and—perhaps most importantly—they didn’t know, except in individual cases, whether cardiac catheterizations had achieved the desired results.

One of the solutions VA developed was a new national repository for VA cath lab data, along with a specialized software application. The effort has involved several



Cath labs can save lives

Having a tube inserted into your heart is a scary proposition. But for millions of people, allowing a cardiologist to do so can help make a critical diagnosis, ease chest pain and even save their lives.

The procedure is known as cardiac catheterization. Most often, it's used as part of a coronary angiogram: Doctors thread a thin tube into an artery in the groin or wrist and gently move it toward the heart. They then inject dye into the tube. The dye fills the coronary arteries, which feed blood to the heart. Watching a live X-ray as the dye spreads, doctors can see where arteries are narrowed or blocked.

Coronary angiograms allow doctors to confirm suspected problems, quantify the severity of heart disease and investigate symptoms that could be related to heart disease. Angiograms are often followed by angioplasty, in which doctors use an inflatable balloon to open blocked arteries and a mesh stent to keep them open.

Several other procedures are typically performed in cath labs, such as an atherectomy—the cutting away of plaque inside arteries; pacemaker implantation and maintenance; and cardioversion, in which a shock is applied to the heart to re-establish a normal beat.

VA offices. Among those spearheading the project have been Fihn and two other physician-researchers with expertise in heart disease: John Rumsfeld, MD, PhD, of the Denver VA Medical Center; and Robert Jesse, MD, PhD, previously with VA Patient Care Services in Washington, DC, and now the agency's principal deputy under secretary for health.

The project, called CART-CL (Clinical Assessment Reporting and Tracking System for Cath Labs), was launched in Denver in 2005 as a joint effort between VA's Quality Enhancement Research Initiative (QUERI) program and the agency's Office of Patient Care Services. It then spread to other sites. Today, CART-CL collects data from all 77 VA cath labs nationwide and has become a model for using data to improve clinical performance.

Software generates reports for electronic medical record

Among other features, CART-CL enables standardized data capture and reporting across all VA cath labs. Every lab provides the same kind of documentation on all cardiac procedures, including information about the health of patients before and after the procedures. The software automatically generates reports that show up in patients' electronic medical records.

Standardizing the data enables VA to make good comparisons of results among cath labs throughout the nation. Those with the highest levels of quality are asked to share their best practices with other VA hospitals; those who rank lowest are reviewed to ensure that they are performing their procedures correctly, or to see if there are problems that can be identified and corrected. VA now also compares its results with non-VA cath labs throughout the nation, using standards developed by the American College of Cardiology's National Cardiovascular Data Registry.

"CART-CL has already had a positive impact on the care of Veterans with heart disease," says Rumsfeld, who oversees the effort and also serves as VA's national program director for cardiology. "We expect this to continue to grow as we use CART to further enhance the quality of care and patient safety for Veterans undergoing cardiac procedures."

Another example of the benefits that CART-CL offers patients and VA cardiologists: Reports of adverse events are shared immediately throughout the VA system, and trained cardiologists at other VA facilities conduct "peer reviews" to determine whether the problem could have been avoided, and, if so, how.

Also, unexpected equipment problems that take place during cath lab procedures are quickly reported to the Food and Drug Administration. The FDA looks for trends to see if there are safety problems that warrant warnings to physicians or even equipment recalls.

Today, the CART-CL database includes more than 200,000 procedures performed at VA cath labs on more than 100,000 Veterans. Among the research projects currently under way using the data is an evaluation of the short-and long-term value of coronary angioplasty, which

Vein pursuits—In cath labs, doctors can watch live X-rays to see where blood vessels are narrowed or blocked.



cardiologists call percutaneous coronary intervention, or PCI. VA researchers are also studying how the radiation from fluoroscopy use (which allows for imaging during catheterization) varies among procedures and across sites, with the goal of improving patient safety.

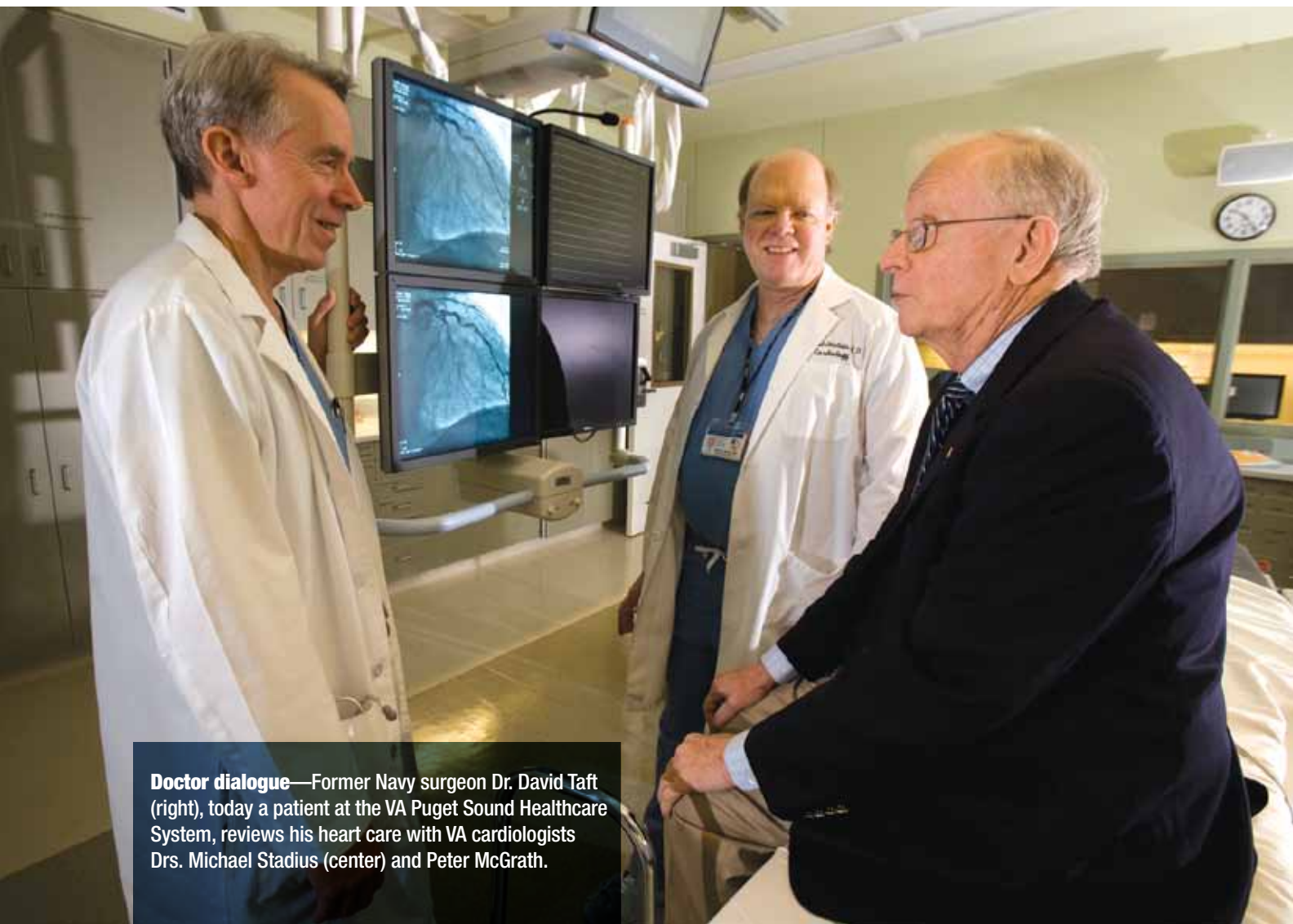
In Denver, a group led by Rumsfeld is testing a new aspect of the CART program that notifies doctors, in real time, whether patients are picking up their clopidogrel prescriptions after a PCI procedure. Clopidogrel (sold as Plavix) is a medication used to prevent blood clots in patients with heart disease; those who have had stents implanted must take it for up to one year, or their risk of an adverse cardiac event increases sharply.

Rumsfeld is also working, along with other VA researchers, on a new database, called CART-CPR, that

will document what happens to patients who go into cardiac arrest while in the hospital and are resuscitated using CPR, or cardiopulmonary resuscitation. They are also working to expand CART to capture the implantation of pacemakers and defibrillators. Both these procedures are used to help control abnormal heart rhythms.

The efforts make good sense to VA patient David Taft, who knows a thing or two about heart care. In fact—gutsy military surgeon that he is—he’s stayed awake during both his stent procedures, watching the catheter work its way up to his heart on the large monitor in the cath lab, chatting with the cardiologist doing the procedure.

“I’ve done a lot of heart surgery myself, both in training and afterwards, and I know my way around,” he says. “I will tell you, they do a great job here.” —



Doctor dialogue—Former Navy surgeon Dr. David Taft (right), today a patient at the VA Puget Sound Healthcare System, reviews his heart care with VA cardiologists Drs. Michael Stadius (center) and Peter McGrath.

MILLION VETERAN PROGRAM: VA-VETERAN PARTNERSHIP EXPLORES GENES' ROLE IN HEALTH AND DISEASE

In what is expected to be a landmark genomics effort, Veteran volunteers will help inform the course of medicine in the future

Toward answering some of the most crucial questions about genes—in particular, how they affect our health—VA Research has launched the Million Veteran Program, or MVP. The program is designed to collect genetic samples and health information from about a million Veterans who volunteer to participate, positioning VA to identify links between genes and health and to then translate this information into better medical therapies. “MVP promises to reshape the field of genomics—a sophisticated science poised to revolutionize health care for Veterans and others throughout the U.S. and around the world,” says Joel Kupersmith, MD, VA’s chief research and development officer.

The promise of super-sized genomics databases

Genes influence personal traits such as our eye and hair color, intelligence and personality. They also contribute to our risk for diseases—including common conditions such as heart disease, diabetes and cancer, and much rarer diseases such as hemophilia and cystic fibrosis. The effects of genes are usually not clear-cut, as they involve complex interactions with the environment and lifestyle factors.

Building on gene-mapping efforts such as the Human Genome Project, which elucidated the basic layout of the human genetic structure, genomic researchers are now seeking new ways to prevent and treat illnesses.

They are asking questions such as: Why are some people at greater risk than others for developing an illness? Why does a therapy work well only for certain patients? Why are some patients more vulnerable to adverse side effects from a certain drug?

Predicting which drugs are going to work for a patient and which might cause harm—a field called pharmacogenomics—is a fertile area for the “first wins” in genomic medicine, according to Eric Wieben, PhD, director of the Genomics Research Center at the renowned Mayo Clinic in Minnesota. No argument from David Oslin, MD, a psychiatry researcher at the Philadelphia VA Medical Center who is studying the role genes may play in the effectiveness of a common alcohol dependence treatment (see sidebar on page 44).

The potentially huge and rich MVP database—together with the rapidly evolving technology that is used to analyze DNA—will be a precious resource for genomics research, according to experts. That’s because meaningful genomics research demands the collection and comparison of genetic samples and health data from large groups of people. Amassing this type of extensive information to support reliable conclusions is one of the major challenges facing genomics researchers today, according to the Mayo Clinic’s Wieben. “Right now,” he says, “in terms of being able to blaze the trail in



Genomics in action—At the Philadelphia VA Medical Center, Dr. David Oslin, center, is leading a study that aims to use patients’ genetic profiles to tailor their treatment for alcoholism. At the computer is nurse Trisha Stump. Read more on page 44.

genomic medicine, one of the big limitations is the lack of sufficient samples that are matched with detailed and accessible medical information.” By helping to quench this research gap, Wieben says, MVP “could speed the science of genomics into medical practice.”

Million-strong partnership

MVP stands to become one of the world’s largest databases of genetic, military exposure and health information, with up to a million Veterans expected to participate during the project’s five- to seven-year time frame. “Veterans who volunteer to participate in MVP,” says VA’s Kupersmith, “are making a crucial contribution to genomics research and, in turn, to an improved understanding of how diseases might be prevented and treated.”

Kicked off in Boston in January 2011 and launched already at several additional VA sites, MVP will

ultimately be open to participation by Veterans across the country who receive VA care. The nationwide roll-out begins this May as part of National VA Research Week. Veterans who volunteer to participate will:

- Provide a blood sample
- Complete a brief survey about health, lifestyle habits, military experience and family history
- Allow access to their medical records

The samples and information submitted will be stored in a secure VA biorepository at VA’s Boston-based Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), with strict measures in place to protect Veterans’ confidentiality. Samples and information will be labeled with a barcode so that no one can directly identify participants. Only a small number of authorized VA employees will have access to the key for the code. And those researchers who are

DNA and data—Dr. Donald Humphries processes blood samples at VA's Massachusetts Veterans Epidemiology Research and Information Center, where a large, secure biorepository and data warehouse exist to serve the Million Veteran Program.



Studying a drug that *sometimes* packs a punch

The anti-craving medication naltrexone, approved years ago to treat alcohol dependence, works very well in some patients but proves strikingly futile for others. Researchers at the Philadelphia VA Medical Center and University of Pennsylvania, led by psychiatrist David Oslin, MD, have identified a genetic change that seems to explain the night-and-day differences in effectiveness.

Oslin is director of a VA Mental Illness Research, Education and Clinical Center and a University of Pennsylvania associate professor. About eight years ago, he was intrigued to observe that family history, known to be a strong factor in alcohol dependence itself, seemed to be a major factor in whether naltrexone worked or fell flat. Oslin and his colleagues conducted a preliminary study suggesting that a fairly common variation in a person's genetic code—specifically, a variation in the “mu-opioid receptor”—can predict naltrexone's effectiveness.

Following up on the study's finding of a strong link between a patient's genetic makeup and treatment response—a finding confirmed by another research group—Oslin's team is now in the midst of a carefully controlled study of the drug. The researchers are about halfway to recruiting the 200 to 250 desired participants. They will compare responses in those with and without the genetic variation to naltrexone or placebo.

Improving the success of treatment is crucial in alcohol dependence, which by Oslin's description is “a very tough disorder” that may be successfully treated in just 50 percent of patients under the best therapeutic circumstances. Previous studies point to the possibility of an 80- to 85-percent response to naltrexone in those with the identified gene mutation. “If this pans out, it's probably one of the most exciting things in the addiction field in a long time,” Oslin notes.

Ultimately, a simple and inexpensive genetic test may be available to identify those most likely to benefit from naltrexone and others who might respond better to an alternative alcoholism therapy. And the naltrexone studies are the “tip of the iceberg,” according to Oslin, in terms of genomics' potential to improve treatment. “Many examples are likely to arise where a simple genetic test will help drive treatment choices,” he says. “The better we understand the disease process, including a condition's genetic components, the better we can treat the disease.”



Breathing easy—A breath alcohol test, given here by nurse Trisha Stump, is part of the clinical exam for volunteers who are taking part in a VA study on naltrexone, a long-standing treatment for alcoholism. Researchers are testing whether a certain genetic variation affects how patients respond to the drug.

approved to analyze samples and data will not receive any Veteran's name, address, date of birth or Social Security number.

Veterans' genetic results, along with additional health information that Veterans provide, will be linked to their VA medical records. These state-of-the-art electronic health records, with the potential to include genetic information, will allow researchers to tap into abundantly detailed medical histories, some of them spanning decades. Importantly, while researchers will be able to make associations between genes and health conditions, all the information will be “de-identified” to protect the identity of individual Veterans.

Pursuing customized care


With the fast-growing focus on genomics research by VA and other top research institutions, experts

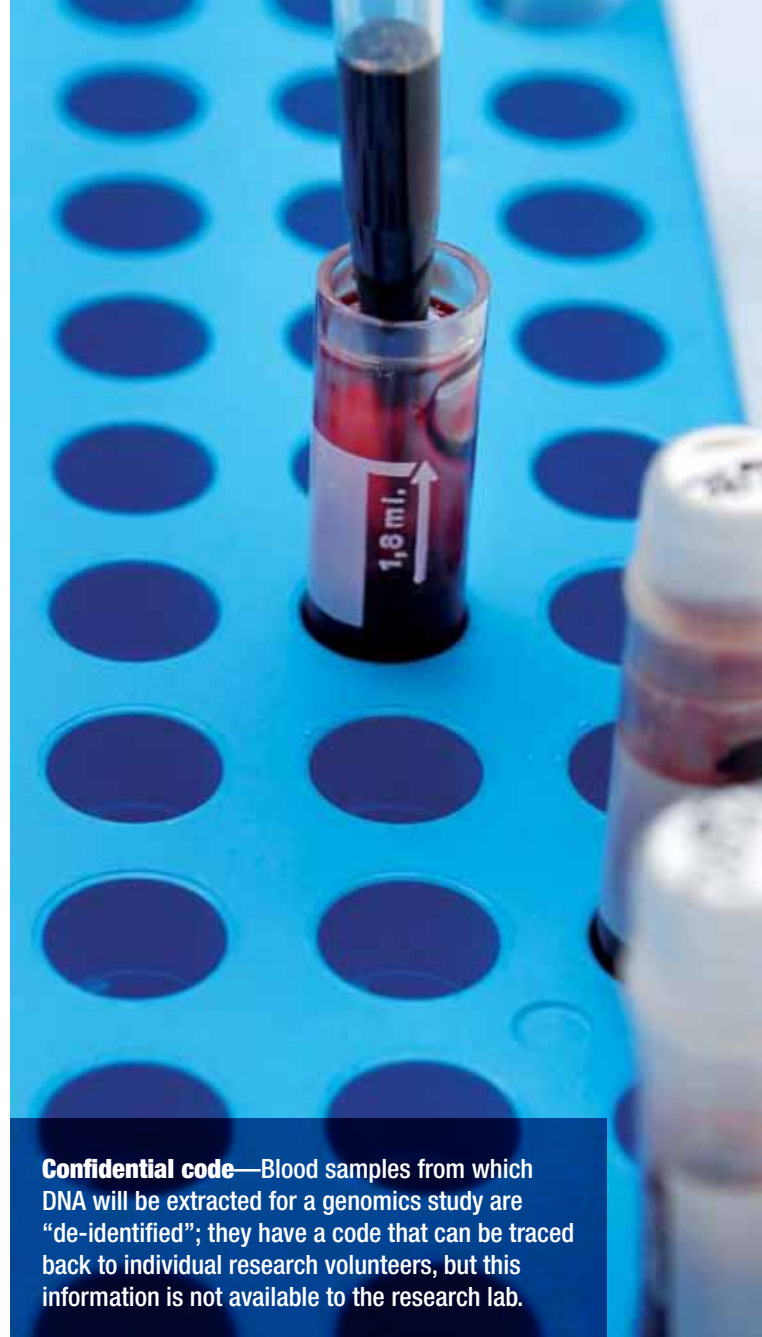
predict that today's one-size-fits-all treatments will gradually be phased out in favor of treatment strategies customized for each person's individual health profile. In Kupersmith's words, "Genomics provides additional information that can be used together by health professionals and their patients to determine the best care, moving one step closer to personalized health care."

Genomics is already being applied to individualize treatments in some cases. For example, a genetic test is sometimes used to help predict a patient's response to the anticlotting drug warfarin and suggest an appropriate dose. And several cancer treatments take advantage of genetic testing. Further broadening of gene-based personalized medicine will come about as researchers learn more about the genes in our genome and the roles they play in our bodies.

Kupersmith believes that within the next few years, researchers may pinpoint many of those genes that are keys to better health.

Wieben, too, is optimistic. "Genomics is a slow process," he acknowledges, "which makes any attempt to look into a crystal ball and set a precise date for routine use in medicine a fuzzy process." But, he emphasizes, "I'm really excited even about the near future, with the first major inroads already being made to bring genomics to medical practice."

More information about MVP is available by visiting www.research.va.gov/mvp. 



Confidential code—Blood samples from which DNA will be extracted for a genomics study are "de-identified"; they have a code that can be traced back to individual research volunteers, but this information is not available to the research lab.



Mini-glossary of genomics terms

DNA	The basic molecule that makes up genes.
Gene	A length of DNA that codes for a protein and helps control a specific hereditary trait, such as hair color or disease risk.
Genome	All the DNA contained in a person or other organism.
Genomics	The study of genes and their functions. (Genetics, on the other hand, is the study of how traits are inherited.)

MAKING THE MOST OF ELECTRONIC HEALTH RECORDS

A consortium of several VA medical centers and universities is exploring new technology to squeeze more value out of electronic records for research and quality improvement

In early 2009, President Barack Obama called for all medical records in the U.S. to be electronic within five years, in an effort to save dollars and lives. His predecessor, President George W. Bush, had set similar goals.

VA is ahead of the game. Since the late 1990s, VA hospitals, clinics and other care sites nationwide have been linked by an electronic records system. A doctor seeing a Veteran in Louisiana, say, can easily find notes, X-rays and lab results from the patient's previous VA visits in New York, Alaska or anywhere else, for that matter. Electronic records at individual VA locations go back even farther, at least to the 1980s.

Very few other health systems can make those claims. A study published in the *New England Journal of Medicine* in 2009 found that fewer than 2 percent of U.S. hospitals had a comprehensive electronic records system.

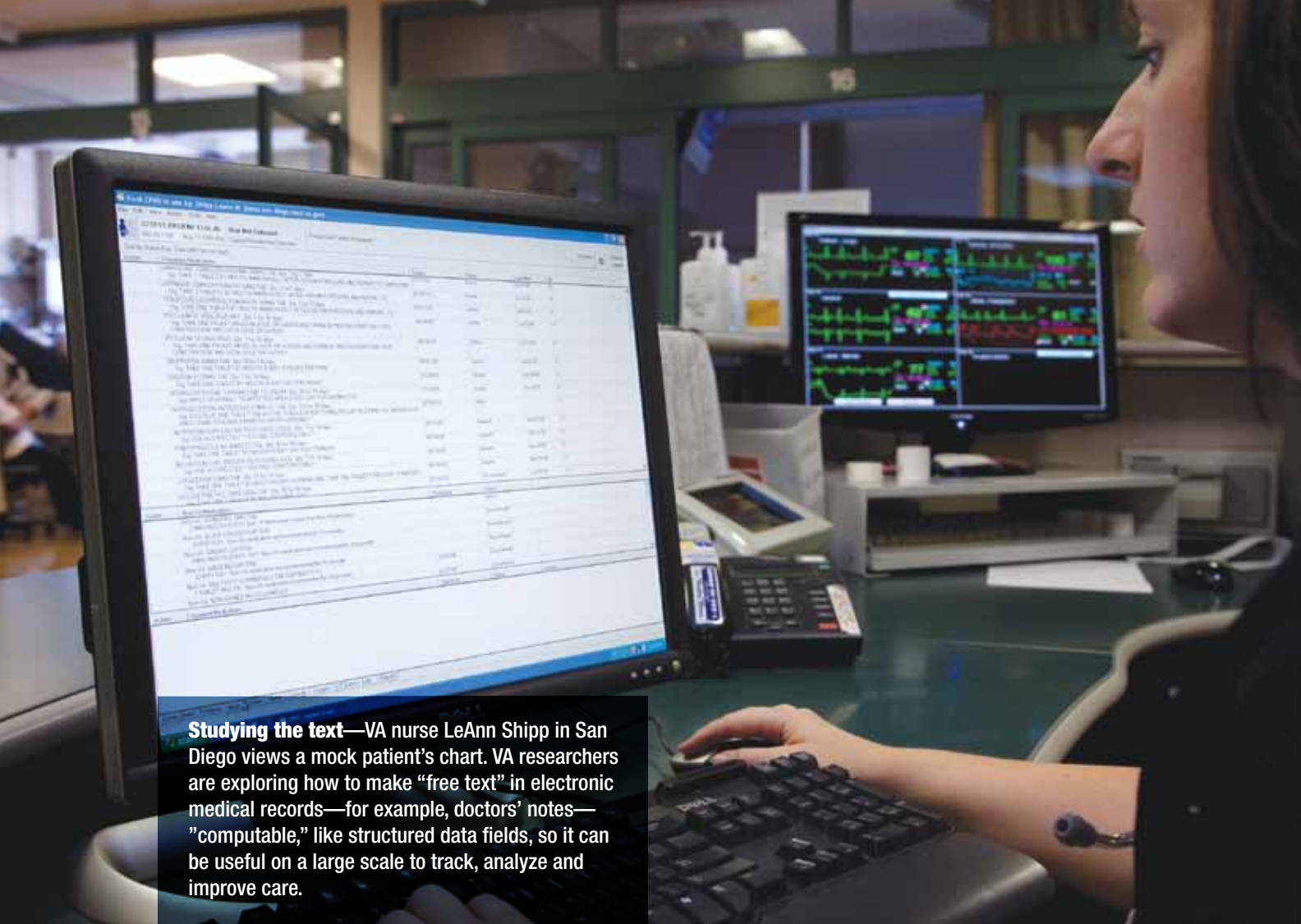
Yet, even VA's state-of-the-art system has drawbacks. Much of the data in the electronic health record is free text—for example, notes typed in by doctors, nurses or therapists. This non-structured information has value in individual patient care, but it can't easily be analyzed on a large scale—from thousands of records—for clinical research, decision-making or quality improvement.

To address this gap, VA has launched the Consortium for Healthcare Informatics Research (CHIR). The project aims to squeeze more value out of VA's electronic health records for researchers, clinicians, managers—and, ultimately, Veterans.

Changing free text into structured data

CHIR lead investigator Matthew Samore, MD, says: "If you can convert narrative text into structured data, you can improve your measurement of quality, improve surveillance of infectious diseases and adverse drug events, create new decision-support systems, and help clinicians improve documentation of problems in the medical record. There are a huge number of applications." Samore is a clinician and epidemiologist at the Salt Lake City VA Medical Center.

Besides his Utah group, CHIR involves research teams at the VA medical centers in Portland, Palo Alto, Indianapolis, Nashville, Tampa, West Haven, Boston and Pittsburgh. The universities affiliated with each of these VA sites serve as research partners. The brain power being poured into the project represents an eclectic mix of specialties, spanning medical research and computer science: clinical epidemiology, health services research, applied informatics, knowledge representation, machine learning, natural language processing.



Studying the text—VA nurse LeAnn Shipp in San Diego views a mock patient's chart. VA researchers are exploring how to make “free text” in electronic medical records—for example, doctors' notes—“computable,” like structured data fields, so it can be useful on a large scale to track, analyze and improve care.

Aspects of natural language processing, or NLP, can be seen at work in products we use every day—search engines such as Google, for example. These applications recognize the combinations of words we type in—even when the grammar and syntax are garbled—and make sense of them.

VA's electronic records were designed to give doctors ample space to use free text to document patient care. Using structured data alone—for example, checkboxes or pull-down menus—wouldn't achieve the same thing. Because free text is likely to endure in the nation's medical records, learning how to make the best use of it is an important goal.

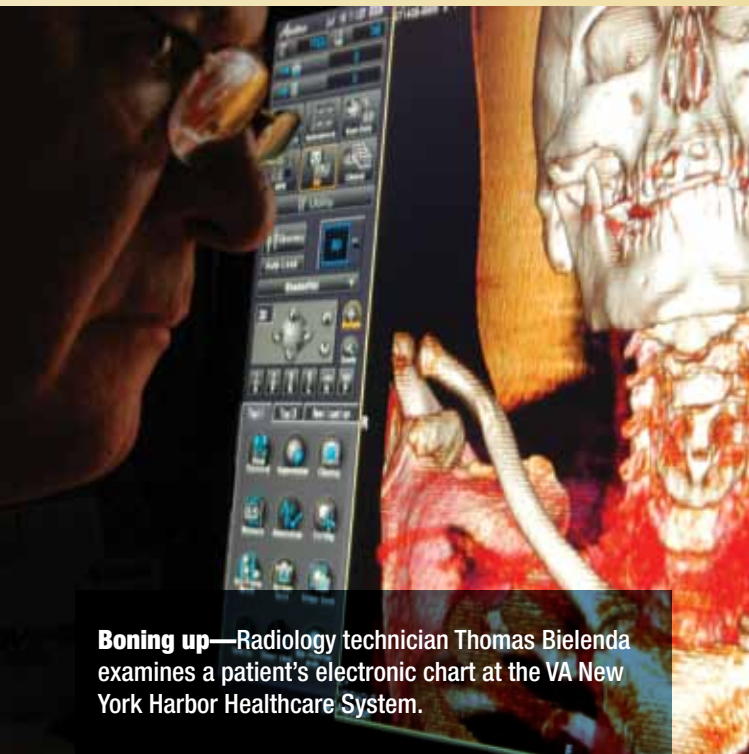
“There's a real limitation to asking clinicians to input only structured data when they are evaluating patients, recording those evaluations, describing what's happening with the patient, documenting

their decisions,” says Samore. “There's a richness to free text, a communication benefit. It allows people to express themselves.”

Merry Ward, PhD, who is overseeing CHIR for VA's Office of Research and Development, agrees. “That narrative is very important for health care providers. Radio buttons, pull-downs, yes-no and other forced choices can only go so far in describing the patient's condition. It's much more complex than that.”

[Project will empower health researchers, improve care](#)

Samore offers an example of how CHIR will expand research: Doctors often enter free-text notes about why they are prescribing certain drugs or how patients are responding. The only way for researchers to study the notes would be to manually review each chart. In studies involving thousands of charts, this would



Boning up—Radiology technician Thomas Bielenda examines a patient's electronic chart at the VA New York Harbor Healthcare System.

VA's electronic medical record

VA's electronic medical record system is often referred to as the Computerized Patient Record System, or CPRS. Actually, CPRS is a Windows interface to the umbrella system known as VISTA (Veterans Health Information Systems and Technology Architecture), which contains more than 100 clinical, financial and administrative programs.

Through VISTA, providers can securely access patient information at any VA care site nationwide. They can update a patient's history, place orders, review test results, and view X-rays and other images.

As of the end of 2009, VISTA contained:

- 1.3 billion text-based clinical documents, such as progress notes or discharge summaries (952,000 added each workday)
- 1.4 billion images (1.7 million added each workday)
- 1.6 billion vital-sign measurements (977,000 added each workday)

take countless hours. The effort would be laborious, inefficient and probably inaccurate here and there.

With NLP, computers could scan tens of thousands of de-identified patient records, find and extract the relevant notes, and convert the information into a structured format. Researchers could use computers to analyze it in huge batches. This could reveal new insights about the drugs that would otherwise remain hidden.

According to Ward, such studies could reveal nuances—as expressed by doctors in free text—about the comparative benefits of one treatment over another. “If we can look at large numbers of patients, large amounts of data, we might be able to get a better sense of what is it about some patients that made them respond better to one treatment over another.”

The technology would also boost genomic research—studies that link patients' genetic information with their health risks, needs or outcomes. Ward says CHIR will allow the electronic medical record to be a “very powerful” tool in this regard—for example, by enabling researchers to analyze free text about clinical traits tied to certain genes.

Along with these applications, Samore says CHIR will also look at new ways to “de-identify” patient charts so researchers can access clinically relevant information without patient names or other identifiers. He says protecting Veterans' privacy is a critical, overarching goal of the project.

'Rolling up' data nationwide

While CHIR will increase the number of data fields within the electronic health record that are available for research, a related project will greatly expand the number of patient records available for any given study.

As of now, the records from each of VA's more than 1,400 care sites are gathered together only at the regional level. Most studies based on patient records use charts only from a facility-wide or region-wide sample—say, from the Southwest. Some administrative data are pulled out and made available in national databases, and VA researchers have been using these for years, but this represents only part of the data available in the actual records.



Learning environment—Nursing students Marissa Hall (left) and Jacqui Stotz from Lewis University, an affiliate of the Hines (III.) VA Medical Center, view a patient's electronic medical record.

Examples of CHIR projects: Tackling bad germs, boosting PTSD care

Within the framework of the Consortium for Healthcare Informatics Research, VA investigators have launched several projects to help advance the development of natural language processing and its clinical applications.

One study, for instance, will look at methicillin-resistant *Staphylococcus aureus*, known as MRSA. The tough-to-treat germ has long been the nemesis of infection-control experts in hospitals. It causes tens of thousands of serious infections each year. The project will aim to capture more MRSA-related information in the electronic medical record, beyond standard coded data, so surveillance and control can be improved.

A second project, on posttraumatic stress disorder, will examine whether free text in the electronic medical record can shed light on how the disorder progresses and how symptoms may vary from one patient to the next.

Other CHIR projects, of shorter duration, will look at several clinical topics that figure largely in care for heart disease, cancer and other diseases.



For the record—Nurse Tanya Woods updates an inpatient's electronic medical record at the Hines (Ill.) VA Medical Center.


That will change, thanks to an initiative called Veterans' Informatics, Information, and Computing Infrastructure. Known by the acronym VINCI, the project will “roll up” electronic medical records from VA sites nationwide into one secure, centralized data repository.

“VINCI will make all the data available for researchers in a highly secure fashion,” explains Samore. “The data will never be taken off the VINCI servers. And the tools to do natural language processing will be installed and available for use within the VINCI environment.”

Adds Ward, “Not only will the data that researchers have access to be much richer [because of the ability to analyze free text], but they’ll be able to include Veterans everywhere.”

She notes that currently, Veterans seen at medical centers with no research program are far less likely to be included in database studies by VA investigators at other sites. The new paradigm will allow for more representative sampling of Veterans nationwide.

Between CHIR and VINCI, experts expect that VA researchers will be in a position to conduct large, nationwide studies—in some cases covering decades of patients’ medical care, as documented in their electronic records—with unprecedented efficiency and precision. The end beneficiaries, notes Samore, will be Veterans.

“VA research is always tied to care of Veterans and efforts to improve care,” he says. “It’s not just research for research’s sake.” 

REACHING OUT TO ALZHEIMER'S FAMILIES: RESEARCH LEADS TO NATIONWIDE VA PROGRAM TO EASE STRESS ON CAREGIVERS

*'REACH VA,' the result of a federal-academic collaboration,
is changing lives for Veterans and their caregivers across the nation*

You deserve a break today,' goes the famous advertising slogan.

Researchers and clinicians may not call it a “break”—an “intervention” would be the more likely term—but that’s exactly what teams at VA sites nationwide are now preparing to deliver to thousands of Americans who have one of the most stressful and demanding jobs around.

The program is called REACH, short for Resources for Enhancing Alzheimer’s Caregiver Health. It’s now being implemented at VA sites nationwide, with the goal of providing much-needed support for a beleaguered caregiver population.

Reducing caregiver risk

About 80 percent of care for those with dementia is provided by family caregivers, but these devoted family members often lack the skills to manage troubling patient behaviors and their own stress. As a result, they can be at risk for depression, anxiety and other health problems. And their aging loved ones with Alzheimer’s are less likely to be able to remain at home.

The REACH effort began with two studies sponsored by the National Institute on Aging and National Institute of Nursing Research and conducted by investigators with VA and several universities. The

researchers tested a six-month intervention designed to ease caregiver stress. It included 12 individual sessions in the home and by telephone, complemented by 5 telephone support-group sessions. The focus is on education, support and skills-building.

In the REACH model, trained “interventionists” teach family caregivers how to reduce stress, solve problems and manage difficult behaviors by their family member. Role-playing and other strategies are used to develop coping skills. A caregiver notebook, written in very easy-to-understand language, covers dozens of topics, ranging from the physical care of the person with Alzheimer’s to emotional and communication issues.

“REACH VA is designed for caregivers who are highly stressed,” says Jennifer Martindale-Adams, EdD, an investigator with the Memphis VA Medical Center and the department of preventive medicine at the University of Tennessee Health Science Center. “It is easy for staff to use because it is structured, with a protocol and scripts. It meets the needs of caregivers and Veterans because it is targeted to their individual concerns through a risk appraisal.”

The material is tailored to family members based on assessments of where they need the most help. For



More in the works for caregivers

Partly as a result of the Caregivers and Veterans Omnibus Health Services Act of 2010, an increasing network of services and resources is now available for family caregivers of Veterans. Here's a sampling of what VA now provides and some of the new programs being tested:

- **Caregiver Support Coordinators**—VA medical centers nationwide have been adding social workers in this role to help coordinate services for caregivers.
- **National VA Caregiver Support Line** (1-855-260-3274)—Established in early 2011, this service offers emotional support, information and referrals. It operates Monday through Friday 8 am to 11 pm, and Saturday 10:30 am-6 pm (Eastern time).
- **Evidence-Based Caregiver Support**—REACH, featured in these pages, is one of two evidence-based programs for caregivers that VA is already putting into action nationwide. Originally for Alzheimer's caregivers, REACH is being modified to also help caregivers of Veterans with spinal cord injury, with plans to further extend it to families coping with traumatic brain injury and chronic diseases. The second effort is Spouse Battlemind. Developed by the Army as a pre-deployment intervention, the telephone-based program has been modified by VA researchers to help prepare spouses to cope with their own reintegration difficulties and thereby ease the return home for Iraq and Afghanistan Veterans.
- **Other help for dementia caregivers**—Partners in Dementia Care, recently tested in five cities, is a joint program between VA and local Alzheimer's Association chapters. Telephone calls provide health information, referrals to services and resources, emotional support, and outreach to family and friends who can help. Another program, the New York University Caregiver Intervention, is being evaluated at two VA sites. In prior studies, caregivers who received counseling and support through the program were able to delay placing their ill spouse in a nursing home by about a year and a half, compared with usual care. According to Kathy Horvath, PhD, RN, of the Bedford (Mass.) VA Medical Center, the program "is being successfully implemented in a variety of non-VA settings, but the unique features of VA are not yet addressed." She says her team will identify the best way to apply the program in VA so "Veterans and their caregivers will have access to this high-quality, evidence-based counseling and support intervention."

For more information on VA's programs for caregivers, visit

www.caregiver.va.gov.

example, some caregivers might simply need more knowledge about available resources or Alzheimer's symptoms, while others need to learn how to reframe their emotional responses.

"Risk priority assessment is the most innovative part of the program," says Linda O. Nichols, PhD, a health educator and lead investigator for REACH. "Targeting the intervention to the caregiver's needs and not just to the behavior problems of the patient helps to individualize the program and to focus on high-risk areas first." She is also with the Memphis VA and the University of Tennessee.

VA acts on positive study findings

Findings from the REACH studies showed improvements across many areas. Caregivers reported less "burden" and depression, and improved emotional well-being overall. They also reported gains in the areas of self-care and healthy behaviors, social support, and management of problem behaviors on the part of their loved ones with Alzheimer's disease. Plus, they gained an hour a day of time that was not consumed with caregiving duties.

"The intervention provided that most scarce of caregiver commodities—time," wrote Nichols and coauthors in a 2008 journal report.

"We think the biggest outcome was in the increase in perceived free time of one hour," adds Martindale-Adams. "The extra non-caregiving time could allow the caregivers to do what they wanted."

Moreover, the extra soul-nourishing hour came relatively cheap—at a cost of about \$5 per day for each caregiver, according to an analysis by the Memphis group. "We showed that you can do behavioral interventions," says Martindale-Adams. "There are a lot of people who have said they won't work due to cost."

Based on these positive results, in 2007 VA began a "translation project" called REACH VA, designed to parlay REACH into an ongoing program to help caregivers of Veterans with Alzheimer's. The first step was showing how the program could work on a wide scale in VA. The six-month intervention was delivered at 24 sites in 15 states through VA's Home Based Primary

World War II Navy Veteran Raymond Boop, of North Charleston, S.C., has Alzheimer's disease and receives round-the-clock care and supervision from his wife, Rose, or one of his five daughters, who live nearby. He also receives visits from the Home-Based Primary Care team at the Charleston VA.





Through the years—Alzheimer’s caregiver and research participant Erma Taylor, of Memphis, tended devotedly to her husband, Robert, a Korean War Veteran, until he passed away last year.

Care programs. The Memphis VA Medical Center coordinated the effort, providing training to the clinical sites, certification of staff and evaluation of the results.

By and large, the 127 caregivers who took part in REACH VA—most of them spouses of Veterans—reported improvements similar to those seen in the earlier research. Significantly, 96 percent said the intervention program should be provided by VA to all caregivers. The full results were reported earlier this year in the *Archives of Internal Medicine*.

‘Most rewarding aspect of my work with VA’

Saudia Major, PhD, a clinical psychologist with the VA Ann Arbor Healthcare System, has been involved with REACH VA since late 2008.

It’s been one of the most rewarding aspects of my work here,” she says. “When I joined the Ann Arbor VA and began making home visits, I experienced a frequent sense of sadness when I observed the caregivers. These people, often times spouses of the Veterans, appeared depressed, teary, isolated, and usually in poor physical condition due to self-neglect. I found that some caregivers would

attempt to monopolize my time during home visits, understandably due to lack of support, and I would have to spend a good bit of time redirecting them and my focus to the Veteran.

The results from REACH, she says, can often be dramatic. “It gives caregivers a sense of validation, helps them realize they are not alone, and that their needs have been heard. With this comes an increase in self-esteem and self-confidence. We see an improvement in their caregiving abilities and skills and then we observe declines in depression and stress. I’ve had a couple of caregivers tell me that that they felt that I, and the REACH VA program, saved their lives.”

Shelby Nemeth, one of the caregivers with whom Major has worked, says she feels “blessed” by the REACH program.

Her husband of 53 years, 85-year-old Lawrence, a Purple Heart Veteran of the Battle of the Bulge, has had Alzheimer’s since 2003. She had looked after him around the clock ever since.

“He has his good days and his bad days,” she says. “No, he doesn’t recognize me. But, he’s comfortable.”



Caregiving, Southern style—Robin Weidberg, daughter of Navy Veteran Raymond Boop, serves him a classic Southern lunch of fried chicken and sweet tea.

Alzheimer's caregiving at a glance

- Almost 11 million Americans provide unpaid care for a person with Alzheimer's disease or another dementia. In 2009, they provided 12.5 billion hours of unpaid care, valued at almost \$144 billion.
- In 2009, these caregivers provided, on average, nearly 22 hours of care per week. About a third have been providing help for five years or longer.
- About 60 percent of these caregivers are women.
- More than 40 percent rate the emotional stress of caregiving as high or very high, compared with 28 percent of caregivers of other older people. These caregivers are more likely than non-caregivers to report that their health is fair or poor.
- Tasks typically handled by caregivers include shopping for groceries, preparing meals and providing transportation; helping the person take medications and follow treatment recommendations; managing finances and legal affairs; supervising the person to avoid wandering and other unsafe activities; bathing, dressing, feeding and helping the person use the toilet or managing incontinence; making arrangements for medical and other care; and managing behavioral symptoms.

Source: Alzheimer's Association (www.alz.org)

When Major and her team offered to enroll Nemeth in REACH and some related respite services, at first she thought she would feel guilty about not being there all the time for her husband. Then, "I realized that my being healthy, letting go of some of that stress, was not only good for me, but it was just what Lawrence needed, for me to be strong enough to take care of him." For Nemeth, preserving her own health was no small task: A few years ago, she suffered a heart attack and underwent a quadruple bypass. She relied on her and Lawrence's children to help care for him while she recovered.

"I am so grateful to the VA for the REACH program," says Nemeth. "I would absolutely recommend it to other Veteran families."

Now, REACH VA is being rolled out on a national basis through VA's Home-Based Primary Care programs. Training has started on a wide scale this year and will continue over the next few years.

"The Home-Based Primary Care staff have been amazing in the translation," notes Nichols. "They do the work because they see a need."

The needs of other Veterans and their caregivers—outside the Alzheimer's community—will be addressed as REACH VA is modified for spinal cord injury and traumatic brain injury.

Says Nichols, "We have had wonderful support from VA in moving REACH from research to a program that will be available to caregivers around the country." —



Reflections of courage—A Naval reservist uses a mirror to check for explosive material under a vehicle at the Iraq-Kuwait border. Troops who are exposed to blasts, even from a distance, are at risk for auditory damage, among other injuries.

FOR VETERANS COPING WITH SUBTLE AUDITORY PROBLEMS, STUDIES MAY POINT TO SOLUTIONS

Researchers and clinicians with VA and the military are learning how to identify and treat cases in which the ear-brain pathway is damaged, despite normal hearing

Blast-induced injuries have been a signature of the wars in Iraq and Afghanistan. Even if the explosion doesn't directly injure through shrapnel or a concussion, the blast wave can have effects from a distance. A few milliseconds of blast exposure can cause damage equal to that of a decade of low-level noise exposure.

But blast damage doesn't always lead to hearing loss; about half of blast-exposed Veterans have normal hearing. Yet an increasing number, even those with normal hearing, are reporting problems with understanding and processing spoken information. This condition, called central auditory processing disorder, is under study by VA researchers—and colleagues in the military—who seek ways to identify affected Veterans and find treatments that could help.

Targeting diagnosis, tailoring treatment

A recent VA-funded study by investigators with the National Center for Rehabilitative Auditory Research (NCRAR) and Walter Reed Army Medical Center (WRAMC) sought ways to identify Veterans with auditory processing disorders. Researchers analyzed the usefulness of five common tests, given to 35 blast-exposed Veterans and 23 non-exposed Veterans.

Abnormal scores on two or more of the tests generally indicate a central auditory processing disorder. In the study, more than 65 percent of blast-exposed Veterans fell into this category, compared with only 20 percent of the "controls." About 40 percent of blast-exposed Veterans had abnormal results on three or more tests, compared with only 3 percent of controls.

"The results were much stronger than I anticipated, in terms of the tests' usefulness," says Frederick Gallun, PhD, who was part of the NCRAR team, based in Portland, Ore. The team was led by Marjorie Leek, PhD, and Stephen Fausti, PhD.

Blast-exposed Veterans without a diagnosis of traumatic brain injury (TBI) had similar test scores as Veterans with mild TBI. This finding underscores the subtlety of the symptoms of mild TBI, points out Gallun. "There are delicate connections between the ear and other parts of the brain, and recent studies suggest that blast exposure stretches and twists these parts of the brain, which could compromise nerve fibers."

WRAMC clinicians have begun to use some of the tests in evaluating active duty service members. Therese C. Walden, AuD, of WRAMC notes that researchers at her facility are now working on a series of studies on how auditory processing disorder affects fitness for duty.



Tuning in—Iraq Veteran Louis Lamp, who experienced auditory-processing problems as the result of his deployment, says he has benefited from a “frequency modulation” (FM) system he was fitted with as part of VA clinical trial. The system uses a microphone that transmits signals to an earpiece via radio waves.

They also hope to establish functional test protocols for auditory processing before deployment, to provide baseline information. Service members already receive a standard hearing test prior to deployment.

Testing a therapy that may help

At the NCRAR in Portland and the James Haley VA Medical Center in Tampa, another study—also funded by VA—is testing two interventions for Veterans with auditory processing problems. One, a frequency modulation (FM) system, uses radio waves to transmit signals directly from a microphone to an earpiece to make a speaker’s voice clearer, relative to other sounds. The second, a “brain-training” computer program, leads users through tasks that involve following spoken instructions or interpreting sounds.

Each of 128 Veterans in the study is randomly assigned to one of four groups. All four groups will receive educational counseling. In addition, one group will receive the FM system for eight weeks; a second group will use the computer program for the same period. A third group will receive both interventions. The researchers hope to learn which combination of these interventions will be most effective at helping these Veterans with auditory processing problems.

Problem may be more widespread than thought

Army Veteran Louis Lamp was deployed to Iraq in 2003. He helped capture Talil Airbase. “We were going through an uncleared mine field, and a couple of mines went off, but nothing within about 100 meters of me,” recalls Lamp, 29. “There were some mortars, a rocket-propelled grenade.”

During his tour, Lamp was also exposed to noise as a gunner in a Humvee, and as an occasional passenger in a Chinook helicopter and C-130 cargo plane.

When he applied to join the NCRAR/Tampa study in 2010, Lamp hadn’t realized how, or how much, he was compensating for his auditory processing problems. He was easily exhausted in social situations because he had to both listen and lip-read to understand conversations. Lamp was an accomplished and passionate violinist, but after returning from Iraq he stopped composing music and performing, except when he felt “duty-bound” to play.

“Once I realized I was compensating and why, I started watching other Veterans,” he says. “A lot of them are locked right on my face as we’re talking.



Sorting sounds—Research audiologist Anna Diedesch works with Jeremiah Oertel in the anechoic chamber at VA's National Center for Rehabilitative Auditory Research. Oertel, a former Marine, took part in a study on the effects of blasts on auditory processing.

I think this will wind up being realized as a much more common problem.”

Lamp may be right. In a recent survey, VA audiology researchers surveyed VA audiologists nationwide, asking them how often they were seeing Iraq or Afghanistan Veterans with normal or near-normal hearing but with auditory-processing problems. Of the 88 audiologists who responded, 53 percent said they saw one to three such Veterans each month. Nearly 40 percent said they saw at least four per month.

Given the absence of an established standard of care in this area, the survey also asked audiologists what they were doing to treat the problem. About one in three said they were providing patients with an FM system. A slightly lower percentage said they were offering auditory training, similar to the computer program offered in the NCRAR/Tampa study. However, 30 percent said they did not know what to do.

That’s why the NCRAR/Tampa trial is so important, says study investigator Gabrielle Saunders, PhD. “From a clinical perspective, it will be good if we can show that either intervention is beneficial. An audiologist can try

a hearing aid or some other interventions, but there’s no evidence that they work.”

Getting back to the violin

Lamp received an FM system as part of the NCRAR/Tampa study. While he has encountered some glitches with the technology, it has helped him in many ways. He finds he doesn’t need to lip-read as much, or at all, so he feels less drained in social situations. He says that his violin now sounds to him like it used to, which has boosted his confidence for playing and composing.

The system also has restored parts of the Veteran’s life that he hadn’t realized were lost.

For example, “I’d gotten used to hearing rain as a dull thudding,” he says. “I was in the airport recently and it started raining really hard. Using the FM, I was hearing a lot more, and the sounds brought back a lot of memories I hadn’t thought of for years. I thought, ‘Oh, this is cool!’

“My long-term memories are coming back in different ways because of this, and I hadn’t the faintest idea that it was even an issue.” —

RECENT ADVANCES BY VA RESEARCHERS

A sampling of important new scientific findings reported by VA investigators

For cardiac bypass, arm artery and leg vein work equally well as grafts

In a clinical trial involving 757 patients at 11 VA medical centers, coronary artery bypass surgery had similar outcomes whether doctors used the radial artery (from the forearm, wrist and hand) or the saphenous vein (from the leg) to reroute blood flow to the heart. Contrary to what many surgeons have come to believe, using the arm artery didn't result in improved patency (the graft remaining open).

Steven Goldman, MD, of the Southern Arizona VA Health Care System and the University of Arizona

Sarver Heart Center in Tucson led a team that compared the two approaches in study volunteers who were undergoing elective, first-time heart bypass surgery. The main outcome measure was graft patency at one year after the operation, confirmed by an angiogram. Other outcomes tracked in the study were graft patency after one week, and adverse events such as heart attack, stroke, repeat revascularization, and death.

The researchers found no significant difference in one-year graft patency between the two methods. Both achieved a patency rate of 89 percent. Also, there was



Solving surgery debate—A clinical trial at 11 VA sites has shed light on which blood vessel works best as a graft for rerouting blood flow to the heart in coronary artery bypass surgery.

no difference in one-week patency or in the number and types of adverse events.

Notwithstanding the new study results, the rates of radial artery grafts have been rising in the U.S. because of widespread belief among doctors that the technique improves patency, says Goldman. VA's Cooperative Studies Program, which funded the initial trial, is now supporting further research that will look at five-year outcomes—especially graft patency—among Veterans in the initial study.

(Journal of the American Medical Association, Jan. 12, 2011)

Alcohol screenings: Do they yield accurate results?

Current methods of identifying patients who have drinking problems may not be good enough, according to a VA study.

The researchers, from the VA Puget Sound Health Care System, compared results from two different methods of alcohol screening among more than 6,800 VA patients nationwide.

The patients had completed a brief, well-validated alcohol questionnaire known as the AUDIT-C in two different settings, no more than 90 days apart: once during a clinic visit, and another time as part of a mailed survey. The three-question form, which VA has used for routine screening since 2006, asks how often people have an alcoholic drink; how many drinks they have on a typical day; and how often they have six or more drinks on one occasion.

The study found that 6 in 10 of those who screened positive for alcohol misuse on the mailed survey screened negative when asked the same questions in VA outpatient clinics. In other words, some patients may have been reluctant to disclose their consumption habits when speaking face-to-face with their doctor or other health care provider, but were more open when filling out the survey at home.

As a result, suggest the researchers, “Many patients who could benefit from brief alcohol counseling are being missing by clinical screening.” They say that while VA overall has excellent rates of alcohol screening, more attention needs to be paid to the accuracy of those

screenings. One idea they recommend: Have patients complete mental health questionnaires—including those relating to alcohol or substance abuse—on paper while they wait, rather than in a conversation with the clinician. They say, also, that VA staff who conduct alcohol screenings should be educated about this potential pitfall of the process.

(Journal of General Internal Medicine, March 2011)



Review sheds more doubt on routine prostate tests

In an update to an earlier study, an international team including Dr. Timothy Wilt at the Minneapolis VA Medical Center and University of Minnesota found that routine prostate cancer screening using the PSA blood test had no impact on how many men died as a result of the disease.

The team reviewed five randomized clinical trials that together included more than 341,000 men. While three of the trials may have been methodologically flawed, according to Wilt and colleagues, an analysis of combined data from the studies found no significant difference between screened and non-screened men in mortality from prostate cancer or any cause.

Current guidelines from the American Cancer Society recommend that men discuss their individual risk factors and the option of screening with their doctors. The ACS says, “Research has not yet proven that the potential benefits of testing outweigh the harms of testing and treatment.” Similarly, the U.S. Preventive Services Task Force says there is not enough evidence to make a recommendation for men under age 75. For those older than 75, the group advises against screening. For these men, the potential benefits are typically outweighed by the risks—for example, unnecessary biopsies, which could involve infection, bleeding or

pain; and anxiety over receiving a cancer diagnosis, even though the tumor might be slow-growing and unlikely to cause any symptoms during the patient's lifetime.

Researchers in VA and elsewhere are working to resolve the question of how and when men should be screened. One idea is to test only for certain forms of PSA that can reliably indicate aggressive cancers—those that undeniably require treatment. Another approach is to clarify how certain risk factors—such as obesity—can be used along with PSA to help predict disease progression.

(British Journal of Urology, March 2011)

Genetic clues to the deadliest staph infections

Staph infections account for some 15 percent of all healthcare-related infections and can often be deadly. VA researchers in Iowa City and colleagues from several universities have discovered a genetic twist they say may provide important clues to guide prevention and treatment.

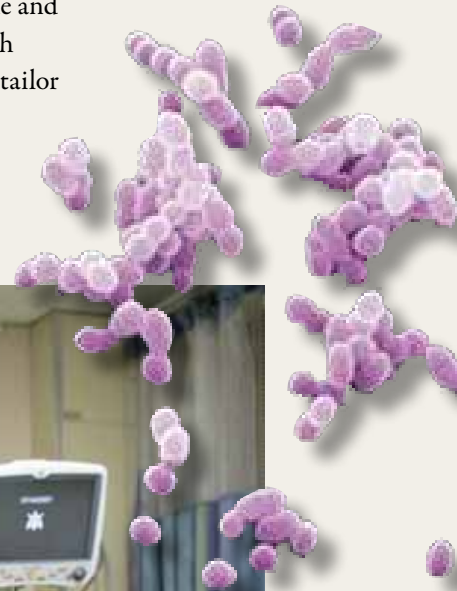
Their study, which took place at a university medical center, found higher death rates among patients infected with isolates of *Staphylococcus aureus* that contain a certain genetic defect. *S. aureus* are the nasty

bacteria that cause staph infections. The data suggest that the defect, known as accessory gene regulator (*agr*) dysfunction, previously linked to longer-lasting infections, may also be a culprit in deadlier infections. The dysfunction involves a system of genes that turn other genes on and off.

Among 814 patients whose hospital stay was complicated by staph infections, 22 percent were infected with *S. aureus* isolates that contained the genetic flaw. Overall, 18 percent of patients with the dysfunction died, compared with 12 percent who were infected with *S. aureus* without the dysfunction—about a 30-percent higher risk.

The study is the first to show a link between *agr* dysfunction and death rates among severely ill hospital patients, according to the authors. To address the issue, they recommend the use of a readily available lab test that they say may be a simple and inexpensive way to predict which patients are most at risk, and to tailor antibiotic therapy accordingly.

(Journal of Antimicrobial Agents and Chemotherapy, March 2011)



Staff against staph—Nurse Rafael Sepulveda dons rubber gloves before tending to a patient in the emergency room at the Miami VA Medical Center. Staff at VA and other health care facilities follow strict measures to curb the spread of staph germs and other pathogens.





Amazing feet—Randall Tipton, wearing the iWalk PowerFoot BIOM, gets a check-up from nurse and certified prosthetist Mark Benveniste at the Houston VA. The computerized ankle-foot prosthesis, developed in part through VA research, is now available to VA patients.

Special Forces Veteran is first in VA to receive bionic ankle

Randall Tipton, a 20-year Army Special Forces Veteran who served in Iraq and Afghanistan, recently became the first VA patient to be fitted with the iWalk PowerFoot BIOM. The computerized prosthesis, in part the product of VA research, replaces the action of the foot, Achilles tendon and calf muscle and offers a near-normal gait for amputees.

Tipton was fitted with the ankle at the Michael E. DeBakey VA Medical Center in Houston, just weeks after the device became available at Brooke Army Medical Center in San Antonio and Walter Reed Army Medical Center in Washington, DC.

The bionic ankle was invented by Hugh Herr, PhD, of the Massachusetts Institute of Technology Biomechanics Group. Herr is also with the Center for Restorative and Regenerative Medicine, a collaboration among VA, MIT and Brown University.

The ankle has been shown to reduce fatigue and improve balance. According to Herr, it also improves amputees' overall health because it leads to higher levels of physical activity.

The device has robotic features: Two microprocessors and six environmental sensors continuously evaluate and adjust ankle position. As a result, users can walk over even ground, slopes and stairs with a fluid, natural gait. They feel far less of the fatigue and back pain associated with older artificial foot models.

“We have seen a significant difference in function in this device over the other 200-plus [prosthetic] feet we have used here at the DeBakey VA,” said certified prosthetist Mark Benveniste. “It is the most improvement over conventional prosthetics in the last 20 years.”

Tipton had this to say about the device: “I feel like I have my leg back and I can do the things I used to do. It just helps out a lot. It takes the strain off my back, my hips. I don't feel as tired at the end of the day.”

(February 2011)

Face-recognition test may help in diagnosing, treating vision problems

Vision problems such as age-related macular degeneration—the leading cause of vision loss among older Americans—can mean a reduced ability to recognize faces, which is a big part of social interaction. But researchers have paid little attention in the past to learning how to measure this problem.

That's why a team of VA vision experts has created a “face discrimination” test. They say it can help quantify the impact of vision loss and track the benefits of low-vision therapy.

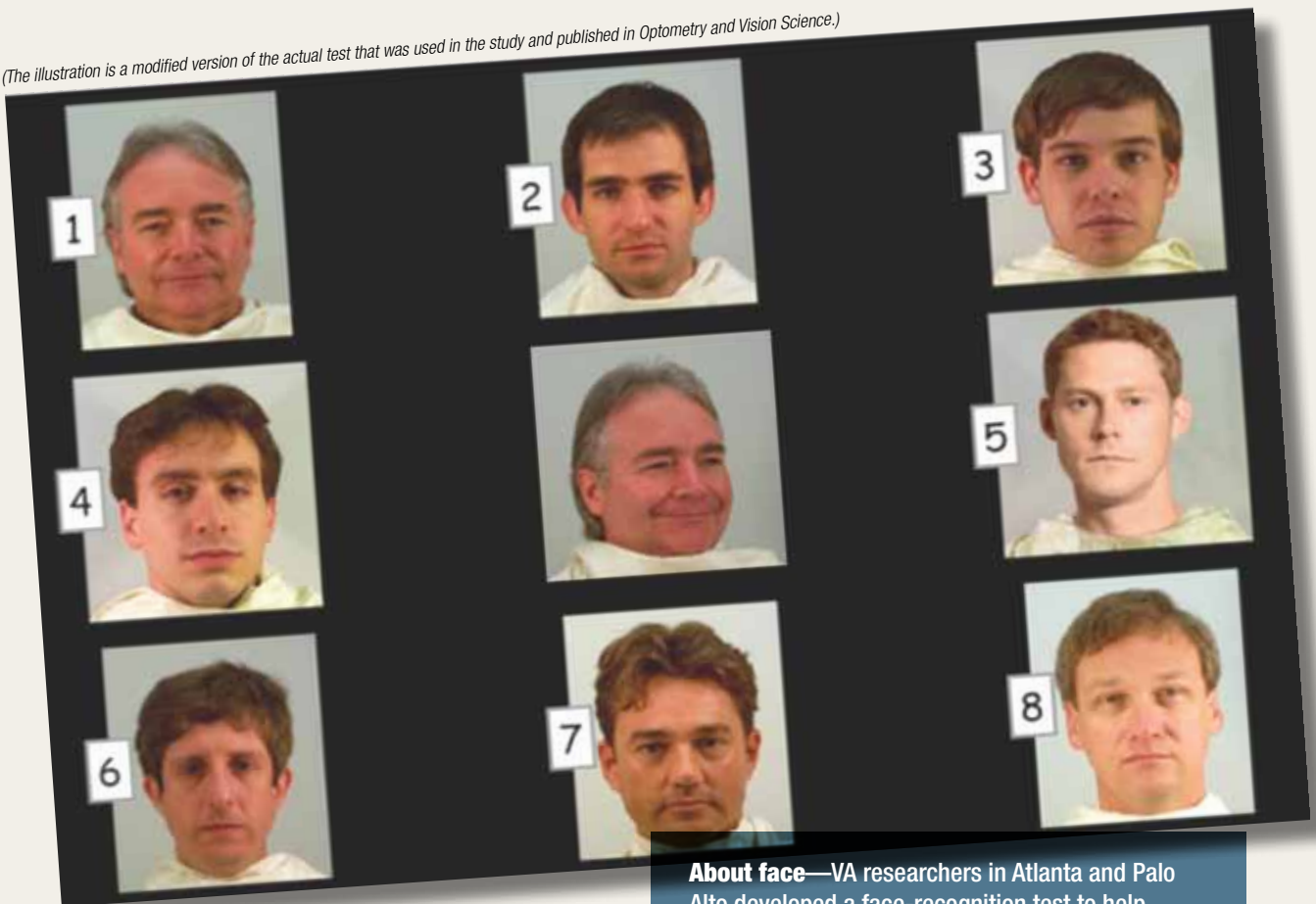
The test involves sets of color photos showing male and female faces. A person being evaluated is shown a “test” face surrounded by eight reference images. One of the reference faces is the same as the test face, although it could be shown from a different angle and with a different expression. The test-taker has to pick the reference image that matches the test image, and determine the expression of the test image—normal, smile or frown.

The researchers tried the test with older people with age-related macular degeneration in both eyes, and with younger and older healthy controls. Not surprisingly, performance was best among the young volunteers. They responded quickly and made almost no mistakes. The older controls—those without macular degeneration—had somewhat slower response times, and made some errors, mainly in identifying the expressions. Those with macular degeneration were slower and made more errors in identification than did the older controls. For all those who took part in the evaluation, visual acuity and contrast sensitivity affected performance.

The researchers say the test would be easy to reproduce across all VA sites and could be used to “quantify low vision patients’ complaints of difficulty with face perception, and to evaluate possible changes in performance with low vision rehabilitation.”

(Optometry and Vision Science, February 2011)

(The illustration is a modified version of the actual test that was used in the study and published in Optometry and Vision Science.)



About face—VA researchers in Atlanta and Palo Alto developed a face-recognition test to help assess symptoms of macular degeneration and other vision disorders.



In high-risk schizophrenia, no edge for injectable, long-acting drug

In a clinical trial led by a VA and Yale University team, Veterans with severe schizophrenia who received biweekly injections of a long-acting antipsychotic drug fared no better than those treated with standard oral drugs. Schizophrenia affects more than 2.2 million Americans and some 100,000 Veterans who use VA health care.

The study results were somewhat surprising, said lead author Robert Rosenheck, MD, a psychiatry researcher with Yale and the VA New England Mental Illness Research, Education and Clinical Center. “Some earlier studies had shown that by ensuring sustained levels of drug in the blood, long-acting injections could improve symptoms and reduce hospitalizations, relative to oral antipsychotics. In our study, though, the injectable drug showed no advantage in symptom control, quality of life or hospitalization for these high-risk patients.”

The study included 369 Veterans. All were considered high-risk because of their recent need for hospital care.

About half received injections of long-acting risperidone (sold as Risperdal Consta). The others received oral antipsychotics chosen by their psychiatrists.

After two years, roughly 4 in 10 patients in both groups had been hospitalized. The two groups also had similar symptoms and overall quality of life. Side effects known as extrapyramidal symptoms—involuntary movements or muscle stiffness—were more common in the injection group, as were headaches and soreness from the injection.

Schizophrenia can be manageable for many patients, but sticking to drug regimens is critical. Long-acting injections have been seen as a way to ensure steadier doses of medication, especially for those with more severe symptoms. The new VA study does not support that view, says Rosenheck. He says further trials with larger groups of patients could provide more conclusive evidence on the benefits and risks of the injectable drug, both for high- and lower-risk schizophrenia patients.

(New England Journal of Medicine, March 3, 2011)

On the horizon: Blood marker for cognitive decline

Low blood levels of beta-amyloid 42, a protein-like substance, were linked with the risk of significant cognitive decline within nine years in a group of nearly 1,000 older study volunteers. The research was led by Kristine Yaffe, MD, chief of geriatric psychiatry at the San Francisco VA Medical Center and a professor at the University of California, San Francisco.

Another finding was that among elders with low blood levels of beta-amyloid 42, cognitive decline was less marked in those who had higher literacy, or more education, or who lacked the APOE e4 gene known to predict a greater risk of dementia. The researchers describe this set of conditions as “cognitive reserve.”

“We show that a blood test for beta-amyloid 42 might be a good way to predict those at risk for cognitive decline,” said Yaffe. “Also, for the first time, we show that cognitive reserve—a general level of resiliency in the brain—might modify that risk in the elderly.”

Yaffe said that currently “there is no reliable method of predicting ahead of time who will experience cognitive decline and go on to develop dementia. A blood test would be a huge step forward.”

Beta-amyloid 42 has long been known to collect in the brain of patients with Alzheimer’s disease. Low levels of beta-amyloid 42 in the blood or spinal fluid, explained Yaffe, indicate high levels in the brain, “which acts as a sink for beta amyloid in Alzheimer’s disease.” Although an experimental test for beta-amyloid in cerebral spinal fluid already exists, said Yaffe, “a blood test would be far easier, less invasive and less expensive than the lumbar puncture required to obtain spinal fluid.”

The researchers saw the “cognitive reserve” finding as good news. “We might actually be able to modify the risk of dementia before it becomes manifest,” said Yaffe. “If you find out that you have low beta-amyloid 42, but you haven’t yet experienced any obvious cognitive decline, you might try and increase your cognitive reserve by staying mentally active—reading, taking classes—and thereby mitigate or at least delay the damage.”

(Journal of the American Medical Association, Jan. 19, 2011)

For those with paralysis, brain implant allows point-and-click cursor control

In one of the latest reports on their innovative BrainGate technology, researchers with VA and Brown University showed that recording signals from only a tiny cluster of brain cells—only 40 or so, out of billions in the brain—can enable effective control of a computer cursor for patients with total paralysis.

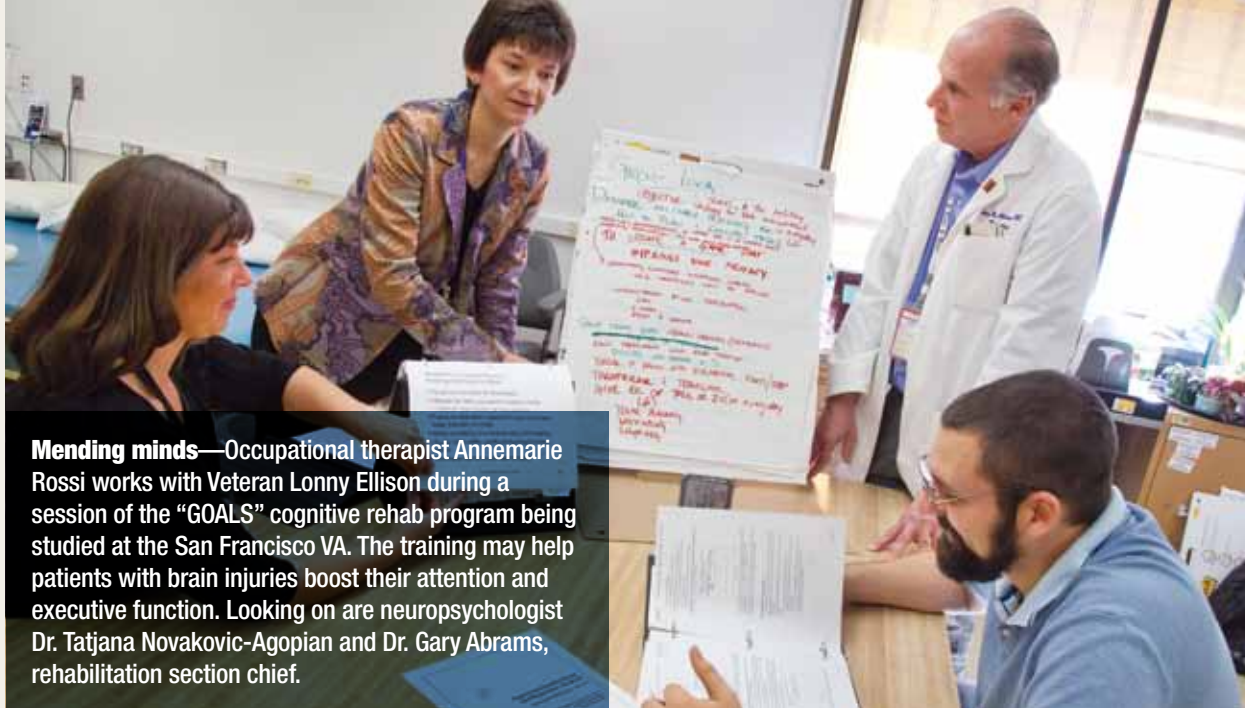
The study, part of ongoing research involving patients with conditions such as spinal cord injury, ALS (Lou Gehrig’s disease) and brainstem stroke, included two patients with paralysis of all four limbs. Using BrainGate, they were able to control the motion of a cursor on a screen and click on targets. The error rate was small—under three percent for one of the participants.

BrainGate (www.braingate2.org) uses a sensor in the brain to pick up signals from neurons. The impulses are decoded by an external computer and translated into commands for electronic or robotic devices.

The implant, an electrode array about the size of a baby aspirin, is made of biocompatible materials such as silicon and titanium and is placed in the motor cortex, which controls movement. A small pedestal is visible on the surface of the skull and allows for the internal sensor to be wired to the external decoder. A wireless version of the system is under development.

“The current investigational device represents the first step in a cycle of innovation and clinical research that we hope will yield ever-improving restorative technologies for people with neurological disorders, injuries or limb loss,” said investigator Leigh Hochberg, PhD. He noted that his group is currently testing BrainGate as a control system for a high-tech upper limb prosthesis, known as the DEKA arm, that was funded by the Defense Advanced Research Projects Agency and is being field tested with Veterans at several VA sites.

(IEEE Transactions on Neural Systems and Rehabilitation Engineering, online Jan. 28, 2011)



Mending minds—Occupational therapist Annemarie Rossi works with Veteran Lonny Ellison during a session of the “GOALS” cognitive rehab program being studied at the San Francisco VA. The training may help patients with brain injuries boost their attention and executive function. Looking on are neuropsychologist Dr. Tatjana Novakovic-Agopian and Dr. Gary Abrams, rehabilitation section chief.

Training boosts cognitive function even in long-term brain injury

In a pilot study led by VA researchers, a new cognitive rehabilitation method helped patients with longstanding brain injury—in most cases from traumatic injuries or stroke—stay focused on goals and complete everyday tasks such as schoolwork or meal planning.

Neuropsychologist Tatjana Novakovic-Agopian, PhD, and neurologist Anthony Chen, MD, both lead authors on the study, said the results show that cognitive function can improve even years after a brain injury. “Developing interventions for these problems is extremely important, given the large number of young men and women coming back from active duty deployment in Iraq and Afghanistan with traumatic brain injury and persistent symptoms of cognitive dysfunction.”

Chen and Novakovic-Agopian co-direct the inter-institutional Program in Rehabilitation Neuroscience and are affiliated with the San Francisco VA Medical Center, VA Northern California Healthcare System, and University of California, San Francisco.

The training method developed by the researchers is called goal-oriented attentional self-regulation, or GOALS. It teaches participants how to focus on goal-relevant information and hold it in mind while managing distractions, and then to apply those skills in managing their own real-life goals.

Chen described one of the GOALS strategies, called Stop-Relax-Refocus: “Stop, relax, refocus on the goal to be accomplished, and when your mind wanders, practice redirecting your attention back to the central goal. This is inspired by mindfulness training that’s been taught for thousands of years. The difference is that we have put a rehabilitation twist to it. This is not traditional meditation, but goal-oriented *applied* mindfulness.”

The 10-week study included 16 participants in two groups. The first group had GOALS training for 5 weeks and educational instruction about brain injury during the second 5 weeks. The other group received the same interventions but in reverse order. After the first 5 weeks, the GOALS group showed significant improvements in attention, executive function and completion of functional tasks. Those who had the education sessions showed no such changes. After 10 weeks, the group that was switched from education to GOALS training showed similar improvements.

Importantly, the first group maintained the gains they had shown after the first 5 weeks. In fact, Novakovic-Agopian said that in follow-up research, almost all the participants reported using GOALS strategies for up to two years after the study.

A larger study of Veterans is under way. The research has been supported by VA and the California Pacific Medical Foundation.

(Journal of Head Trauma Rehabilitation, online Dec. 16, 2010)



You've got mail—Dr. Richard Hoffman, with VA and the University of New Mexico, shows the stool-test kits that were mailed to eligible Veterans at home as part of a study. The kits boosted colorectal cancer screening rates.

Sending test kits to patients' homes boosts colorectal screening

Researchers with the New Mexico VA Health Care System and University of New Mexico found that mailing stool tests to eligible patients' homes—rather than waiting for them to be routinely screened during office visits—was an effective preventive measure for colorectal cancer.

In the study, more than 200 Veterans—many of them in rural areas—received fecal occult blood test kits in the mail, along with consent forms and a pre-paid return envelope. Nearly 6,000 patients in the region served as “controls” and did not receive the kits. All the Veterans were between ages 50 and 80. All were eligible for this type of screening, based on their medical status, and were due for the test.

Nearly half of those who received the kits by mail completed the test, which is widely used as an initial screening for colorectal cancer. Those who tested positive were referred for further screening, usually a colonoscopy.

Among the control groups, who did not receive the kits by mail, fewer than a fifth of patients ended up getting screened for colorectal screening during the study period, either by stool test or colonoscopy.

The findings suggest the mail method may be more effective than waiting to screen patients during routine primary care visits—especially for people who are healthier overall and less likely to show up for regular check-ups. The researchers also point to the value of VA's electronic health record, which was used to identify patients eligible for the study and to track their care.

Colorectal cancer is the third most common cancer in the U.S. and the third leading cause of cancer-related deaths. In the VA health system, there are some 4,000 new cases each year.

(American Journal of Managed Care, January 2011)



VA RESEARCH TODAY

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Homeless no more—Army Veteran Andre Guyton, 50, was living on the street four years ago when he first came to a VA primary care clinic for Veterans coping with homelessness. Today, he has a job and a roof over his head. Read more on page 19.

