

VA RESEARCH TODAY

Building on 85 Years of Discovery, Innovation, and Advancement

- New technology for spinal cord injury, limb loss
- TBI-PTSD: Helping clinicians toward better diagnosis and treatment
- Looking back—and ahead—at VA comparative effectiveness research
- Polytrauma: Focus on family care
- Personalized medicine: What the future holds



A DIFFERENT WORLD, YET AN ENDURING COMMITMENT TO VETERANS

Eighty-five years ago, the first generation of VA researchers began publishing the *U.S. Veterans' Bureau Medical Bulletin* to "promote research along practical lines."

Today, we live in a different world. Medical research, in particular, has advanced beyond anything those early VA researchers could have imagined. Yet one thing has not changed: The research conducted by the Department of Veterans Affairs is designed to be practical, and it is wholly focused on Veterans' needs. It is designed to directly address the health issues affecting Veterans and improve their lives in tangible, significant ways.

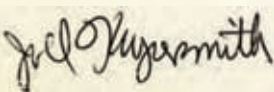
This publication, which we've called *VA Research Today*, helps tell our story. The magazine was produced to help commemorate the 85th anniversary of VA Research, which is the theme of National VA Research Week 2010.

The articles in this magazine speak to the tremendous spirit of discovery, innovation, and advancement that has characterized VA research for so many decades. Some of the stories showcase state-of-the-art technology we are developing—such as advanced prosthetic devices, or new electrodes for implantation in the brain. Other articles tell of innovative studies that have already made a difference in the lives of Veterans—for example, those with chronic obstructive pulmonary disease, or serious mental illness. Other features explain work in progress that aims to revolutionize cancer treatment, for instance, or greatly improve the diagnosis and treatment of traumatic brain injury or posttraumatic stress disorder. You'll also find inspiring stories of Veterans who have returned from combat in Iraq and Afghanistan with polytrauma injuries and read how VA researchers are learning the best ways to involve family members in their care.

The common theme throughout these pages is the focus on Veterans. As it was in 1925, so it is in 2010.

We hope you enjoy this magazine and gain a new understanding of the scope and impact of the work being done by talented, dedicated investigators at VA medical centers nationwide. Thanks to their brilliant efforts, and the many Veterans who volunteer to take part in VA research, we proudly carry forth our longstanding tradition of discovery, innovation, and advancement.

Sincerely,



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



85 Years of **DISCOVERY,**
INNOVATION, 
ADVANCEMENT

For Veterans

VETERANS AFFAIRS RESEARCH & DEVELOPMENT

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85 YEARS OF DISCOVERY, INNOVATION, AND ADVANCEMENT

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Cover: Navy Veteran and VA employee David Haldane (left) and research assistant Doug Benedicto test the Lokomat—a robotic treadmill that supports the patient's weight and helps restore walking ability after certain types of injury—at VA's Center for Restorative and Regenerative Medicine. See feature on page 41.



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APT CENTER IS HOME TO EMERGING TECHNOLOGY FOR VETERANS WITH DISABILITIES

From 'smart' electrodes to electric bandages, APT researchers are creating a new generation of adaptive and therapeutic devices

What goes on at the Advanced Platform Technology (APT) Center might sound more like something out of a novel by Asimov or Heinlein. At this research center of excellence, based at the Louis Stokes VA in Cleveland, some scientists and engineers are developing a material that can mimic brain tissue. Others are refining a muscle-powered brace that could allow paraplegics to walk easily and climb stairs. Still others are creating disposable electric bandages for wounds that won't heal, and artificial limbs that sync up with the nervous system.

"We try to capitalize on advances in materials science and microelectronics, and focus them on the needs of Veterans with disabilities," says APT Center executive director Ronald Triolo, PhD.

A case in point is a new type of electrode for use in brain-computer systems. Groups within VA and elsewhere are testing technology wherein electrodes are implanted in the brain to pick up signals that can be changed into commands for computers or robotic limbs. Electrodes like this already exist, but they have limitations: Because they are made of stiff silicon, they don't fit well in the watery environment of the brain. An APT Center team has created a material that softens once inside the brain, rendering it mechanically invisible. Results were published in *Science* in 2007.

Now APT director of research and scientific affairs Christian Zorman, PhD, and others are working out how to incorporate the new material into a device that can record neural activity or stimulate nerves. The device must be extremely small: 1 mm long and 0.05 mm wide (by contrast, a sheet of paper is about 0.1 mm thick).

"If we can perfect the design, we hope to mass produce it, and at low cost," says Zorman. "But the main attribute is the miniaturization, so a surgeon could implant many of these, and not just a few." A prototype electrode is in preclinical testing.

Another early-stage project is the design of a wireless system for recording brain waves. In some people with epilepsy, brain tumors or brain injuries, neurologists pinpoint the damage by placing a grid of electrodes on the brain and reading the resulting waves. Currently, the electrode contacts are embedded in a silicone rubber sheet that is placed directly on the brain, with wires running from the sheet to the recording device. Any tests using this grid require surgery, a hospital stay and precautionary antibiotics. APT Center researchers want to make it possible to record brainwave information wirelessly, without needing to expose the brain or run wires.

APT engineers are working on new devices to stimulate nerves and record brain-cell activity.

Dr. Christian Zorman's team is developing an electronics interface board, seen here, along with implantable brain electrodes that will be only 1 mm long and .05 mm wide. The board, external to the body, would allow brain signals from the implants to be decoded and used to control devices such as prosthetic limbs.



Veteran Don Crago (center) has been helping APT engineers test a dynamic brace that uses electrical stimulation to excite paralyzed muscles and controllers that lock and unlock leg joints, allowing patients to walk after full or partial paralysis. With Crago are Dr. Musa Adu, Curtis To, Rudi Kobetic and Thomas Bulea. The inset shows the brace with the knee joint in the unlocked (sitting) position.

Says Triolo, “If we could get this device to last for years, we could have something like a Holter monitor for brain disease.” (Holter monitors are used to track the heart’s electrical activity. Worn for days at a time, they have several electrodes that are taped to the patient’s chest.) This would revolutionize the field of neurology, asserts Triolo, providing continuous, long-term data on what’s going on in the brain. It also could improve patient selection for surgery and surgical accuracy.

Like the grid of brain electrodes, other medical equipment doesn’t translate well to the battlefield, or the living room. Heart-lung machines can save lives,

but only in the hospital. Center engineers are researching ways to create a portable heart-lung machine that could provide life-sustaining oxygen just about anywhere, at least until the patient could be transported to a medical center.

Electrodes also are helpful—but unwieldy—when it comes to wound healing. For slow-healing wounds, the standard of care involves applying low-intensity current to the area. “It’s commonly accepted but not commonly used, and we think that’s because it’s so inconvenient,” Triolo says. Patients must receive treatment in a hospital, and placing the electrodes on fragile skin can be tricky.

To solve the problem, APT engineers are at work on an electronic bandage. “If we can combine the electrical current with a bandage and make it disposable, we’d have a sterile, occlusive dressing,” says lead investigator Kath Bogie, D.Phil. “The bandage would apply current through the wound until the battery wore down. It could then be thrown out and replaced.”

Once made, the bandage might be easily tweaked into a wireless patch for pain control. Transcutaneous electrical nerve stimulation (TENS) is used to treat chronic pain, but portable units have electrodes and wires that keep the system—and the patient—homebound. “We might be able to make a disposable TENS patch that would relieve pain for a week,” notes Bogie. “And thanks to wireless technology, a physician could change the type and pattern of electrical stimulation as easily as he or she makes a phone call.”

Given the number of Veterans affected by partial or total limb loss, a main focus of the APT Center is prosthetics and orthotics. Several ongoing projects aim to find ways to restore some sense of feeling to the residual limb. By activating nerves in the residual limb, says lead researcher Dustin Tyler, PhD, “We hope to provide some sense of how hard the prosthesis is squeezing something, for example, and where the prosthesis is in relation to the rest of the body.”

By combining multiple disciplines and technologies, an orthotics project led by Triolo hopes to build a better brace, one that would allow a paralyzed Veteran to walk at variable speed and climb stairs.

Today’s full-leg braces—called reciprocating gait orthotics—are designed to help paraplegics to stand and walk in a straight line over a level surface. The braces are constructed such that when one leg extends, the other flexes. “Walking is slow and awkward, and not cosmetic or functional,” says Triolo. “You can’t go up a curb, or up or down steps.”

The center’s biomedical engineers, working with a robotics lab at Case Western Reserve University, are developing a more dynamic brace. The ankle, knee and hip joints can be locked and unlocked using a small, wearable computer. The group also is working on hydraulics that slowly release the knee joints. Lock one hip, unlock the other and flex the knee slowly, and stairs become possible.

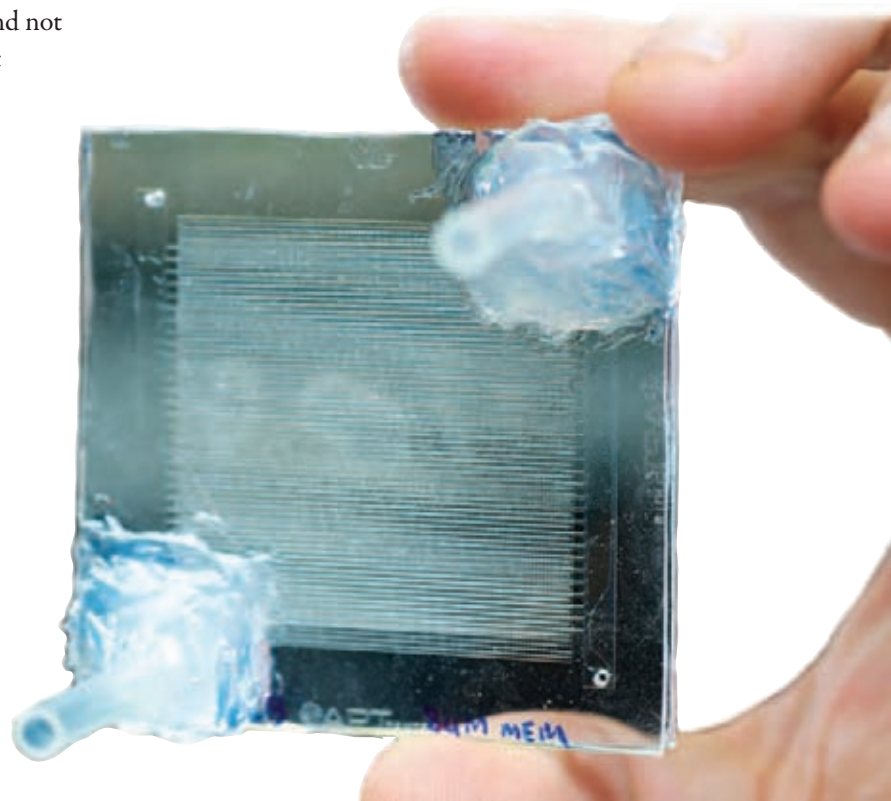
Another APT device in the works: a micromachined artificial lung with air inlet and outlet ports and tiny channels for blood and air flow.

The brace also uses electrical stimulation to excite paralyzed muscles, inciting movement and avoiding the need for a bulky battery.

Veteran Don Crago, 48, is one of two people testing the brace at the center. Crago was paralyzed from the chest down in an automobile accident in 1983. He’s adept with a wheelchair, but limitations abound. This past winter, Crago was able to go down the slopes at a Maryland resort on a monoski, but had to be carried up a set of stairs to a restaurant that night.

Crago has been testing the brace technology with APT researchers for three years. “The first time [the brace] worked for me, it felt great,” he remembers. “It was like my steps were effortless. It’s still a prototype, but when it works, it feels really stable.”

The brace is still too heavy and continues to be refined, says co-investigator Rudi Kobetic, MS. One day, APT researchers hope it will be ready for technology transfer and eventual U.S. Food and Drug Administration approval, making it an option for the hundreds of thousands of Americans who are paralyzed due to spinal cord injury or disease. —



FROM CANCER TO CARDIOLOGY, NOBEL-WINNING SCIENTIST IS CLOSING IN ON CURES

Dr. Andrew Schally is still going strong in VA after nearly five decades of groundbreaking research

VA Distinguished Medical Research Scientist and University of Miami researcher Dr. Andrew Schally may not yet have found the fabled “cure for cancer,” but he’s come about as close as any medical researcher. Nowadays, at age 80-plus, this winner of the 1977 Nobel Prize in Physiology or Medicine is hot on the trail of compounds he believes will revolutionize cancer treatment. But over his decades-long career, Schally has been credited with weighty advances in a wide range of additional specialties—among them, gynecology, gastroenterology and endocrinology. And now, cardiology can be added to the list (*see sidebar on page 8*). All told, the European-born scientist and proud naturalized American for 48 years has published more than 2,200 papers, more than 1,200 of them after winning the Nobel Prize.

Schally is a “national asset,” says Norman Block, MD, a 30-year professional colleague of Schally’s who gave up his surgical career in urology about five years ago to support the Nobel laureate’s research full-time. “It was an easy choice,” says Block of his professional transition. “Doing surgery, I was helping one person a day to stay alive. Working with Dr. Schally, I may be helping a couple of hundred a day to stay alive.”

Joining VA in 1962, Schally set up a lab devoted to research on the hypothalamus. His early work established the fact that the pituitary gland and certain other glands of the endocrine system are regulated by the region in the brain called the hypothalamus. This work, which has been called the foundation of modern endocrinology, earned him his Nobel in 1977. The prize was shared with Rosalyn Yalow, a friend and VA colleague who pioneered the field of radioimmunoassay, and hormone researcher Roger Guillemin.

In those early years, Schally’s focus was in the field of human reproduction, leading to the development of both fertility and contraceptive compounds. His work since then has pyramided on these initial scientific breakthroughs. It’s his scientific curiosity, Schally says, that has fueled his long line of achievements in medical science. “This is a trait I still have,” says the scientist. “I want to know how nature controls these mechanisms.”

It was this curiosity—along with a strong sense of ethical responsibility as a scientist—that in the 1970s caused Schally to shift the focus of his earliest hormone research from reproductive health to oncology. “I began to see the role of hormones in breast and prostate cancer was much greater than originally demonstrated,” he



“I want to know how nature controls these mechanisms.”

Dr. Andrew Schally, with VA Research since 1962, has won a Nobel Prize and numerous other awards for his biomedical discoveries.

remembers. “We had patients with various tumors. We could inject our hormones and show inhibition of the tumor. So I realized I would be a fool—even scientifically criminal—to not use in oncology some of the hormones which I discovered in the brain.”

Harnessing anti-cancer hormones

One example of Schally’s revolutionary discoveries in the fight against cancer: The current treatment for testosterone-dependent prostate cancer—used successfully in hundreds of thousands of men around the world—is derived from a brain chemical called luteinizing hormone-releasing hormone (LHRH), which he discovered. Schally calls LHRH the “biggest prize” of his long career. “After I gave my lecture on the discovery of LHRH to 2,000 people in San Francisco in June of 1971,” Schally recalls, “the audience disappeared suddenly to phone the structure all over the world, in view of its expected medical importance.”

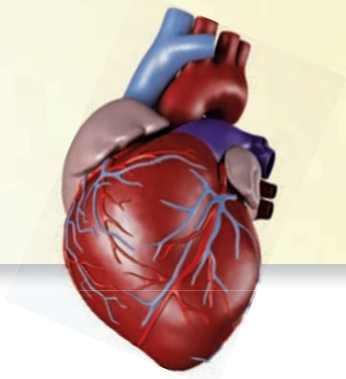
More recently, a Schally-led research team found that a synthetic compound called JMR-132 stops the spread of human prostate cancer cells and also acts as a strong antioxidant. Like some other compounds that Schally has explored, the compound works as an antagonist to a tumor-nourishing natural body chemical called growth hormone-releasing hormone.

Schally has studied thousands of potential therapies, including analogs—modified compounds that can pack 100 times the punch of natural hormones—and out of this far-reaching investigation has created several auspicious cancer therapies. Schally is now exploring hormone-based treatments for breast, ovarian, pancreatic, lung and other tumors, and his team is involved in several clinical trials of hormone-based therapies. “I believe we are very, very close to new methods for cancer treatment,” says Schally, who recently received a Meritorious Service Award from VA for his work on innovative cancer therapies.

Heart-protective compound identified

In a potentially important advance in the study of congestive heart failure—a leading cause of disability—Dr. Andrew Schally and his University of Miami colleagues have found a compound that sparked major recovery in rats after heart attack, which often leads to heart failure. The compound is a derivative of growth hormone-releasing hormone (GHRH), and the research team’s findings were published earlier this year in the *Proceedings of the National Academy of Sciences*.

Schally has studied GHRH extensively for its cancer-fighting potential, and his laboratory synthesized the compound used in this study. He and his colleagues plan to study the mechanisms further so they can move the compound into human testing, and Schally predicts that GHRH will prove able to repair the heart in humans, too. “This should be possible in human beings because the hormone works well in all species,” Schally says. In a University of Miami press release, the study’s principal investigator, Joshua Hare, MD, said, “This discovery is a major step forward in harnessing a new therapeutic opportunity for heart disease that avoids unwanted side effects.”



Schally is now set on developing “smart” chemotherapies to zap cancer cells while leaving surrounding tissue unscathed. While Schally is careful to distinguish between effective treatments and “cures,” he brims with excitement when describing this latest work. “The beauty of these methods is that they are targeted to

tumors,” says Schally of his approach, which combines cancer drugs with synthetic versions of hormones and then hunts down tumors that have receptors for those hormones. “They go to the tumor and they can destroy malignant cells. If you repeat it two, three times, you can perhaps totally destroy the tumor. In such a case, you have a treatment that comes very close to being a cure.”

A half-century of uninterrupted research

In all, Schally is approaching 50 years in his VA research career, without any interruption worth mentioning. When Hurricane Katrina threatened to disturb his work, then based at the New Orleans VA Medical Center, Schally moved to the Miami VA to avoid disruption, telling a reporter from the *Sun Sentinel* in Fort Lauderdale, “What worried me most was my research would come to a standstill for two or three months. It’s a tremendous relief to be among friends and be able to do something practical to continue my research.”

One of the friends welcoming Schally to Miami was urologist Block, who calls Schally a “genius,” but stresses his kindness above all. “It’s unbelievable that the same person can have his credentials and accomplishments and be so caring.” The Nobel laureate’s self-described “hardest blow and the biggest tragedy in my life” came with the death in 2004 of the person he cared most about—his wife of 28 years, Ana Maria Comaru-Schally, MD, an endocrinologist and his research partner for many years. Schally’s solace after her death, he has written, came from his ongoing medical investigation: “I am seeking consolation and comfort by continuing my work in cancer research.”

While he continues to work as hard as ever, Schally also finds time to relax—watching soccer, and carving out time in his pressing schedule to swim a mile several days each week. He shows no sign of slowing down. “I am in good health,” says Schally, “and Nobelists never retire.” —

FACING DOWN COPD: LEARNING TO LIVE WITH CHRONIC LUNG AILMENTS

A trial at the Phoenix VA and 21 other sites is teaching Veterans better ways of coping with chronic obstructive pulmonary disease

Ron Greenberg is a Korean War Veteran and a retired newspaper pressman. He's sung in musicals and coached baseball, and he loves to golf. Greenberg, 76, is a "wherever you are, that's where you're supposed to be" kind of person. But when chronic obstructive pulmonary disease (COPD) took hold, Greenberg found himself intimately acquainted with a place that no one really wants to be: a hospital emergency room.

He visited the Phoenix VA Medical Center ER four days in a row. On the fourth day, he met Pat Jacobs.

Jacobs is the Phoenix coordinator of a five-year VA study on the effects of patient education and case management on hospitalizations for COPD. The Phoenix center, one of 22 VA study sites, enrolled 59 Veterans.

After joining the study in November 2007, Greenberg spent a couple of hours each week reviewing patient education information with Jacobs. He learned what COPD was, how his medicines worked, and how to handle flare-ups. He also received case management that included 24/7 support. Jacobs gave out her cell-phone number and email address to the Veterans. "If they got in trouble or had a question, they called me," she says.

When John Snyder joined the study in August 2008, he'd had five years of treatment for his COPD. Snyder got around via scooter. "I couldn't really walk. I was always out of breath," he recalls.



John Snyder has been able to stay more active since taking part in a VA study aimed at improving care and self-management for COPD.



“You have to be your own best friend,” says Paul Glessing, 82, about looking after his health and coping with COPD.

The study helped him in two ways: It taught him about his condition and what he could do to control it, and helped him get his medications in order.

“I was on the wrong medications, and wasn’t taking them properly,” he said. Snyder was taking inhaled steroids up to six times a day before he entered the study. Now he takes them once a day, always at the same time. “I have specific times to take everything, and I’m consistent with that, which has helped enormously,” he says.

Jacobs, the study coordinator, explains that fine-tuning medication regimens for COPD can often be tricky and involves a learning curve for patients. In the study, she spent up to two hours a week one-on-one with patients. “I think it’s the individual attention as much as anything that helped,” she says.

Another stumbling block for Snyder—and for many with COPD—was anxiety. Not surprisingly, he became anxious when it became difficult to breathe. He learned that giving in to the fear only made things worse, and practiced techniques to calm himself.

“I tell myself, ‘All right Snyder, take over, don’t let it rule you. Stay calm and use some common sense,’” he says. “And that pulls me out of it. You don’t learn that

one overnight, that’s for sure. But taking control has changed my life.”

The education materials helped immensely, says study participant David Richards, 74. “You read them, practice what is said, and there’s no reason you won’t get better.”

Richards had been relying on a scooter to get around since 1999. When he entered the study in January 2007, he had been in and out of the hospital several times each year with bronchitis.

He also wasn’t taking his medications properly, and he didn’t know when to rest. “The study helped me understand what COPD was and how it worked,” says Richards. “I learned to know my limitations and control the COPD without it controlling me.”

After seven months in the study, Richards was walking again. He sold the scooter in 2008. “I’m 100 percent better. I can do housework and laundry and shopping. I walk on a treadmill. Before, I couldn’t take a shower without resting.”

Another study volunteer, Paul Glessing, says the study taught him how to be kinder to himself. “You have to be your own best friend,” he reflects. “There are bumps in the road, and you have to resolve them.”

The Veterans learned what COPD was, how their medicines worked, and how to handle flare-ups.



Top: Ron Greenberg, 76, is back on the golf course, able to play nine holes, since learning how to better manage his COPD.

Left: Dave Richards, 74, says the VA study has helped him regain the ability to exercise, do household chores and get around without a scooter.

COPD at a glance



Try breathing through a drinking straw, and you'll have some idea what it's like to have chronic obstructive pulmonary disease (COPD). COPD is an umbrella term for a group of lung diseases that complicate breathing. The most common types are emphysema and chronic bronchitis. (Asthma is not included in the definition of COPD, however.) People with COPD usually have several of these symptoms:

- Shortness of breath
- Tiredness
- Wheezing
- Coughing
- Coughing up mucus (phlegm)
- Frequent lung infections

Between 80 and 90 percent of COPD cases are caused by smoking. Air pollution, frequent childhood lung infections, secondhand smoke, and rare genetic diseases also can cause COPD.

According to the National Heart, Lung, and Blood Institute, COPD affects about 24 million people, but only half have been diagnosed. About 13 percent of adults in nursing homes, and 6 percent of adults outside nursing homes, have the disease.

COPD has been linked with lung infections, high blood pressure, heart problems, lung cancer and depression. It is the fourth-leading cause of death in the U.S. (behind heart disease, cancer and stroke), causing more than 120,000 deaths each year and about 670,000 hospitalizations.

Glessing, 82, found himself in critical care at least once a year due to his COPD. After entering the study in August 2007, he attended his first support-group meeting. The study requires that Veterans attend at least one such meeting, but Glessing kept coming back. "You never leave without picking up at least one thing that might help," he says.

The other patients agree. "In the group, I learned what worked for other guys, and you're grateful for that," says Snyder. "You bring your own experience to bear too, in case it can help someone else."

The four found the group meetings so useful that they chose to meet monthly long after their study requirements had been met. Now they are working with Jacobs on establishing an ongoing group for Veterans with COPD at the Phoenix VA. The group would include an educational component. "They're going to be doing some of the teaching," says Jacobs. "They know they can be of help to other people with COPD."

Richard Robbins, MD, the site principal investigator for the study, adds that "programs stressing patient education are of great benefit to our Veterans and have been shown to improve their quality of life."

He notes that the Phoenix VA has one of the highest admission rates in the country for COPD. Part of it is demographics—many older retirees live in the area. Also, Arizona's dry air has made the area a target locale for those with lung and sinus problems.

Even with decades of experience as a respiratory therapist, Jacobs was surprised at the positive changes seen in the study. She believes that if the education and case management strategies could be applied around the country, they could bring measurable improvements for people with COPD.

"Case management is done all the time in diabetes and I think it's feasible to do on a large-scale basis [with COPD patients]. It's the idea that you have someone you can call whenever you need it."

Also, she notes: "We started this study with people who were very sick. These Veterans could not walk. If we could provide education and support when people are first diagnosed, I think we'd see an extension of life and an improvement in quality of life."

The study outcome won't be known for at least a year, but the program already has changed at least four lives. "I'm proud to be a Veteran and to know these people," says Glessing. "I didn't think I'd live this long." —

GENOMICS RESEARCH: PAVING THE WAY TO PERSONALIZED CARE

VA researchers are helping to unlock genetic keys to health risks and treatment responses

Finding out in her early 20s about a gene that puts her at extremely high risk for some types of cancer was more of a blessing than a blow to Lisa Collins, says the now-25-year-old Air Force Veteran whose mother was diagnosed with breast cancer in her 30s and experienced a recurrence several years later.

Collins discovered, through testing at the Tampa VA Medical Center, that she has a variant of the gene BRCA1 that compounds her risk for breast and ovarian cancer. Normally, the gene suppresses tumors; a change in it can have the opposite effect. “[The BRCA mutation] isn’t a good thing, but being enlightened about it is,” says Collins, who is now using strategies recommended by her VA health care providers to try to preserve her health.

VA scientists specializing in the field of genomics are hunting down disease-associated genes and gene mutations, such as the one affecting Collins, to improve Veterans’ health. New discoveries in this area can enhance screening and diagnosis and point toward more effective therapies. Some cancers, for instance, may be shut down by subduing a damaging gene or activating a beneficial one. Advances in genomics could also help predict a person’s response to a medication or other treatment.

Joel Kupersmith, MD, VA’s chief research and development officer, says the role of genomics in medical research during the coming years can’t be over-emphasized. “The future of medicine is determined by research, and genomics is *the* direction for research in the 21st century.”

The more researchers learn about the effects of different genetic variations, the better doctors will be able to individualize care—in terms of both treatment and prevention. For her part, Collins gets an annual mammogram to screen for breast cancer. That’s more frequent and earlier in life than what is recommended for average-risk women. Moreover, Collins says she is leaning toward a double mastectomy within the next year. To thwart ovarian cancer, she gets a twice-a-year

Weleetka Carter works with DNA samples at the Pharmacogenomics Analysis Lab at the Little Rock VA Medical Center.





At VA's Pharmacogenomics Analysis Lab, this carrier contains slides loaded with common gene variants and DNA from research volunteers. A laser scanner will detect matches and help researchers learn which variants are linked to which health conditions. The slides are bar-coded for privacy.

screening ultrasound and may choose to have her ovaries removed by the time she's 35. "True, this is a huge ordeal for any woman to have to go through, especially at my age," she reflects. "But so many people are walking around with no clue about their risk and their cancer is detected too late."

Today's medical literature is replete with new discoveries relating to genes and disease, particularly with regard to cancer. For example, one team of VA researchers recently found that genetic variations associated with a protein called macrophage migration inhibitory factor may signal an increased risk for prostate cancer recurrence. Another VA team found that while one variant of the BC12 gene is generally associated with longer survival in patients with kidney cancer, another variant of the gene may actually predict worse outcomes.

But experts say research has just skimmed the surface of the potential of genomics in disease prevention and treatment. VA's ongoing research in this area includes studies of:

- **Schizophrenia and bipolar disorder.** In what is expected to be one of the largest studies of its kind to date, a VA-funded research team will probe the genetic basis of schizophrenia and bipolar disorder, which together affect some 170,000 patients in VA's

health system. Researchers will scan DNA from up to 38,000 Veterans at some 25 VA sites, looking for gene variants found in those with mental illness but not in others.

- **Lou Gehrig's disease.** VA researchers are seeking to identify genes that contribute to the risk of amyotrophic lateral sclerosis (ALS), commonly known as Lou Gehrig's disease. The study is also evaluating possible environmental triggers by looking at participants' family and medical histories, diets, medications, and exposures to toxins.
- **Posttraumatic stress disorder.** VA researchers are working to identify genes that may affect how service members cope with deployment and combat. By conducting clinical assessments in those affected by combat-related PTSD and analyzing their genetic samples, researchers hope to pinpoint genetic variants that contribute to PTSD and other post-deployment adjustment disorders, such as depression.

New technology speeds quest for disease-linked genes

There's only a small portion of our DNA—less than one percent—that's of special interest to researchers. That's where individual variations called SNPs (pronounced "snips") occur. SNPs—short for single nucleotide

As many as a million Veterans expected to take part in ‘MVP’

A major initiative called the Million Veteran Program (MVP) is being launched this year in VA to gain new knowledge about the role of genes in health. The study is expected to involve as many as a million Veterans over the next five to seven years.

According to VA deputy chief research and development officer Timothy J. O’Leary, MD, PhD, the effort will be among the largest of its kind to date, worldwide. “We have a unique opportunity in VA to make discoveries in this area that will impact not only the care we provide to Veterans, but medical care in general,” he says. “This opportunity stems, in large part, from the altruistic volunteering of so many VA patients who become involved in research because they want to help make a difference for others. The generosity of today’s Veterans who become part of this effort will improve the health care of tomorrow’s Veterans.”

Volunteers in the study will donate a blood sample from which their DNA will be extracted. They’ll also fill out a survey about their health and health-related behaviors, and allow access to their VA medical records. The records will be added to the secure VA Central Research Database. By comparing the genetic profiles of large numbers of people and studying their health information—for example, which medical conditions

they have, or how they respond to certain drugs—the researchers hope to pinpoint the genetic factors involved. This could lead to new treatments or preventive measures.

More information about MVP will be available on the VA Research website (www.research.va.gov) later this year.



Dr. Donald Humphries processes blood samples at VA’s Massachusetts Veterans Epidemiology Research and Information Center. The center will securely house DNA and data for the Million Veteran Program.

polymorphisms—are changes in one of the chemical bases that make up the DNA sequence, such as guanine or cytosine. Some of these changes might be of little consequence. Others might raise our risk for a serious disease. There are millions of these SNPs—among the three billion chemical base pairs that make up our DNA—so finding the critical ones is like finding the proverbial needle in the haystack. But thanks to recent advances in technology, researchers are able to make far quicker progress than they could even just a few years ago.

“We can do in a few weeks what we couldn’t do in years,” says Steven Schichman, MD, PhD, director of

the Pharmacogenomics Analysis Lab at the Little Rock VA Medical Center. “We’re using technology that enables you to simultaneously detect a million SNPs at a time in the genome [the entire genetic material] of a person.”

Detecting SNPs in an individual patient is one thing. Solving the mystery of which SNPs have crucial health effects is another.

Anjanette Stone, a biomedical technician who helps run Schichman’s lab, explains: “You have to study hundreds of patients to see if there’s a ‘phenotypic’ effect to a particular SNP. That polymorphism may not do



To accommodate large-scale genomics studies, VA has created significant infrastructure at its Massachusetts Veterans Epidemiology Research and Information Center.

anything. It may not change a thing in your body. Or it could: What if it changes an amino acid sequence in a protein, and it totally changes the function of that protein? Once again, that may not do anything, or it may change how you metabolize a drug, for example. There could be many effects of a polymorphism, and the only way to understand them is to do these studies with huge numbers of patients.”

The studies Stone refers to are called genome-wide association studies, in which DNA samples are obtained from large numbers of people with and without a particular disease. SNPs that show up more commonly in the affected population become prime suspects in the hunt for disease-related genes. The schizophrenia study mentioned above is one example. Another is the Million Veteran Program, being launched by VA this year (*see sidebar on page 15*).

To accommodate these large-scale genomics studies, VA has created significant infrastructure at the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC), housed at the Boston VA. Several years ago, the facility began housing DNA samples from Veterans taking part in clinical trials through VA’s Cooperative Studies Program. More recently, the facility has been expanding into a state-of-the-art central biorepository for VA, adding robotic processing equipment and storage capacity as the agency ramps up its genomics program. MAVERIC is also developing a powerful data warehouse that will enable VA researchers to securely access and analyze genomic and other health data on millions of Veterans.

Veterans express support for genomics research


Large-scale VA genomics studies are possible only with the cooperation of many Veterans. In fact, a majority of Veterans who have received health care through VA would participate in genomics research, according to

a recent VA-initiated study conducted by a group at Johns Hopkins University. Survey participants’ greatest concern was privacy. That issue is addressed through strict safeguards put in place by VA. For example, specimens from those participating in genomics studies are coded and “de-identified” so researchers don’t know who the specimen came from. The key that links the code to the identity is kept in a secure location and only a few authorized VA personnel have access to it.

Addressing concerns about privacy is just one of the challenges facing VA as its genomics program evolves. For example, VA has a state-of-the-art computerized system of health records for its patients, but researchers still have to determine the best ways to incorporate genetic information into those records. A Genomic Medicine Advisory Committee, made up of genetics experts and representatives from Veterans’ groups, helps guide VA on various issues related to the development of its Genomic Medicine Program, including privacy.

While the use of genomic medicine is still limited in scope—within VA and in the U.S. generally—research in the field is growing, and genomics-based medical knowledge is increasingly playing a role in the lives of patients.

Lisa Collins finds peace of mind in knowing she can take steps to minimize her risk of the disease for which her mother—cancer-free since 2004 and turning 50 in July—underwent arduous treatment.

“With my risk being as high as it is, I can go through preventive treatment now, while I’m healthy and have the best support,” says the Veteran. “Being aware of a high risk for cancer makes it a fair fight.” She adds that she is passing along what’s she’s learned to her three sisters so they, too, can opt to take a preemptive stand against cancer. 

Christine Govans prepares to remove frozen biospecimens from a liquid-nitrogen tank at VA’s Massachusetts Veterans Epidemiology Research and Information Center, housed at the Boston VA.

LIFELONG DISABILITY CAN'T KEEP HER DOWN

Determination and a soaring spirit underpin Dr. Lisa Hannold's work on behalf of injured Veterans

When severely injured Veterans talk with Elizabeth (Lisa) Hannold, PhD, about “freedom,” she understands they are not talking about the same freedom they fought for on the battlefield. When they share their struggles, she empathizes, and they know they have found a friend.

An investigator at VA's Rehabilitation Outcomes Research Center (RORC) in Gainesville, Fla., Hannold was born with a rare disease called spinal muscular atrophy. She has never walked, and as a result of severe curvature of the spine, she is only 4 feet 10 inches tall. Poor range of motion in her arms and overall weakness keep her from reaching and lifting everyday objects. She is prone to respiratory infections and fatigue. Despite its physical impact, however, the disease does not affect the mind: People with the condition tend to be bright, sociable and highly verbal, and Hannold is no exception.

Home-tutored from elementary through high school, Hannold attended Gannon University in her hometown of Erie, Pa., where she loved chemistry and biology. “Science was my thing,” she says. In her sophomore year, when a department chair refused to allow special accommodations for her to complete lab experiments—he felt it gave her an unfair edge—Hannold gained a lesson that would steer her future career: “At the time, I was devastated, but it was one of those life-defining

moments that really caused me to re-focus and find another way to accomplish my goals. It also showed me the importance of vocational evaluations and in-depth job exploration to enable people with disabilities to establish realistic work goals.”

She switched her major to avoid having to meet lab requirements, earned her bachelor's degree in 1986 and began looking into PhD programs in neuroscience and psychopharmacology. At the time, though, relatively few people with disabilities were in the sciences, and the issue of lab accommodations came up again.

Rethinking her options, she enrolled in a residential independent living skills training program. She also began volunteering at a nearby center that provided similar services. After a week, she was offered a job there. Within two years, she became director of the independent living skills program at a complex of affordable, wheelchair-accessible apartments for people with disabilities. Hannold cites this as an example of how fate “always intervenes just as it is supposed to. My work experience provided a phenomenal foundation for my current research.”

While working full-time, she returned to Gannon to earn a master's in counseling. She and her parents moved to Gainesville in 1999 so she could pursue a PhD



“Thinking outside the box is really important. When you have a disability, you are forced to think of different ways of doing things.”

Dr. Lisa Hannold is an investigator at VA's Rehabilitation Outcomes Research Center in Gainesville, Fla.

in rehabilitation science from the University of Florida. It was here she was introduced to VA: She was awarded a fellowship at the RORC in 2002 and became a research health scientist at the center in 2004, after she earned her doctorate.

In the years since, she has co-authored several publications and presentations about topics such as the effects of locomotor training. The therapy is used for patients with incomplete spinal cord injury: They walk on a treadmill, their body weight supported in a harness, and gradually improve their walking ability. Hannold has also studied how to redesign outcome measures so they

incorporate the perspectives of disabled Veterans and address the issues they consider important.

Last year, she received VA funding to study the challenges faced by Iraq and Afghanistan Veterans with polytrauma as they reintegrate into the work force. She relies not only on her research expertise but also her unique personal perspective. “Historically, there has been a tendency in vocational rehab to get people with disabilities back to work immediately, but the necessary foundation of independent living skills is not always in place,” she reflects. “From my personal experience, it is imperative that individuals can meet their daily needs



Left: When a company designed Hannold's avatar for a virtual conference, she asked that her wheelchair be included: "It's an extension of me. It symbolizes my freedom." Right: In her office at the Gainesville VA, Hannold uses voice-recognition software that helps her enter text into her computer.

in the home and community first—independently or with support. If not, life falls apart and stacks the deck against success in the workplace.”

The research is now in the pilot phase. Hannold and colleagues are interviewing small groups of Veterans, caregivers and service providers. The results will guide a larger proposal. “The goal of this work is to help answer several questions about the daily living skills of this unique Veteran population,” notes Hannold. “What’s easy? What’s difficult? What’s going well? What’s not? How will this translate to a work setting and successful employment?”

As Hannold’s research career moves forward, she is determined to help her colleagues with disabilities succeed as well. She organized a symposium at the 2009 joint educational meeting of the American Congress of Rehabilitation Medicine and the American Society of Neurorehabilitation. Her event was titled “Rehabilitation Researchers with Disabilities: Empowering Full Participation.” Appropriately, it was simulated—in real time, to sync with the live meeting—in the Web-based virtual world known as Second Life so that researchers who couldn’t physically attend could still take part.

Navy Veteran Dan Parks, founder of the company Virtualis, had his team create a computer-generated conference space identical to the actual meeting setting. They custom-designed avatars—3D graphical representations of people—to resemble the panel members. Some panelists preferred to be designed

without their assistive device, while others—Hannold among them—wanted it included. “I love my wheelchair,” she says. “It’s an extension of me. It symbolizes my freedom.”

Hannold hopes the approach will be used for other conferences. “It was a remarkable opportunity for collaboration. Without this technology, none of us would have been able to participate.” She adds that “thinking outside of the box is really important. When you have a disability you are forced to think about different ways of doing things.”

Hannold’s VA office is fairly typical, except for features such as a document turntable and voice-recognition equipment that helps her enter text into her computer. One item she is rarely without is her “elevator stick.” She jokes about it being “high-tech. It cost all of \$1.50 for a wooden dowel with an eraser on the end. Without it, I can’t push elevator buttons or door-opener push pads!”

Now that her parents are aging—she calls them the “best caregivers anyone could ask for”—Hannold relies on a team of attendants to help with day-to-day activities such as showering and dressing. Hannold enjoys hiring and mentoring rehabilitation students as attendants.

Thinking about the future, she hopes to enjoy a long career with VA. “My dad is a Veteran, all of his brothers were Veterans, and so is my mom’s brother. I have always been interested in empowering Veterans, so I’d love to still be doing research at the VA many years from now.” —

RESEARCH TARGETS WARS' SIGNATURE INJURIES

Researchers are probing new types of brain scans and other tools to boost diagnosis and treatment for traumatic brain injury and posttraumatic stress disorder

Since 2001, more than 1.6 million U.S. troops have been deployed to Iraq and Afghanistan. The “signature injuries” of these wars—posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI)—can’t easily be diagnosed with a blood test, brain scan or other lab test.

What’s more, they often co-occur: Nearly half of military personnel with TBI also report symptoms of PTSD. The association seems natural; the traumatic event of being injured in combat may induce PTSD in some cases. Though early reports showed that TBI protected against PTSD, perhaps due to the loss of

consciousness and amnesia surrounding the trauma itself, newer research shows that two in five returning troops with mild TBI also have PTSD. Current thinking is that TBI might make someone more vulnerable to PTSD, or the two conditions might simply result from the same traumatic event.

Currently, VA has a comprehensive screening process that aims to identify depression, substance abuse, TBI and PTSD. The screening is designed to cast a wide net. “We don’t want to take the chance that we’re missing someone who needs attention,” says physician-researcher David Cifu, MD. Cifu is chief of physical medicine and



To help troops returning home from Iraq and Afghanistan with brain injuries, Drs. Mingxiang Huang (standing) and Roland Lee at the VA San Diego Healthcare System are exploring new combinations of brain-imaging techniques.



Dr. Apostolos Georgopoulos, with the Brain Sciences Center at the Minneapolis VA, has used a technology called magnetoencephalography to try to identify brain-wave patterns unique to PTSD.

rehabilitation at the Richmond VA Medical Center and chair and professor of the department of physical medicine and rehabilitation at Virginia Commonwealth University. “About 20 percent of those screened have a positive screen, but only about 5 to 7 percent are confirmed as having TBI,” he says.

Many mild TBIs don’t require treatment, and 85 to 95 percent of patients with mild TBI recover in 3 to 12 months. However, Cifu advocates for an aggressive approach to treating TBI symptoms, especially if PTSD might be complicating the picture.

“Watching and waiting is not the best approach,” says Cifu. “While it’s always optimal to have a definitive diagnosis before starting treatment, many times there are multiple co-occurring conditions, and identifying a specific cause of all the symptoms isn’t feasible. You may never get a confirmed diagnosis, so instead you treat the symptoms and monitor closely to see what happens. Very often you can get a clearer picture of the diagnosis based on the response to treatment.

“If the Veteran appears to have both TBI and PTSD, for example, then treat elements of both conditions—because if you don’t, the small percentage of people who won’t get better on their own will get worse.”

In Iraq and Afghanistan, TBI most often results from blasts, usually from improvised explosive devices (IEDs). Mild TBI may go undiagnosed: Troops may stay in combat and not report symptoms, such as headache or ringing in the ears. Cifu points out that this may lead to exacerbations, even without further combat injuries.

“When you get a brain injury in a setting where you don’t eat or sleep well, where you’re under stress, it’s going to look worse. When the brain tries to heal in that sort of environment, it may not recover well. That’s why we can see slow recovery rates and a higher rate of persistent symptoms.”

Newer imaging methods may help

In December 2009, a panel of experts, including Cifu, developed clinical practice guidelines for diagnosing and treating mild TBI. Though created by VA and the military, the guidelines apply to anyone affected by concussion. The panel included sports medicine specialists, psychiatrists, neurologists, and experts from other disciplines.

While the guidelines take advantage of the best existing technology, VA researchers are eager to put new tools in clinicians’ hands.

For example, in a small pilot study, a team with VA and the University of California, San Diego, found that a combination of two imaging technologies—magnetoencephalography (MEG) and diffusion tensor imaging (DTI)—can show subtle brain injuries that go undetected in conventional CT and MRI scans. The first type of scan picks up the signals that neurons give off when they fire. The second picks up abnormalities in the brain’s nerve fibers. According to lead researcher Mingxiong Huang, PhD, injured brains generate pathological low-frequency brain waves—like those seen in normal patients during deep, dreamless sleep. And he believes that damaged neurons may become like frayed wires, unable to conduct impulses efficiently.

Researchers agree that the damage from TBI can take various forms. In addition to head wounds from IED shrapnel, troops are exposed to tremendous, near-instantaneous changes in air pressure that can rupture eardrums. The effects of these pressure changes on the brain aren’t clear, but VA researchers are working to understand them.

VA investigator Pamela VandeVord, PhD, an associate professor in the department of biomedical engineering at Wayne State University in Detroit, is studying the effects of IED pressure waves at the cellular level.



“When you get a brain injury in a setting where you don’t eat or sleep well, where you’re under stress, it’s going to look worse.”

Members of Bravo Section, 2nd Brigade Recon Troop, in action in Iraq in 2004.



Facts on PTSD and TBI

According to a 2009 report in the *American Journal of Public Health* by VA researchers, about one in five returning Veterans who enrolled in VA health care between 2002 and 2008 received a diagnosis of posttraumatic stress disorder, a form of anxiety.

Anyone, military or civilian, can develop PTSD after a traumatic event. Such events include combat, automobile accidents, assault, abuse and natural disasters.

Most people have short-term psychological reactions to these events, but in people with PTSD, symptoms last for at least a month and interfere with everyday life. Symptoms appear in four key areas:

- Reliving the event—Nightmares are common. Many people have flashbacks that can be triggered by sounds, news reports or other experiences.
- Avoiding situations that trigger thoughts of the event—People may refuse to discuss the event, or keep busy so they won't think about it.
- Feeling numb—People may find it hard to express feelings, positive or negative. They can lose interest in activities and in being with people.
- Feeling keyed up—People are hyperalert for danger. They can be easily angered, have trouble sleeping, have concentration problems and be overly worried about safety.

Estimates vary on how many returning Veterans have traumatic brain injury, but VA statistics show that mild TBI is diagnosed in about six to seven percent of all Iraq and Afghanistan Veterans who are screened.

TBI can be caused by a direct blow to the head—from a bullet or shell fragment or in a motor vehicle accident—or from changes in air pressure caused by a nearby explosion.

TBI's immediate effects run the gamut from a temporary woozy, "off" feeling to concussion to coma. About 15 percent of all TBIs are moderate or severe; they involve a loss of consciousness, hospitalization and usually other injuries. Only about half of military personnel with mild TBI seek care, although DoD and VA have significantly boosted screening efforts in this area. Currently, more than 22,000 Veterans are being compensated for TBI, including more than 5,800 Veterans of the current wars.

Blast waves cause different injuries than blunt trauma, VandeVord says. "With trauma from impact, you get a pressure wave that can last up to 100 milliseconds. The pressure wave from a blast causes a less than 5-millisecond change in pressure."

The pressure wave from an IED is so fast, in fact, that it's difficult to measure. Only about a dozen places in the United States have the technology to replicate such pressure waves. Wayne State is one of them, and VandeVord has tested two types of brain cells—neurons and glial cells—by exposing them to the same type of compression wave that affects troops.

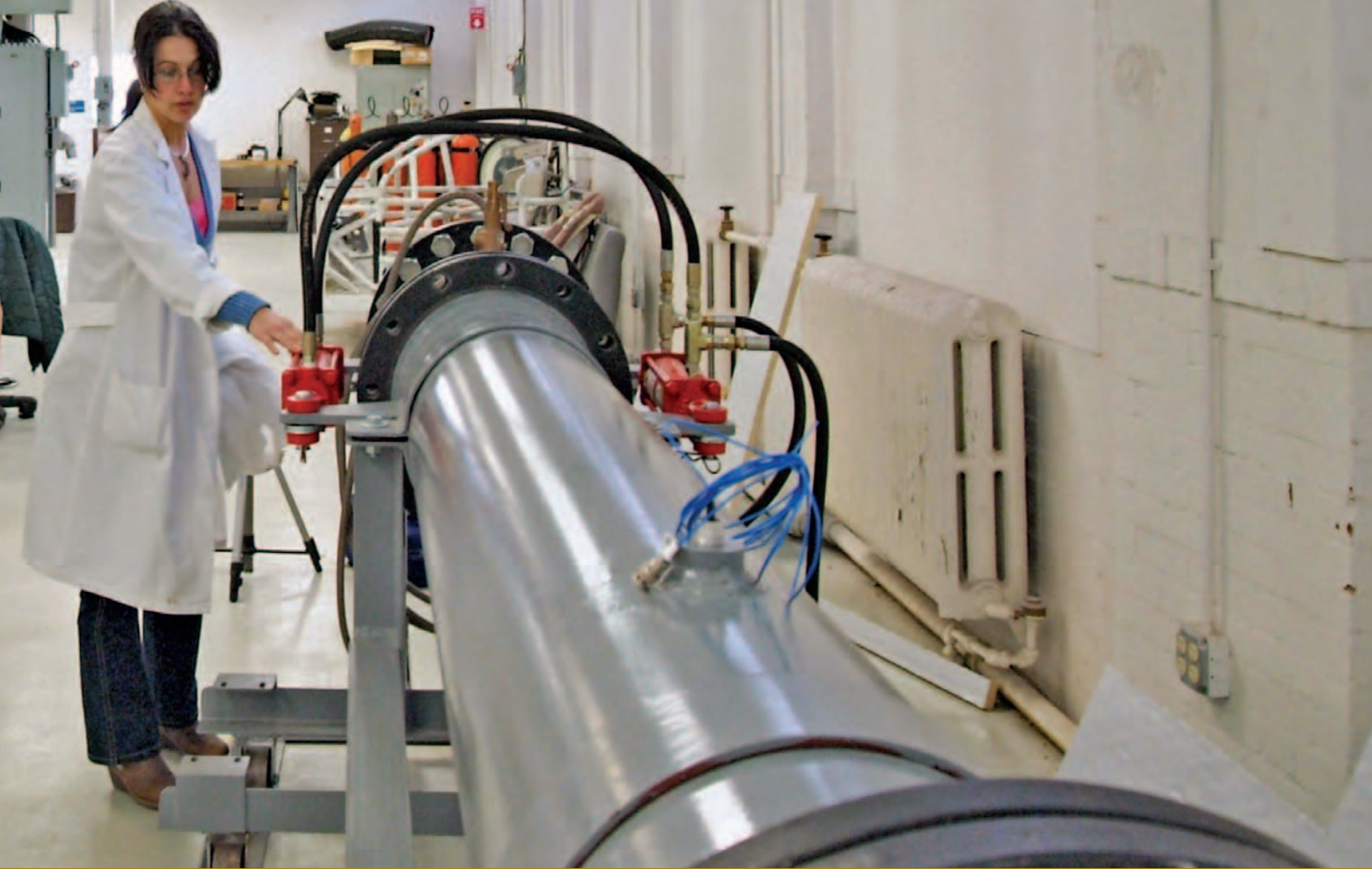
Neurons are hardy, surviving at even extremely high pressures. But at relatively low pressures, glial cells produce chemicals that might damage neurons. VandeVord is now conducting studies using mixtures of both cell types, to see if such damage occurs.

"If it does, we could look for drugs that block the synthesis of those chemicals," she says. "We could find pharmacologic agents for blast-related brain injury."

Non-human studies by her group have shown that certain pressures result in behavioral and microscopic anatomical changes, as well as decreases in blood flow to the brain, hallmark signs of brain injury. One surprising finding was that the pressures that caused these effects were not the *highest* pressures. "Now we're looking at the biomechanics in this specific pressure range," VandeVord says. "The shock wave appears to have a unique interaction with the skull, so we're trying to figure that out." The studies might result in the development of new types of helmets or other protection to block the transmission of specific pressure waves to the brain and reduce the risk for injury.

Seeking signature brain changes

Other VA research is looking for signature brain changes associated with PTSD, TBI or both. Michael Weiner, MD, is director of the Center for Imaging of Neurodegenerative Diseases at the San Francisco VA Medical Center, as well as a professor of radiology, medicine, psychiatry, and neurology at the University of California, San Francisco. He emphasizes that PTSD involves physiological and anatomical changes



Alessandra Leonardi Dal Cengio checks the settings on the “shock tube” that a VA and Wayne State University team is using to simulate the effects of bomb blasts.

in the brain, even though—unlike TBI—it may not be brought on by external forces to the head.

“Generally, you can say that there are structural and functional biological changes that can be detected in people with PTSD, and that these changes affect areas that make sense: They are areas involved in our fear response,” Weiner says.

Weiner and colleagues have studied subjects with PTSD only, TBI only, and both PTSD and TBI. He says early results suggest that the changes in the brain are different in the two conditions, but he emphasizes that “much more work needs to be done.”

“Research like this will give us a better understanding of what’s going on—why people have symptoms, who’s at risk,” Weiner says. Ultimately, “We could use it for better diagnosis, to tailor treatments, or in treatment trials.”

In the past couple of years, VA funded several new centers to advance TBI-PTSD research and bolster

efforts under way at other sites. A new program in Houston, led by Harvey Levin, PhD, is using MRI as a study tool, along with tests that resemble computer games to measure problem-solving ability, short-term memory, and other brain functions. In Boston, a group led by Henry Lew, MD, PhD, is exploring a range of new approaches to the diagnosis and treatment of TBI and PTSD. Another key site is the Center of Excellence for Research on Returning War Veterans in central Texas, where a mobile functional MRI unit travels between the Waco VA and Fort Hood, the largest Army base in the United States. In still other work, San Diego VA psychiatry researcher Murray Stein, MD, MPH, is leading a \$60-million, five-year, 10-site clinical consortium focused on preventing and treating PTSD and TBI. The effort is funded by the Department of Defense (DoD).

Much of this work is still in the early stages. But results such as those reported earlier this year by a Minneapolis

VA team may be a harbinger of things to come. The researchers published findings of distinctive MEG scans in Veterans with PTSD. They were able to differentiate between those with PTSD and healthy controls with better than 90 percent accuracy.

“These findings document robust differences in brain function between the PTSD and control groups that can be used for differential diagnosis,” says neuroscientist Apostolos Georgopoulos, MD, PhD, who led the study along with psychologist Brian Engdahl, PhD. Both are with the Brain Sciences Center at the Minneapolis VA Medical Center and University of Minnesota. Georgopoulos says MEG technology could also be used to track disease progression and the effects of therapy. He noted that if the PTSD biomarker holds up in further study, VA and DoD could use it to help determine the medical status of service members and Veterans.

Removing the stigma from PTSD

Beyond being able to more easily identify TBI and PTSD, clinicians and the military also want to find ways to prevent the conditions. PTSD, in particular, is the focus of a large collaborative effort toward that end. The San Diego-based Marine Resilience Study involves VA and DoD researchers and more than 2,000 Marines. The troops are evaluated one month before deployment and then at three time points after they return.

The researchers are looking at many factors that might be associated with resistance to, and risk for, PTSD,

ranging from biological to psychological, social and environmental factors.

Some of what’s learned may help guide DoD efforts to better prepare and support troops before and after combat deployments. Also, to the extent the study helps pinpoint the physical changes linked to PTSD, it may help change the way some people think about the illness.

Study co-leader William Nash, MD, a former Navy psychiatrist who deployed to Iraq with the 1st Marine Division in 2004, says: “The Marine Corps would love for us to find objective, physical markers for PTSD in our study because that would go a long way toward reducing the stigma that surrounds PTSD. There are still too many military service members, including health care professionals, who don’t believe PTSD is a real illness resulting from real injuries to the mind and brain, but instead think it is caused by a personal weakness. If we can show them biological markers for PTSD, Marines will better accept that PTSD is no more their own fault than any other wound of war.”

In the future, a clearer picture is likely to emerge of who is at risk for PTSD, how to differentiate between PTSD and TBI, and how imaging and other technologies can inform diagnosis and treatment of both conditions. Until then, Cifu says, diligence and vigilance are the best strategies. “You do your best to clarify the problem, treat the symptoms aggressively, and then monitor the patient long term,” he says. “Doctors love one-time fixes, but that’s not life.” —

Subtle visual impairment is common in mild traumatic brain injury, and VA researchers are testing new methods to detect and treat the problem. Here, therapist Paul Koons of the VA Palo Alto Healthcare System uses a Neuro Vision Technology scanner with Veteran Angie Stoltz to help improve her visual function.



HISTORICAL MILESTONES

On the following pages, a snapshot of milestones in VA's rich 85-year history of research on behalf of Veterans

Dr. Rosalyn Yalow was one of two VA researchers to win the Nobel Prize in 1977.



1925: Conducted the first hospital-based medical studies to be formally considered part of VA's newly established research program. Began publishing the *U.S. Veterans' Bureau Medical Bulletin*, designed, in part, to "promote research along practical lines."

1928: Reported findings from early VA studies looking at treatments for malaria, the long-term health effects of chemical warfare, and hospitalization and mortality among Veterans with mental illness.

1932: Published data comparing outcomes at VA clinics with those at other hospitals. The VA facilities compared favorably. Also, established the Tumor Research Laboratory at the Hines (Ill.) VA—the first research lab to receive funds from VA Central Office specifically for research.

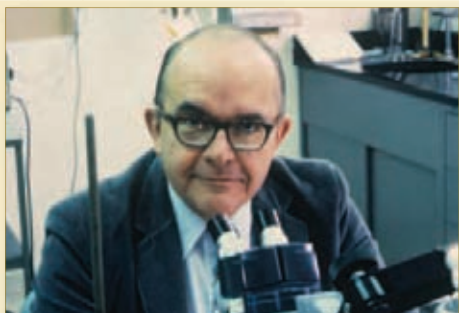
1935: Published a series of articles in the *New England Journal of Medicine* about heart disease among Veterans.

1941: Established a research lab at the Northport (N.Y.) VA medical center to conduct clinical and biomedical research in neuropsychiatric disorders; contribute to the nationwide standardization of diagnostic and treatment methods; and teach the latest concepts and methods in neurology, psychiatry, and neuropathology to VA doctors.



1946: Developed and tested effective therapies for tuberculosis following World War II. These tuberculosis studies were among the first-ever large-scale clinical trials and led to development of the Cooperative Studies Program, which has since produced effective treatments for diseases and conditions including schizophrenia, diabetes, depression, heart disease, and stroke.

1958: Contributed to the development and early use of the implantable cardiac pacemaker, helping many patients prevent potentially life-threatening complications from irregular heartbeats.



1960: Pioneered concepts leading to development of computerized axial tomography (CAT scan).

1968: Performed the first successful liver transplants and developed techniques for suppressing the body's natural attempt to reject transplanted tissue.

1970: Published the results of a landmark VA cooperative study on hypertension, showing that drug treatment was effective in controlling blood pressure and reducing the incidence of major cardiovascular events.



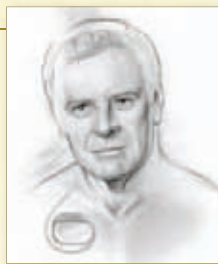
1977: Nobel Prize awarded to VA researchers Dr. Andrew Schally, for his research on peptide hormone production in the brain; and Dr. Rosalyn Yalow, for her development of radioimmunoassay to detect and measure various substances in the blood.

1984: Developed the nicotine patch and other therapies to help smokers give up the habit.

1989: Invented a computer system that provides patients on ventilators with more accurate respirator settings, fewer medical complications and better outcomes.



- 1991:** Developed Functional Electrical Stimulation (FES) systems that allow patients to move paralyzed limbs.
- 1994:** Demonstrated that one aspirin tablet a day reduced by half the rate of death and nonfatal heart attacks in patients with unstable angina. Also, identified a gene associated with a major risk for schizophrenia.
- 1999:** Established, through a large clinical trial using the drug gemfibrozil, that raising HDL (“good”) cholesterol and lowering triglycerides could prevent heart attacks and coronary deaths.
- 2000:** Conducted the first large clinical trials of hearing aids, documenting that the devices can help the hearing-impaired in both quiet and noisy environments.



- 2001:** Initiated a landmark clinical trial to assess the effectiveness of deep brain stimulators for Parkinson’s disease.
- 2002:** Published, together with National Institutes of Health colleagues, the main results from the landmark ALLHAT study, the largest hypertension study ever, which found that conventional diuretics were better than newer medicines for treating high blood pressure.



- 2003:** Launched the largest-ever clinical trial of psychotherapy to treat posttraumatic stress disorder (PTSD).
- 2004:** Took on leadership of a five-year, \$60 million nationwide study—funded by the National Institute on Aging and other partners—to identify brain changes linked to Alzheimer’s disease.

2005: Showed the effectiveness of a new vaccine for shingles, a painful skin and nerve infection that affects older adults.

2006: Launched a Genomic Medicine initiative to advance knowledge of how genes affect health and to promote personalized medicine for Veterans.

2007: Unveiled the first powered ankle-foot prosthesis, developed in collaboration with researchers at MIT and Brown University.

2008: Sponsored an international conference on traumatic brain injury and expanded VA research in this area, including studies looking at TBI in association with posttraumatic stress disorder, hearing and vision loss, chronic pain, and other conditions.

2009: Began first-of-its kind study at VA medical centers to optimize the design of an advanced prosthetic arm, made by DEKA Research and Development through funding from the Defense Advanced Research Projects Agency. Also, initiated the largest health study ever of Vietnam-era women Veterans, with up to 10,000 women expected to take part.




2010: As part of the VA Genomic Medicine Program, announced a groundbreaking genetics study—the Million Veteran Program—to study the effects genes have on health, with as many as a million Veterans expected to take part over the next five to seven years.



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—70 percent 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



As we mark the 85th year of VA's research program, we celebrate our innovative researchers who helped turn so many hopes into realities. VA's forward-looking contributions to medical research continue to bring life-improving treatments and pharmaceuticals to our Veterans and the Nation. We will maintain our steadfast commitment to lead the way as we transform VA into a 21st century organization.

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

INTRAMURAL PROGRAM, COLLABORATIVE SPIRIT

The VA Research program consists of four main research services working together 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 2009, VA Research and Development supported more than 2,000 research projects at VA medical centers nationwide, ranging from preclinical studies to health services research to multisite clinical trials. The types of research that VA Research sponsors are:

- 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 31*)

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.

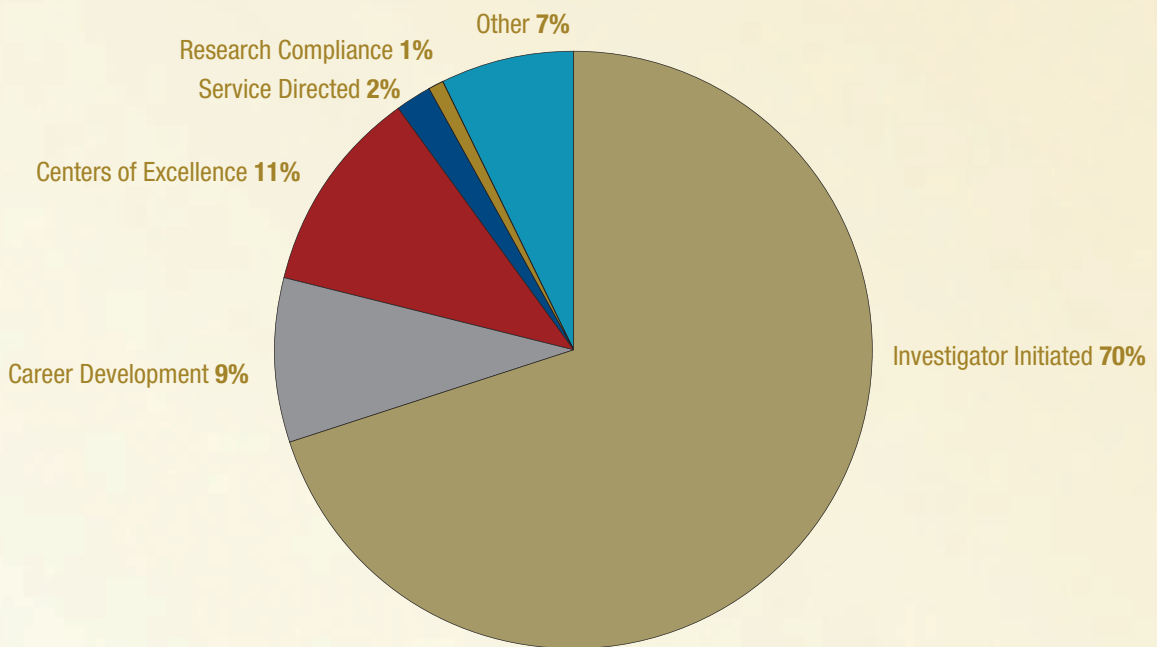
The congressional allocation for VA Research for fiscal year 2010 is \$580 million. VA studies are also supported in part by VA medical care dollars, as well as funding from non-VA sources, such as other federal agencies, nonprofit associations and industry partners. In fact, VA researchers are expected to leverage their VA funding whenever possible—that is, seek additional support from 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 2009



VA'S COOPERATIVE STUDIES PROGRAM: LARGE-SCALE TRIALS TO INFORM EVIDENCE-BASED MEDICINE

From heart disease to mental health, CSP comparative effectiveness trials and other studies yield valuable data to help guide health care for VA and the nation

During the Vietnam War, Allen Wright served aboard the *USS Oriskany*. He helped fix and maintain the Skyhawk fighter jets and other aircraft that would fly from the ship.

Today, the Baltimore resident has trouble using his right hand—one of the effects of a stroke he suffered in 2000. “I use dumbbells and do stretching exercises at home,” says Wright. “My hand still feels weak and slow sometimes, but it’s better than it would be if I weren’t doing anything.”

Wright recently got some help moving his hand from a robot called the MIT-Manus. He was one of 127 Veterans who took part in a VA study that used robots to deliver high-intensity therapy. Other study volunteers received high-intensity therapy without the robot. Both methods proved effective. The results, presented at the 2010 International Stroke Conference, provide compelling new evidence that people can gain back function even years after a stroke.

The study is one of many examples of the impact of VA’s Cooperative Studies Program. By conducting innovative trials across multiple VA sites—often including thousands of Veterans—CSP is able to generate strong evidence to help guide clinical practice.


Findings from CSP studies not only inform VA care but also contribute significantly to medical care throughout the United States and the world.

CSP’s innovative clinical trials and epidemiological studies (research looking at causes and risk factors for disease) cover a wide range of health topics, such as heart disease, diabetes, cancer, infectious diseases, mental health and prosthetics. Always, the first focus is on health problems affecting Veterans.

Roots in tuberculosis care

While CSP was established in its present form in 1972, the program’s roots date back to just after World War II. The program conducted the first-ever large-scale clinical trials, looking at the effectiveness of tuberculosis treatments. In the decades since, CSP has conducted numerous landmark studies—many of which have appeared in prominent medical journals such as the *New England Journal of Medicine* and the *Journal of the American Medical Association*.

CSP typically has more than 30 clinical trials in progress at a given time—most of them “comparative effectiveness” studies that compare treatment options head to head. By seeing how therapies stack up against each other in defined groups of people, CSP studies

A photograph of a man, Benson Belo, sitting at a desk in a clinical setting. He is wearing a grey sweater and a black harness. He is holding a black robotic arm that is attached to a desk. The arm has a white cup-like base and a black handle. In the background, there is a computer monitor displaying a blue circular graphic with several black dots. The man is looking towards the right side of the frame.

A recent CSP study provided compelling new evidence that people can gain back function even years after a stroke.

Benson Belo uses a robotic system to strengthen his stroke-weakened right arm at the Baltimore VA Medical Center.

help fill critical gaps in medical knowledge. Some prime examples from recent years:

- *“On-pump” method of heart bypass surgery.* The traditional “on-pump” method—which uses a heart-lung pump to stop the heart while doctors conduct the bypass—achieved better outcomes after a year than a newer “off-pump” technique.
- *Angioplasty in stable coronary artery disease.* VA researchers, working with Canadian colleagues, found that patients with stable coronary artery disease—in which plaque buildup narrows the arteries and restricts the heart’s blood supply—often fare well with medication and lifestyle changes alone. A commonly used treatment called percutaneous coronary intervention (PCI, commonly called angioplasty) might best be reserved for patients with more severe forms of heart disease.
- *Prolonged-exposure therapy for posttraumatic stress disorder.* VA researchers showed that prolonged-exposure therapy—in which therapists help patients recall their trauma memories under controlled conditions—helped women reduce their PTSD symptoms more than emotional support and counseling that focused on current problems.
- *Intensive therapy to support kidney function.* VA investigators, in collaboration with NIH investigators, showed that delivering more intensive therapy—for example, dialysis six times a week instead of three—did not benefit patients with kidney failure, compared with conventional treatment.

Genetics studies, which look at how patients’ genes influence their susceptibility to certain diseases and their responses to drugs or other treatments, account for an increasingly significant portion of CSP’s portfolio. As part of its role in VA’s Genomic Medicine

Half-decade snapshot of CSP studies

VA's Cooperative Studies Program dates back, in its earliest form, to the 1940s, when it ran tuberculosis clinical trials. Since then, it has conducted numerous landmark trials, such as a 1970 study showing that drugs for lowering blood pressure can help prevent or delay serious cardiovascular events. Fast-forward more than 30 years, and here's a glimpse at just the last half-decade of CSP history:

2009

Launched a study of up to 10,000 Vietnam-era women Veterans to better understand their long-term health status and risks.

2008

Published the results of the seven-year VA Diabetes Trial, which found that intensive control of blood glucose in type 2 diabetes does little to cut the risk of heart disease, compared with standard treatment.

2007

Began a study of prazosin, an inexpensive generic drug used for high blood pressure and prostate problems that was shown in a pilot study to improve sleep and lessen trauma nightmares in Veterans with PTSD.

2006

Published, with colleagues from the National Institutes of Health, the results of a major study of the dietary supplements glucosamine and chondroitin sulfate for arthritis.

2005

Also in collaboration with NIH, showed the effectiveness of a new vaccine for shingles, a painful skin and nerve infection in older adults.



Program, CSP established a repository to securely store biological specimens donated for genomics research. CSP plans to expand its genomic medicine capacity, keeping up with rapidly evolving technology for DNA analysis and expanding the numbers of Veterans involved in such studies.

Studies include up to thousands of Veterans

The CSP studies mentioned above—and hundreds more in the program’s long history—are conducted by research teams that include clinicians as well as statisticians, epidemiologists, pharmacists, and regulatory experts. CSP investigators also team up with experts outside VA, including federal, university and private industry partners.

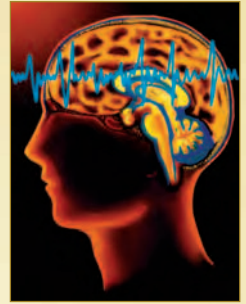
The most important partners in the studies, though, are the Veterans who get their health care from VA and who choose to participate in research. Crucial to VA research overall, the efforts of these volunteers are especially important in CSP’s multisite trials. The largest health study ever of Vietnam-era women Veterans, for example, is expected to include up to 10,000 women. Another CSP study, on the genetics of schizophrenia and bipolar disorder, is expected to enroll some 38,000 Veterans. Study co-chair Larry J. Siever, MD, of the Bronx VA and Mount Sinai School of Medicine, says, “We’ve been hunting for genes of susceptibility for these two diseases, and you need a very large sample to establish genomic-wide association.”

For more information about the VA Cooperative Studies Program, go to www.csp.research.va.gov. 

A CSP-NIH study published in 2006 found little benefit overall for two supplements used widely by patients with osteoarthritis. Here, Dr. Saïd Ibrahim examines a Veteran who has arthritis of the knee at the Pittsburgh VA.

Spotlight on a CSP trial: Brain stimulation for Parkinson’s

George Schmid, a 63-year-old Army Veteran living in southern New Jersey, decided three years ago with his VA doctor that it was time to try a new treatment for his Parkinson’s disease. His left side would often stiffen up, and the drugs he took to tame the symptoms were wearing off faster and faster.



Schmid participated in a six-year study sponsored by VA’s Cooperative Studies Program and the National Institutes of Health, in which some patients received “best medical therapy” (carefully managed medication plus speech, physical, or occupational therapy as needed), while another group of patients, including Schmid, received a procedure called deep brain stimulation. In DBS, electrodes are implanted into the brain, with thin wires running under the skin to a small pacemaker-like device placed under the skin near the collarbone. Electrical stimulation from the battery-operated device aims to jam the brain signals causing the symptoms.

The study involved 255 patients, ages 38 to 83—all of whom were no longer helped adequately by drugs. VA’s Cooperative Studies Program coordinated the trial, which took place at VA’s national network of Parkinson’s centers (www.parkinson's.va.gov) and six university hospitals.

Researchers found that DBS, while riskier than drug therapy, may hold significant benefits for those with Parkinson’s disease who, like Schmid, no longer respond well to medication alone. The results, published last year in the *Journal of the American Medical Association*, would come as no surprise to Schmid, who says he’s felt “very, very good” after DBS—“at least 30 to 50 percent better” than before the procedure.

Overall, after six months, patients who received DBS gained more than four hours per day, on average, of “on time” periods with good motor control and few or no involuntary movements of the face or limbs. Also, DBS patients showed significant improvements in several quality-of-life measures, compared with little change for the other patients. On the down side, there was a higher likelihood of serious side effects with DBS compared with drug therapy. Also, while DBS generally improves movement, the procedure does little to help other Parkinson’s symptoms such as depression, declines in mental ability, and gait and balance problems.

MAJOR MEETING MARKS MILESTONE FOR VA RESEARCH ON WOMEN'S HEALTH

Top experts are gathering to help plan the next steps for VA women's care

When retired Army Staff Sgt. June Moss came home from her 2003 deployment to Iraq, she found herself crying unexpectedly. And not sleeping. And “checking the perimeter” around her home to make sure she and her two children were safe.

Moss eventually got divorced—her husband, also an Iraq Veteran struggling to readjust, was resistant to seeking help. She and her children became homeless at one point, relying on cheap motels to have a roof over their heads.

The single mom would eventually receive a diagnosis of posttraumatic stress disorder and get help through VA treatment. She found the strength to be open about her illness partly through her children. “They helped me realize it’s not bad to tell other people that I was getting help, that I was taking medication.”


Moss’ story is not uncommon among the hundreds of thousands of women Veterans who turn to VA for health care. To make their care the best it can be, VA relies on research: studying how and where care is delivered, and how well it meets women’s needs.

In summer 2010, a major conference is being held to promote and expand research on issues affecting women Veterans.

The National Meeting on Building the Evidence Base to Improve Health Care and Outcomes for Women Veterans, July 15 – 16 in Washington, DC, is the first event of its type since 2004, when VA first set out to develop a comprehensive research agenda focused on women. Women now account for 14 percent of active duty military and nearly 6 percent of VA health care users, and VA has continued to build a diverse research portfolio targeted to their needs.

“This year’s meeting is an opportunity to gauge how far we have come since the establishment of the research agenda and to accelerate our growth towards research that will directly impact the care that women receive in VA,” says Elizabeth Yano, PhD, MSPH. Yano is co-director of VA’s Center for the Study of Healthcare Provider Behavior and an adjunct professor of health services at the University of California, Los Angeles, School of Public Health.

Known nationally as a leading investigator in the area of health care for women Veterans, Yano was lead author on a paper published in the January 2010 *Journal of General Internal Medicine* that gave an overview of VA health care for women, outlined VA’s research focused on their needs, and proposed ways to increase their representation in VA studies aimed at quality improvement.



Women now account for 14 percent of active duty military and nearly 6 percent of VA health care users.

Veteran Gladys Colón receives care at the Providence (R.I.) VA Medical Center.

Yano said the July conference will “partner senior VA leaders with researchers in the field” to explore how to best use research to guide care and services for women. As of the printing of this magazine, leaders from several VA offices, such as the Center for Women Veterans, are expected to attend, as are researchers and women’s health experts from the military, other federal agencies, and the nonprofit and private sectors.

Dozens of VA researchers will present their study results in areas such as:

- access to and quality of care for women Veterans;
- interventions to improve care and outcomes;
- post-deployment mental health care for women;
- the overall effects of military service on women’s health; and
- transforming VA care for women.

In the past few years, VA has been funding an active and varied portfolio of research for women Veterans that has resulted in upwards of 75 scientific publications each year. Here are examples of key findings from recent studies:

- **Homelessness and women Veterans—** Unemployment, disability and unmarried status are among the strongest predictors of homelessness for women Veterans, according to a VA study of

nearly 200 women in Los Angeles. Homeless women were also more than four times as likely to have experienced military sexual trauma, and five times as likely to screen positive for posttraumatic stress disorder. Notably, the homeless women in the study were just as likely as housed women to have a regular health care provider, and were twice as likely to have used any VA health care in the past year. The researchers said this may both illustrate the impact of VA’s homeless outreach and represent an opportunity for further interventions to help this population. (*Journal of Health Care for the Poor and Underserved*, February 2010)

- **Emerging issues among women OEF/OIF Veterans—** Following the Gulf War, policy changes and new legislation eased rules excluding women from combat-related positions. As a result, women deployed to Iraq and Afghanistan serve in support positions that involve leaving military bases, working side-by-side with combat troops, and coming under fire. In this review study, a VA team found that combat exposure in particular is not associated with a higher risk of mental health problems for women compared with men. However, women are more likely than men to develop PTSD following a range of traumatic experiences. The authors also found evidence that women who suffered abuse prior to their military



Left: Air Force medical technician Kabliha Love works at an U.S. expeditionary hospital in Chile after being deployed there in March to help earthquake victims. Right: Veteran June Moss, seen here with children Briona and Jacob, struggled with PTSD and homelessness after returning from Iraq in 2003.

service may be more likely to develop PTSD after combat exposure. Another finding: Among women, concerns about family or relationships play a stronger role in the development of PTSD. (*Clinical Psychology Review*, October 2009)

- **Men and women receive equal heart attack care in VA**—Women, in general, are less likely than men to undergo cardiac catheterization and receive other evidence-based therapies for heart attack, but no prior studies had examined how VA patients fare in this regard. This VA study, which included 236 women and 13,259 men, found similar care and survival rates between the two groups. For example, catheterization was provided for about 35 percent of men and 37 percent of women. More men were prescribed aspirin and angiotensin-converting enzyme inhibitors, but there were no differences with regard to other platelet inhibitors, beta-blockers, or lipid-lowering medications. (*Journal of Women's Health*, May 2009)

Ongoing VA research on women's health is exploring issues such as barriers to VA care for women; military sexual trauma; mental health issues such as PTSD, anxiety, depression and suicide; and the development of new models of health care and psychosocial reintegration for women Veterans, including those who are raising children. Among current studies being conducted:


- **Vietnam women Veterans**—VA has launched the largest and most comprehensive study to date of Vietnam-era women Veterans. The \$5.6 million study, aimed at understanding the long-term effects of military service on women's mental and physical

health, will enroll as many as 10,000 women who served during the war in Vietnam, elsewhere in Asia, or in the U.S.

- **Studying access to care**—VA recently undertook the first national survey of women Veterans since 1985. This survey of 3,611 women has amassed comprehensive data on health care needs and VA experiences, differences among cohorts of women Veterans by military era, and their preferences and perceptions about access to VA care and its quality. The data will guide future efforts to improve outreach, access and care.
- **Synthesizing research results**—A synthesis of published research on women Veterans from the past five years will be completed by summer 2010—in time for the July conference—and will help guide further efforts to improve VA care for this fast-growing segment of VA's patient population.

For Veterans like June Moss, VA health care is integral to recovery. Ongoing weekly therapy has helped Moss restore her life. Today, she is a valued program assistant for the chaplaincy program at the Palo Alto VA. She also takes part in research on PTSD—another way to help her fellow Veterans in need.

"If it hadn't been for my faith and my family and the VA and my medical attention," she says, "I could not be here today."

For more information on the National Meeting on Building the Evidence Base to Improve Health Care and Outcomes for Women Veterans, sponsored by VA's Health Services Research and Development Service, visit www.research.va.gov. 

A BIOHYBRID APPROACH TO REBUILDING THE BODY

At VA's Center for Restorative and Regenerative Medicine, leading-edge scientists are working on innovative ways to help injured Veterans regain their independence

Researchers with the Center for Restorative and Regenerative Medicine (CRRM) are content to leave Superman's bounds over tall buildings and the Six Million Dollar Man's bulldozer-strength bionic arm in the realm of implausible fiction. It's the natural body's real-life feats of movement and function that CRRM researchers are bent on mimicking. The center's investigators, representing the Providence (R.I.) VA Medical Center, Brown University and the Massachusetts Institute of Technology, are studying new-millennium methods for restoring quality of life to those hurt by disease or injury. A primary focus is the marrying of human tissue and mechanical elements into lifelike "biohybrid" limbs that handily outperform currently available prostheses.

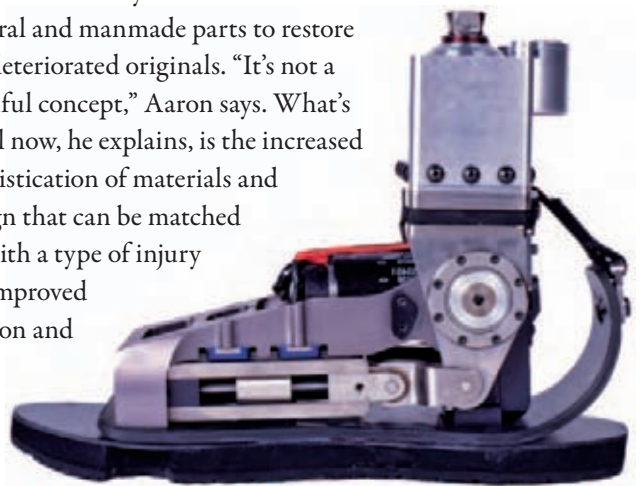
The center—which was founded in 2004 and will be rededicated this year with a new 24,000-square-foot, state-of-the-art research space—specifically targets problems experienced by Veterans, notes the director of CRRM, Brown University professor of orthopedic surgery Roy Aaron, MD. "People in civilian life are affected by the conditions we study," he says, "but mostly we're focused on conditions such as devastating limb injury, burns, traumatic brain injury, and

posttraumatic stress disorder, which are much more prevalent in Veterans."

The CRRM collaboration addresses these needs through a team approach. Its researchers boast expertise in tissue engineering, orthopedics, neurotechnology, prosthetic design and rehabilitation. "At the end of the day, the science and medicine of limb restoration and advanced rehabilitation are creative processes that benefit from all sorts of disciplines," says Al Lo, MD, PhD, a neurorehabilitation expert and CRRM's associate director.

Bionic ankle embodies 'biohybrid' concept

Today's hip and knee replacements are examples of the use of biohybrids that blend natural and manmade parts to restore the deteriorated originals. "It's not a fanciful concept," Aaron says. What's novel now, he explains, is the increased sophistication of materials and design that can be matched up with a type of injury for improved motion and



PowerFoot, a bionic ankle developed by Dr. Hugh Herr of the Massachusetts Institute of Technology and VA's Center for Restorative and Regenerative Medicine.

function. Every battlefield injury is different, for example—sometimes it’s better to rely on biological reconstruction to salvage a limb, and in other cases it’s preferable to do an amputation and prosthetic fitting. “The biohybrid concept allows the unification of metals and other disparate materials that influence biological tissue differently depending on their shape, texture and other characteristics,” Aaron explains.

The first powered ankle-foot prosthesis, constructed by MIT prosthetics engineer Hugh Herr, PhD, is an example of a biology-mimicking (“biomimetic”) component developed through the center. The computerized below-the-knee prosthesis, called PowerFoot, propels a user forward with tendon-like springs and an electric motor. “This design releases three times the power of a conventional prosthesis to propel you forward, and for the first time, provides amputees with a truly humanlike gait,” says Herr, who many years ago lost both of his own legs below the knee from frostbite suffered during a mountain-climbing expedition.

Garth Stewart, a 24-year-old Army Veteran who lost his left leg below the knee from an injury in Iraq, demonstrated the new prosthesis at its unveiling at the Providence VA Medical Center. “One of the first things I noticed was a huge relief in back pressure,” said Stewart of the prosthetic, which was designed to reduce fatigue and improve balance better than previously available alternatives.

Joel Kupersmith, MD, VA’s chief research and development officer, points out that “up to now, prosthetic devices have not been able to duplicate the complex functions of our feet and ankles as we walk and run. The ingenious computerized design of this new prosthesis changes all of this. It constantly ‘thinks’ and responds, allowing the person to walk or run in a more natural and comfortable way.”

Optimizing a space-age artificial arm

For those who have lost an arm from a battlefield injury or other cause, a CRRM-led VA study will help put the polish on the design of a sophisticated prosthetic arm that supports tasks as intricate and diverse as picking



Iraq Veteran Garth Stewart helped Dr. Hugh Herr’s lab test PowerFoot, which propels users forward with tendon-like springs and an electric motor.

up a key, holding a pencil, and using a power drill. The artificial arm, developed by the DEKA Research and Development Corporation through funding from the Defense Advanced Research Projects Agency, is being tested at four VA sites before being commercialized. Frederick Downs Jr., director of VA’s Prosthetic and Sensory Aids Service, who lost his left arm during combat in Vietnam, says he was “brought to tears” recently when the device allowed him to smoothly bring a water bottle to his mouth and drink—a task that may sound simple but that requires fine control to accurately maneuver the bottle without crushing it.

“The device has six different grips, including a fine pinch for picking up paper clips, a spherical grip to pick up a round ball, and a lateral pinch to cut with scissors,” explains study leader Linda Resnik, PhD, a VA research scientist and Brown University associate professor. The other extraordinary feature of the arm under



“Our studies will help amputee patients by improving their function and ability to navigate through different terrains and obstacles.”

Dr. Susan D'Andrea directs the Gait and Motion Analysis Lab, part of the Center for Restorative and Regenerative Medicine at the Providence VA.



A study volunteer runs on a treadmill in the Gait and Motion Analysis Lab at the Center for Restorative and Regenerative Medicine, his legs taped with reflective markers that are tracked by motion-capture cameras. Meanwhile, researchers check the results from software that creates a 3D representation of the volunteer's leg movements.

study, according to Resnik, is a fully powered shoulder, which allows people who have lost an arm at that high a level to function far better than they could with any previously available artificial arm. “Many people who have lost their arm including their shoulder don’t even use a prosthetic limb,” Resnik points out, “because they can get so little function out of it.”

Turning brain waves into action

CRRM researchers are working on additional prostheses to respond more accurately to the user’s intent. “You can have the most beautiful prostheses, but if people can’t power them to perform as they intend,” they’re hardly useful, says CRRM director Aaron.

A system called BrainGate, developed by Brown-VA researcher John Donoghue, PhD, allows signals from the brain to be picked up by a sensor implanted in a part of the brain that controls voluntary movement. The signals are then decoded into commands that drive prosthetic or other robotic and electronic devices. In a pilot study, the BrainGate system enabled a 25-year-old man with quadriplegia to operate a computer cursor and perform other tasks solely through his thoughts. When

the BrainGate study team, led by Leigh Hochberg, MD, PhD, published the results, the research earned headlines worldwide: A London newspaper, for example, referred to the trial participant as “the first bionic man” and a Canadian newspaper proclaimed, “Movement by Thought: Science Fiction to Fact.”

The BrainGate research team is now focused on extracting the neural signals related to the intention to move one’s limb, and in turn a computer cursor, to use applications such as e-mail and word processing. The researchers are also working on allowing people to use the system to control prosthetic limbs or even their own limbs that have lost function. The device has the potential to restore the fundamental ability to communicate and to increase independence for those with spinal cord injury, stroke, ALS (also known as Lou Gehrig’s disease) and other disorders of the nervous system.

High-tech approaches to PTSD

Many other sophisticated tools are in early testing at CRRM to improve Veterans’ physical, as well as mental, functioning. For example, a recently launched study



Dr. Roy Aaron is director of VA's Center for Restorative and Regenerative Medicine and a professor of orthopedic surgery at Brown University.

is evaluating whether a “Virtual Iraq” virtual reality program, used for years in exposure-based therapy to recreate distressing situations in controlled clinical settings, can identify someone at increased risk for posttraumatic stress disorder before major symptoms appear. “Experts believe that early intervention will

make a difference,” says William Unger, PhD, chief of the PTSD program at the Providence VA Medical Center and a Brown University assistant clinical professor. “What we’re working on now is an objective way to identify those at higher risk who might benefit from such early treatment.”

In another example of forward-looking research, Aaron and a team of CRRM researchers are developing a method to measure blood flow in bones noninvasively, just by an MRI, to distinguish live from dead tissue. “Surgeons have a tough time telling live from dead tissue in a fresh wound,” Aaron explains. “This distinction is extremely important for wound management because we want to save all live tissue, but dead tissue can become dangerously infected.”

Because Veterans wounded in the conflicts in Iraq and Afghanistan are returning with devastating injuries that would have been fatal in past wars, there is a heightened need for these types of progressive healing approaches. It’s a prime example of scientific inquiry driven by real-world needs. Sums up Aaron, “We’re cranking up our research base to catch up with the clinical need.” —

Terms in restorative and regenerative medicine



Biohybrid Limbs. Artificial arms and legs that incorporate human tissue with manmade elements to perform like natural limbs.

Tissue Engineering. Replacement, repair, or regrowth of tissues using synthetic materials and human cells.

Biomimetics. Creation of materials that imitate natural biology.

Neurotechnology. Application of science to elucidate and harness the brain’s power to improve the body’s ability to function.

BRAIN BANKS—PROVIDING PRECIOUS CLUES ABOUT WHY A BRAIN BREAKS DOWN

A collection of specimens at the Bedford VA is providing insights on Alzheimer's disease and traumatic brain injury

The brain, running right, is a staggeringly capable instrument—commander of thought and behavior. But degraded by disease or injury, this three-pound organ is associated with some 600 neurological disorders, according to the National Institute of Neurological Disorders and Stroke.

The brain has long kept scientists baffled: What biological changes are to blame in medical conditions such as traumatic brain injury and Alzheimer's disease? Its elaborate structure makes the brain uniquely difficult to study. Also, brain biopsies are too risky, as a rule, and diagnostic images generally fall short of the desired detail. So neurology researchers rely heavily on brain banks, including some housed at the Bedford VA Medical Center in Massachusetts, for collecting clues about the biological nature of brain-related medical conditions. People with these types of diseases—and others without—arrange to donate their brains after death to advance scientists' understanding of the ravages wreaked by various ailments.


"We can't treat what we don't understand," says Ann McKee, MD, head of the neuropathology service for the VA New England Healthcare System and director of the Bedford VA-based brain banks. "The idea with these banks is to learn as much as possible about brain

diseases, including their origins and any environmental or genetic triggers."

Concussions: The sports-military link

At the Boston University Brain Bank at the Bedford VA Hospital, McKee studies the enduring effects of repeated head injury from contact sports and military combat. In the last couple of years, she has focused her investigation on the brains of deceased athletes who received many concussions during their careers—commonly boxers, football players and hockey players. In many of these athletes, researchers have identified a degenerative neurological condition called chronic traumatic encephalopathy, which during life can cause memory loss and erratic behavior.

"We're starting to understand so much about the parts of the brain involved in traumatic injury, and about links between brain structures and clinical symptoms," explains McKee, who is now also studying whether military troops with traumatic brain injury from blasts or other exposures on the battlefield experience the same types of effects. "There are clear parallels with Veterans," notes McKee—chronic traumatic encephalopathy is associated with brain trauma, and exactly how the trauma occurs may not be critical in some of the scientific questions being studied.

The image shows three men in light blue scrubs standing in a laboratory or classroom setting. They are looking towards the right side of the frame. In the foreground, two human brains are displayed on black stands. The brain on the left is a full-sized adult brain, while the one on the right is a smaller, child-sized brain. The background is slightly out of focus, showing some laboratory equipment and a white wall.

“We’re starting to understand so much about the parts of the brain involved in traumatic injury, and about links between brain structures and clinical symptoms.”

Medical students visit one of the brain banks housed at the Bedford VA Medical Center.

McKee believes researchers “are on the brink of a huge breakthrough” in understanding what people go through after a traumatic injury, and that brain banks hold promise, too, for studying mental health conditions such as posttraumatic stress disorder. “We really need to do exactly what we’re doing with other conditions—establish a special brain bank to allow us to fully analyze the brains of those who are diagnosed with PTSD,” says McKee, who surmises that many people with this “very heterogeneous condition” may have structural brain lesions leading to their symptoms.

To help researchers resolve remaining questions, 29-year-old Iraq Veteran Will Reynolds III has already decided to donate his brain for study after his death. He plans to make the donation through the Sports Legacy Institute, which studies the effects of concussion and often partners in its research with McKee and the Boston University Brain Bank. Reynolds, a West Point alum, was exposed to multiple blasts while serving in Iraq, including an IED explosion that left his left leg and arm severely injured. “Being in my unique scenario, exposed to so many blasts, my brain and other organs may be useful to help Veterans down the line with the same kinds of trauma,” he says.

This type of altruistic donation, to spare others suffering, is common, says McKee. “With Veterans, as with athletes, donations are driven by an esprit de corps—I hope by donating my brain I will help my fellow soldiers in the future.” In other situations, people want to understand what their family member went through, or if a disease such as Alzheimer’s may run in their family.

How Alzheimer’s unfolds

Alzheimer’s disease—which affects some 4.5 million Americans, including many aging Veterans, with the figure expected to triple by 2050—is a primary focus of brain bank research along with traumatic brain injury. VA researchers approach the study of Alzheimer’s from many perspectives, but the far-reaching role of brain banks in such investigation is hard to overstate, according to Neil Kowall, MD, director of the VA New England Geriatric Research, Education and Clinical



Center and the NIH-funded Boston University Alzheimer’s Disease Center.

Currently, brain autopsy is the only way to definitively diagnose Alzheimer’s disease, Kowall points out. Looking at the brain under a microscope after death is far superior to diagnostic imaging for scrutinizing the telltale brain changes in Alzheimer’s: protein clumps called amyloid beta “plaques” and twisted protein fibers called neurofibrillary “tangles.”

Animal models have helped scientists understand certain molecular events that the disease involves, but these models’ usefulness is extremely limited, says Kowall: “Even between the brain of a monkey and that of a person, there’s a massive difference in complexity. They say ‘You can’t teach an old dog new tricks,’ but there’s no animal analog to a person not being able to do something that once was easy—balancing a checkbook, or taking apart an engine.”

Ruth Henry says difficulty balancing a checkbook was one of the first signs of Alzheimer’s disease for her husband, John, who was diagnosed with the condition at age 62 and donated his brain to the Bedford VA, where he received care for several years before his 2004 death. “Math had been a game to John,” she says of the post-World War II Army Veteran, who, perhaps ironically, fully embraced the standard recommendations for reducing Alzheimer’s risk. He stayed mentally and physically active and ate a healthful



Research based at the Bedford (Mass.) VA Medical Center is examining the underlying biological damage that may be common to combat troops who survive blasts and football players, boxers and other athletes who sustain head injuries.

diet. “He just wanted to do whatever he could to help other people avoid what he was going through,” Henry says about her husband’s reasons for donating his brain for scientific study. John’s gift to medical science may be especially valuable to researchers because his identical twin brother, Charles, also contributed his brain after death from a cause unrelated to Alzheimer’s disease.

By studying donated brains from those with and without Alzheimer’s, says Kowall, VA and other researchers are already homing in on some of the early brain changes in the disease, and how Alzheimer’s differs from typical memory loss. “Many people have memory trouble. We are uncovering clues to tell us

when mild cognitive impairment is an opening shot of Alzheimer’s.”

Identifying early changes, Kowall says, could steer scientists toward interventions to halt the progression of Alzheimer’s disease before it becomes disabling. “This is a disease without a cure right now. Blocking the early biological processes in Alzheimer’s disease requires an understanding of how the dominos fall as the disease unfolds.” For understanding how Alzheimer’s and other neurological diseases evolve—and in turn, how they might be effectively treated—brain donation is, in Kowall’s words, a “unique gift with no adequate substitute.” —

Bedford VA houses several brain banks

Dr. Ann McKee of VA and Boston University oversees several brain banks, all housed at the Bedford VA Medical Center. They include those of:

- The Boston University Alzheimer’s Disease Center and the school’s New England Centenarian Study, the largest and most comprehensive study of centenarians and their families in the world
- The Center for the Study of Traumatic Encephalopathy, a major collaboration with the Sports Legacy Institute that is partly funded by the VA New England Geriatric Research and Clinical Center and several other agencies, including the National Institute on Aging
- The Framingham Heart Study, a project of Boston University and the National Heart, Lung and Blood Institute



EXPLORING THE FAMILY'S ROLE IN HELPING SEVERELY WOUNDED VETERANS

Caregivers and family members are at the heart of new polytrauma research

It was shortly after Christmas 2006 when an insurgent-made missile tore through Juan Roldan's Humvee and changed his life forever. The young Army staff sergeant suffered major injuries to his spinal cord, brain and other organs and would eventually need both legs amputated. The gunner on the vehicle was also severely wounded, and the driver—a private who Roldan says was “one of the best soldiers you could ever ask for”—was killed instantly. Today, Roldan wears a memorial bracelet engraved with his name.

Roldan, now 25, bears painful memories of the incident and struggles to keep a positive attitude. He relies on his devoted mother, Carmen, for day-to-day help in the Silver Spring, Md., apartment provided to him by Operation Homefront. He goes to the Washington, DC, VA Medical Center or Walter Reed Army Medical Center for care at least weekly. Now divorced, he proudly shows visitors a picture of his little daughter, Bryana, and says she's a big part of his motivation to keep going.


Families such as the Roldans are the focus of research based at the Minneapolis VA Medical Center, home to one of VA's four main polytrauma centers, where the nation's most severely wounded Veterans receive care.

One study under way is called Family and Caregiver Experiences with Polytrauma, or FACES. Lead

investigator Joan Griffin, PhD, says the study should provide much-needed information about the current and long-term needs of families—people who, in many cases, will continue to be involved in their loved ones' care for years or even decades to come.

“That's the big question for us—the long-term needs,” says Griffin, who is with VA's Center for Chronic Disease Outcomes Research and the polytrauma and brain-injury wing of VA's Quality Enhancement Research Initiative (QUERI). “These Veterans, for the most part, are a young population. So you've got parents who are in the prime of their working years and looking forward to retirement, who are all of a sudden thrown into a whole new experience they weren't expecting. Or you've got a 21-year-old wife who may not have the coping skills to deal with a husband who has a brain injury and who now may not be employable. What are these families going to do over the long term?”

The FACES study team is analyzing survey responses from 565 families and conducting in-depth interviews with some of the respondents. Most of the respondents are the parents, spouses or significant others of Veterans with polytrauma injuries. In some cases, the caregiver may be a friend or other relative. The situations are diverse: In some cases, the Veteran has improved and no



*One study under way is called
Family and Caregiver Experiences
with Polytrauma, or FACES.*

*Carmen Roldan is helping to care for her son, Army Veteran
Juan Roldan, as he continues to struggle to regain his
independence. He was severely wounded in Iraq in late 2006.*

longer needs substantial help. In others, intensive family caregiving is still required. In these families, the burden on caregivers can be grueling:

- Many caregivers are spending more than eight hours a day helping their loved one.
- They are often struggling to hold down a job and care for other family members.
- Many have had to stop working and drain their savings or retirement accounts to help pay for care.

Besides focusing on long-term needs, the study is also yielding insights on what families go through immediately after their loved ones are injured.

“Both the literature and the first glimpses of our data are showing that it’s those first few months that are very difficult for families,” says Griffin. “They’re difficult emotionally and financially. They are often taking off a lot of work, and possibly paying for travel and hotels on top of everything. Financially it’s a burden, and emotionally they’re still in a state of shock.”



For perhaps the first time in U.S. history, says Griffin, many military families are involved in the care of their seriously injured loved one from a very early stage. That’s partly because in the past, far fewer military personnel survived grievous wounds. It’s also because jet travel is now easier and more common, and people know about the injuries a lot faster.

“You might find out 24 hours afterward, get on a plane and be there [in Germany] within three days, whereas before it might have taken weeks,” says Griffin.

Severely wounded troops are typically evacuated from the war zone to the main U.S. military hospital in Germany. The next stop is generally a stateside military hospital such as Walter Reed, which specializes in acute and rehab care for polytrauma, followed by a VA polytrauma center, where rehab care continues with a multidisciplinary team of experts.

Those first few weeks and months may be just the beginning of a very long haul for polytrauma Veterans and their loved ones, says Griffin, but this period is what breaks some families—especially if there was underlying economic or emotional stress or poor relationships to begin with. Other families seem able to withstand the strain. Griffin hopes her research will reveal factors that help families rebound from adversity.

“We’ve heard countless stories that are inspiring, to the point where they bring us to tears,” she says. “Some families have been through this horrible thing but found purpose in it and become stronger through it. The human spirit is resilient. It’s a powerful thing.”

Other studies by the Minneapolis group aim to make VA polytrauma care more family-centered. That means involving families in the care plan, giving them the right resources, and seeing to their needs.

“If we keep families informed and involved in a way that they want to be involved, and in which the *patient* wants them to be involved, adherence to treatment, and outcomes, are likely to be better,” says Nina Sayer,

Marine Cpl. Jason Poole, seen here with his mother, Trudie, suffered a brain injury and other severe wounds in Iraq in 2004.

PhD, research chairperson for the polytrauma-brain injury QUERI.

The researchers have looked to other areas of medicine—such as pediatrics—for guidance on how to best involve family members in a patient’s care. The polytrauma population, though, is obviously different in many ways. And finding the right balance—how much to involve the family—can be tricky, says Carmen Hall, RN, PhD, also with the QUERI.

“We’re learning how to do that,” she says. “We don’t have a lot of guidance on this issue from the previous work in pediatrics. For an autonomous adult, family involvement and support looks different. It’s a little more challenging, because of privacy rules and our wish to optimize the autonomy of the Veteran. With younger Veterans whose parents may become very involved in their lives, a tension can develop between the Veteran’s need for independence and the parents’ instinct to take care of their son or daughter.”

One tool developed by the researchers is called the Family Care Map. It’s a Web-based guide that lays out each stage of VA rehab care in a user-friendly way. Care teams use it as a reference with families during the Veteran’s inpatient stay. In addition to it being available on the Web, families receive it in notebook form, with worksheets and references. For one thing, it allows for consistent terminology—otherwise, different clinicians may talk about the same thing using different jargon, and families may get confused.

“We wanted to provide a tool for both families and clinicians so they had the same ‘playbook,’” says Hall. “The Family Care Map creates a common framework from which to talk about the polytrauma rehab plan and how the family can participate.”

The Family Care Map has been tested and continues to evolve as researchers and clinicians learn more about families’ needs. “It’s a dynamic document,” notes Sayer.

She points out that the map is just one tool; more broadly, a family-centered culture is developing at the polytrauma centers. Some of the changes being guided and tracked by research:



Juan Roldan displays a photo of himself with his three-year-old daughter, Bryana.

- Training for registered nurses at the sites now includes more family-centered skills.
- Treatment goals are posted in patients’ rooms, along with white boards for family and staff to exchange information.
- Family peer support groups are being expanded.

Above all, says Hall, family-centered care is about “recognizing the uniqueness of each family and trying to explore with them and with the Veteran the ways in which the family will be involved in care.”

Today, Juan Roldan is looking forward to moving to Florida, where the organization Homes for our Troops is building him a house. His mother, Carmen, is prepared to continue caring for her son—but only in a way that works for him.

“I do whatever I have to do for my son. When he says ‘I don’t need you anymore,’ I will go out of the picture. But until that time, I’ll be here for whatever he needs.” —



USAF

“It simplifies my taking [my medications] and lets me know if I have or haven’t taken them.”

MANAGING MEDICATIONS MADE EASIER

Patients with serious mental illness may benefit from a new pharmacy approach, says a study at the Ann Arbor VA

Call it pill bottle sprawl. For millions of Americans—especially the elderly and those with chronic illnesses—kitchen cabinets and counters are increasingly taken up by white and amber plastic bottles containing their myriad medications. It's not uncommon for people to be on as many as 15 or so prescription drugs, not to mention vitamins and over-the-counter remedies.

Managing it all can be a burden. Those for whom adherence is most critical—such as patients with serious mental illness—often have the hardest time keeping track of what drug to take when. Store-bought pill organizers can help, but filling them each day or week is a challenge in itself. Staying on top of refills adds another layer of confusion.

There's a better way, according to a recent study at the VA Ann Arbor Healthcare System. Researchers there worked with clinicians and pharmacy staff to develop and test a system they call MedsHelp. It involves innovative packaging, personalized refill service, and close cooperation among pharmacy staff, social workers, nurses and doctors.

“What's unique about MedsHelp is that VA is trying to meet the needs of patients with daunting medical conditions and medication regimens with very personalized care,” says Agnes Jensen, a health services research associate and pharmacy technician who was part of the randomized clinical trial that led to the program.

Central to the new approach is “unit of use” packaging. Patients receive custom-made blister packs straight from the pharmacy, with their medications for each time of day—breakfast, lunch, dinner and bedtime—packed into separate plastic bubbles. There's a row for each day of the week, a column for each time of day. Colorful graphic icons and clear instructions are printed right on the packs.

The concept isn't totally new. The packaging components of MedsHelp have been applied in other settings and have proved effective for patients, especially older ones, with conditions such as diabetes and heart disease. But the VA Ann Arbor team expanded on the idea in several ways—for example, by packaging all the meds for a whole week into one visually friendly sheet format, with complete labeling for all the drugs.

Air Force Veteran Jeanette Eastham took part in a research project at the Ann Arbor VA that helped her manage her medications.

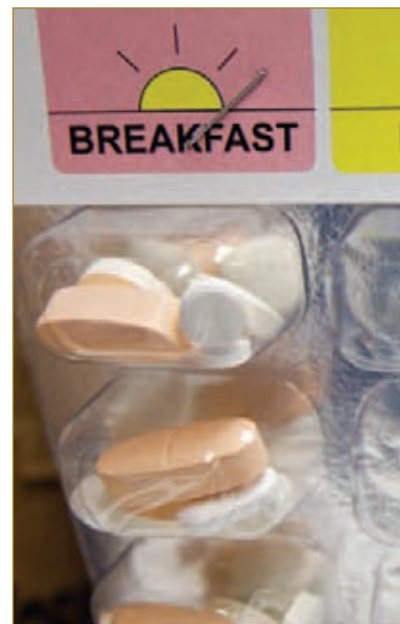
The packaging is only part of MedsHelp, but it's the feature that seems to elicit the most effusive feedback from patients who no longer have to cope with assembling—and remembering to take—their daily meds. This is critical for those with serious mental illness, as they often have impaired thinking skills.

“They have a system by which I can't make a mistake,” says Paul Getzen, 67, a Vietnam Veteran who developed bipolar disorder later in life. “It's all organized for you.” He adds that if he goes to a non-VA hospital, it's easier for him to give all his information. “On the back, it describes in great detail each pill—the size, shape, color, dose. So if I have to go to a civilian hospital, I just take that with me and everything is there. I don't have to explain to the doctor what I'm on, or how often I take it, or the dose.”

Veteran Jeanette Eastham, 56, who has mood and personality disorders and lost her voice from cancer, says, “It simplifies my taking them and lets me know if I have or haven't taken them.” She points out that the social worker who visits her home can also tell easily whether she has missed any doses. “The pills are loaded right in the containers and she can see if I've taken them.”

Adds Ann Whaley, 48, “I don't have to think about getting [my medications] ready.” She has struggled with bipolar disorder since her 20s.

Whaley's doctor is Marcia Valenstein, MD, MS, a physician and health services researcher at the Ann Arbor VA. She led the randomized clinical trial of MedsHelp that led to its being implemented at her VA hospital and four others in the region. The study team, which included researchers from the Ann Arbor VA and University of Michigan as well as other VA and academic sites, reported their results recently in *Schizophrenia Bulletin*. They found that patients using MedsHelp were significantly more likely to be taking their antipsychotic medication at 6 and 12 months. The study, which involved 118 Veterans with schizophrenia, schizoaffective disorder or bipolar disorder, did not show any easing of symptoms—even with the increases in adherence. But the study may not have been long enough to capture that, suggests Valenstein. Also, those in the study had to be able to understand key elements of the program, so they were “not at the higher end of the severity range,” says Valenstein, noting that symptom improvement may have been easier to see in patients with more severe illness.



The study didn't track drug adherence for other medical conditions, even though MedsHelp includes all of a patient's various drugs.

"I will have their antipsychotic, multivitamin, calcium, water pill, cholesterol medication, diabetes and hypertension drugs, all in one packet. That helps them be more compliant," says pharmacist Mary Moy-Sandusky, citing a typical regimen for patients in MedsHelp.

Moy-Sandusky, who now manages the program, says another important feature of MedsHelp is the personalized service.

"Patients have a social worker through the program, and they can also call us in the pharmacy with any problem. We have a really good rapport with them."

Adds Jensen: "Even in a large setting like a VA medical center, patients and pharmacy staff develop familiar, trusting relationships. MedsHelp patients know their pharmacist and pharmacy technician by name."

The extra care coordination and pharmacy services involved in MedsHelp cost VA about \$125 per patient per month. Valenstein says that "this cost should be

placed in the context of the high costs of the many medications that these patients are prescribed and the waste that occurs when meds are not taken regularly."

Also, the program handles refills on a custom basis so that "if a doctor is going to be changing a medication, I can send the patient only a one- or two-week supply," says Moy-Sandusky. She notes that the newer-generation antipsychotics commonly prescribed for those with serious mental illness can cost up to \$400 per month.

For now, the program is limited to five VA hospitals in one Midwest region. As the benefits of MedsHelp are confirmed in larger trials, Valenstein believes it will be practical for VA to implement the system at more facilities.

Meanwhile, most MedsHelp patients are clamoring to stay on the program—which now services more than 215 Veterans—because they like it so much.

Says Navy Veteran Getzen, "I feel great, and my kids say I'm on-target 110 percent." —

From left: Pharmacist Mary Moy-Sandusky meets with MedsHelp participant Ann Whaley; a close-up of the "unit of use" packaging used in the program; MedsHelp participant Paul Getzen displays the medication pack that is regularly mailed to his home through the program.



RECOGNIZING EXCELLENCE

An overview of major awards presented to outstanding VA investigators during National VA Research Week 2010

Barnwell Award

The Barnwell Award was established by VA in 2007 to honor John Blair Barnwell, MD, director of research and education for VA in the 1940s. He formed the Veterans Administration-Army-Navy Cooperative Studies in the Chemotherapy of Tuberculosis Program, which pioneered the model of the multi-site clinical trial. The award recognizes senior VA investigators who have achieved international acclaim for clinical research in areas of prime importance to VA's research mission.

William C. Duckworth, MD



Dr. William C. Duckworth is director of diabetes research at the Phoenix VA Medical Center and a professor of clinical medicine and biochemistry at the University of Arizona Medical School.

His lab focuses on insulin degradation and the role of insulin metabolism in insulin action. Duckworth's primary clinical interest is type 2 diabetes and its complications, and he serves as co-chair of both the VA Diabetes Trial and a separate VA study on diabetic nephropathy. He has also studied the delivery of diabetes care to Veterans. Duckworth is a

renowned author and lecturer, as well as a distinguished member of the *Journal of Cardiometabolic Syndrome's* editorial board. He is a diplomate of the American Board of Internal Medicine and is certified by the American Board of Endocrinology and Metabolism. He has received numerous honors and awards beyond his many research grants and contracts, and has participated in various National Institutes of Health research reviews.

William C. Cushman, MD



Dr. William C. Cushman is chief of the preventive medicine section at the Memphis VA Medical Center; lead hypertension consultant for VA at the national level; and professor of preventive medicine,

medicine and physiology at the University of Tennessee College of Medicine. Cushman served on the executive committee that wrote the 2003 Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) and is currently on the JNC 8 panel. A fellow of the American College of Physicians and American Heart Association, Cushman has been an investigator on



PECASE winner Dr. Melina Kibbe is a vascular surgeon and biomedical researcher at the Jesse Brown VA Medical Center in Chicago.

many clinical studies relating to hypertension, lipids and type 2 diabetes. He served as VA chair for the National Heart, Lung, and Blood Institute (NHLBI)-sponsored Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)—the largest hypertension trial ever—and is currently principal investigator for the VA Clinical Center Network and chair of the Blood Pressure Working Group of the NHLBI-sponsored Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. Cushman's research has led to a VA-wide performance measure that promotes the evidence-based use of drugs known as thiazide diuretics to manage hypertension.

Paul B. Magnuson Award

This award, established in 1998, honors Paul B. Magnuson, MD, who, as a bone and joint surgeon in VA, continuously sought new treatments and devices to help Veterans. The award is given annually to a VA rehabilitation investigator who exemplifies the entrepreneurship, humanitarianism and dedication to Veterans shown by Dr. Magnuson during his career.

Robert L. Ruff, MD, PhD



Dr. Robert L. Ruff is the Veterans Health Administration's national director for neurology. His research interests include stroke rehabilitation and combat-related traumatic brain injury. Ruff, who received his MD and PhD degrees from the University of Washington, has been chief of the neurology, rehabilitation and spinal cord injury services at the Louis Stokes VA Medical Center, and is medical director of the FES Center in Cleveland, a VA Rehabilitation Research Center of Excellence. A professor of neurology and neurosciences at Case Western Reserve University, Ruff has been on the editorial board of the *Journal of Rehabilitation Research and Development* since 1999, serving as the journal's deputy editor since 2004 and as editor-in-chief from 2005 to 2007. He was associate editor of the journal *Neurology* from 1994 through 1996 and a member of the editorial board of *Muscle & Nerve* from 2004 to 2007.

Middleton Award

VA established the Middleton Award in 1960 to honor William S. Middleton, MD, an educator and physician-scientist who served as VA's chief medical director from 1955 to 1963. The award is given each year to one or two senior VA investigators for major achievements in areas of prime importance to VA's research mission.

Michael D. Norenberg, MD



Dr. Michael D. Norenberg, a VA clinician-researcher for more than 36 years, is currently on staff at the VA Miami Healthcare System. He is also a professor of pathology and director of neuropathology at the University of Miami,

Miller School of Medicine, where he holds appointments in the departments of biochemistry/molecular biology, neurology and neurosurgery. In addition, he is an affiliate faculty member with the Miami Project to Cure Paralysis. Norenberg has made essential contributions in a range of research areas. Among other accomplishments, he has played a key role in elucidating the biology of astrocytes, the main supporting cells of the central nervous system; characterized pathological changes and identified potential targets for therapeutic intervention in spinal cord injury; and contributed to a better understanding of brain edema (swelling from excess fluid) as a consequence of brain trauma. Also, his research laid the groundwork for a new treatment approach for hyponatremia—a sodium imbalance—that has dramatically reduced the incidence of a related complication called central pontine myelinosis, which affects the brainstem. All told, Dr. Norenberg has some 240 scientific publications to his name. He has served on the editorial boards of his field's leading journals and has won numerous awards for research and teaching.

Edward J. Weinman, MD



Dr. Edward J. Weinman, with the VA Maryland Healthcare System, has been a VA clinician-investigator for 27 years and has made seminal contributions to the understanding of kidney function. His pioneering

achievements have included mapping out the molecular processes involved in kidney function and isolating, cloning and demonstrating the function of two proteins, NHERF-1 and NHERF-2, that regulate kidney function. Dr. Weinman's discoveries have proved clinically relevant not only in nephrology but also in gastroenterology and neurology. In addition to 173 peer-reviewed publications, Dr. Weinman has authored or co-authored 27 invited reviews and several editorials and letters to the editor in leading medical journals. He has also contributed various chapters to medical textbooks, including *Cecil Essentials of Internal Medicine*. His research is currently funded by both VA and the National Institutes of Health.

Presidential Early Career Award for Scientists and Engineers (PECASE)

The PECASE program was established by the White House in 1996 to recognize and nurture outstanding scientists and engineers who are in the early stages of their careers and "who show exceptional potential for leadership at the frontiers of scientific knowledge during the twenty-first century."

Melina R. Kibbe, MD



Dr. Melina R. Kibbe, of the Jesse Brown VA Medical Center in Chicago, studies the effects of nitric oxide on vascular smooth muscle cell proliferation, with a focus on minimizing blood vessel damage associated

with vascular bypass grafting and arterial injury. A VA Career Development awardee, she has established a vibrant and robust vascular research laboratory located within Northwestern University's Institute for BioNanotechnology in Medicine. Kibbe has received the university's Drew Senyei, MD, Translational Research Award to develop a nitric oxide-releasing graft for better recovery following vascular surgery. Her research has been recognized and supported by diverse public and private grants, and she has also exhibited an award-winning dedication to teaching and a sustained commitment to charitable causes. Kibbe has published more than 50 peer-reviewed manuscripts and 10 book chapters, and her work has been presented at numerous national and international meetings.

Alexander Sox-Harris, PhD



Dr. Alex Sox-Harris earned graduate degrees in counseling psychology and statistics at Stanford University. Based at the VA Palo Alto Health Care System, Sox-Harris plays key roles in three VA research centers: He is a health services researcher at the Center for Health Care Evaluation; a statistician and methodologist at the Bone and Joint Rehabilitation Center; and associate director of the Program Evaluation and Resource Center. A main focus for Sox-Harris has been improving the quality of addiction treatment. He has led efforts to examine and refine process-quality measures widely used to predict outcomes for patients treated for drug or alcohol addiction. Sox-Harris also examines system-wide variability in the use of Food and Drug Administration-approved medications in the treatment of alcohol dependence, and studies the relationship between alcohol misuse screening data and subsequent medical outcomes. He has more than 50 scientific articles and nine book chapters to his credit.

Under Secretary's Award for Outstanding Achievement in Health Services Research

This award is presented annually by VA to an investigator whose health services research has added significantly to the understanding of factors that affect the health of America's Veterans or has led to a major improvement in the quality of their health care, and who has demonstrated leadership in the research community and excellence in the training and mentorship of young investigators.

Mary K. Goldstein, MD, MS



A health services researcher at the VA Palo Alto Health Care System for more than 18 years, Dr. Mary K. Goldstein has focused on studying functional status in geriatrics, hypertension management, clinical guideline compliance, and automated clinical decision support systems. Her work in health informatics is known nationally and internationally. Within the Consortium for Healthcare Informatics Research, funded by VA Health Services Research and Development, Goldstein is principal investigator for the project on translational use cases. As a VA Career Development awardee, Goldstein led a team that developed an automated clinical decision support system for hypertension management known as ATHENA-CDS. The system combines patient information from VA's electronic medical records system with an automated knowledge base of hypertension to generate patient-specific recommendations for managing hypertension. The recommendations are displayed on clinicians' computer screens when they see patients. Goldstein serves as director of the Geriatric Research, Education and Clinical Center at the Palo Alto VA and shares her expertise and experience by actively mentoring VA researchers and clinicians.

RECENT ADVANCES BY VA RESEARCHERS

A sampling of important new scientific findings reported by VA investigators during the past few months

ACCORD trial reports blood pressure, lipid results

In a surprising result, intensive treatment of high blood pressure to reach normal levels—below currently recommended levels—did not further reduce the risk of stroke and heart attack in people with type 2 diabetes who were at very high risk for cardiovascular disease, according to the Action to Control Cardiovascular Risk in Diabetes (ACCORD) clinical trial, one of the largest studies ever conducted in this population. The study also found that treating multiple blood lipids with a fibrate and a statin did not reduce risk more than treatment with a statin alone.

The study was sponsored by the National Institutes of Health and included more than 10,000 patients with diabetes, including Veterans at 10 VA sites. The study tested three strategies to lower the risk of major cardiovascular events: intensive control of blood sugar, intensive control of blood pressure, and treatment of cholesterol and triglycerides.

VA's involvement in ACCORD was led by William Cushman, MD, of the Memphis VA Medical Center. "Our results provide no conclusive evidence that targeting a normal systolic blood pressure—less than 120 mmHg—compared with targeting a systolic blood pressure of less than 140 mmHg lowers the overall risk



Dewey Ratcliff has his blood pressure taken by nurse Margaret Penry at the Central Arkansas Veterans Healthcare System.

of major cardiovascular events in high risk adults with type 2 diabetes," said Cushman.

He pointed out, however, that the "study suggests that lower blood pressure levels in patients like those in ACCORD may reduce the risk of stroke. This finding is consistent with other blood pressure trials." He also noted that more intensive blood pressure control resulted in a higher risk of adverse events, and that people with diabetes should carefully weigh the risks and benefits of treatment with their physicians.

(New England Journal of Medicine, online March 14, 2010)



Researchers at the VA Palo Alto Healthcare System used a mathematical model to project the effects on Americans' health of proposed reductions in the amount of sodium in processed foods.

Food industry effort to cut sodium would save lives, study suggests

A voluntary effort by the U.S. food service industry to cut salt in processed foods could have far-reaching implications for the health of the U.S. population, preventing strokes and heart attacks in nearly a million Americans and saving \$32.1 billion in medical costs, according to a study by researchers with Stanford University and the VA Palo Alto Health Care System.

In the study, the researchers developed a computerized model that simulates the effects of reduced sodium intake on a large population of people between the ages of 40 and 85. Based on a similar salt-reduction campaign in the United Kingdom, the researchers estimated that a collaborative industry effort could lead to a 9.5 percent decline in Americans' salt intake. That, in turn, would lead to a very modest decline in blood pressure among American consumers, minimizing a major risk factor for cardiovascular problems.

"In our analysis, we found these small decreases in blood pressure would be effective in reducing deaths due to cardiovascular disease," said Crystal Smith-Spangler, MD, a postdoctoral scholar with VA and first author of the study. "The numbers of affected people are huge, so even a small decrease is significant if you have large numbers of people involved."

By the researchers' calculations, some 513,885 Americans would be spared from potentially fatal strokes in their lifetimes, and another 480,358 would not suffer heart attacks as a result of the reduced salt campaign.

(Annals of Internal Medicine, March 2, 2010)

Stress-affected brain region is smaller in Veterans with PTSD

A specific region of the hippocampus, a brain structure essential to memory, is significantly smaller in Veterans with posttraumatic stress disorder than in those without the condition, according to a study by a team with VA and the University of California, San Francisco.

The researchers used MRI to scan the brains of 40 Veterans—20 with combat-related PTSD and 20 without—and found that the region known as the CA3/dentate gyrus was at least 11 percent smaller, on average, in those with PTSD.

Also, the CA1 region of the hippocampus, which



shrinks as a part of normal aging, was not significantly affected in the Veterans with PTSD, according to lead investigator Norbert Schuff, PhD. “This is the first time in human subjects that PTSD has been shown to be associated with changes in certain specific hippocampal regions and not in others,” said Schuff.

The hippocampus, a small structure found on both sides of the brain, helps establish and retrieve memories, said co-author Thomas C. Neylan, MD. He noted that recurring or intrusive memory of traumatic events is a common symptom of PTSD, “and thus the hippocampus is of great interest in PTSD research.” Neylan said the results raise the possibility that since the dentate gyrus has the ability to create new neurons, “These changes might actually be reversible through treatment.”

The authors cautioned that the findings need to be replicated in larger studies. “This is an incremental step toward establishing a physical biomarker for PTSD,” said Neylan. “A biomarker is our ultimate goal, since currently PTSD is diagnosed based on a subjective neuropsychiatric examination rather than on physical symptoms. He added that a biomarker would provide clinicians and researchers with an objective way to measure the progress of PTSD treatment, and “would also allow us to no longer think of PTSD as a mental health diagnosis, with all of its associated stigma for our Veteran and military patients, but to view it as a physical wound instead.”

(Archives of General Psychiatry, March 2010)

Study finds potential Alzheimer’s use for immune drug

Rapamycin, a drug that keeps the immune system from attacking transplanted organs, may have another use: fighting Alzheimer’s disease. The drug—a bacterial product first isolated in soil from Easter Island in the Pacific—reversed learning and memory deficits in a mouse model of the disease, reported a team with VA and the University of Texas Health Science Center in San Antonio.

Rapamycin also reduced lesions in the brains of the mice, the team found. The lesions are similar to those seen in the brains of people who died with Alzheimer’s. Last year, researchers at three institutions—including the Texas group—announced that rapamycin extended the lifespan of aged mice. It was the first pharmacologic intervention shown to extend life in an animal model of aging.

“While it remains to be determined whether our results obtained in mice could be translated in people, we are very excited as these findings may lead to a new therapeutic intervention to treat Alzheimer’s,” said lead researcher Salvatore Oddo, PhD.

(Journal of Biological Chemistry, Feb. 23, 2010)

Antibody boosts therapy for multiple sclerosis

An international team co-led by a researcher with VA and the University of Utah found that adding a treatment called daclizumab, a type of antibody, to standard drug therapy cuts the number of new or enlarged brain lesions in patients with relapsing multiple sclerosis.

About 85 percent of MS patients are initially diagnosed with a relapsing form of the disease, in which clearly-defined attacks are followed by partial or complete recovery periods.

John Rose, MD, of the VA Salt Lake City Health Care System and the University of Utah, said previous clinical trials that were not randomized suggested benefits from the antibody. The new findings, he said, confirm that “daclizumab significantly reduces MS lesion formation in people with active relapsing disease.”

The study included 230 patients at 51 sites in the U.S., Canada and Europe. In addition to taking a standard MS drug called interferon beta, the volunteers were randomly assigned to add-on treatment with high-dose daclizumab, low-dose daclizumab or placebo. In addition to finding that add-on treatment with high-dose daclizumab resulted in a significantly lower number of new or enlarged MS lesions, the researchers

found that patients treated with either high- or low-dose daclizumab had far more natural killer cells, which the researchers believe may account for the treatment's benefits.

(Lancet Neurology, online Feb. 15, 2010)

Orthopedic surgery outcomes better at specialized hospitals

The more specialized a hospital is in orthopedic surgical care, the better the outcomes appear to be for patients undergoing hip and knee replacement surgery, according to a study of Medicare data by a team with VA and the University of Iowa.

Among more specialized hospitals, there were fewer serious post-surgical complications such as blood clots, infections and heart problems, as well as fewer deaths.

The findings were based on data for nearly 1.3 million older patients who received hip or knee replacement surgeries between 2001 and 2005 at 3,818 U.S. hospitals. The study adjusted for differences in the types of patient seen at each hospital, as well as the number of surgeries that each hospital performed. Compared with the least specialized hospitals, the more specialized hospitals treated a lower proportion of women and African Americans. These hospitals also treated patients who had better health overall.

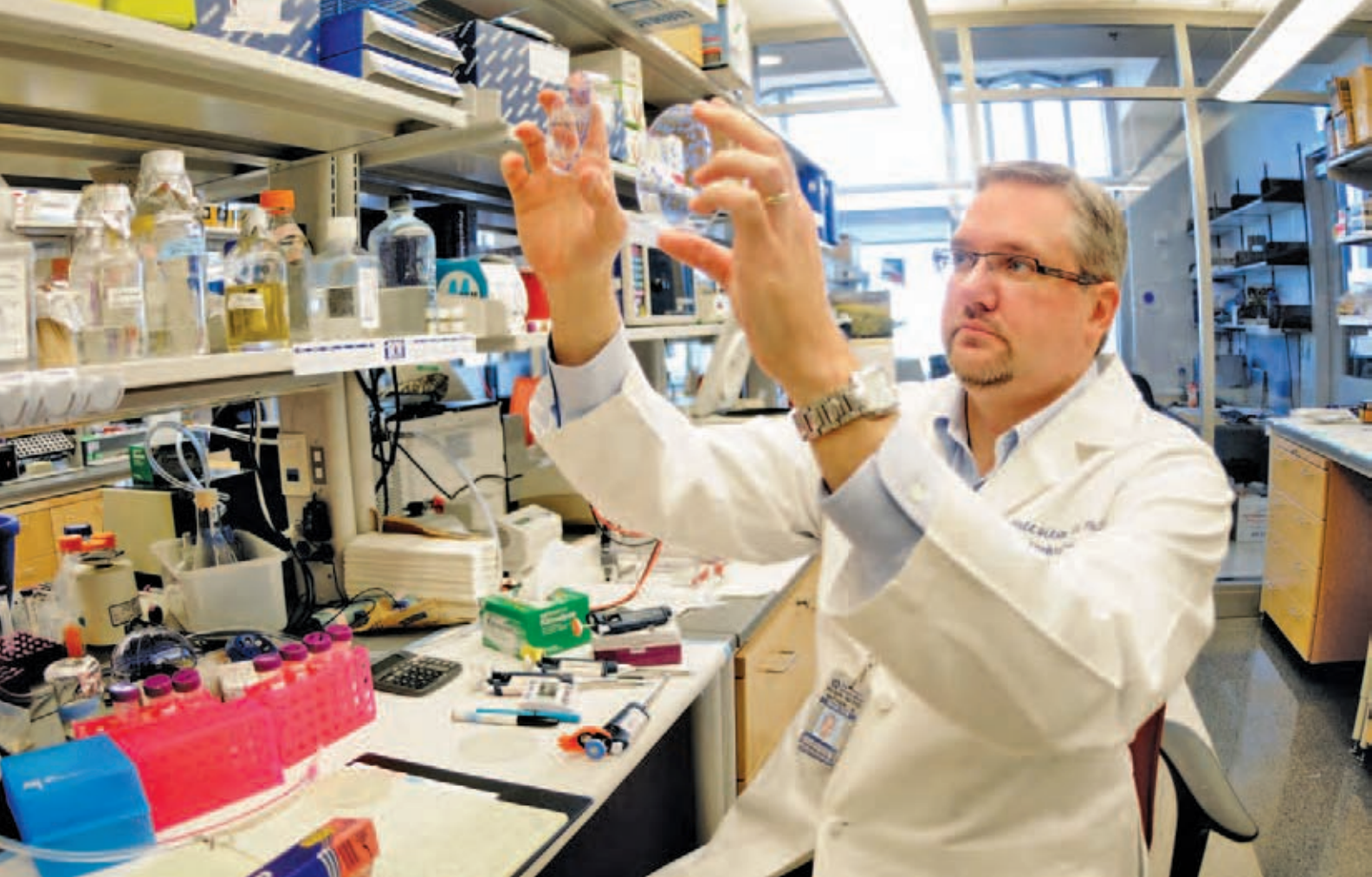
In addition, the rate of post-surgery infection for patients who got hip and knee replacements decreased from 2.6 percent at the least specialized hospitals to 1.6 at the most specialized hospitals.

“Learning more about orthopedic specialization could help us to better understand how to organize care and take ideas from more specialized hospitals to less specialized hospitals and result in better outcomes all around,” said senior author Peter Cram, MD, with the Center for Research in the Implementation of Innovative Strategies at the Iowa City VA Medical Center.

(British Medical Journal, online Feb. 11, 2010)



Surgeons in action at the VA Palo Alto Healthcare System.



Dr. Matthew Wilson of the Houston VA Medical Center and Baylor College of Medicine says a gene-transfer method his lab is developing could come to play a key role in drug discovery and gene therapy.

New genetic-engineering technique could speed drug discovery

Drug discovery in biomedical labs worldwide may benefit from a new gene-insertion method being developed by a group with VA and Baylor College of Medicine in Houston. Until now, researchers have generally been able to insert only one gene at a time into cells or lab mice to study its effects. The new method will enable them to insert several genes at once. Lead researcher Matthew H. Wilson, MD, PhD, said the new gene-transfer technique “allows you to ask a whole new level of questions that you couldn’t ask before.”

The new method uses carrier genes called transposons. Discovered in the 1950s, transposons are also known as “jumping genes” because they spontaneously hop around to different spots on the DNA strands that make up an organism’s genome. Several different transposons have been studied in recent years because they offer an efficient way to ferry new genes into the

DNA of cells or lab animals. Wilson’s lab has focused on one transposon in particular, known as piggyBac. In their experiments, the team used the gene and its related enzyme to efficiently transfer up to eight genes at once into human kidney cells.

Besides drug discovery, transposons hold promise for gene therapy. They are seen as potentially safer, faster and more cost-effective than current methods that use viruses to transfer beneficial genes into patients’ DNA.

The recipient of Career Development funding from VA, Wilson specializes in nephrology research. He hopes to eventually develop a treatment for an inherited kidney disease called Alport Syndrome, which affects 1 in 5,000 people. His group’s breakthrough in transposon-based gene transfer came as they sought the best ways to deliver genes to the kidneys of mice.

(Proceedings of the National Academy of Sciences, Jan. 26, 2010)

Blood pressure benefits seen from low-carb diet

In a head-to-head comparison, two popular weight-loss methods proved equally effective at helping overweight and obese Veterans shed pounds. But, in a surprising twist, a low-carbohydrate diet proved better at lowering blood pressure than the weight-loss drug orlistat, according to researchers with VA and Duke University Medical Center in Durham.

The findings send an important message to those with hypertension who are trying to lose weight, said lead author William S. Yancy Jr., MD. “If people have high blood pressure and a weight problem, a low-carbohydrate diet might be a better option than a weight-loss medication. It’s important to know you can try a diet instead of medication and get the same weight-loss results with fewer costs and potentially fewer side effects.”

The 146 people in the year-long study had a range of health problems typically associated with obesity—diabetes, high blood pressure, high cholesterol, arthritis. Nonetheless, they saw impressive results from the study treatments: The average weight loss for both groups was nearly 10 percent of body weight. Yancy attributes the success in large part to the group counseling that was offered for 48 weeks. “People tolerated orlistat better than I expected,” says Yancy, noting that use of the drug is often limited by gastrointestinal side effects, but that “these can be avoided, or at least lessened, by following a low-fat diet closely. We counseled people on orlistat in our study fairly extensively about the low-fat diet.”

The two methods proved equal not only for weight loss, but also for reducing levels of cholesterol and blood sugar. With regard to blood pressure, though, there was a distinct edge to the low-carb approach. Some 47 percent of patients in the low-carbohydrate group were able to decrease or discontinue their blood pressure medication, while only 21 percent of the orlistat group were able to do so.

(Archives of Internal Medicine, Jan. 25, 2010)

Hypertension drugs may thwart dementia

Drugs known as angiotensin receptor blockers (ARBs)—brand names such as Atacand or Avapro—are used mainly to treat high blood pressure and heart failure because they block a hormone that narrows blood vessels. A team at the Bedford (Mass.) and Boston VA medical centers found that the drugs may also help prevent dementia, adding to similar results from some previous studies.

The study, based at VA’s Center for Health Quality Outcomes and Economic Research, analyzed the records of more than 800,000 older Veterans who had been treated for hypertension or heart disease. They found that those taking ARBs were up to 24 percent less likely to develop dementia than those taking other drugs. Moreover, of patients who had Alzheimer’s disease at the study’s outset, those on ARBs were half as likely to enter a nursing home, compared with those taking ACE inhibitors or other heart drugs.

In an interview with *Business Week*, senior author Benjamin Wolozin, MD, PhD, with VA and Boston University, said improved blood flow to the brain is the likely mechanism behind the drugs’ apparent cognitive benefits. “If you get no blood to the brain, you’re not going to think well,” he said.

Wolozin pointed out that randomized clinical trials will be needed to test whether ARBs are truly responsible for the Alzheimer’s-thwarting effect seen in his group’s large database study. Meanwhile, he cautioned that the new evidence is not enough to warrant routine clinical use of ARBs to halt dementia, adding that the drugs could pose significant side effects for some patients, such as drops in blood pressure that lead to falls.

(British Medical Journal, Jan. 12, 2010)



Soldiers with the Second Infantry Division walk through a local market in Ebnkathwer, Iraq, in March 2010.

OEF/OIF Veterans with mental health conditions use more VA medical services

In a study of nearly 250,000 Veterans of the wars in Iraq and Afghanistan, those with mental health diagnoses used non-mental health medical services in VA at higher rates than those without mental health disorders.

The most striking finding was that Veterans whose mental health diagnosis was PTSD used VA medical services at almost twice the rate of those whose mental health diagnosis was another disorder, such as depression.

The overall results are consistent with studies of Veterans from earlier wars, says lead author Beth Cohen, MD, MAS, a staff physician at the San Francisco VA. “What we don’t know from this data,” she says, “is whether these Veterans are using medical care more often because they simply have more medical diseases, or because they need help with mental health concerns but seek care in other medical settings” because of the stigma associated with mental health treatment.

The authors found that Veterans with PTSD used non-mental health medical services, including primary care, emergency care, and visits to other medical specialists, at a 91-percent higher rate overall than those without mental health diagnoses. Veterans with a mental health diagnosis other than PTSD had a 55-percent higher use rate than those without mental health diagnoses.

To explore the factors driving the Veterans’ use of non-mental health medical care, Cohen and colleagues plan to evaluate the effects of different models of care delivery on utilization. One such model, says Cohen, is the OEF/OIF Integrated Care Clinic at the San Francisco VA, where all patients, whether or not they screen positive for mental health concerns, are seen by primary care, mental health, and social work providers, potentially reducing the stigma of seeking mental health care.

(Journal of General Internal Medicine, January 2010)

VA RESEARCH TODAY

CREDITS

VA Research Today is produced by:

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Korean War Veteran Ron Greenberg, 76, is back on the golf course after learning how to better manage his chronic lung ailment through a VA study. See the story inside.