

# STATE OF VA RESEARCH

Improving Veterans' Lives



2011

DISCOVERY → INNOVATION → ADVANCEMENT



Veterans Health Admin

Improvi



# A Message from the Chief

For 86 years, the Office of Research and Development of the Department of Veterans Affairs (VA) has been improving the lives of Veterans and all Americans through health care discovery and innovation. Because more than 70 percent of VA researchers are also clinicians who provide direct patient care, VA is uniquely positioned to quickly move scientific discovery from investigators' laboratories to patient care. In turn, VA clinician-investigators identify new research questions for the laboratory at the patient's bedside, making our research program one of VA's most effective tools to improve Veterans' care.

Our fundamental goals are to address the needs of the entire Veteran population, from the young recruit who returns from combat with injuries to the aging Veteran, and to use our research findings proactively to benefit future Veterans. The data our researchers generate are used not only in our current projects, but also as the foundation for future work.

VA Research is an intramural program that is fully integrated with the larger biomedical research community through our academic affiliations with other organizations. Our investigators foster dynamic collaborations with colleagues in other federal agencies, academic medical centers, non-profit organizations, and private industry nationwide, further expanding the scope and reach of our work.

From effective therapies for tuberculosis, to implantable cardiac pacemakers, to the first successful liver transplants, to the development of the nicotine patch, to the discovery of new genes, and beyond, VA's rich research history and trailblazing accomplishments are a source of great pride to our

Department and to the nation. While our research is principally focused on benefiting current and future Veterans, it also impacts Veterans' families and caregivers, VA health care providers, Veterans Service Organizations, other components of the Federal research establishment, academic health centers, and health care practitioners throughout our country.

VA research is a valuable investment with remarkable and lasting returns. The state of VA research today is stronger than it has ever been. I invite you to learn more about the many ways in which our researchers are improving Veterans' lives.

Joel Kupersmith, M.D.  
Chief Research and Development Officer  
Department of Veterans Affairs



**Joel Kupersmith, M.D.**  
Chief Research and Development Officer  
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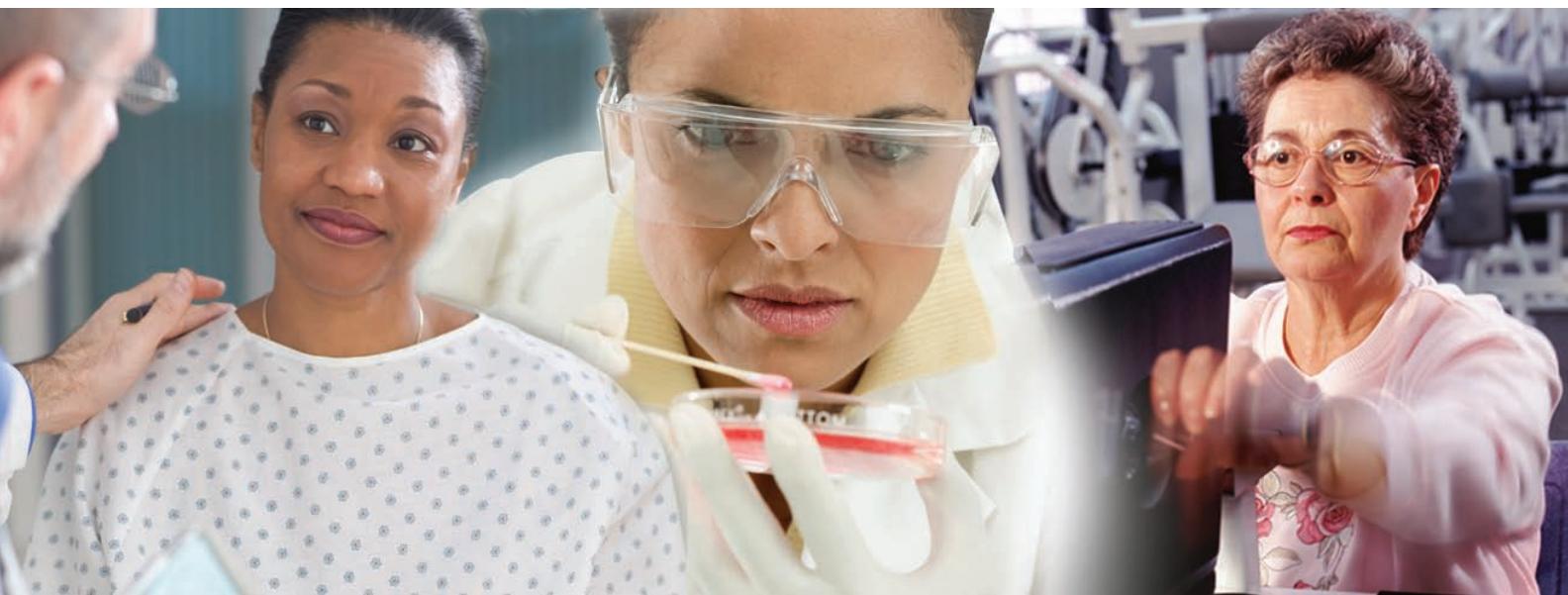
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# VA Research plays key role in advancing health care for Veterans

VA's Office of Research and Development (ORD, also R&D, or VA Research) plays a key role in advancing the health and care of America's Veterans. As part of the largest integrated health care system in the United States, VA Research relies on committed clinician-investigators, engaged patients and families, and an unparalleled national health care delivery infrastructure to help the VA deliver the world-class health care Veterans have earned through their service, and to develop cutting-edge medical treatments for Veterans, their families, and our nation.

VA researchers regularly find ways to improve Veterans' health care. Our focused missions enables VA Research to demonstrate, in the 21st century, how scientific inquiry and innovative thought can transform medicine in America—and to help lead the national transformation of health care that is now underway.

In testimony last year before the United States House of Representatives, Eric A. Hilleman, Director of the Veterans of Foreign Wars of the United States, said, "VA Research is a national asset. Research conducted in the Department of Veterans Affairs has led to such

innovations and advances as the cardiac pacemaker, nuclear scanning technologies, radioisotope diagnostic techniques, liver and other organ transplantation, the nicotine patch, and vast improvements in a variety of prosthetic and sensory aids."

Blake C. Ortner, Senior Associative Legislative Director of the Paralyzed Veterans of America, told the House, "We are particularly pleased that Congress has recognized the critical need for funding in the Medical and Prosthetic Research account in the last couple of years. Research is a vital part of Veterans' health care, and an essential mission for our national health care system."

VA Research is proud of its heritage of service to Veterans and our nation. This report highlights some of VA's major research accomplishments, with an emphasis on the progress made in 2010. It presents a snapshot of the types of health studies that have made VA Research an acclaimed model for conducting bench-to-bedside research.



## Value of an intramural research program with priceless partnerships

VA Research and Development is an intramural program where clinical care and research occur together within VA's health care system. This partnership enables VA to bring scientific discovery from the patient's bedside to the laboratory and back, making the program one of VA's most effective tools for improving care for Veterans. Embedding research within an integrated health care system with a state-of-the-art electronic health record creates a national laboratory for the discovery of new medical knowledge and for translating that knowledge into improved health. VA Research's fundamental goal is to address the needs of the entire Veteran population, from the recruit who returns wounded from war to the oldest Veteran. Ultimately, VA research benefits all who receive health care.

VA is able to conduct innovative research across multiple VA sites—with studies often including thousands of Veterans—thanks to the Department's Cooperative Studies Program (CSP). CSP organizes research involving multiple medical centers within VA to reap greater benefits than can be achieved from a single-site study. CSP's clinical trials and epidemiological studies cover a wide range of health topics, including heart disease, diabetes, cancer, infectious diseases, mental health, and prosthetics. The program's large-scale leading-edge trials allow VA to generate strong evidence to help guide clinical practice.

## Translating knowledge into improved health: Study examines long-term effects of HIV/AIDS treatments

Dr. Amy C. Justice, a clinical investigator who cared for VA patients with HIV infections and AIDS, noticed that patients on combination antiretroviral therapy were living longer, but seemed to have an increased risk for "non-AIDS" events (illnesses not specifically tied to AIDS infection). She began a longitudinal clinical trial to follow these patients over a long time to understand how treatment approaches were working and better understand the risks associated with the illness.

The trial is called SMART (Strategies for Management of Antiretroviral Therapy). Dr. Justice and her coworkers learned that there were 1.7 times as many major coronary artery disease, renal, and liver disease events among those whose treatment involved structured interruptions of medications because of problems involved with their long-term use, compared with those who received their medications on a regular basis.

In addition, models accounting for varying CD4 (T-cells, or cells particularly vulnerable to the AIDS virus) count and HIV-1 RNA (a retrovirus that causes AIDS by infecting CD4 cells) did not fully explain these differences in outcome. The study team concluded that the risk of common non-AIDS conditions was indeed greater for patients using this therapy; however established modifiable risk factors, such as smoking, played a greater role in this finding than patients' CD4 count, the principal biomarker for AIDS.



# VA Cooperative Studies Program

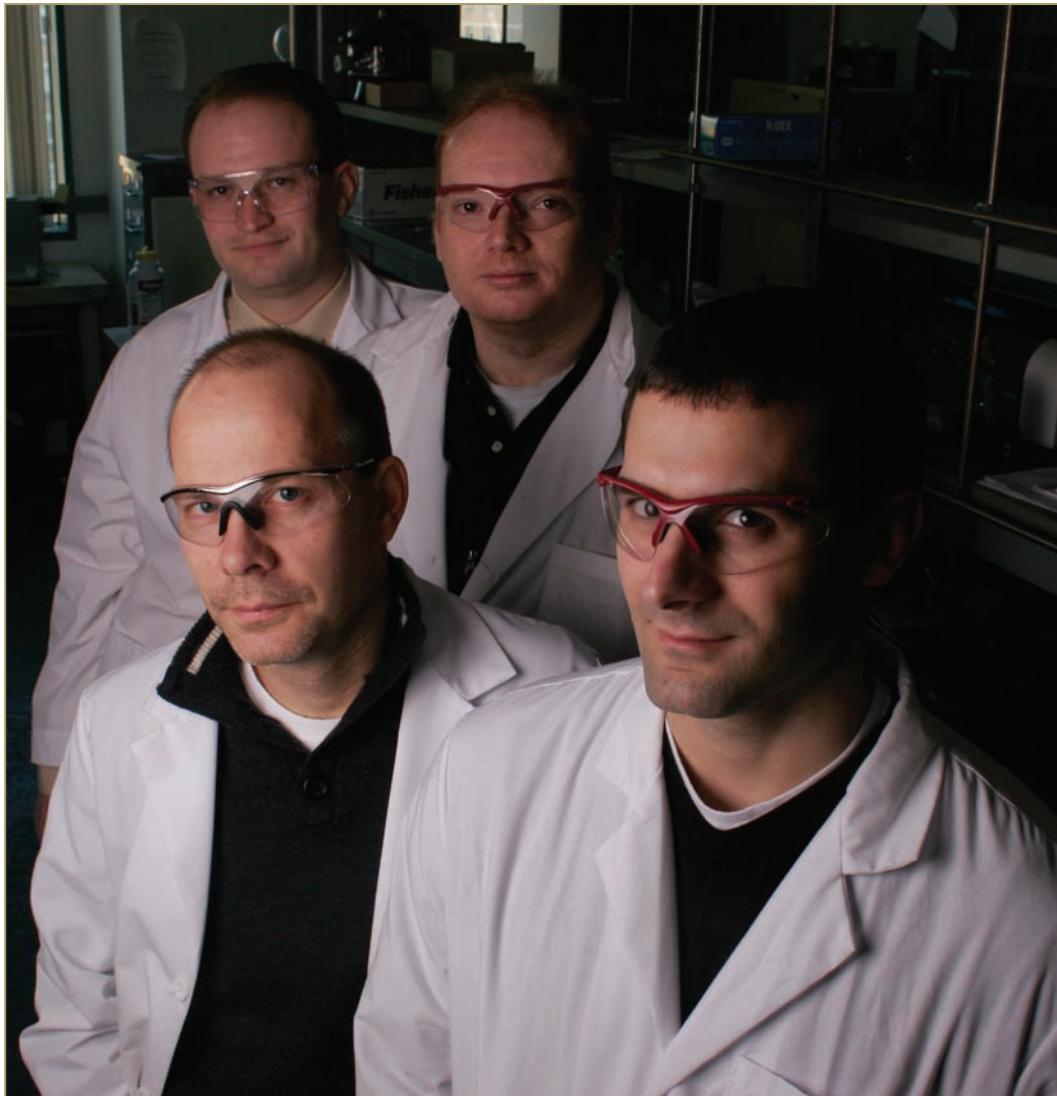
*New heart study highlights the benefit of embedded research system*

A recent Cooperative Study Program (CSP) study highlights the benefits of an embedded research system. The study looked at whether the use of heart-lung pumps during cardiac surgery yielded better outcomes than surgery without the pump. The clinical trial involved 18 VA medical centers and its results were published in the *New England Journal of Medicine*.

The 2,203 Veterans in the study all had clogged or narrowed coronary arteries, resulting in less blood flow to the heart. This can cause chest pain and increase the risk of heart attack. In bypass surgery, also known as coronary artery bypass grafting (CABG), doctors take a healthy piece of vein from elsewhere in the body and sew it in place as a “detour” between the heart and a point in the problem artery below the blockage.

As long as the graft remains open, and doesn't close down over time, the heart enjoys a renewed flow of blood and oxygen.

For more than 30 years, most bypass procedures have been done with the use of a cardiopulmonary bypass pump, or heart-lung machine. During an “on-pump” procedure, the heart is stopped with medication and the machine takes over blood circulation. This allows doctors to work on a still heart.



An alternative “off-pump” method that has gained popularity in the past decade is also known as “beating heart” surgery. As the name implies, the heart keeps beating during the procedure, and no heart-lung machine is used. Doctors use special devices to stabilize only the small section of the heart in which they are stitching in the graft.

There is controversy over which method is safer and more effective. Some studies have suggested that



using the pump could weaken heart function after surgery, harm the lungs and kidneys, result in more blood use during surgery and longer hospital stays, and bring on problems with memory and thinking. Many experts came to see the off-pump method as enabling a quicker recovery, with lower health care costs and less risk of cognitive decline.

Recent studies, though, have raised concerns about the newer procedure as well: Is it too technically difficult? Are surgeons sometimes unable to complete multiple grafts on a patient? Are the grafts more likely to fail? And as a result, are patients more prone to heart attacks or repeat procedures?

VA's Cooperative Study found that both methods were generally safe and effective. However, the more traditional "on-pump" method yielded better outcomes after one year on a composite measure that included death, repeat cardiac procedures, or nonfatal heart attacks. The vein grafts of patients whose surgeons had used the pump were also more likely to remain open.

Another interesting study finding was that patients from both groups scored equally well a year after surgery on neuropsychology tests. Some experts had believed the on-pump method was riskier for cognitive health. According to first author A. Laurie Shroyer, PhD, though, the findings of the large, multisite VA study contradict findings from earlier studies that showed "some advantages of [heart bypass] surgery using the off-pump procedure, including quicker recovery and less impact on cognitive function. This study indicated a consistent trend toward better outcomes in patients who had undergone the conventional on-pump technique."

To date, no studies have been conclusive, but the new VA trial results should greatly inform the debate. Frederick L. Grover, MD, another author of the study, said "the results may influence cardiology referrals and cardiac surgery practice," but stresses that individual patient differences still need to be taken into account. "Patients with certain risk profiles and patterns of coronary damage," he said, "may still be strong candidates for the off-pump method, notwithstanding the general results seen in the trial."



## Research Spotlight



# CSP trial looks at brain stimulation for Parkinson's disease

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

Schmid was enrolled in a six-year study sponsored by VA's Cooperative Studies Program and the National Institutes of Health, in which some patients with Parkinson's disease received "best medical therapy" (carefully managed medication plus speech, physical, or occupational therapy as needed), while another group of patients, including George, 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 of the illness.



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 (for more information, visit [www.parkinsons.va.gov](http://www.parkinsons.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*, came as no surprise to Schmid, who's felt "very, very good" after DBS—"at least 30 to 50 percent better" than before the procedure. Patients

who received DBS saw significant improvements in several areas, though DBS was also associated with more serious side effects.

## VA RESEARCH BY THE NUMBERS

Many VA articles appear in the top medical journals, including highly respected publications such as the *Journal of the American Medical Association* and the *New England Journal of Medicine*.



# Continuing care across a lifetime

Although Kevlar helmets and improved body armor save lives, they cannot fully protect against blasts and impacts, especially to the head and face and to the cervical region of the spinal cord. Traumatic brain injuries (TBIs) from impacts or blasts can range from mild to severe. Concussive or mild TBI is the most common form of combat-related injury, often associated with problems with memory, concentration, anxiety, and irritability, and sometimes with hearing and visual disturbances. For the vast majority of mild TBI cases, the most pronounced symptoms occur immediately after injury, with complete recovery within days or weeks. However, questions still remain about the possibility of long-term effects even for those with mild TBI.

Service men and women with moderate to severe TBI have similar symptoms to those with mild TBI, but also have more severe cognitive impairment. They may experience symptoms such as worsening headaches, repeated vomiting or nausea, posttraumatic concussions, visual disturbances, sleep disturbances, slurred speech, weakness, numbness, and loss of coordination. Unlike in mild TBI, problems can persist long-term or result in permanent difficulties with memory, reasoning, emotion, and expression.

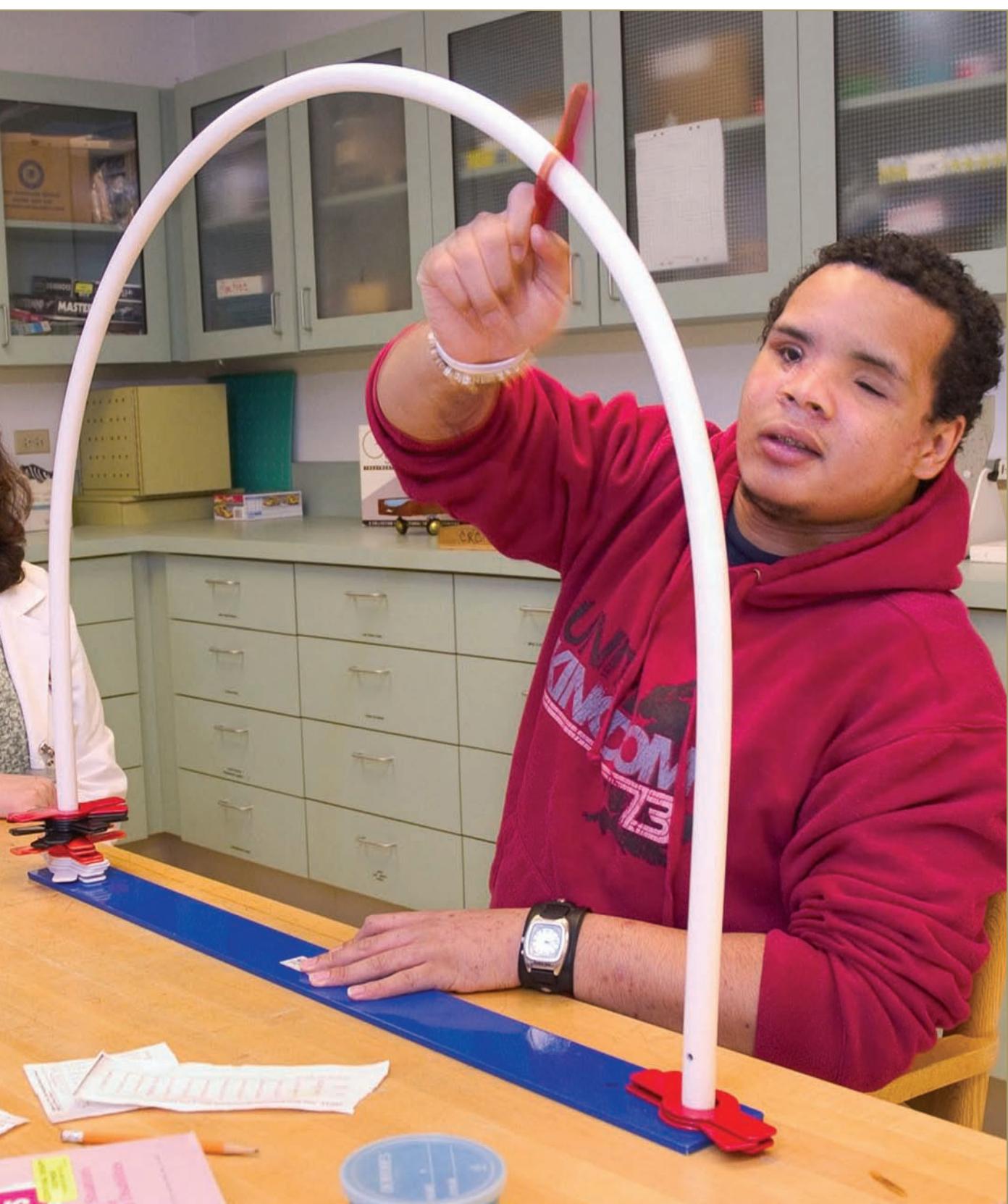
VA's research is focused on identifying those Veterans who need care for their TBI; treating them once they are identified and continuing that care throughout their lives; supporting their caregivers; and reintegrating Veterans back into their communities. Highlights of the research that VA is doing to improve functional recovery and quality of life for Veterans with TBI include neuro-imaging and simulation techniques.

*ORD-funded research is focused on identifying those Veterans who need care for their TBI*

VA supports a range of imaging research in technologies such as magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI). The goals of this research are to better "map" the brain changes associated with long-term TBI; develop effective evidence-based rehabilitation strategies to improve the quality of life of Veterans with TBI; define the nature of blast-related TBI; and track actual improvements in brain function associated with the intervention. In the area of simulations, new VA research suggests that modern driving simulators may be useful in cognitive rehabilitation because they can track responses to realistic scenarios that approximate the driving activities that are so important to independent functioning. Driving simulators and other virtual reality technologies are being applied to develop therapies to improve not only cognitive function, but also other psychological health issues associated with TBI, such as PTSD and substance abuse.



# Traumatic Brain Injury





## VA studies looking at wide variety of mental health-related issues

VA investigators are pioneering advances in the understanding and treatment of mental health disorders, an important issue for Veterans. Current studies are looking at a wide range of mental health-related issues affecting Veterans of all ages, including depression, generalized anxiety disorder, and posttraumatic stress disorder (PTSD).

Researchers are looking at various potential approaches to understand, treat, and prevent mental health disorders. They are also reviewing related issues such as developing and evaluating collaborative primary care models and improving access to services for Veterans living in rural areas by using the Internet and other modern technologies.

Areas in which they are focusing include mood disorders, such as depression and bipolar disorder; anxiety disorders, including PTSD; psychotic disorders, such as schizophrenia, dementia, and memory disorders; and substance use disorders. VA investigators also focus on the ways in which mental health issues and physical disorders often combine, such as depression in those with spinal cord injury or substance abuse by patients with chronic pain.



*Researchers are looking at various potential approaches for treating and preventing mental health disorders.*

### VA RESEARCH BY THE NUMBERS

In fiscal year 2010, VA R&D supported more than 2,100 research projects at VA medical centers nationwide, ranging from preclinical studies to health services research to multisite clinical trials. VA's program is intramural, meaning only VA employees can conduct research under VA's auspices. Typically, however, VA researchers collaborate with academic colleagues and others outside VA.

In addition to VA R&D funding, VA studies are also partially supported by VA medical care dollars and by 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 additional funding for VA investigators. Another benefit of NIH funding is assuring the public that VA and NIH research projects are of equally high 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.



## Veterans win with VA sensory loss research

One of the most common conditions in returning Iraq and Afghanistan Veterans who were exposed to a blast is tinnitus—a ringing, swishing, or other type of noise that originates in the head. It is experienced by 10 to 15 percent of all Americans, though 80 percent are not particularly bothered by it. Investigators are addressing its debilitating effects in the other 20 percent of people with this condition, which is the single most prevalent service-connected disability for America's Veterans and is commonly seen at VA otolaryngology and audiology clinics because of its association with hearing loss. Tinnitus is also the single most prevalent service-connected disability for America's Veterans, with nearly 640,000 Veterans currently receiving compensation for this problem.

In a collaborative study between the National Center for Rehabilitative Auditory Research (NCRAR) and the James A. Haley (Tampa) VA Medical Center, researchers developed, tested, and evaluated

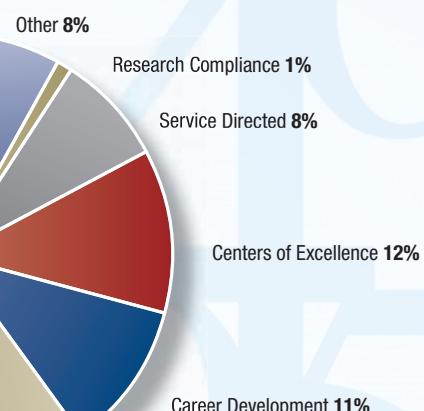
a comprehensive tinnitus management program developed by NCRAR for Veterans, called Progressive Tinnitus Management, or PTM. PTM takes into account that most Veterans who complain of tinnitus do not require extensive intervention, and clinical services are provided only to the degree needed by individual patients.

PTM includes five level of clinical care: triage, audiologic evaluation, group education, interdisciplinary evaluation, and individual support. Its overriding philosophy is that patients primarily need education to learn how to manage tinnitus on their own—an outstanding example of patient-centered care. If patients can be taught to provide self-management, they can avoid using many unproven and often costly therapies and successfully live with the problem. In 2010, NCRAR published handbooks for both patients and audiologists to help them use this new and exciting therapy.

### VA RESEARCH BY THE NUMBERS

VA Research funds spent in fiscal year 2010 for all areas of research.

Investigator Initiated 60%





# Investigators battle PTSD on many fronts

*Answers on treatment will come from many medical disciplines*

VA investigators have made important strides recently in understanding how the brain works in posttraumatic stress disorder, or PTSD, an anxiety disorder often associated with Veterans exposed to combat that also occurs in the general population. VA researchers have established much of the evidence now available relating to the biological basis of PTSD—a disorder that during past wars was called “soldier’s heart,” “shell shock,” or “combat fatigue.”

To effectively understand, prevent, and treat PTSD, investigators must understand the psychological and biological impact of trauma exposure in the Veteran population. VA investigators have established much of the evidence relating to the biological basis of PTSD, and they continue to learn about changes in the body that are linked to the condition. Currently, VA Research is supporting more than 100 PTSD studies at a cost of more than \$25 million, including studies in women Veterans and research across different deployment eras.

In addition to a groundbreaking study of prolonged exposure therapy for PTSD in women (see box next page), VA has recently completed two large PTSD treatment trials. One evaluated the use of a drug, risperidone, for chronic, unremitting PTSD. Another examined the way PTSD care is delivered to Veterans. These studies have the potential to positively affect VA’s ability to care for Veterans for many years to come.

Additional treatments currently being studied are the use of an inexpensive medication, Prazosin, to relieve trauma-related sleep disturbances; an early-stage trial of a novel drug to alleviate PTSD symptoms; complementary and alternative therapies for PTSD; and strategies to engage Veterans in treatment at early stages of their illness, when it is most treatable. In Veterans of the Iraq and Afghanistan wars, extensive work is underway to identify PTSD-related risk and resilience factors, early intervention and prevention strategies, and new treatments, as well as other conditions associated with the illness.



One landmark study, called the Marine Resiliency Study, will assess cognitive and emotional changes that occur after deployment to Iraq based on critical baseline assessment information that was collected prior to deployment. The study will characterize physiological reactivity in a large cohort of Veterans through repeated post-deployment assessments.

To understand long-term consequences of PTSD and health care needs in Vietnam-era Veterans, several efforts are underway to assess this cohort’s current PTSD and mental and physical health status. Research includes a male-twins 20-year follow-up study; a study of Vietnam-era women Veterans; and the continuation of the National Vietnam Veterans Longitudinal Study (NVVLS).

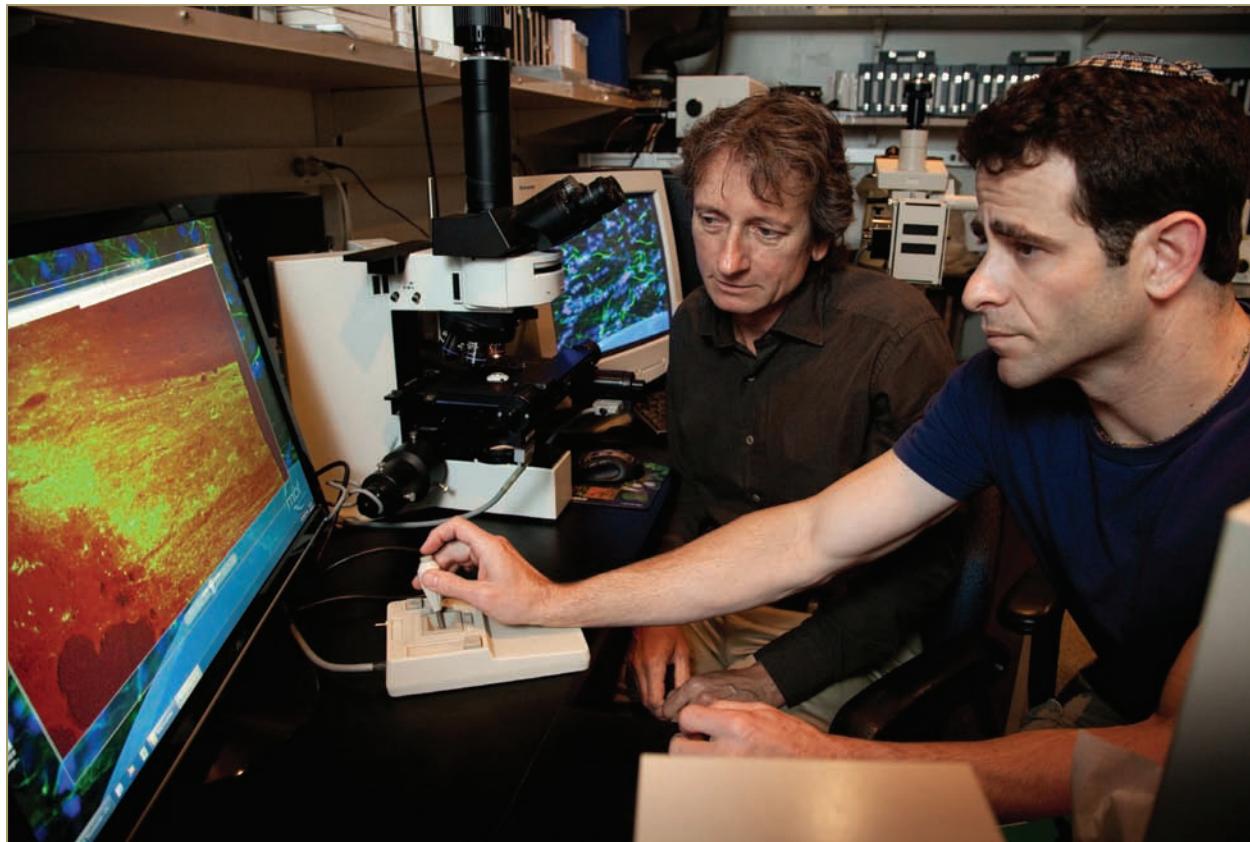


### Women Veterans with PTSD use exposure therapy as way to gain hope, greater functionality

In the largest randomized clinical trial to date involving women Veterans with PTSD, VA investigators and their colleagues recently demonstrated that prolonged exposure (PE), a type of cognitive behavioral therapy, is an effective treatment for PTSD in female Veterans and active-duty military personnel. Women who received this therapy experienced greater reduction in PTSD symptoms, were more likely to no longer meet the PTSD diagnosis criteria, and were more likely to achieve total remission of their PTSD symptoms.

VA's investment of \$6.6 million in the PE therapy study directly resulted in the national dissemination and

implementation in the Veterans Health Administration of evidence-based psychotherapies for PTSD, depression, and serious mental illness. PE is currently considered one of the most effective treatments available for PTSD, and is now recommended for PTSD in the VA/DoD Clinical Practice Guidelines for PTSD at the highest level, indicating "a strong recommendation that the intervention is always indicated and acceptable." As of May 2010, VA had trained more than 2,700 mental health staff in the delivery of PE, greatly increasing the Department's capacity to offer this treatment for PTSD.



## Gene therapy gives hope for SCI patients' recovery

*VA researchers study variety of ways to help Veterans recover or rehabilitate*

VA operates the nation's largest network for the care of spinal cord injuries (SCI). In 2010, VA treated more than 25,000 Veterans with the condition. VA's research program leads all others in defining new methods of treatment and rehabilitation for Veterans with SCI, and information from VA studies also help the approximately 250,000 Americans with spinal cord injuries.

VA researchers are studying a variety of ways to help Veterans recover or rehabilitate after SCIs. Several teams of VA researchers are addressing the issue of functional recovery. For example, a team at the San Diego VA Medical Center pioneered the use of combinational therapies to treat SCI with a focus on the recovery of upper limb function. This

is an area of vast importance to returning Iraq and Afghanistan Veterans as well as older Veterans who have suffered a stroke. The VA research team recently demonstrated the feasibility of using gene therapy to deliver neurotropic factors (proteins responsible for the growth and survival of neurons) to damaged neural (nervous system) tissue to promote repair and recovery of function.

Along with clinical care in VA's polytrauma centers and other points of care, VA researchers are convinced stem cell research and other SCI research will soon lead to breakthroughs for those living with this disorder—and to breakthroughs in other neurological disorders such as stroke and multiple sclerosis.

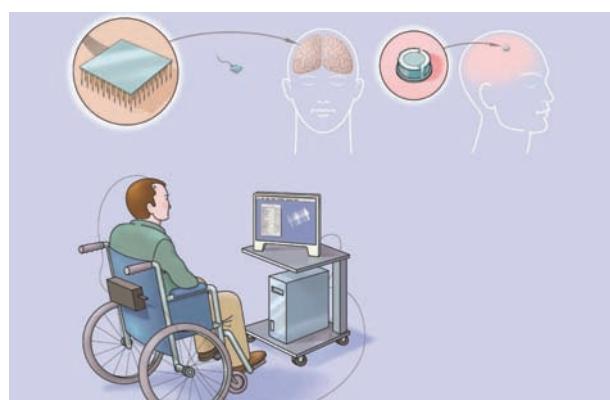


# Turning brain waves into actions

Researchers at VA's Center for Restorative and Regenerative Medicine (CRRM) are working on prostheses that will respond more accurately to a 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 Roy Aaron, MD.

A system called BrainGate, developed by Brown University and 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 neural signals related to the intention to move a limb, and in turn computer cursors, to enable paralyzed Veterans to more easily 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.



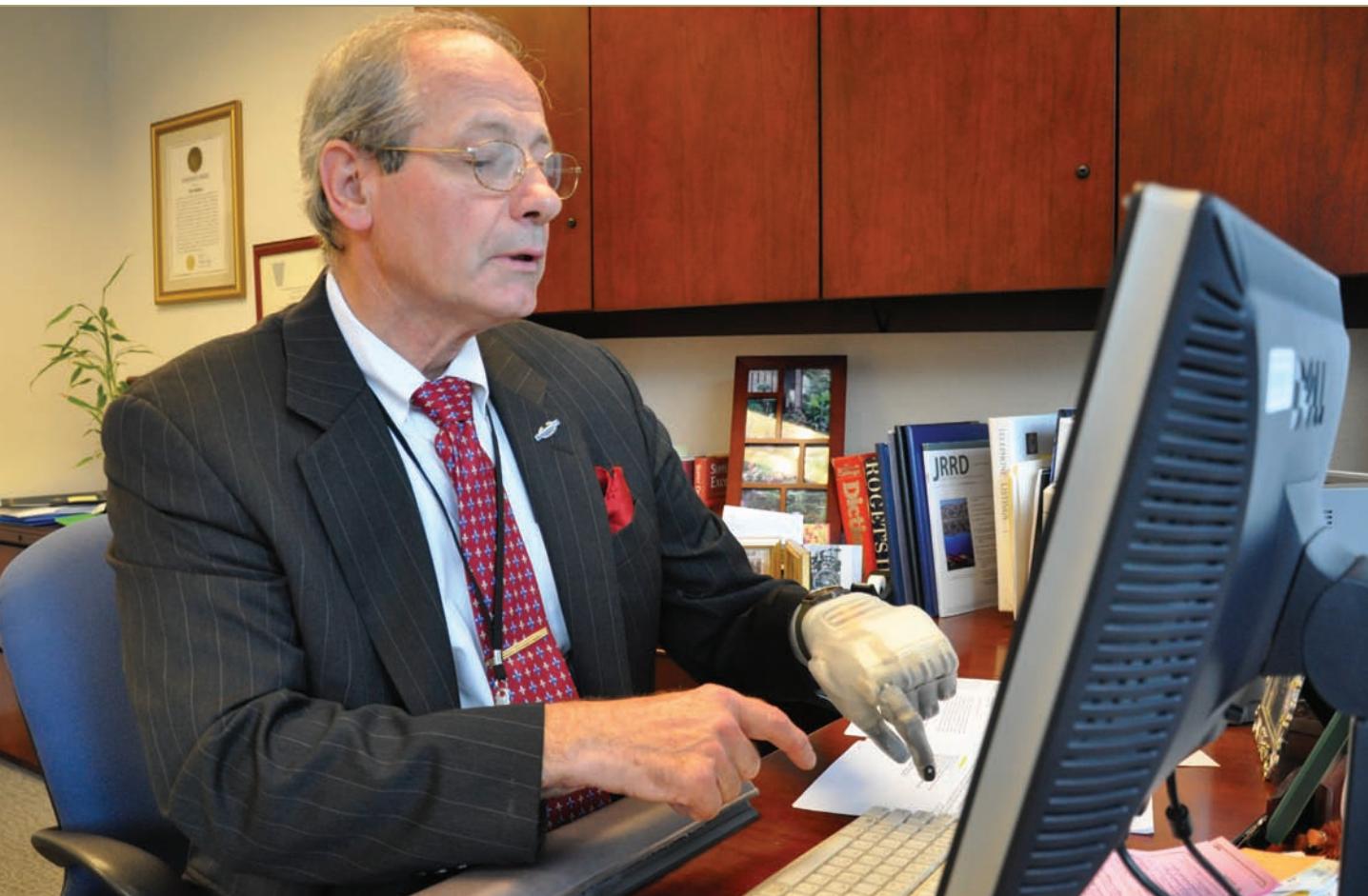
## VA partners with pioneering SCI investigators

VA investigators often partner with other pioneering spinal cord injury investigators to advance SCI research as quickly as possible. Leading VA-affiliated Centers with this research focus include the Advanced Platform Technology (APT) Center, a VA Research Center of Excellence established in partnership with Case Western Reserve University that supports rehabilitation research by adapting cross-cutting foundational technical platforms to meet specific needs for advanced prosthetic systems, sensory aids, and other clinical applications.

Other VA partnerships include the Functional Electrical Stimulation Center (FESC) in Cleveland, Ohio, and the Center for Restorative and Regenerative Medicine (CRRM) in Providence, Rhode Island. FESC—a consortium of the Louis Stokes Cleveland VA Medical Center with Case Western Reserve University and MetroHealth Medical Center—focuses on the application of electrical currents to either generate

or suppress nervous system activity. This technique, known as functional electrical stimulation, or FES, is being studied to help those with paralysis from spinal cord injury, impaired movement from stroke, and other neurological and muscular skeletal conditions to grasp an object with their hand; stand or walk; control bladder and bowel function; and achieve other bodily functions to improve quality of life.

CRRM investigators, representing the Providence (RI) VA Medical Center, Brown University, and the Massachusetts Institute of Technology, study new-millennium methods for restoring quality of life to those hurt by disease or injury. A primary focus of the center is marrying human tissue and mechanical elements into lifelike "biohybrid" limbs that handily outperform currently available prostheses. The Center's staff includes investigators with expertise in orthopedics, tissue engineering, neurotechnology, prosthetic design, and rehabilitation.



## The future of prosthetics is now

*Trauma from IEDs becomes signature injury of Iraq and Afghanistan theaters*

While nearly two-thirds of adult amputations are due to peripheral vascular disease of a lower extremity, the remaining number are associated with trauma, such as those related to high-explosive blasts or other combat scenarios. High-impact explosive trauma from improvised explosive devices is all too common in Iraq and Afghanistan Veterans, and a primary mission of VA research is to restore Veterans injured in this way to their greatest possible functional capacity in their families, communities, and work places.

Today's VA researchers are using leading-edge technologies such as robotics, tissue engineering,

and nanotechnology to build better prostheses for the 21st century, and are studying ways to best match available prosthetic components to the needs of individual amputees.

A modern prosthesis allows Luke Cassidy, a Veteran who lost his left foot and right toe in Operation Iraqi Freedom, to maintain his active lifestyle and a normal relationship with his young children. "I felt I wasn't going to be able to function and be able to do 'dad' things with them," he says. With a prosthesis matched to his needs, the Veteran can now coach softball and his mindset has changed to "Okay, I can do this."



# Prosthetics & Amputation Care



## New prosthetic arm enables wide range of tasks

One huge leap forward in the field of prosthetics is the launch of a three-year VA “optimization study” of an advanced prosthetic arm developed by DEKA Integrated Solutions through funding from the Defense Advanced Research Projects Agency (DARPA).

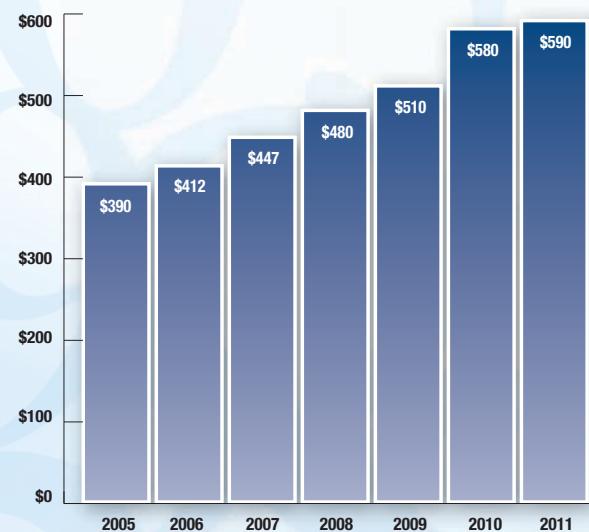
This revolutionary arm is programmed with various hand grasps to allow users to perform a wide range of tasks, from picking up a key to using power tools. Users can raise, twist, and bend the arm and even raise it overhead, almost as they would a natural arm. The eight-pound DEKA arm also has a device called a “tactor” that sits on the user’s skin and vibrates to signal the strength of the grasp.

Frederick Downs Jr. lost his left arm during combat in Vietnam. Downs was “brought to tears” recently when the DEKA arm allowed him to smoothly bring a water bottle to his mouth and drink. In a VA study—the first large-scale clinical trial to play an

ind development of ts with upper-limb ed with the arm, use edback to guide further refinements.

## VA RESEARCH BY THE NUMBERS

Total congressional allocation for the VA Research and Development program (*in millions*)



A futuristic tack is being taken by researchers at the Center for Restorative and Regenerative Medicine. Researchers at the center are working to merge biological and nonbiological materials into high-tech “biohybrid” limbs.

VA prosthetics research doesn’t stop with state-of-the-art limbs, but extends to wigs, eyeglasses, hearing aids, wheelchairs, GPS devices to help individuals with brain injuries become mobile, and adaptive equipment for cars and homes. According to Frederick Downs Jr., the Veterans Health Administration’s Chief Prosthetics and Clinical Logistics Officer, VA offers “everything that’s necessary to help Veterans regain their mobility and independence.”



# Managing chronic disease remains high priority for VA Research

Promoting good health and managing chronic conditions remain high priorities for VA health care and VA research. Among the chronic conditions that rank high among VA's health research priorities are:

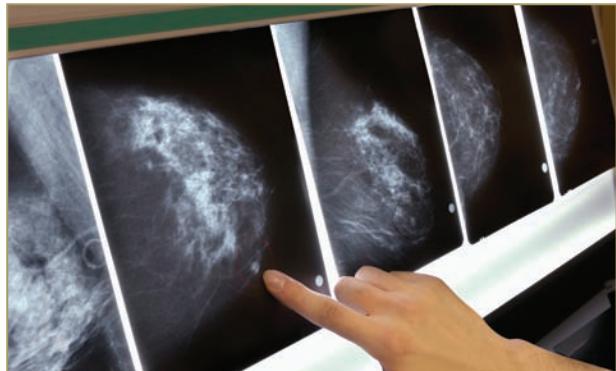
## Cardiovascular Disease

Cardiovascular disease is the number one killer of Americans and the leading cause of hospitalization in the VA health care system. VA researchers in the field of cardiovascular disease are conducting groundbreaking studies ranging from lab experiments on heart disease to large, multistate trials involving thousands of patients. Recent VA studies have demonstrated that patients can effectively monitor themselves for the effects of the anti-clotting drug Warfarin, and that even low doses of a natural antioxidant called Resveratrol, found in grape skins, preserved the heart and musculoskeletal system of middle-aged mice.



## Cancer

VA's research program supports improved methods of diagnosing and treating cancer that have already directly improved Veterans' lives and the lives of other Americans with the disease. A recent innovative study at the VA Palo Alto Health Care System in California has contributed significantly to the understanding of colon cancer and its ability to be



detected through colonoscopy. Traditionally, doctors have searched for potentially cancerous polyps—abnormal growths protruding from the lining of the colon. However, the VA study suggests that difficult-to-detect flat abnormal growths are more common in Americans than previously thought, and are much more likely to be cancerous than polyps. About 10 percent of patients in the study had these flat growths, which were previously thought to be only an Asian-Japanese phenomenon.

## Diabetes

Diabetes affects about one million Veterans within the VA health care system—nearly 20 percent of the population. Diabetes is also the leading cause of blindness, end-stage renal disease, and amputation in the VA. VA supports an innovative and comprehensive diabetes research program directed at a range of immediate clinical concerns such as hyperglycemia, glaucoma, and high blood pressure; long-term complications such as amputation and kidney failure; and care delivery issues through a range of facilities such as outpatient clinics and nursing homes, as well as home-based care. VA investigators continue to examine mechanisms and risk factors for susceptibility to diabetes and its complications. In



212 dpi



addition to cellular and molecular-based research, VA is supporting genetic studies on this complex disease, including one that is measuring gene expression and insulin resistance simultaneously in human fat, muscle, and blood samples from Mexican-American Veterans and their family members.

### Parkinson's Disease

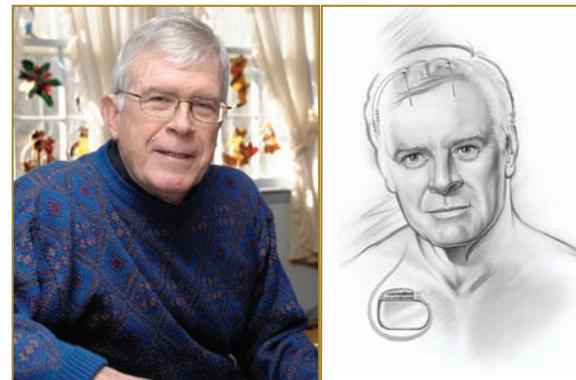
VA treats at least 40,000 Veterans each year who have Parkinson's disease, a debilitating central nervous system disorder that can cause muscle rigidity, delayed movement, poor balance, and tremors. Besides researchers' work on direct brain stimulation as a treatment for Parkinson's (see pages 6 and 7), VA researchers have recently learned that a protein called beta-catenin plays a key role in the development of the illness, and may boost the effectiveness of new therapies. They have also learned that patients with Parkinson's who communicate with their health care providers by videophone for follow-up care have a high degree of satisfaction with their care.

### Pain Management

Pain is one of the most common reasons Americans consult a physician, and has been cited as the most common symptom in service members returning from combat. VA's pain research program covers a wide range of topics, from drug discovery to alternative treatments to the impact of pain on daily function and quality of life. In three studies that represent VA's diverse research approaches on this issue, one VA research team has looked at whether yoga can help in pain reduction; another is testing a high-tech approach for delivering a pain-relieving gene to the nervous system; and a third is examining changes at the cellular and molecular levels for clues about what causes pain and how to treat it.

## VA RESEARCH BY THE NUMBERS

About 7,500 articles based on VA-sponsored research are published yearly.



### VA investigators tackle blood sugar control



In a groundbreaking 7-year, multisite clinical trial recently completed, VA investigators found that intensive blood sugar control, primarily using higher doses of medication, did not reduce cardiovascular risks

compared with recommended targets in older patients with longstanding diabetes. The trial also found that an intensive approach provided no added benefits for the kidneys or eyes, which are often harmed by the high blood sugar levels in poorly controlled diabetes. These findings will help physicians to better manage this complex disease, and are changing the prevailing thought among clinicians that a more intensive approach to treating the disease is always advantageous.



# Research focuses on deployment-related exposure to hazardous environmental agents

*VA investigators seek to understand fundamental causes, best treatments*

Veterans, while in service to their country, may be exposed to environmental agents that are later found to be a health hazard. VA is committed to advancing knowledge about ways to identify health concerns associated with environmental exposure to hazardous agents, as well as improving the care and treatment options available to affected Veterans. While much progress has been made, new advancements in genetic analysis and medical knowledge bring opportunity for further exploration, discovery, and advances in health care. VA researchers are therefore planning to advance and implement methodologies using personalized medicine to understand individual responses to deployment-related exposure to hazardous environmental agents and identify the best treatment for the resulting health concerns.

VA Research supports a broad portfolio of research on diseases associated with Agent Orange exposure. VA investigators seek to understand the causes and best treatments for conditions affecting Veterans related to possible exposure to herbicides. They are also studying the optimal methods for ensuring this knowledge is incorporated into the health care received by Veterans, and ultimately the entire nation.

A major focus of VA research is on the causes of and treatments for medical conditions currently compensable for Agent Orange exposure. VA currently has 597 projects on this subject, funded at \$79 million per year. Ongoing studies include work on prostate cancer, lymphoma, leukemia, myeloma, lung cancer, head and neck cancer, Parkinson's disease, cardiovascular disease, metabolic syndrome, and diabetes. One such project is an epidemiologic study of the risk of Parkinson's disease in Veterans exposed to Agent Orange. Others are looking at how dioxin causes lymphoma, health outcomes of women Veterans, and health outcomes of Vietnam Veterans.

Another Agent Orange-related research focus is to evaluate the association between specific diseases and herbicide exposure in Vietnam by working with the Institute of Medicine (IOM). IOM provided \$1.5 million for a biannual update on "Vietnam Veterans and Agent Orange." A new contract is in place with the IOM to review the literature related to "Blue Water Navy" Veterans (Veterans who patrolled the oceans off of Vietnam) and exposure to Agent Orange. VA is working with IOM to make available to researchers the records and biologic samples of the most highly exposed U.S. service members who took part in the Air Force Health Study and Operation Ranch Hand. VA and IOM will also solicit proposals for an evaluation of the impact of Agent Orange on hypertension, in addition to other pilot studies designed by investigators across the nation.

Examples of [ongoing projects](#) examining diseases associated with Agent Orange exposure include:

## Diabetes

### [Nonalcoholic Fatty Liver Disease in Type 2 Diabetes Mellitus: Prevalence in Hispanics and Role of Treatment](#)

**Treatment:** Nonalcoholic fatty liver disease and type 2 diabetes mellitus are major public health problems, particularly for the aging Veteran minority population. Type 2 diabetes is a major problem among patients treated at the San Antonio VAMC, with 5 percent of the population having Hispanic ancestry. Hispanics are two to three times more likely to have diabetes than Caucasians. This novel study will be the first to define the prevalence of nonalcoholic fatty liver disease in diabetic Hispanics and to characterize the metabolic and molecular defects in a large population of Hispanics with nonalcoholic fatty liver disease. Clinical, metabolic, and molecular evaluations, including liver biopsies, will identify variables associated with disease progression and help understand how pioglitazone,

# Agent Orange



Retired U.S. Marine Corps Capt. Ronald E. Hoover Sr. sits near the Three Soldiers Statue following a rededication ceremony at the Vietnam Veterans Memorial on the National Mall in Washington, D.C.



Laotian and U.S. team members of recovery team two are hard at work in the excavation area, located in the Xiangkhoang province of the Lao People's Democratic Republic. The mission of the Joint POW/MIA Accounting Command is to achieve the fullest possible accounting of Americans lost during our nation's past conflicts. (U.S. Marine Corps photo by Sgt. Kara L. Coonrod/Released)

a state-of-the-art drug used to help maintain normal blood glucose levels in diabetics, alters physiological and biochemical pathways leading to fat accumulation in the liver. Without this knowledge, we are limited to lifestyle recommendations (the current standard of care) that frequently fail and have not been shown to reduce liver damage resulting from fat accumulation in large controlled trials. VA hopes this study will lead to a new understanding of the disease and provide a blueprint for a novel intervention to prevent complications associated with nonalcoholic fatty liver disease in Hispanic Veterans with type 2 diabetes.

### Ischemic Heart Disease

#### Estrogen Receptor and Cardiovascular Function:

A VA study involving 25,000 post-menopausal women showed that estrogen replacement within 10 years of menopause reduced the incidence of heart attacks by 34 percent; however, this reduction in heart attacks did not occur if women started estrogen replacement more than 10 years after menopause. Furthermore, it is known that estrogen reduces the incidence of heart enlargement and rescues the heart from injuries due to restricted blood supply in isolated cells and in mouse models. This study will determine how estrogen protects the heart against heart attacks and associated damage. The results will help improve cardiovascular health in post-menopausal women Veterans.

## Agent Orange



## Prostate Cancer

### Vitamin D Supplementation in African-American

**Veterans with Prostate Cancer:** Vitamin D deficiency is widespread among African-American populations; furthermore, urban African-Americans are 1.7 times more likely to exhibit vitamin D deficiency than their rural counterparts. It is believed that vitamin D deficiency over time may promote the progression of prostate cancer. This is particularly relevant to African-American men since they have higher death rates from prostate cancer than Caucasians. A clinical study will measure the value of vitamin D supplementation in African-American Veterans diagnosed with low-risk, early-stage prostate cancer who elect to have their disease monitored through expectant management (close monitoring without treatment until symptoms appear or change). The successful completion of this proposed clinical study will determine whether correcting widespread vitamin D deficiency in African-American Veterans diagnosed with early-stage prostate cancer will prevent progression of their disease, improve their prognosis, and pave the way to mitigating a well-documented health disparity through vitamin D supplementation.



Richard Crepeau receives the Bronze Star Medal with combat distinguishing device. Crepeau received the medal for his actions as a sergeant with 3rd Force Reconnaissance Company during a four-day patrol in Vietnam in the spring of 1967. (Marine photo/Staff Sgt. Ethan E. Rocke)

### Radical Prostatectomy Versus Palliative Expectant Management for the Treatment of Clinically Localized Prostate Cancer:

Cancer confined to the prostate is believed to be curable, with the most frequently recommended therapy being surgical removal of the tumor with radical prostatectomy (removal of the entire prostate gland and some surrounding tissue). However, existing evidence does not demonstrate the superiority of this procedure compared to expectant management (close monitoring without treatment until symptoms appear or change, otherwise known as "watchful waiting") in the treatment of localized prostate cancer. While prostatectomy provides potentially curative removal of the cancer, it subjects patients to the risks of surgery and may be neither necessary nor effective. Expectant management does not offer a potential cure. However, it emphasizes disease management approaches focused on relieving symptoms and minimizing complications. The primary objective of this study is to determine which of the two strategies is superior for the management of clinically localized prostate cancer. Outcome measures to be reviewed include overall death, prostate cancer-related death, disease-free and progression-free survival, morbidity, quality of life, and cost effectiveness.

Examples of **recently completed** projects examining diseases associated with Agent Orange exposure include:

## Diabetes

- Dr. Andrew Schally, a Nobel Laureate who works at the Miami VAMC, discovered that synthesized analogs of the natural growth hormone-releasing hormone can promote increased proliferation of pancreatic islets, which are the pancreatic cells responsible for insulin release. This study has direct implications for improving the survivability of transplanted islets into diabetics who lack sufficient number of functional islets to release insulin and thereby regulate blood glucose levels.
- Drs. William Duckworth and Carlos Abraira, physicians at the Phoenix and Miami VAMCs, respectively, demonstrated in a large, multisite, controlled clinical trial that intensive control of blood glucose levels in poorly controlled type

## Agent Orange



Vietnam Veterans share stories prior to the annual POW/MIA reveille at Kadena Air Base, Okinawa. This ceremony pays tribute to those who were imprisoned during wartime. (U.S. Air Force photo by Staff Sgt. Darnell T. Cannady/Released)

2 diabetic Veterans had no significant effect on the rates of major cardiovascular events (such as stroke and heart attack), death, or microvascular (small blood vessel) complications. This study demonstrated that interventions other than closely controlling blood glucose levels, such as diet, exercise, and blood pressure and lipid control, would reduce the illnesses and death associated with vascular disease in diabetic Veterans.

### Lung Cancer

- Dr. Suresh Ramnath, a physician at the Ann Arbor VAMC, discovered that the activity of an enzyme (CYP24A) involved in breaking down vitamin D could be used as a predictive marker in lung cancer patients—higher levels of the enzyme result in poorer survival of lung cancer patients. This work suggests that maintaining vitamin D levels may contribute to improving the prognosis of patients with lung cancer.

### Agent Orange

### Prostate Cancer

- Dr. Rajvir Dahiya of the San Francisco VAMC discovered that genistein (a natural, non-toxic, dietary isoflavone found in soy extracts) can activate a tumor suppressor gene and thereby potentially inhibit the growth of prostate cancer cells. Dr. Dahiya demonstrated similar effects on the tumor suppressor gene by genistein and the compound 5-AZA-C currently being tested in clinical trials. If this compound shows value in inhibiting the growth of prostate cancer, then that genistein, a non-toxic agent, may also be a useful therapeutic agent for treating prostate cancer.

*A major focus of ORD research is on the causes of, and treatments for, medical conditions currently compensable for Agent Orange exposure.*



## Parkinson's Disease

- For Parkinson's disease patients who suffer from the long-term complications of levodopa (L-DOPA) treatment or who no longer respond well to medication alone, deep brain stimulation (DBS) has become increasingly accepted as a surgical alternative for symptom management (see pages 6-7 for one Veteran's story). In DBS, surgeons implant electrodes in the brain and run thin wires under the skin to a pacemaker-like device. Electrical pulses from the battery-operated device jam the brain signals that cause motor symptoms such as stiffness and tremors. A VA Cooperative Study (CSP #468) enrolled 316 patients from seven VA medical centers and six affiliated university hospitals across the U.S. This study had two phases:

**Phase I** of the study, which compared best medical therapy (medications and non-drug therapy) to DBS for improving motor symptoms at six months, found that DBS is somewhat riskier than drug therapy but may hold significant benefits for those with Parkinson's who no longer respond well to medication alone.

**Phase II**, which compared long-term (two-year) outcomes (improving motor function and reducing symptoms of PD) for two different surgical DBS targets in the brain, showed that stimulation of either of two sites in the brain can effectively control Parkinson's motor symptoms and improve quality of life.





# VA Research addresses pressing issues for female Veterans

As the number of women Veterans grows past 1.8 million, or roughly 8 percent of the Veteran population, it is critical for VA to have a proper evidence base for guiding women's health care. Current VA research is examining the complex interaction of physical and mental health, military service effects, military sexual trauma (MST), PTSD, barriers to care, and the impact of VA's organization and structure of health care delivery to women Veterans, in order to better address the needs of recent women Veterans.

Screening and treatment for, and the health consequences of, sexual assault, military sexual trauma, and other trauma on women Veterans are important components of VA's research portfolio. An early-stage evaluation of VA's sexual trauma screening program demonstrates the importance of universal screening to guide the best mental health and behavioral health treatment. Screening also promotes detection and measurement of trauma, ultimately leading to better care and access to mental health care. Follow-up studies are examining the prevalence

of MST in Veterans returning from Iraq and Afghanistan and the association of MST with mental health diagnoses and risk of depression, PTSD, and substance use disorders.

Armed with this growing and comprehensive body of research, VA is working to transform care for women Veterans through a research infrastructure focused on intervention, implementation, and dissemination of best practices centered specifically on this important population. VA Research is embarking on an expansive program to establish a women's health research consortium to build VA women's health research expertise, and develop a national VA practice-based research network. The research consortium and research network will greatly facilitate women's research and implementation of research results into practice.

### VA RESEARCH BY THE NUMBERS

VA, through ORD, currently funds more than 2,100 projects.



## VA examines access to care from rural areas

A major goal of VA research is ensuring access to health care for all Veterans. For certain Veteran populations, such as Veterans in rural areas, racial and ethnic minorities, women Veterans, and caregivers of Veterans, there are barriers that affect access to care. Much of VA's research is focused on identifying barriers that affect access and discovering ways to overcome them. Research in this area is centered on interventions to improve access. Examples of such interventions include telemedicine, Web-based interventions, and health literacy. The outcomes of these projects directly inform VA policy. They provide guidance for developing outreach programs and improving access to services such as mental health and substance use services; care for chronic diseases such as diabetes; specialized care for conditions such as PTSD, HIV, and hepatitis C; and rehabilitative services such as pain management and wound care.

Returning Veterans provide a new set of research issues in terms of access to VA care. VA Research is identifying the best approaches to providing

services to Veterans with spinal cord injuries, TBI, and amputations and is identifying those geographic areas with the greatest need for specialized VA rehabilitation care and modeling methods to meet those needs. Research initiatives are examining new methods of providing caregiver support and training for family members of recently returned Veterans to facilitate their transition to civilian life, new methods of adapting care to different social and cultural settings, and innovative ways to expand telehealth to portable devices such as smart phones.

"Store-and-forward" photographic technology (a procedure in which data are stored at some point between the sender and the receiver and are later forwarded to the receiver) offers an important potential tool for improving access to care through telemedicine. Its diagnostic accuracy has been assessed for teleretinal screening and teledermatology. The value of teleconsultations to freestanding VA clinics and sites, and remote monitoring of chronic conditions such as diabetes and heart failure, are also being examined.





### Caring for those who care for our Veterans

Meeting the long-term care needs of Veterans is growing in importance as the number of Veterans most in need of these services—those 85 years old and older—is expected to reach 1.3 million by 2012. In addition, a younger population of Veterans with different long-term and care coordination needs is emerging as a result of our nation's current wars.

The Minneapolis VA Medical Center's Family and Caregiver Experiences with Polytrauma (FACES) study is looking at the current and long-term needs of families of Veterans with major injuries—people who, in many cases, will be involved in their loved ones' care for years and even decades to come.

The FACES study is analyzing survey responses from 565 families on their caregiving needs. They have learned that many caregivers spend more than eight hours a day helping their loved one; struggle

to hold down a job and care for other family members; and often have had to stop working and drain their savings or retirement accounts to help pay for care. Study managers hope to find ways to help them cope, while recognizing the uniqueness of each family and exploring with them and with the Veteran the ways in which the family will be involved with care.

Already, researchers have come up with a Web-based guide, called the Family Care Map, that lays out each stage of VA rehabilitation in a user-friendly way. Care teams use it as a reference with families during the Veterans' inpatient stay, and every family of a newly wounded service member receives a copy of the map in notebook form. In addition, VA nurses are being trained in family-centered skills; treatment goals are posted in patients' rooms along with white boards for family and staff to exchange information; and family peer support groups are being expanded.

**VA Caregiver Support Line 1-855-260-3274**



# Program helps researchers, VA, and all Americans

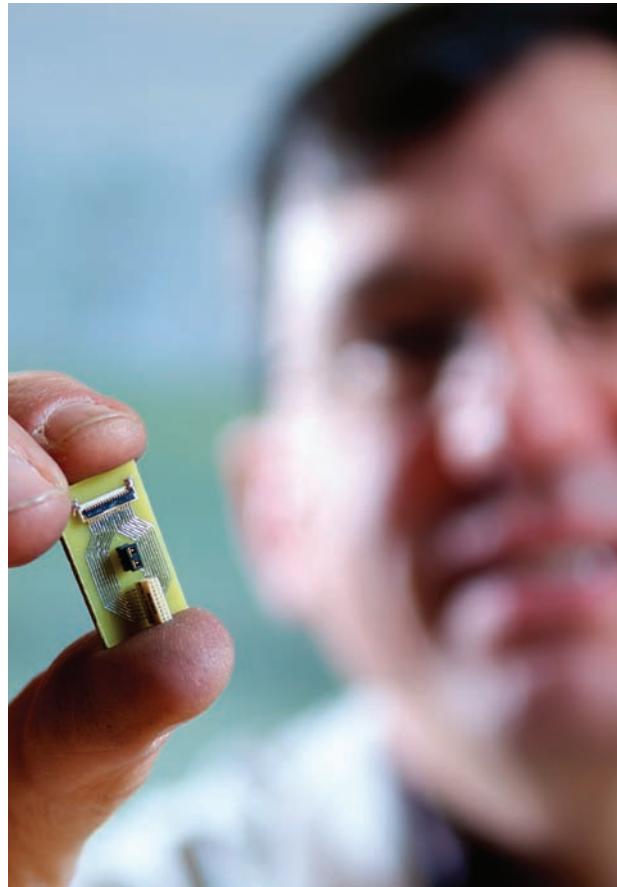
Every year, VA researchers develop dozens of new technologies and other inventions that benefit patients and other Americans. VA's Technology Transfer Program translates the results of VA employees' discoveries into practice. The program educates VA inventors on their rights and obligations; rigorously evaluates inventions; obtains patents; and helps commercialize new products.

The first step in the process is for the VA inventor to file an invention disclosure, or ID. VA receives approximately 150 invention disclosures per year—and the Department believes there could be more. Many of these are early-stage technologies, and the Department asserts an ownership interest in between 100 and 120 of them.

Because most VA researchers work part-time for VA and part-time for the university affiliated with their VA medical center, there is no clear delineation on which institution owns the intellectual property generated by research. VA's Office of General Counsel, the Veterans Health Administration, and the National Association of Veterans' Research and Education Foundations are developing a series of model agreements for research collaborations benefiting our nation's Veterans.

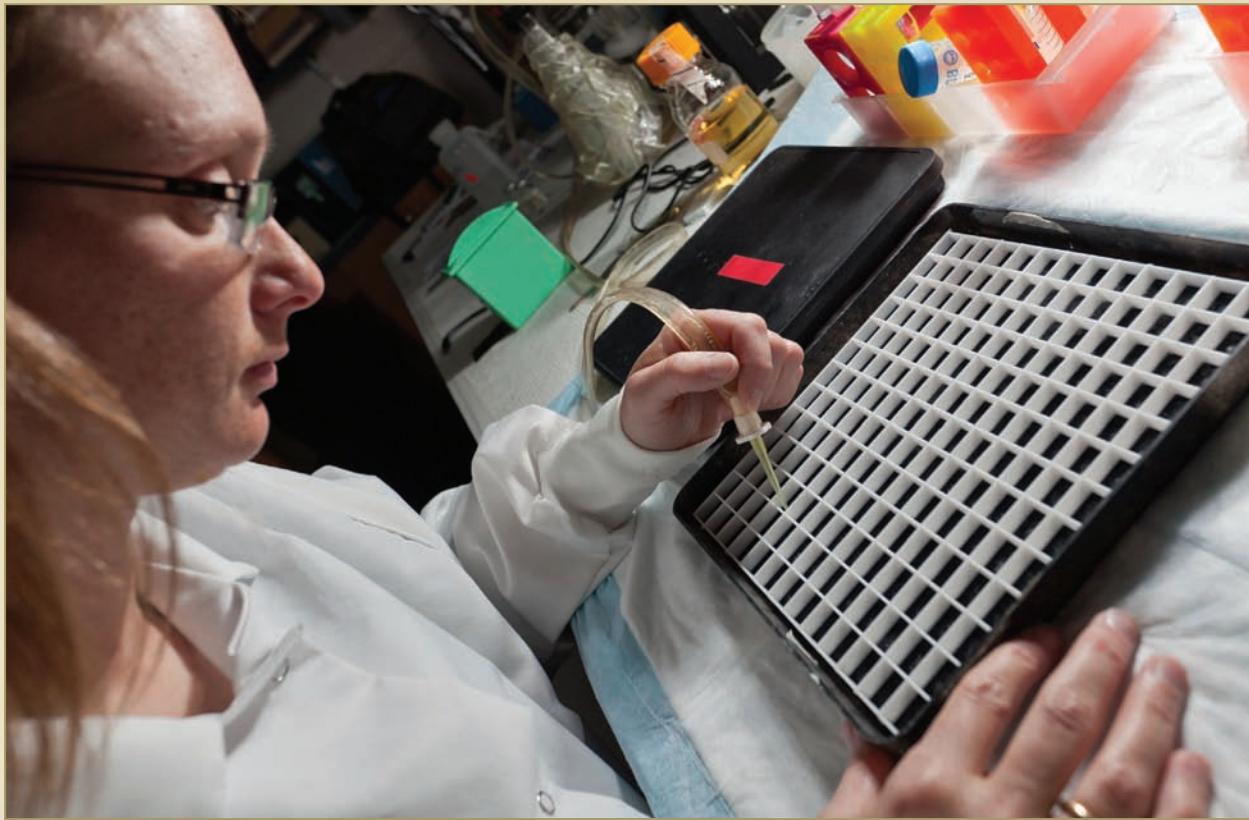
In 2000, when the Technology Transfer Program began, there was only one such Cooperative Research and Development Agreement, or CRADA. As of October 2010, there were 897. VA also has developed 59 Cooperative Technology Administration Agreements to help manage inventions VA jointly owns with its academic affiliates throughout the nation. These agreements represent partnerships between VA and universities, foundations, and industries that have led to new drugs, devices, and other interventions becoming quickly available. If there is no agreement with an affiliate, then VA itself takes the lead in this area.

If an invention has the potential for commercial success, VA and its academic affiliates will attempt to protect their intellectual property with a patent.



On average, 35 patent applications are filed a year for VA-related products and approximately eight patents are issued. VA also helps commercialize inventions developed by its employees by licensing the process to companies that have an interest in bringing the product or service to the marketplace. VA currently has 169 active licenses with pharmaceutical and other companies, and the number is growing every year.

In short, the Technology Transfer Program is an important link in the process of ensuring Veterans receive access to the latest technologies developed by VA researchers. It also helps VA, and American taxpayers, to receive their fair share of royalties from patents and joint ventures with non-governmental agencies and private companies.



# Genomic medicine takes VA Research into 21st century

New knowledge about the role of genes in health and disease promises to lead to safer, more effective treatments for an entire spectrum of diseases. VA Research is at the forefront of genomic analysis efforts throughout the nation and the world. VA is superbly fitted to study genomics—the use of patients' individual genetic profiles to customize care—because of its large and diverse patient population; world-class investigators; integrated network of basic research and clinical applications; and an unequalled electronic medical record system that will in time incorporate genetic information. As stated by Joel Kupersmith, MD, VA's Chief Research and Development Officer, "The future of medicine is determined by research, and genomics is the direction for research in the 21st century." Genomics is the key to personalizing medicine—that is, tailoring disease

screening, treatment, and monitoring according to an individual patient's genetic makeup.

Genetic-based tests for colon and breast cancers are already being used at VA. In recent years, VA has focused on further building its capacity in the genomics field. The Pharmacogenomics Analysis Laboratory (PAL) at the Little Rock VA Medical Center in Arkansas is capable of conducting cutting-edge genomics research using innovative technologies including robots, laser genome scanners, and other sophisticated genomic research tools. The PAL is poised to perform pharmacogenomic polymorphic marker testing to identify how people react to various medications and other treatments due to genetic differences. For example, this testing will look at the best drug dosage combinations for patients with certain genetic makeups.



"What we're learning will make medical diagnosis and treatment in the future so much better than what it is today—not just in VA but in the world at large," says Marc Blackman, MD, Associate Chief of Staff of Research and Development at the D.C. VA Medical Center.

### Research Spotlight: Gene Under Study Shows Promise for Diverse Health Problems

One of VA's many genomic research projects is being led by Dr. David Lovett, of the San Francisco VA Medical Center. Besides seeing kidney patients on a regular basis, nephrologist Lovett has made a career of studying one particular gene—the matrix metallopeptidase 2, or *MMP2*—and has published more than 100 scientific papers on the properties of this gene. "It's a gene I've worked with forever," Lovett said. "And its effects on the body when it is expressed inappropriately are widespread and varied."

The *MMP2* gene is a protein involved in many physical processes, such as the development of embryos, repair of damaged tissue, tumor invasion, and reproduction. As a nephrologist, Lovett is particularly concerned with *MMP2*'s effects on kidney function and its implications for those who have undergone kidney transplants. His studies have sparked great hope in wide-ranging medical contexts—not only promise for improved monitoring of kidney transplant for possible problems, but also for speeding up soldiers' recovery from battlefield injuries and patients' recovery from heart failure.



Stacey Whitbourne (left), PhD, MVP National Program Director, discusses informed consent procedures for the Million Veteran Program with research participant and Veteran Barbara Barnes.



### Million Veteran Project: A giant stride for genomics Research

VA is launching an unprecedented effort to improve Veterans' health care by redefining the sophisticated science of genomics. The Million Veteran Program, or MVP, is VA Research's trailblazing partnership with up to a million Veterans who are volunteering to help build one of the world's largest databases of genetic, military exposure, and health information, which will be applied to identify the connections between genes and health. This new understanding is aimed at enhancing disease screening, diagnosis, and prognosis. It may further point the way toward more effective therapies for a wide range of diseases, and could also help predict a person's response to a medication or other treatment.

By providing their genetic information in the form of a blood sample, completing a survey on health and military exposure, and allowing access to their medical record, Veterans who volunteer to participate in the MVP program are making a crucial contribution to this type of genomics research that could transform health care for Veterans and others throughout the U.S. The study will be rolled out in phases over the next five to seven years.

With the launch of a program that takes advantage of VA's unrivaled resources, VA expects to retain its position at the forefront of genomics research. MVP's kick-off represents another turning point on the road to a new era of improved, patient-tailored health care—a new day in which research will help medical professionals and their patients have more information so that together they can make better, personalized health care decisions.



# VA seeks to lead national health care efforts

*Agency provides ideal environment for comparative effectiveness research*



Comparative effectiveness research (CER)—research seeking to provide better information on different strategies for preventing, diagnosing, treating, and monitoring health conditions—has been a hallmark of VA research for decades. Such research is a prime example of how VA's combined approach to

research and health care can help ensure that the care the Department provides Veterans is the best care possible, and how VA can serve as a model for national health care reform efforts.

VA provides an ideal environment for CER efforts, which are driven by three major elements within the Department:

- **The Cooperative Studies Program (CSP)**, which conducts national, multi-site clinical trials and epidemiological studies comparing different treatments on health outcomes and costs.
- **A large portfolio of health systems-oriented projects** that examine questions related to health care delivery and quality of care. VA researchers also possess expertise in using the VA electronic health record and other large databases essential for efficiently comparing commonly used treatments in real-world settings.
- **The Quality Enhancement Research Initiative (QUERI)**, a program that seeks to improve Veteran health care by studying and facilitating the implementation and spread of evidence-based clinical practices and research findings into routine clinical practice in the VA. The QUERI program has provided critical information on what it takes to actually translate the findings of CER into effective and more cost-effective care.



## From cancer to cardiology, Nobel-winning scientist breaking ground



The VA research program has often been called the “jewel in the crown” of VA health care. VA research focuses on areas of concern to America’s Veterans, and has earned an international reputation for excellence in areas including aging, chronic disease, prosthetics, and mental health. VA investigators and clinicians collaborate across many disciplines, resulting in a synergistic flow of inquiry, discovery, and innovation between laboratories and clinics.

If one person can be said to embody the skills, imagination, and lifelong commitment to medicine of VA’s research team, it would be Dr. Andrew V. Schally, Distinguished Medical Research Scientist and Head of the Endocrine, Polypeptide and Cancer Institute of the Miami VA Medical Center. Dr. Schally started in medical research in 1950, and



# Malcolm Baldrige National Quality Award bestowed on VA

*VA Research Center receives nation's highest award for organizational excellence*

Among the many recent honors bestowed on VA and its world-class researchers is the 2009 Malcolm Baldrige National Quality Award, America's highest honor for innovation and performance excellence. This significant reward was conferred on VA's Clinical Research Pharmacy Coordinating Center in Albuquerque, NM.

"This prestigious recognition is a demonstration of VA's commitment to excellence and innovation in meeting Veterans' needs and the priority that this Department places on quality," said Secretary of Veterans Affairs Eric K. Shinseki. "It is through such dedication, ingenuity, and people-centered service that VA will provide exceptional service to our nation's Veterans in the 21st century."

As part of VA Research and Development, the Coordinating Center manufactures drugs, placebos, and devices, distributing them throughout the VA system to various clinical trial sites. In the last three years, the Coordinating Center supported studies involving 90,000 patients per year across the country, ultimately benefiting millions of Veterans and other Americans. Recent VA research trials supported by the Center include the use of robotic arms to help

stroke patients regain limb function, treatments for posttraumatic stress disorder, a comparative effectiveness research study of optimal medical therapy to angioplasty for coronary artery diseases, and effective approaches for diabetes management.



From left to right: Vice President Biden; Thelma P. Salazar, Associate Center Director for Administrative Operations, Veterans Affairs Cooperative Studies Program Clinical Research Pharmacy Coordinating Center; Mike R. Sather, Center Director; U.S. Commerce Department Secretary Gary Locke

by now has published more than 2,300 research papers in his long and distinguished career—the highlight of which was sharing the Nobel Prize for Physiology or Medicine in 1977 with his VA colleague Dr. Rosalyn Yalow. Recently, Dr. Schally said: "I am very fortunate to have spent my career at VA. I was lucky to have been allowed to do the work I have done, and to work with the people with whom I have worked, which enabled us to produce medical breakthroughs."

Over his decades-long career, Schally has been credited with weighty advances in a wide range of specialties—among them, not only cancer but also gynecology, gastroenterology, cardiology, and endocrinology. And now, a finding on the exciting effects of a growth

hormone antagonist on the aging process in mice can be added to the list of his groundbreaking findings. A paper published in the Proceedings of the National Academy of Sciences in December 2010, prepared by a VA research team led by Schally, offers evidence that the aging process in humans can be halted, or even reversed. By administering the growth hormone antagonist to mice, the team found that their average life expectancy increased; that cells in treated mice were able to live longer and replicate themselves longer; that learning and memory improved, especially in younger mice; and that treated mice developed fewer tumors than untreated mice. The next step will be to test the growth hormone antagonist in humans, with the promise that someday it may slow down the aging process.



# New workgroup recommends ways to maximize VA Research impact

*How VA Research runs its program is key to future success*

Translating discoveries in the laboratory to health care improvements at the patient's bedside is a top priority for VA Research, and health services research is crucial to the swift delivery of the best medical treatments to Veterans who need them.

VA leads the way in health services research, thanks to such unique attributes as its standout investigators and research centers with diverse expertise and interests; affiliations with world-class academic health centers and universities; research that is integrated with a national health care system, which allows the involvement in patient care of VA's many clinician-researchers; and advanced electronic medical records and centralized databases.

VA is committed to continuing as a pioneer in this field, building on new developments such as the growth of health informatics; expanding reliance on patient-aligned care teams that bring broad expertise to a Veteran's care; and the national focus on fundamental health care reform. To further increase the impact of health services research on health care within the VA and beyond, VA's Office of Research and Development has formed a workgroup of VA researchers and leaders with expertise in the area, to focus on enhancing research opportunities and impact on health care.

Workgroup members identified three factors influencing the potential impact of health services research: the appropriateness of the experimental design and methods; the robustness of existing evidence relevant to the question being studied; and the relevance of research to current health systems issues. Members also identified areas for

enhancements to existing processes. Among their recommendations:

- Encourage long-term relationships between researchers and clinical and health system leaders, establishing communication links within an investigator's own medical center as well as throughout the research enterprise.
- Encourage a focus on carefully defining research parameters so that questions are influential



and practical to address, and findings are methodologically sound and can be implemented within a relevant timeframe.

- Ensure clinicians and health system personnel are included in the initial study discussions to help identify potential research areas that would have the greatest impact on improving the health care system.

VA's Health Systems Research and Development (HSR&D) Service is committed to supporting research that can lead to measurable improvements in Veterans' care. To enhance coordination among all interested researchers and other stakeholders, the workgroup members proposed a new award initiative, to be called the Collaborative Research to Enhance and Advance Transformation and

## VA RESEARCH BY THE NUMBERS

Of VA's 153 medical centers, 116 have the capacity to conduct research.



Excellence (CREATE), to support cross-Veterans Health Administration collaboration and support coordination throughout the conduct and implementation of studies.

CREATE topics would focus on areas most clinically important to Veterans and the health system, and ones that generate research interest and opportunity. Project grants would be made to advance the understanding of clinical and policy options in priority areas, including their impact on health outcomes and their costs and suitability for wider VA implementation.

The ultimate aim of VA health services research is to improve the health of the Veteran population, and for this to be achieved, VA research findings must be taken up and disseminated throughout the VA health system. To this end, a specific focus on implementation science and translation research has been a hallmark of VA health services research for the past decade. Health services research funds proposals that focus on implementation of evidence-based practice and new clinical programs. In addition,

VA's Quality Enhancement Research Initiative (QUERI) has served as a research-operations-clinical partnership to advance implementation in high-priority clinical areas such as diabetes, mental health, and polytrauma.

QUERI's experience has reinforced the importance of considering implementation throughout the research process rather than just as an afterthought. More attention to implementation issues could be embedded within a variety of health services studies, according to the workgroup, including research into variations in practice and early effectiveness studies of new models of care. Also, implementation science can help in the real-world experiments as VA addresses critical issues such as suicide prevention, post-deployment care, and PTSD.

Finally, workgroup members noted, creating new QUERIs could support implementation of positive research findings not confined to a single clinical condition. Incorporating QUERI principles, the workgroup concluded, could benefit various health services research areas.



# History of Research Accomplishment

- **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.
- **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.
- **1994**—Identified a gene associated with a major risk for schizophrenia.
- **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 study 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 (TBI) 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 a 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.
- **2009**—Initiated the largest health study ever of Vietnam-era women Veterans, with up to 10,000 women expected to take part.
- **2009**—Launched one of the largest studies to date on the genetics of schizophrenia and bipolar disorder, to involve 38,000 Veterans at more than 20 VA sites.
- **2009**—Launched a four-year study of long-term health and social outcomes of OEF/OIF Veterans with serious burn injuries.
- **2009**—Showed that the traditional “on pump” method of heart bypass surgery yields better outcomes after one year than a newer method that does not use a heart-lung machine.
- **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 some one million Veterans expected to take part over the next five to seven years.
- **2010**—Combined efforts with the U.S. Army to study ways to prevent suicide among active-duty service members, Veterans, and reservists and to build on existing suicide research in VA, the Department of Defense, and the civilian sector; and conducted research with the U.S. Marines to determine why certain service members develop PTSD while others do not.
- **2010**—Began work on a computerized vision system to bridge the limitations of handheld GPS devices for blind users and offer additional mobility and independence for Veterans with vision loss.
- **2010**—Determined that Veterans with a mental health condition, especially PTSD, tend to have more physical ailments than those who do not, and that older veterans with chronic PTSD had a higher risk for dementia than their peers without the disorder.
- **2010**—Found evidence that prior head injury may double the risk of developing amyotrophic lateral sclerosis (ALS), commonly known as Lou Gehrig’s disease.
- **2010**—Determined that robots can be used to provide repetitive, high-intensity therapy for stroke patients, and confirmed previous findings that patients can recover function through therapy even years after a stroke.
- **2010**—Found that the immune system is likely to have a role in the development of Parkinson’s disease.
- **2010**—Identified a potential biomarker for PTSD through the use of a super-fast scanner that captures cross talk between groups of neurons in the brain.
- **2010**—Found that smoking cessation treatment that is made part of mental health care for Veterans with PTSD improves quit rates in those Veterans.
- **2011**—Expanded the REACH (Resources for Enhancing Alzheimer’s Caregiver Health in VA) program to support caregivers of Veterans with Alzheimer’s disease throughout the nation. In the program, based on earlier research by VA and university investigators, caregivers are provided individual and group counseling, a caregiver guide, education on safety and patient behavior management, and training for their individual health and well being.
- **2011**—Identified a potential blood marker for cognitive decline, through a study of nearly 1,000 older volunteers.
- **2011**—Published study results showing that the tiny, biocompatible brain implant that is part of the BrainGate neural control system remains viable and continues to effectively record brain signals for at least 2.7 years. The technology promises to help those with paralysis achieve more independence, and is also being studied as a prosthetic control system.



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