

**STATEMENT OF**  
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**UNDER SECRETARY FOR HEALTH**  
**DEPARTMENT OF VETERANS AFFAIRS**  
**ON THE VA MEDICAL AND PROSTHETIC RESEARCH PROGRAM**  
**BEFORE THE**  
**HOUSE COMMITTEE ON VETERANS' AFFAIRS**  
**JUNE 7, 2006**

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Mr. Chairman and Members of the Committee,

Thank you for the opportunity to appear before you today to discuss the Department of Veterans Affairs (VA) medical and prosthetic research program, including the relevance of VA research to the clinical treatment of veterans; description of priorities for Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) research; discussion of the Genomic Medicine initiative; and the need to upgrade and modernize VA research facilities. I am pleased to have Dr. Robert Ruff, Acting Director, Rehabilitation Research and Development Service; and Dr. Matthew Friedman, Director, National Center for Post Traumatic Stress Disorder. In addition, I am especially honored to introduce Dr. Joel Kupersmith, Chief Research and Development Officer, to the Committee. We appreciate this invitation to discuss the important work of VA research.

## **History of VA Research**

The original design for the Veterans Health Administration (VHA) Office of Research and Development (ORD) was clear: VA shall carry out a program of medical research to provide health care more effectively and contribute to the Nation's knowledge about disease and disability with emphasis on injuries and illnesses particularly related to service. We hold to that same purpose today.

The history of VA research is full of examples of how VA clinical investigators have improved clinical care.

- VA pioneered the first effective therapies for tuberculosis in the 1940s; veterans returning from the Pacific theater and POW camps in World War II were some of the first to receive these treatments.
- From the 1940's to the present, VA researchers have led the development of better fitting, lighter, more functional artificial limbs. In the late 1970s and early 1980s the Veterans Administration, as it was called then, supported research that led to the Seattle Foot, a prosthetic device for lower limb amputees. This revolutionary device has allowed thousands of amputees from the Vietnam War to return to an active life and participate in activities like basketball, skiing, or running, all of which were impossible with traditional artificial limbs. By 1991, more than 70,000 Seattle feet were in use in the United States. Later, I will describe the exciting work VA research is doing today in the area of robotics and other cutting edge prosthetics.
- In the 1950s and 1960s, the VA cooperative studies program developed the essentials of the multi-site randomized controlled clinical trial that is the standard for testing the safety and efficacy of new treatments today. VA cooperative studies in the 1960's, 70's, and 80's proved the value of such widely used therapies as coronary artery bypass, the use of lithium in bipolar disorders, and

aspirin's ability to ward off heart attacks. More recent VA clinical trials have led to non-surgical treatments for gastro-esophageal reflux disease and prostate enlargement, demonstrated the value of advanced cochlear implants in veterans with profound hearing loss, and established effective treatments for post-traumatic stress disorder (PTSD). Such results have extended life and improved the quality of life for veterans and non-veterans alike.

- In the 1960s, the VA invented the radioimmunoassay, a procedure that is now a mainstay of clinical laboratory testing through the world for detecting biological markers associated with health and disease such as prostate-specific antigen (PSA).
- Also in the 1960s, VA was instrumental in the invention and use of the first implantable cardiac pacemaker. William C. Chardack, chief of surgery at Buffalo's Veterans Administration Hospital, collaborated with Wilson Greatbatch in a partnership to develop the device and surgical techniques that have helped millions of Americans, including our aging veterans.
- VA research contributed significantly to the development of the CT scanner and MRI machine. VA's basic science research in 1960 and 1961 contributed to the development of the computerized axial tomography (CAT scan) in the early 1970s and modern radioimmunoassay diagnostic techniques in the mid-1980s. This illustrates that the progress of discovery is not an overnight task. Sometimes, scientists must work for decades to find solutions to complex problems. Today, veterans and all of us benefit from the basics discovered by VA investigators.
- Smoking and military service have coincided for many years, so VA has a longstanding history of investigating treatments for nicotine dependence. In the early 1980s VA's investigator, Jed Rose at the Durham VA Medical Center (VAMC), worked with others to invent the nicotine patch. Today, VA continues to

support a strong portfolio of research about the effects of nicotine and its relationship with substance abuse, a major concern for many veterans.

- More recently in 2005, the New England Journal of Medicine published the results of a 15 year VA clinical trial that showed an experimental vaccine for shingles cuts its incidence in half and dramatically reduces severity and complications in those that develop the disease. FDA recently approved a license for this vaccine.
- Also, researchers from VHA, Stanford University, and Duke University reported in the October 2005 *New England Journal of Medicine* that the implantable cardioverter defibrillator, although a costly device, is a relatively cost effective way to help prevent sudden cardiac deaths for some high risk patients. This is a good example of collaboration involving our academic partners with funding from another federal agency (the Agency for Healthcare Research and Quality) as well as industry (Blue Cross Blue Shield Technology Evaluation Center).

But, past success is not enough. Research must be future oriented. We must look at how we practice health care today and ask: how can we do better? Our research program builds on its past by identifying and confronting the important questions and challenges of today and then doing the hard work to find solutions for the future.

### **Genomic Medicine**

VA's plans for a Genomic Medicine Program are part of this future. VHA, as a large healthcare system with an integrated research network and an unrivaled electronic medical record system, is distinctively positioned to develop a national Genomic Medicine Program, a program that will be targeted to address veteran-specific concerns.

Value of Genomic Medicine. While it is crucial that VA research address the issues of today and this current conflict, it is equally important that we invest in the achievable possibilities of genetic medicine to understand the role of genetics in the prevention and cause of disease; to improve how clinicians prescribe medications; to prevent adverse drug reactions; and to learn how to use genetic information effectively in everyday practice. I want to emphasize the importance of this especially with the treatment of chronic disease which is a major part of VA's clinical care. In fact, we already have evidence of the value of genomic medicine.

- Prevent adverse drug reactions. When persons who have certain cancers and low levels of a specific enzyme (thiopurine S-methyltransferase) receive standard doses of specific immunosuppressants (mercaptopurine and azathioprine), they risk life-threatening, drug-induced suppression of blood cell production. Genetic testing can identify these people, and then physicians can treat them with greatly reduced doses that are much less toxic than the standard dose.
- Personalize clinical care. Patients with two copies of the gene for an abnormal clotting factor face a risk of developing blood clots in the leg that is 50-100 times greater than that of the general population. We can use this information today to improve the quality of care for patients who may be immobilized for a substantial period, such as following major orthopedic surgery.
- Customize drug treatments. Individuals with mutant allelic variants of the cytochrome P450 (CYP) 2C9 genotype slowly metabolize warfarin, a drug used to thin blood. The slow metabolism of warfarin may increase the risk of hemorrhage when warfarin is first used. A small pilot study conducted at the Marshfield clinic suggests that by obtaining the genotype prior to initiation of therapy, clinicians can reduce the dose of warfarin given the patients most at risk, and that this intervention may result in fewer drug-induced bleeding episodes.
- Improve care. Genetic analysis is becoming part of standard care for treatment of many cancers, including most leukemias and lymphomas, brain tumors, colon cancer and breast cancer. These analyses are used both to diagnose the disease and to determine responsiveness to both chemotherapy and radiation.

Cancer screening based on molecular genetic and proteomic tests will help to catch disease earlier, enabling cures for patients who now go on to develop metastases and die.

These examples show that the move to genomic medicine has begun and that the potential exists for major advances in customizing care to the needs of each individual veteran. Just as VA has pioneered the advantages of the electronic health record, we can do the same in genomics.

Privacy and Ethical Foundations. I want to assure the Committee that VA will maintain the integrity of the privacy of veterans' records. We have built-in safeguards today within the electronic health record to assure privacy, and we will build the necessary protections into our genomics program. As a first step, VA has appointed a Genomic Medicine Program Advisory Board composed of nationally renowned medical experts in genomic research, bioethics, and disease management. While the Committee will assess the potential impact of a VA genomic medicine program on existing VA patient care services; recommend policies and procedures for tissue collection, storage and analysis; and develop a research agenda and approaches to incorporate research results into routine medical care, its first priority will be to provide expert counsel about protecting veterans' privacy and establishing a strong ethical foundation for VA's use of genetic information. Questions about consent, identification of samples, and disclosure of information are a few of those that the group will address. And, we will be sure to consult with veterans about their concerns by using focus groups and other contacts to learn about and then appropriately address issues expressed by veterans themselves. Genomics medicine is the next step into the future to improve and customize health care. We want to take the time necessary to construct a strong ethical and scientific foundation in partnership with the veteran community.

## **VA Research as a Unique Laboratory**

A special advantage of the VA research program is that it is nested within a health care system that serves more than 5 million veterans. This creates a unique national laboratory for the discovery and application of new medical knowledge. Translating research into clinical practice is talked about throughout the medical community, but VA is one place where we apply research every day. VA research has made direct contributions to current clinical practices for hypertension, PTSD, diabetes, and other chronic diseases. VA clinicians who have responsibility for providing care for patients and for training future health care providers are the same scientists who initiate our research projects; nurture the proposal through VA's rigorous scientific merit review; identify and secure additional funding from other Federal agencies, non-Federal sources, and industry; conduct the research; publish the results in prestigious medical journals; and then complete the circle back to the bedside. VA research truly brings scientific discovery from bedside to bench and then back to the bedside.

In fact, the chance to conduct research has been a strong tool for VA to recruit and retain high quality physicians and other clinicians. This directly and continually leads to enhanced quality of care for veterans. Other health care systems rarely provide physicians and other clinicians with the opportunity to research questions that are most relevant to patient care. VA's healthcare system allows that we promote the idea of research within our unique research setting with tools such as the computerized patient record system and protected time for research.

Studies by the Institute of Medicine, RAND, and others have highlighted the delays that occur from the time of scientific discovery to the time an evidence-based practice becomes routine – in US healthcare, on average, the likelihood of receiving a treatment based on credible scientific evidence is only about 50 percent. VA far exceeds that level of performance on virtually every evidence-based indicator. Furthermore, VA has established a unique program, the Quality Enhancement Research Initiative (QUERI), whose mission is to bring researchers into partnership with health system leaders and

managers in order to ensure the care we provide to veterans is based on the most current scientific evidence.

The record of translation is clear. For example

- VA clinicians have long noted that veterans with schizophrenia often have extremely high rates of tobacco usage, and found that nicotine receptors have a critical role in processing sensory input in such patients – in essence, such veterans were medicating themselves with tobacco to correct their brain abnormality. A team from the Denver VA Schizophrenia Research Center discovered that a gene coding for part of the brain’s nicotine receptor is responsible for the inheritance of risk for schizophrenia. Subsequent work by VA researchers has successfully translated these insights to develop potential new clinical treatments for schizophrenia, including a compound derived from sea worms that works like nicotine but does not have its adverse health effects. VA studies of this compound in an animal model of schizophrenia have enabled the Food and Drug Administration (FDA) to approve the first experimental use in humans, and the drug holds the promise of recovery for many persons with schizophrenia that fail to respond to existing therapies.
- VA investigators have demonstrated that intravenous infusion of adult-derived, bone marrow stem cells can protect against brain damage in a rat model of cerebral ischemia. The ability to reverse brain damage has important implications for such disabling conditions as stroke, brain trauma, and spinal cord injury.
- Translation of findings occurs outside of basic science as well. VA investigators at Hines, Illinois and Cleveland, Ohio are developing and testing electronic microstimulators which may have important implications for the quality of life of individuals with spinal cord injury (SCI). Such stimulators, when implanted into leg muscles, may recreate the ability to walk and maneuver in their local environment. When implanted into breathing muscles, they may recreate breath and cough patterns that will avoid respiratory complications that are currently the leading cause of death in SCI patients.

These specific examples illustrate how VA take issues of concerns to veterans and improves care directly through research by VA clinical investigators.

### **Emerging Priorities of VA Research**

Although in any given year the bulk of VA's research budget is committed to on-going investigation, each year we re-evaluate our priorities based on the changing needs of the veterans we serve, and attempt to fund high quality science that meets those priorities. I would like to highlight our current areas of focus for VA research.

Operation Iraqi Freedom and Enduring Freedom (OIF/OEF). In order to better serve military personnel injured during OIF/OEF, VA has implemented a new research agenda which brings all parts of ORD together to develop new treatments and tools for clinicians to use to ease the physical and psychological pain of the men and women returning from conflicts, to improve access to VHA services, and to accelerate discoveries and applications, especially for PTSD diagnosis and treatment, state-of-the art amputation and prosthetics methods, and polytrauma.

Neurotrauma (including traumatic brain injury and spinal cord injury). Traumatic Brain Injury (TBI) accounts for almost 25 percent of combat casualties suffered in OIF/OEF by US Forces. SCI is also a possible consequence of these combat casualties. In November 2005, VA issued a program announcement to stimulate research in the area of combat casualty neurotrauma. This research initiative seeks to advance treatment and rehabilitation for veterans who suffer multiple traumas from improvised explosive devices and other blasts. Eighty-five letters of intent to submit a research proposal were received, indicating a high level of interest among our investigators. Complete proposals will be reviewed in the next several months, and we plan to fund as many high quality projects from this initiative as the budget will allow.

*Polytrauma and Blast-Related Injuries.* Improvements in body armor and battlefield medicine have resulted in higher survival among wounded soldiers but also new combinations of critical injuries, including head injuries, vision and hearing loss, nerve damage, infections, emotional problems, and in some cases amputation or severed spinal cords. This is a new challenge for VA, and we need to develop the knowledge base to manage these conditions over the remaining lifetime of the veteran. VA has devoted its newest QUERI center to polytrauma and blast-related injuries with a focus on using the results of research to promote the successful rehabilitation, psychological adjustment, and community reintegration of these veterans. Other VA scientific studies are currently underway to characterize these injuries and determine their outcomes and costs, and to identify geographic areas where the need for rehabilitation is greatest. Such information is critically important in helping VA redesign its care delivery system to meet the needs of these veterans.

*Amputation and Prosthetic Research.* VHA ORD currently supports a broad research portfolio pertaining to amputation and prosthetics, and more research in this area is planned. Areas of interest include:

- Nanofabrication, microelectronics and robotics to create lighter, more functional prostheses. ORD is funding two new Prosthetics Rehabilitation Engineering and Platform Technology Centers that are national resources to develop computerized state-of-the art prosthetic limbs with the goal of using the latest advances in orthopedic surgery, tissue engineering, nanotechnology, and microelectronics to create prosthetics that look, feel, and act more like one's own limb.
  - The Providence VA Medical Center, in collaboration with Brown University and the Massachusetts Institute of Technology, is working to develop a "biohybrid" limb that will use regenerated tissue, lengthened bone, internal and external implants and sensors to allow amputees to use brain signals and residual limb musculature to have better control of their limbs and reduce the discomfort and

secondary complications associated with current prostheses. These researchers are already publishing and presenting about their work.

- The Advanced Platform Technology (APT) Center at the Cleveland VA Medical Center focuses on sensory and implanted control of prosthetic limbs, accelerated wound healing, and biological sensors for the detection of health and function to accelerate the use of new materials and innovative micro-mechanical or nanotechnologies to provide more independence to veterans with disabilities.

- ORD is partnering with the Department of Defense (DoD), Walter Reed Army Medical Center, the Defense Advanced Research Projects Agency and Brooks Army Medical Center to compare prosthetic designs; define standards of function; evaluate psychological issues faced by returning service personnel; determine psychosocial issues that challenge successful reintegration; and initiate longitudinal studies to study veterans care over time.
- VA investigators are examining rehabilitation for the visually impaired; new treatments for burn victims; restoration of hearing and maximizing function for those with hearing loss, especially for polytrauma victims; and natural mechanisms of neural regeneration to return function to paralyzed veterans and those with brain injuries. VA investigators also plan to study advanced tissue engineering and the manufacturing of artificial skin to accelerate wound healing.

*Mental Health and PTSD Research.* Special attention is being paid to the circumstances of the returning OIF/OEF veteran related to mental health and Post Traumatic Stress Disorder (PTSD) research. Examples include:

- *Long-Term Studies.* Baseline data has been collected on military personnel prior to their deployment to Iraq. These soldiers will be reassessed upon their return and several times after that to identify possible changes that occurred in emotion or thinking as a result of their combat exposure. In another program, a VA

scientist is collecting information prior to deployment, however in this study, from Army Reserve personnel. This is important because Reserve personnel have not been as well studied as active military and may have different readjustment issues. They will be reassessed twice afterwards to determine whether they have increased symptoms, distress, or increased utilization of healthcare services. Information from these types of programs will help identify factors that change as a result of military service and those which may be important in healthy readjustment. Support of these types of prospective, longitudinal studies is important and should be able to provide insight about the effect of combat exposure and the ability of soldiers to return to high levels of functionality afterwards.

- *Interagency Collaboration regarding OIF/OEF Mental Health.* VA, the National Institutes of Health (NIH) and DoD jointly issued a Request for Applications (RFA) in FY 2006 to address questions of risk evaluation, risk reduction, psychotherapies, internet treatments, etc. involving active-duty or recently separated National Guard and Reserve troops from OIF/OEF. This RFA specifically encouraged participation of clinicians and researchers who screen, assess or provide direct care to at-risk, combat exposed troops, and emphasized interventions focusing on building resilience for veterans suffering from mental health problems, including PTSD, and developing new modes of treatment that can be sustained in community-based settings. Among the approaches being considered are novel pharmacological, psychosocial and combination treatments as well as the use of new technologies (e.g., World Wide Web, DVD, Virtual Reality, Tele-health) to extend the reach of VA's health care delivery system. Fifty-five proposals were received earlier this year in response to this RFA, and those proposals deemed to have scientific merit and relevance to veterans will start October 1, 2006.
- *Women and PTSD.* An estimated 8 - 10% of active duty and veteran women currently have PTSD resulting from having experienced some form of trauma. A

large multi-site cooperative study is targeted to determine the best treatment for women veterans by providing either prolonged exposure therapy (PE) or a comparison therapy focused on current problems (PCT). The initial results from this study show that women with PTSD who were treated through PE therapy had more improvement in their PTSD symptoms and functioning than the women receiving PCT. This study is important because it is dedicated to treating female veterans who may experience PTSD differently than male veterans, and also because it identifies the more effective psychotherapeutic strategy, which essentially allows the patient to reorganize and eventually control some aspects of their disruptive memories and symptoms.

Projects in Planning. ORD is currently considering solicitations for studies involving the long-term care needs of veterans with TBI; an assessment, in collaboration with DoD, of the long-term changes in health status resulting from combat deployment; and burn treatment and recovery.

General Mental Health. Mental health research is spread throughout many parts of the ORD research portfolio including aging, health systems, special populations, military occupations and environmental exposures, substance abuse, and other chronic disease. In FY 2005 the total mental health research portfolio totaled \$67,323,105 in active mental health research projects to understand the underlying causes and to effectively diagnose and treat mental disorders. This is nearly 17 percent of the FY 2005 Medical and Prosthetic Research appropriation of \$402,348,000. This total does not include support from non-VA research sponsors or support from other VA resources such as the Quality Enhancement Research Initiative (QUERI), Mental Illness Research, Education, and Clinical Centers (MIRECCs, and medical care support for clinicians engaging in research. The scope of mental health research includes studies about substance abuse, cognitive and behavioral issues, PTSD, stress, TBI, as well as brain diseases and mechanisms.

Depression. Implementation of an evidence-based collaborative care model for depression called “TIDES” (or Translating Initiatives in Depression into Effective Solutions) has demonstrated significant improvements in depression symptomatology among patients referred by their primary care providers. This study plus two companion evaluations of the processes, outcomes, and costs of implementation (called WAVES or Well-Being among Veterans Enhancement Study and COVES or Cost and Value of Evidence-based Solutions for Depression) are part of national VA strategic planning and rollout for improving the quality of depression care.

Other projects. One study involves research about the role of smoking and nicotine dependence among veterans with PTSD. This fall, ORD will begin a multi-site clinical trial to study the effects of risperidone on PTSD. ORD will continue to support other studies that test the effectiveness of virtual reality therapy and other new treatments for PTSD. It is important to note that this research will also have direct applications for all veterans and not simply those involved in OIF/OEF.

Gulf War Veterans’ Illnesses. VA research places a high priority on scientific research aimed at improving the quality of life for veterans of the 1990-1991 Gulf War affected by chronic multisymptom illnesses commonly referred to as Gulf War Veterans’ Illnesses (GWVI). Some veterans who participated in Operations Desert Shield and Desert Storm have reported conditions and chronic symptoms such as fatigue, weakness, gastrointestinal difficulties, cognitive dysfunction, sleep disturbances, persistent headaches, skin rashes, respiratory problems, and mood changes at rates that significantly exceed those reported by comparison groups. VA research continues to expand its efforts to understand and treat GWVI. The core objective is to improve the health of ill Gulf War veterans. It is important to note that Gulf War veterans with chronic unexplained symptoms are eligible for disability benefits even when the cause of their illness cannot be determined.

VA has committed \$15 Million in FY 2006 for a collaboration with the University of Texas – Southwestern Medical Center and has also funded VHA ORD investigators for

on-going projects. These ongoing studies address areas of interest that include: chronic multisymptom illnesses (CMI) affecting GW veterans; conditions and/or symptoms frequently reported by GW veterans; long-term health effects of potentially hazardous substances, alone and in combination, to which GW veterans may have been exposed during deployment; and any of the 21 Research Topics forming the framework for the Annual Report to Congress of Federally Sponsored Research on GWVI.

Women's Health. According to information from the VA's Center for Women Veterans, in 1973, women in the active duty military accounted for 2.5 percent of the armed forces. By fiscal year 2001, however, the number of women significantly increased making up 15 percent of the armed forces and those numbers are expected to increase. To respond to this demographic change and develop a more comprehensive VA women's health research agenda, a VA Women's Health Research Planning Group recently identified the needs of women veterans and a corresponding research agenda. VA researchers currently are investigating optimal strategies for conducting preventive health and disease screening activities among women veterans (e.g., cervical cancer screening) and developing and evaluating computerized, interactive educational programs to enhance VA staff awareness of women veterans and their health-care needs.

### **Chronic Disease**

VA researchers conduct extensive research to discover how to prevent and treat chronic disease.

Diabetes. According to the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health, 20.8 million people—7 percent of the population—have diabetes. An estimated 4.6 million people are diagnosed and 6.2 million people are undiagnosed. In 2005, 1.5 million new cases of diabetes were

diagnosed in people aged 20 years or older. Diabetes affects nearly 20% of veterans receiving health care from VA: 1 million veteran users. An estimated 2 million veterans without diabetes have metabolic syndrome, which places them at high risk for diabetes. The cost is tremendous: 30% of VA health care costs (in- and out-patient and pharmacy) are attributable to patients with diabetes. This includes 1.7 million days of hospital care. VA investigators have completed the first study to compare the quality of diabetes care among patients in VA and commercial managed care organizations. Quality of care measures were compared for seven diabetes processes of care, three diabetes intermediate outcomes, and four dimensions of satisfaction. Results from this study showed that VA patients had better scores than commercially managed care patients on all assessed quality of care measures. VA patients also had better low-density lipoprotein control and were slightly more satisfied with the overall quality of diabetes care at VA.

Identifying the most effective treatment methods is crucial to reducing the incidence of diabetes among veterans. Although more patients are accessing medical information on the Internet, few studies have examined the effects of web-based interventions that incorporate an interactive component requiring feedback from patients. A VA study tested diabetes care management using a web-based system for veterans with poorly controlled diabetes. Results showed that web-based care management improves poorly controlled diabetes in veterans. Veterans participating in the web-based management program had significant improvements in HbA1c over one year compared to usual care, and persistent website users had even greater improvements compared to intermittent users.

ORD has also initiated the VA Diabetes Trial to determine whether intensive control of blood sugar, compared to standard methods, can reduce macrovascular blood vessel damage and other complications. Smaller trials to determine the value of the interventions will come first, with more research to follow.

Obesity. Results from the 2003-2004 National Health and Nutrition Examination Survey (NHANES) indicate that an estimated 66 percent of U.S. adults are either overweight or obese. The problem is similar or worse among VA's patient population, with 73% of veteran patients overweight or obese. Obesity contributes to increased heart disease, diabetes, and sleep apnea, and an estimated 300,000 Americans die annually from illnesses related to overweight and obesity.

Findings from VA studies to assess the efficacy and safety of weight loss medications, as well as the effectiveness and adverse events associated with the surgical treatment of obesity, demonstrated that surgical treatment is more effective than non-surgical treatment for weight loss in severely obese patients; weight loss was maintained for up to 10 years and longer and was accompanied by significant improvements in several comorbid conditions.

Other examples of VA research include studies on traditional and new approaches to prevent and treat obesity, such as a comparison of lower extremity functional electrical stimulation on obesity and associated co-morbidities in comparison to upper extremity aerobic exercise for persons with paraplegia; an assessment of the impact of walking aides on quality of life and physical activity in overweight and obese veterans with osteoarthritis; and explorations of drug therapies.

Alzheimer's Disease. Alzheimer's Disease (AD) and related dementias affect 7.3% of veterans over age 65. VA research is helping to discover new facts about AD and other diseases and conditions that affect older veterans. For instance, researchers at the Bronx VA medical center have reported that diet-induced insulin resistance, a cause of type II diabetes, promoted beta-amyloid production concurrent with decreased insulin-degrading enzyme (IDE) activity in an animal model of AD. Beta-amyloid is the major component of amyloid plaques, the hallmark of AD pathology. IDE has been proposed to be responsible for the degradation and clearance of beta-amyloid in the brain. Such research is needed to form the basis of future interventions to prevent or reverse this devastating condition.

Influenza. VA health services researchers have been instrumental in improving vaccination rates for veterans with chronic diseases that place them at high risk for complications from influenza, as well as enhancing vaccination among health care workers and veteran groups that historically have had low vaccination rates, such as minorities, smokers, and those with spinal cord injuries and disorders.

Pandemic influenza infection has the potential for causing significant morbidity and mortality in the United States and elsewhere. ORD is responding, along with other federal agencies, to this unprecedented public health threat by initiating studies that examine optimal dosing strategies for the antiviral agent oseltamivir (Tamiflu®) in the event of an emerging pandemic of human infection with an avian or other influenza strain for which an effective vaccine is lacking.

HIV/AIDS. AIDS (acquired immunodeficiency syndrome) is caused by HIV (human immunodeficiency virus). The virus kills or damages the body's immune system, which lowers the body's ability to fight infections and certain cancers. According to the Centers for Disease Control, at the end of 2003, an estimated one million persons in the United States were living with HIV/AIDS, with 24-27% undiagnosed and unaware of their HIV infection. VHA is the largest single provider of HIV care in the US, with nearly 20,000 patients seen annually with the disorder. Accordingly, ORD funds a full range of studies from bench research aimed at elucidating the underlying mechanisms of HIV to implementation projects that improve VHA's effectiveness in caring for this population. Researchers at the VA South Texas Health Care System and the University of Texas Health Science Center recently showed that people who have a below-average number of copies of a particular immune-response gene have a greater likelihood of acquiring HIV and, once infected, of progressing to full-blown AIDS. These findings, cited as one of the top articles published in the eminent journal *Science*, have important implications for the treatment and prevention strategies for HIV/AIDS and possibly other infectious diseases as well.

## **Infrastructure**

It is crucial that VA investigators have the equipment and facilities necessary to conduct cutting-edge research in the twenty-first century. To identify where improvements may be needed, ORD has initiated a comprehensive review of VA's research facilities to identify deficiencies and corrective actions. The objectives of the Research Infrastructure Evaluation and Improvement Project are to review the overall adequacy and utilization of research space and infrastructure (including animal research facilities); to develop a plan to update and maintain facilities; to ensure compliance with biosafety and research laboratory security requirements; to enhance collaborations between the local VA Medical Center and its academic affiliate; and to ensure that the needs for highly specialized research programs (e.g., Rehabilitation Research and Development (RR&D) and Health Services R&D (HSR&D) Centers of Excellence) are met.

Survey teams including VA research administrators and scientists, as well as other VA employees and engineering contractors, will review documentation and visit facilities to evaluate the physical infrastructure (including the animal facility, research laboratories and common equipment rooms); operational infrastructure (capability to conduct research while meeting requirements for compliance with safety, animal welfare, and human subjects protection regulations); and equipment (major items of equipment used for the conduct of research) of VA facilities with active research programs. The data collected from the surveys will be used to develop financial needs and an asset management plan. We expect to have a report to Congress early in 2007.

In addition, ORD recently funded proposals as part of the Shared Equipment Evaluation Program that is managed by the Biomedical Laboratory and Clinical Science Research and Development Services. The purpose of this program is to fund new or replacement research and animal facility equipment. The program requires that facilities identify dollar-for-dollar matches in order to leverage the VA contributions. As a result of a December 2005 request for applications, a total of \$2,086,173 for facility projects and research equipment has been funded for the following sites: Decatur, GA; Chicago, IL; Cleveland, OH; Miami, FL; Loma Linda, CA; Memphis, TN; Nashville, TN; New Orleans,

LA; Omaha, NE; Palo Alto, CA; Philadelphia, PA; Portland, OR; Richmond, VA; San Francisco, CA; Seattle, WA; San Diego, CA; San Antonio, TX; and Los Angeles, CA.

Other proposals for research equipment are pending funding with decisions expected later this fiscal year. This program was suspended for a number of years, but plans are to begin funding proposals on an annual basis after a review to determine merit and priorities.

### **VA Research Past, Present, and Future**

Past. The achievement record for VA research is impressive. VA physicians and scientists developed practices that have revolutionized medicine. They pioneered tuberculosis treatment, developed the cardiac pacemaker, the nicotine patch, and contributed to development of the high-tech diagnostic procedures of magnetic resonance imaging (MRI). The first successful drug treatments for high blood pressure and schizophrenia were pioneered by VA researchers, as were kidney and home dialysis techniques. The Seattle Foot, created by VA, allows amputees to walk, run and jump.

In 1977, the Nobel Prize for Medicine went to two VA physicians -- Dr. Rosalyn S. Yalow of the Bronx VA Medical Center, who was recognized for her landmark work in the development of the radioimmunoassay; and Dr. Andrew V. Schally of the New Orleans VA Medical Center, for his research on brain hormones.

In 1998, Ferid Murad, M.D., Ph.D., shared the Nobel Prize in Medicine in part for research he conducted while at the Palo Alto VA Medical Center. Studies by Dr. Murad have been instrumental in illuminating the role of nitric oxide in body functions, including the relaxation of blood vessels and regulation of blood pressure.

And, a most recent accomplishment is the FDA licensure of a vaccine to prevent shingles. VA researchers conducted the clinical trials that tested the efficacy and safety

of this new vaccine that will help millions of veterans and the nation as a whole.

Present. Today, we are briefly discussing what VA researchers are presently doing. For example, in rehabilitation research, we have described how VA researchers are developing and testing cutting edge artificial limbs. Also, VA's Center of Excellence on Innovative Visual Rehabilitation in Boston is developing a microelectronic retinal implant to restore vision to patients with age-related retinal degenerative disorders, including macular degeneration (the leading cause of legal blindness in the VA healthcare system) and retinitis pigmentosa. The implant is beginning to be tested in patients. Stimulation is applied to the retina where damaged cells had been which makes it easier for the nervous system to interpret or make sense of the images.

In biomedical and clinical research, we are searching for more effective treatment for cancer and other problems. For example, one of the most common treatments for cancer is chemotherapy or drugs that kill cancer cells. The problem is that these drugs also harm healthy cells, so VA researchers are studying targeted chemotherapy drugs to disrupt the ability of cancer cells to divide and multiply, but generally not affect healthy cells. Some of these drugs are already in clinical use. One well-known example is Gleevec, approved to treat a rare type of gastrointestinal cancer and some leukemias. This drug, developed and tested with the help of VA researcher Dr. Michael Heinrich in Portland, "turns off" an enzyme that enables cancer growth.

Another example comes from the lab of VA scientist Dr. Andrew Schally, a Nobel Prize winner. Schally, formerly in New Orleans and now in Miami, is testing compounds that stop tumors by blocking a hormone that fuels their growth. He is also developing another form of smart chemotherapy: His group identifies tumors with an affinity for certain hormones, and then packages manmade versions of those hormones with tumor-suppressing drugs. In animal and cell-culture studies, the resulting compounds appear to zap cancer cells without harming healthy cells.

Future. But, past success and present efforts are not enough. Research must be future oriented. We must look at how we practice health care today and ask: how can we do better? Our research program builds on its past by identifying and confronting the important questions and challenges of today and then doing the hard work to find solutions

As an academically trained researcher, I understand the complexities of the research process, and I am fascinated by the results. I fully support this program and advocate to you that its value, both to veterans as well as the nation, far exceeds the costs. The history of VA research is impressive, and the future promises even more important advances. Can we apply genomics to improve the quality of care for veterans? Can we prevent infections that hamper the use of biohybrid limbs? Can we develop artificial retinas so that wounded OIF/OEF soldiers and our aging veterans can regain their sight? Can we use our computerized medical record system and genetic samples to individualize drug and clinical treatments, or identify those veterans who may have a predisposition for a particular disease and prevent the onset of, rather than treat, the symptoms? Can we continue to examine ourselves to find out how to deliver patient care more effectively? The answers to these questions must be “yes”, as no other health system is better positioned than VHA to make these discoveries, and no other group of patients is as deserving as America’s veterans to receive the benefit of such innovation.