



# Gulf War Veterans Illness Research Program

# VA Research Mission

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- Mission: *“To discover knowledge and create innovations that advance the health and care of veterans and the nation.”*

# VA Research Standards

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- Is the research based on rigorous science?
- Will the research produce data that drives clinical policy and translates to improved health care?
- Will the research help veterans?
  - Is it *veteran-centric*?
  - The only research program focused entirely on veteran's needs

# Rich 60 Year History

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- 3 Nobel Laureates, 6 Lasker Award Winners
- Important Discoveries and Inventions
  - Devices
    - First liver transplant
    - Early work on the Cardiac Pacemaker
    - Radioimmunoassay
    - CT Scanner
  - Treatments
    - TB – First large scale clinical trial
    - Hypertension
    - Heart Failure

# Rich 60 Year History (cont)

- First rehabilitation program for blind persons
- Linked smoking with cancer of the respiratory tract and lung
- Developed the nicotine patch for smoking cessation
- Found that the insulin pump controls diabetics blood sugar and weight better than multiple daily injections
- Identified best treatments for colon cancer, psychoses, stable angina, high blood pressure and other conditions
- Developed a computer-controlled ventilator system for critically ill patients
- Developed the Seattle Foot, first prosthesis allowing amputees to run and jump

# Important Recent VA Research Advances

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- Pinpointing genes for diabetes and obesity
- Brain-computer interface to restore independence to paralyzed veterans
- Proper use of coronary angioplasty - COURAGE trial
- Vaccine for Shingles
- Prolonged Exposure Therapy for PTSD
- Long term study of PTSD & TBI starting pre-deployment
- Mechanism of Respiratory Distress Syndrome
- Mechanism of pain in spinal cord injury
- Effects of reduced work hours of medical residents on patient outcomes



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# General Characteristics of VA Research

# Intramural Program

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- VA Research is an intramural program
  - Researchers must be employed by VA (usually 5/8s or more)
  - Having research and clinical care under the same roof is a unique strength

# Intramural Program

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- VA Research connected directly to nation's largest health system (being "Intramural")
  - >70% of investigators are physicians
  - Links researchers directly veterans' needs
  - Facilitates implementation of research results
- Unique research resources include
  - *Electronic Health Record*
  - Cooperative Studies Program – Clinical Trials
  - Telemedicine
  - Drug safety center
  - Rehabilitation research

# VA Research

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- Office of Research and Development does not oversee all VA research
  - RECC's, etc
  - Epidemiology section

# Research Services

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- Biomedical Laboratory R&D Service
  - Molecular, Genomic, Physiologic
- Clinical Science R&D Service
  - Test new treatments & compare existing therapies
- Health Services R&D Service
  - Quality and organization of care
  - Cost effectiveness
  - Basis of VA's ability to present its excellence in quality
- Rehabilitation R&D Service
  - For the disabled individual, improve functional capacity in their persons, families, communities and workplaces

# Organization of VA Research



- **U.S. News & World Report attributes the high quality of VA patient care to**  
*“consistent examination of the processes and procedures that go into care giving systems...”*

# Areas of Research Sponsored

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- Designated Research Areas
  - Age and Age Related Changes
  - Acute and Traumatic Injury
  - Military Occupation and Environmental Exposures
  - Sensory Disorders and Loss
  - Mental Illness
  - Substance Abuse
  - Special (Underserved, High Risk) Populations
  - Health Services and Systems

# Types of Research Sponsored

- Investigator-Initiated Research (Merit Review)
- Large-scale, multi-site clinical trials (Cooperative Studies Program)
- Centers of Excellence (all Services)
- Service-Directed Research
- Special Initiatives (e.g., Gulf War Illnesses Research)
- Research Career Development Awards
- *All projects undergo strict scientific review*



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**OEF/OIF**

# OEF/OIF

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Laura Kluch / W

# OEF/OIF

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- Deployment-related research – current and all conflicts
  - Prosthetics
  - Hearing and vision research
  - PTSD
  - Rehabilitation
- Deployment-related research highlighting specifics for current conflicts
  - Traumatic Brain Injury and other Neurotrauma
  - Polytrauma
  - Access
  - Chronic care and the new veteran
- Collaborations with DoD



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# Gulf War Veterans Illness Research Program

# Background

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- A proportion of veterans returning from the 1990-1991 Gulf War reported various chronic health problems to a greater degree than non-deployed Gulf War era veterans
  - Persistent headaches
  - Joint pains
  - Extreme fatigue
  - Cognitive problems
  - Gastrointestinal difficulties
  - Sleep disturbances
  - Skin abnormalities

# Background

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- More than 30% of veterans who served in the 1990-1991 Gulf War have had military service-connected conditions
- $\approx 3300$  have been service-connected for the special “undiagnosed illness” category

# Federal Research Portfolio

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- To better understand the health conditions and health problems experienced by Gulf War veterans, VA, DoD and HHS have supported research projects related to Gulf War Veterans Illness (GWVI)
- VA/DoD funding for research on GWVI totaled \$326 million from FY1997 to FY2007
- The federal research portfolio has five focus areas
  - Brain and Nervous System Function
  - Environmental Toxicology
  - Immune Function
  - Reproductive Health
  - Symptoms and General Health

# Federal Research Portfolio



- While each Department carries out its GWVI research portfolio independently, there is coordination to avoid duplication
- The Research Subcommittee of the Interagency Deployment Working Group is currently the group that coordinates this research
  - It compiles an Annual Report to Congress on Federally Sponsored Research on GWVI
- Annual Reports for 1997-2006 have been posted at the following URL:

[http://www.research.va.gov/resources/pubs/pubs\\_individual.cfm?Category=Gulf%20War%20Reports](http://www.research.va.gov/resources/pubs/pubs_individual.cfm?Category=Gulf%20War%20Reports)

# VA Research Portfolio on GWVI

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- VA research program has been at the forefront of the field from the onset

# National Health Survey of GW Veterans and their Families

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- In 1995, VA initiated the National Health Survey of Gulf War Veterans and Their Families
- First two phases use surveys of self-reported symptoms
- 15,000 GW veterans and 15,000 non-deployed veterans
- GW veterans were twice as likely to report symptoms/problems
  - Joint
  - Muscle
  - Respiratory
  - Gastrointestinal
  - Skin
  - Chronic fatigue
  - Symptoms of PTSD

# National Health Survey of GW Veterans and their Families

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- Final phase completed recruitment in 2001
- Relied on complete physical exams of 1,061 GW veterans and 1,128 non-deployed veterans
- 10 years after deployment, military service in the Gulf War was associated with:
  - Increased of chronic fatigue syndrome
  - Increased prevalence of PTSD, other psychological disorders, and poorer self-reported quality of life
- No significant physical health outcomes of clinical concern among spouses of deployed or non-deployed veterans
- Gulf War deployment was not associated with significant differences in frequency of birth defects

# Clinical Trials

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- In 1998 VA began planning for 2 large, multisite clinical treatment trials
- Exercise-behavioral therapy trial (EBT)
- Antibiotic treatment trial (ABT)
- Eligibility to participate:
  - All veterans of the 1990-1991 Gulf War with at least 2 of 3 symptoms (fatigue, musculoskeletal pain, or cognitive dysfunction)
  - Symptoms must have begun after August 1990 and persisted for more than 6 months
  - Veterans must have been symptomatic when the study began

# Exercise-Behavioral Therapy Trial (EBT)

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- VA conducted the \$9.6 million EBT study between 1999 and late 2001
- 1,092 veterans participated at 18 VA and 2 DoD medical centers
- All groups continued their usual healthcare
- 3 experimental groups
  - Cognitive behavioral therapy (CBT)
  - Exercise
  - Combination of CBT + exercise

# Exercise-Behavioral Therapy Trial (EBT) - REsults

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- CBT, with or without exercise, provided modest but significant improvement in
  - Physical functioning (primary outcome) - O.R. 1.84 (both CBT & ex.)
  - Mental health functioning
  - Cognitive symptoms
  - Fatigue
  - Distress
  - No significant effect on pain

# Antibiotic Treatment Trial (ABT) - Results

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- ABT enrollment began in May 1999 and included 491 Gulf War veterans at 26 VA and 2 DoD sites
- Trial was completed in December 2001 at a cost of \$10 million
  - Primary hypothesis
    - Antibiotic treatment with doxycycline for 12 months would improve the health status of patients with chronic symptoms who tested positive for *Mycoplasma* infection at baseline
  - Secondary hypotheses
    - Doxycycline treatment would reduce symptoms of fatigue, pain and memory problems
    - Doxycycline treatment would convert patients who were *Mycoplasma* positive to *Mycoplasma* negative
- Study did not identify a new treatment modality for Gulf War veterans

# VA Clinical Studies

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- VA supported a study (Eisen et al, 2005) to assess and compare the prevalence of health conditions in deployed and non-deployed Gulf War veterans:
  - Fibromyalgia
  - Chronic fatigue syndrome
  - Skin conditions
  - Dyspepsia
  - Physical health-related quality of life
  - Hypertension
  - Obstructive lung disease
  - Joint pains
  - Peripheral neuropathy

# Additional VA Clinical Studies

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- Study concluded that 10 years after the Gulf War, the physical health of deployed and non-deployed veterans was generally similar
- Four conditions were more prevalent among deployed veterans
  - Fibromyalgia – O.R. 2.32
  - Skin conditions – O.R. 1.38
  - Dyspepsia – O.R. 1.87
  - *Chronic fatigue syndrome* – O.R. 40.6



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# Ongoing Research in GWVI

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- Clinical Trials of treatments
- Biomarkers
- Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease)
- Multiple Sclerosis
- Funding and other studies

# Clinical Trials

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- Three pilot clinical trials are currently underway to test new therapies for ill Gulf War veterans
  - Sleep disturbances - CPAP
  - Gastrointestinal problems
  - Feasibility of performing CBT via telemedicine

# Objective Markers Biomarkers

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- Another major focus of VA's Gulf War research portfolio is to identify objective markers that can distinguish ill Gulf War veterans from their healthy counterparts
- Such biomarkers serve several purposes
  - Provide vital clues to understand mechanisms responsible for how and why these veterans are ill
  - Identify potential targets for the development of new therapies
  - Provide objective measures for testing the effectiveness of new therapies

# Objective Markers Biomarkers

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- VA currently funds 12 such projects, ranging from:
  - Genetics and genetic markers
  - Advanced neuroimaging procedures
  - Altered protein profiles in blood or cerebrospinal fluid
  - One of these projects recently identified differences in the coagulation system in the blood of ill Gulf War veterans compared to their healthy counterparts

# Amyotrophic Lateral Sclerosis

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- A review of the available published literature and concluded that Gulf War and other combat veterans may be at increased risk for developing amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease) as a result of their military service
- The largest prevalence study included in this review was funded by VA, in cooperation with DoD
  - The study included all Gulf War era veterans
  - Identified and confirmed ALS cases occurring over a 10-year period by medical record review
  - The rate of ALS in Gulf War veterans was 6.7 per million, versus 3.5 per million for other military populations

# Other Health Conditions

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- VA expanded the study to include a national registry for veterans with ALS and a genetic tissue bank
  - Identify all veterans with ALS (not just Gulf War veterans)
  - Provide a mechanism for VA to inform veterans with ALS about clinical trials and other studies they may be eligible to participate in
- VA continues to fund other ALS research, including clinical trials and animal models of the disease, to study potential disease mechanisms and test new therapies

# Multiple Sclerosis

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- There are persistent concerns about the risk of developing multiple sclerosis (MS) in Gulf War veterans
  - VA will begin a large study in 2008 to identify the date of onset and clinical subtype of service-connected cases of MS occurring in Gulf War veterans between 1990 and 2006
  - The study will also attempt to quantify the risk for developing MS in deployed versus non-deployed Gulf War veterans,, as well as the risk for developing MS in Gulf War veterans potentially exposed to smoke from oil well fires or sarin
- Another VA project is examining the overall and cause-specific mortality risk of ALS, MS or brain cancer in more than 620,000 Gulf War veterans and assessing in-theater exposure characteristics associated with those deaths

# Ongoing Research Portfolio on GWVI

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- FY 2006, VA supported \$12.9 million in 67 GWVI research projects
  - These projects examined brain and nervous system function, treatments,, environmental toxicology, GW exposure models, immune function and symptoms, general health, biomarkers and epidemiologic studies
- FY 2007 VA supported \$22 million in GWVI projects
  - \$15 million was for a contract between the Dallas VAMC and University of Texas Southwestern medical Center for research related to illnesses affecting Gulf War veterans
- FY2007 Annual Report is currently in concurrence