

VA Biorepository Brain Bank Gulf War Veterans' Illnesses Biorepository VA Boston

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Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
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Department of Veterans Affairs Biorepository Brain Bank



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VA Biorepository Brain Bank (VABBB) Background

- The VA Biorepository Brain Bank (VABBB) was developed as an amyotrophic lateral sclerosis (ALS) brain bank in 2006 by VA in response to findings that linked ALS to deployment to the Persian Gulf and military service in general
- The VABBB is coordinated at VA Boston Healthcare System (VABHS)
- Veterans/next-of-kin receive regular follow-up from VABBB staff via telephone and mailed surveys
- Tissue is analyzed, processed and stored at the Southern Arizona VA Healthcare System (SAVAHCS) in Tucson, AZ
- Diagnostic neuropathological analyses are conducted at VABHS
- Tissue/data releases to investigators are ongoing

Gulf War Veterans' Illnesses Biorepository Overview

- Given the development of the VABBB as a national tissue recovery model, this model was adapted to develop the Gulf War Veterans' Illnesses Biorepository (GWVIB) brain bank
- New challenges for the development of the GWVIB were:
 - GWVIB open to all 1990-1991 Gulf War Veterans regardless of whether they receive care at VA
 - Research tissue needs of investigators
 - Recruitment and enrollment procedures
 - Data acquisition and management
 - Ongoing follow-up

Research tissue needs of investigators

The value of postmortem CNS tissue had already been established via feedback from the Gulf War Illness experts and the literature:

- Accurate diagnoses of neurodegenerative diseases can only be obtained through post-mortem pathology
- Necessary for clinicopathological correlation
- Human tissue is required to study human disease and to test the relevance of results from animal models
- High quality DNA, RNA, and protein required for accurate and reproducible results
- May aid in the understanding of disease, the discovery of new diagnostic targets, and the development of therapeutics

Research tissue needs of investigators

- The need for non-CNS tissue had not been established
- Collecting non-CNS tissue presented considerable logistical hurdles
- Poll conducted by VABBB of 33 VA Gulf War researchers did not presently support the need to collect non-CNS tissue
- Based on this feedback it was decided to begin the GWVIB as a CNS tissue biorepository
- Non-CNS tissue collection could be considered in the future if the need arises

GWVIB Site Responsibilities

- Boston
 - Operations and data coordinating center
 - Recruitment/enrollment/follow-up
 - Pager coverage/tissue recovery coordination
 - Medical informatics
 - Data management
 - Diagnostic neuropathology
- Tucson
 - CNS tissue processing/storage
 - CSF processing/storage
 - Tissue data management
 - Tissue requests/disbursements

GWVIB Recruitment

- Web site
https://www.research.va.gov/programs/tissue_banking/gwvib/
- Brochure
- Nationwide toll-free number- **855-561-7827**
- Postings on GW Veteran web sites and newsletters
- Outreach to GW Veteran organizations
- Social media
- Other GWV treatment centers/research projects

GWVIB Web Site

The screenshot shows the GWVIB web site interface. At the top left is the U.S. Department of Veterans Affairs logo. To its right is the text "U.S. Department of Veterans Affairs". Further right is a search bar with the text "Search ORD" and a "VA SITE MAP [A-Z]" link. Below this is a navigation menu with tabs for "Health", "Benefits", "Burials & Memorials", "About VA", "Resources", "Media Room", "Locations", and "Contact Us". The main content area is titled "Office of Research & Development" and features a sidebar on the left with a tree view of "Programs" including "See All Programs", "Animal Research", "Biosafety & Biosecurity", "Cooperative Studies Program (CSP)", "Health Disparities & Minority Health", "Million Veteran Program (MVP)", "Nonprofit Program Office (NPPO)", "PRIDE - Human Research Protection", "REQUIP", "Technology Transfer Program (TTP)", and "VA Specimen Research and Biobanking Program". The main content area has a heading "Gulf War Veterans' Illnesses Biorepository" and a sub-heading "What is the Gulf War Veterans' Illnesses Biorepository?". The text describes the biorepository's purpose and includes two images: one of a fighter jet and one of a soldier with a biorepository container. A "RESOURCES" sidebar on the right lists "FAQ", "GWVI Brochure (977 KB, PDF)", and "GWVIB in the News".

U.S. Department of Veterans Affairs

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Office of Research & Development

ORD Home

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 - Health Disparities & Minority Health
 - Million Veteran Program (MVP)
 - Nonprofit Program Office (NPPO)
 - PRIDE - Human Research Protection
 - REQUIP
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 - VA Specimen Research and Biobanking Program

Biobanking Overview

Gulf War Veterans' Illnesses Biorepository

What is the Gulf War Veterans' Illnesses Biorepository?

About 697,000 men and women served in the 1990-1991 Gulf War. Nearly 250,000 Veterans have come down with illnesses in the 20 years since returning from the Gulf. These illnesses, known collectively as Gulf War Veterans' Illnesses (GWVI), have affected Veterans with medically unexplained chronic symptoms that can include tiredness, headaches, joint pain, indigestion, trouble sleeping, dizziness, breathing disorders, and memory problems. The exact cause of GWVI is not yet known. Researchers have been studying various hazards in the environment that Veterans experienced during their Gulf War service.



The Gulf War Veterans' Illnesses Biorepository (GWVIB) brain bank is seeking Veterans from the 1990-91 Gulf War era who would like to participate in research about conditions affecting Gulf War Veterans. A biorepository is a human tissue bank that collects, processes, stores and gives out research specimens and health information for future scientific studies. Veterans enrolled in the GWVIB brain bank complete surveys about their health every six months, and upon their death, donate their brain and other body tissue for future Gulf War Veterans' Illnesses research. Veterans can begin helping now by enrolling today, even though the tissue donation may occur many years from now.

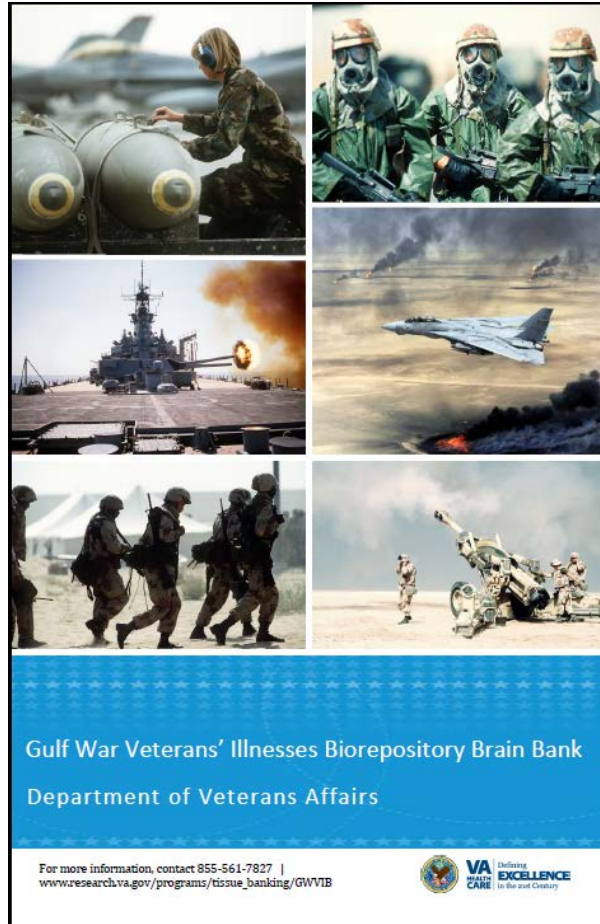


RESOURCES

- FAQ
- GWVI Brochure (977 KB, PDF)
- GWVIB in the News

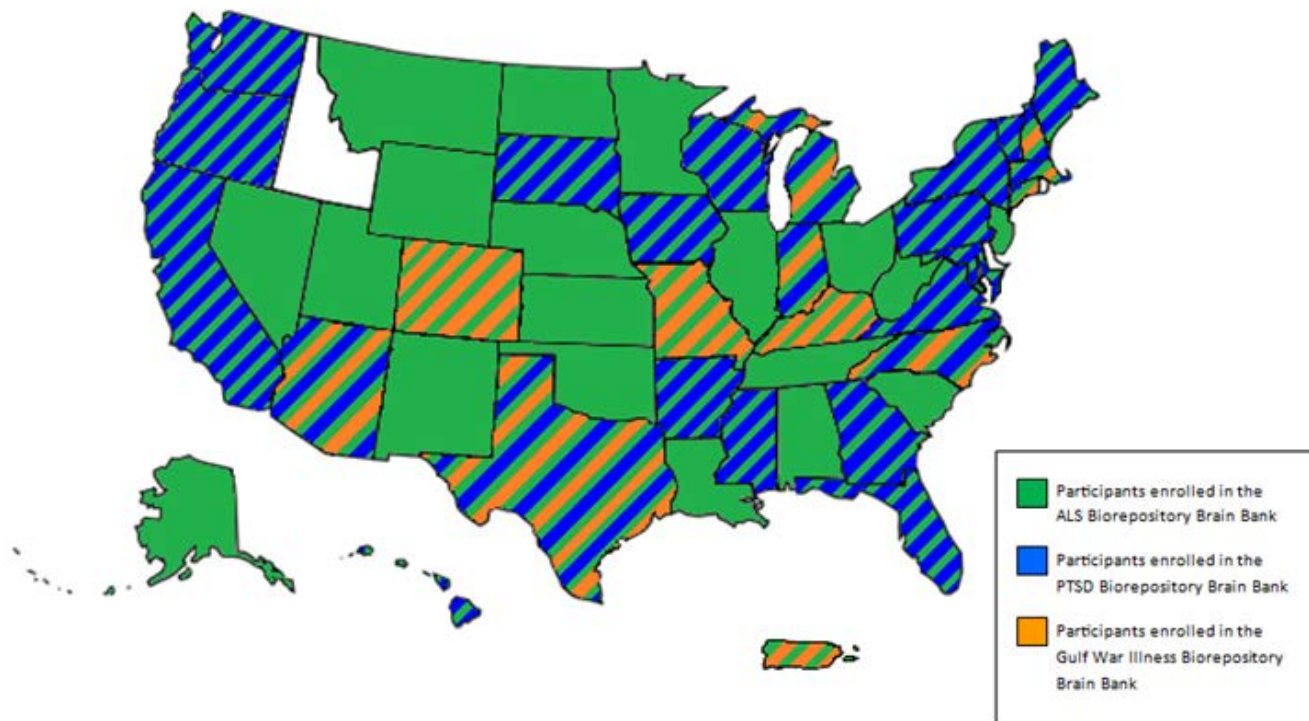
http://www.research.va.gov/programs/tissue_banking/gwvib/

GWVIB Brochure



VABBB Historical Enrollment Map (GWVIB Enrollees Shown in Orange)

States and U.S. Territories Where Veterans Have Enrolled in the VABBB



GWVIB Data Acquisition

- Data collected at enrollment
 - Health information via telephone interview and mailed survey
 - Telephone Interview of Cognitive Status – Modified (TICSm)
 - Medical history from VA electronic medical record if present
- Data collected during semi-annual follow-up
 - Updated medical history and contact information via telephone interview and mailed survey
 - TICSm

GWVIB Health Survey

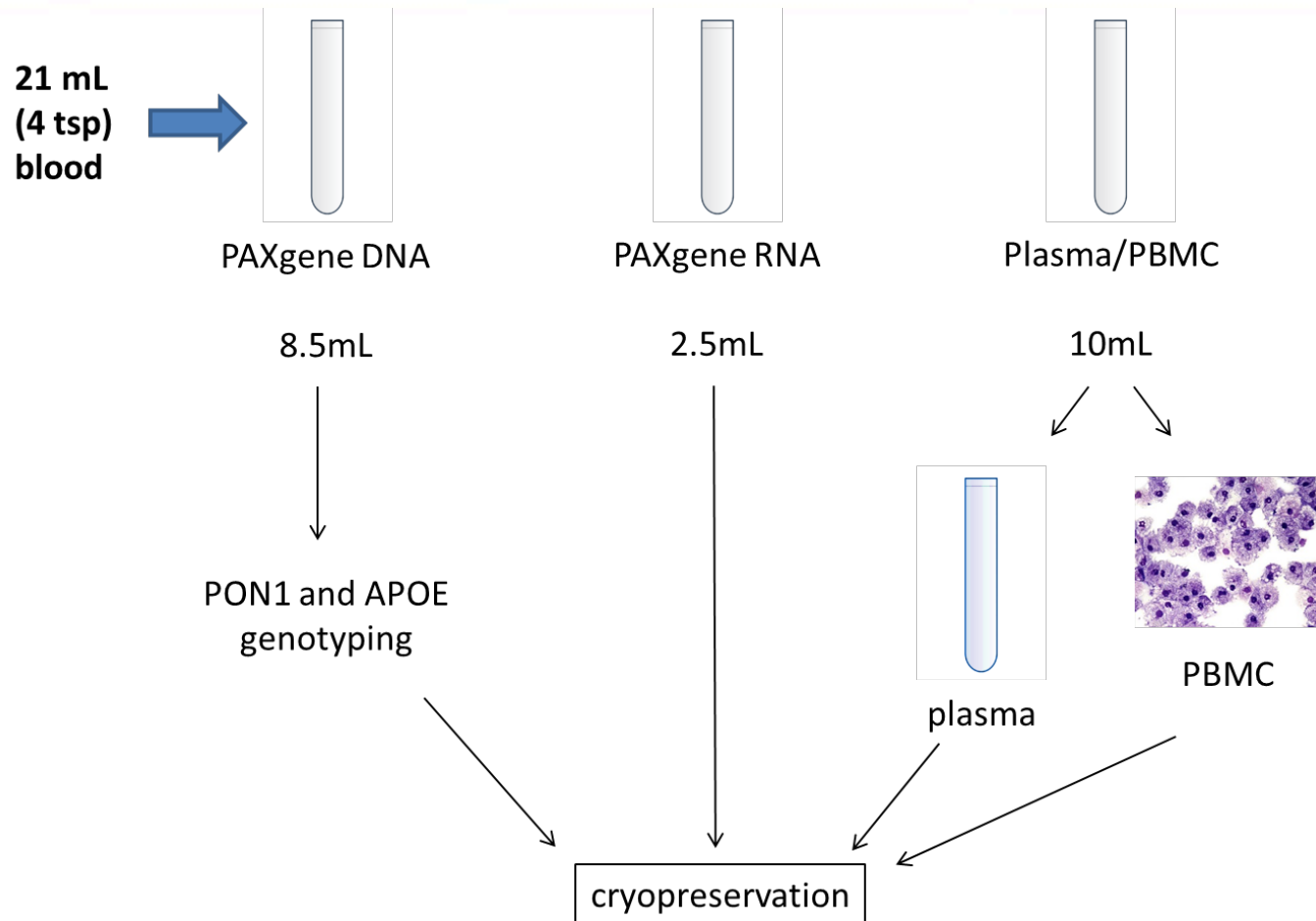
Domains assessed:

- Demographics and physical features
- Gulf War Veterans' illnesses symptom checklists
 - Gulf War illness by Kansas case definition and chronic multisymptom illness by Fukuda case definition
- Military and occupational exposures (SNAC-Short Form)
- Health history and healthcare use
- Family health history
- Military service and combat exposure
- Tobacco and alcohol use

GWVIB Tracking and Tissue Recovery

- Annual or less if health is failing
- Blood samples collected on willing Boston enrollees and processed/stored in Tucson
- Tissue recovery portfolio development:
 - Arrange for tissue recovery
- Brain, spinal cord & cerebrospinal fluid recovery
 - 24/7 coverage with delivery to Tucson by special door-to-door courier service

Blood collection strategy for GWVIB project



Multiple formats allow for a diverse range of study possibilities

DNA: Gene sequencing and polymorphism studies

RNA: Gene expression and microRNA studies

Plasma: Blood protein and cytokine studies

PBMCs: Cellular studies

Genotyping GWVI Blood

PON1 and APOE genotyping allows investigators to select and pool specimens for more targeted studies

PON1:

Serum enzyme that detoxifies organophosphate poisons

Gene contains 2 polymorphisms which can result in 4 isozymes

1. Position 192 (Q to R)
2. Position 55 (L to M)

R isozyme more efficiently hydrolyzes paraoxon produced from the insecticide parathion

Q isozyme more efficiently hydrolyzes diazoxon and nerve gases sarin and soman

L/M polymorphism contributes to genetic susceptibility to paraoxon

Genotyping GWVI Blood

APOE:

A major cholesterol carrier and maintains lipid homeostasis in the brain

APOE is polymorphic at 2 single nucleotides

1. rs429358
2. Rs7412

These polymorphisms result in 3 alleles

1. $\epsilon 2$
2. $\epsilon 3$
3. $\epsilon 4$

ApoE isoforms determine risk levels for vascular and neurodegenerative diseases

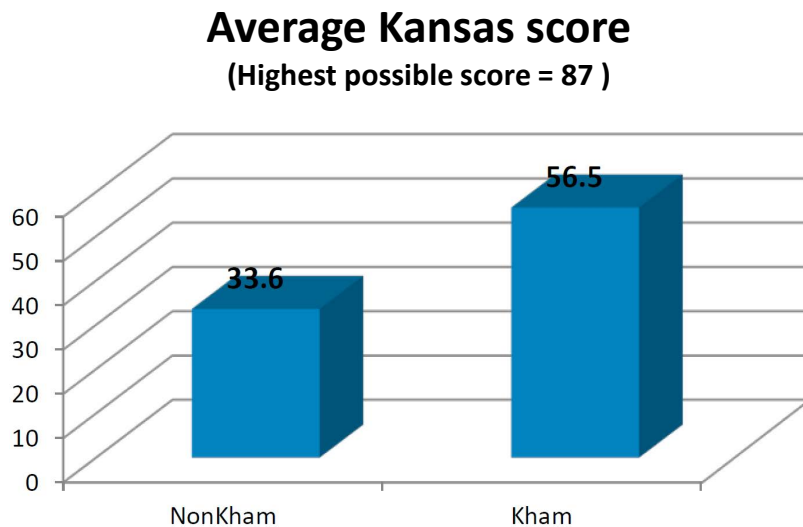
GWVIB Cohort Characteristics (n=15 so far)

Table 1. Cohort Characteristics

Characteristic	
Current age, mean (SD), y	51.1 (7.4)
Age range, y	44 - 70
Men (%)	80
Education (%)	
High school/GED	10
Some college	40
Associates degree	10
Bachelor's degree	20
Master's degree	20
Military exposures (%)	
Combat exposure	70
Blast exposure	30
Pyridostigmine Bromide pills (sure/unsure)	80/20
Chemical/biological warfare agents (sure/unsure)	40/60
Anthrax vaccine (sure/unsure)	70/30
Health history (%)	
> 1 concussion	70
Traumatic brain injury diagnosis - ever	20
Memory loss diagnosis - ever	50
Cancer diagnosis-ever	30
Chronic Multisymptom Illness – Fukuda criteria (%)	70

Effects of Sarin Exposure: Khamisiyah GWV

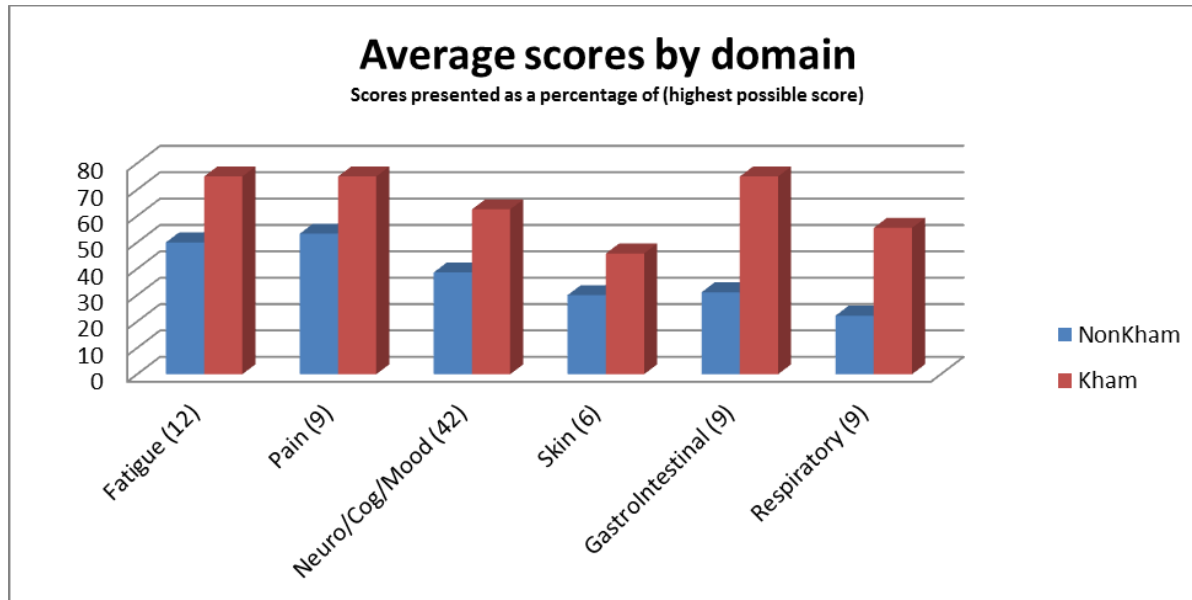
Gulf War Illness by Kansas case definition (Steele)



- DoD-reported Khamisiyah GWV
- Khamisiyah GWV report more GWI symptoms

Effects of Sarin Exposure: Khamisiyah GWV

Kansas case definition scores (% of total) by symptom domain



- Khamisiyah GWV report relatively more GI & respiratory symptoms

GWVIB Results Summary

- Gulf War Veterans who have enrolled are exhibiting high rates of symptoms
- 70% have chronic multisymptom illness by Fukuda criteria
- Khamisiyah Veterans exhibit greater rates of Gulf War Illness symptoms than those not at Khamisiyah
 - Khamisiyah Veterans exhibit higher rates across all symptom domains
 - GI and respiratory symptoms exhibit greatest relative difference

GWVIB Accomplishments

Outreach

- Extensive outreach via multiple outlets
- Web site
- Boston area GWI researcher collaboration with web site in development

Recruitment/enrollment

- Development of national telephone/mail consenting and data collection model
- 50% success rate in consenting referrals when we are able to make telephone contact

GWVIB Challenges

Outreach and recruitment

- Despite extensive national outreach, enrollment thus far has been disappointing
- Current tensions between GWV and VA has affected GWV enthusiasm to participate in VA research and research without a treatment focus
- Our focus has been to encourage GWV to enroll even though their future donation may be many years away
 - Longitudinal health data is useful now and for subsequent tissue donation
 - Blood donation now can be used for current studies

GWVIB as a Resource for Other GWI Research

GWVIB can provide value added collaborations to current and future studies of GWI to provide:

- Long-term longitudinal follow-up
- Blood processing and storage
- CNS tissue samples

GWVIB can provide tissue and data to collaborating studies via data use/ material transfer agreements

Cost-effective as infrastructure in place

GWVIB

Thank you