



Gulf War Veterans' Illnesses Biorepository Brain Bank (CSP501B)

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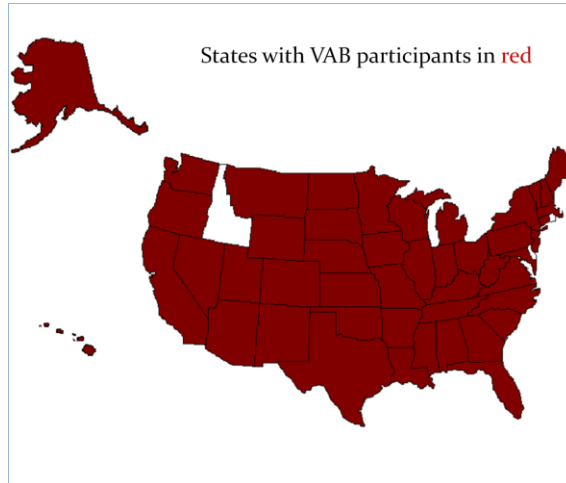
Research Advisory Committee on Gulf War Veterans' Illnesses Meeting
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VAB Brain Bank Background

- The VA National Registry of Veterans with ALS and VA Biorepository Brain Bank (VABBB) were developed by VA in response to findings that linked ALS to deployment to the Persian Gulf and military service in general
- The VABBB (CSP 501) is coordinated at the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC) at VA Boston Healthcare System (VABHS)
- Veterans/next-of-kin receive regular follow-up from VABBB staff
- Tissue is analyzed, processed and stored at the Southern Arizona Core Tissue Laboratory (SACTL) at the Southern Arizona VA Healthcare System (SAVAHCS) in Tucson, AZ
- Diagnostic neuropathological analyses are conducted at the VAs in Bedford/Boston, MA
- Tissue/data releases to investigators are ongoing

National Coverage

VABBB has consented Veterans from 47 states



VABBB National Tissue Recovery Network



Red markers – VA pathology department; Blue markers – non-VA diener

VABBB Enrollment / Recovery Rate

VABBB has a:

55% success rate in consenting referrals

100% success rate in tissue recovery when we have been contacted and next-of-kin wants to proceed

88% of recovered tissue is high quality (RIN > 4) for research

Gulf War Veterans' Illnesses Biorepository

- 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) 2-year pilot study (CSP501B)
- 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

GW Veterans by Enrollment Priority *

Table HC-1: Cohorts by Enrollment Priority Group – FY 2009

Priority Group	Pre-9/11	Deployed to Persian Gulf	Gulf War	Stabilization Period
1. S/C 50% +	373,820	104,775	78,493	38,220
2. S/C 30% - 40%	260,877	67,626	48,100	27,797
3. S/C 10%-20%/POW/Special	403,332	96,364	69,237	38,666
4. AA/Housebound or Catastrophic	11,559	2,725	2,269	693
5. NSC Below Income	337,646	72,148	50,528	28,379
6. All Other Not Req to Make Co-Pay	194,796	44,159	37,315	10,131
7. Non-Compensable 0% S/C-Below GMT	1,229	290	219	98
7. NSC Vets-Below GMT	12,125	2,281	1,673	860
8. Noncompensable 0% S/C-Above GMT	31,000	8,492	6,513	2,946
8. Noncompensable 0% S/C-Above GMT > 1_16_03	6,705	1,487	1,080	577
8. Noncompensable 0% S/C-Above GMT > 6_15_09	140	32	24	11
8. NSC Vets-Above GMT	244,172	56,333	42,042	19,802
8. NSC Vets-Above GMT > 1_16_03	56,902	10,745	7,997	3,934
8. NSC Vets-Above GMT > 6_15_09	1,396	253	190	94
90. Vet User Not Enrolled	16,034	2,212	1,240	1,202
91. Non-Vet User Not Enrolled	20,900	3,932	2,289	2,183
Unknown*	4,543,397	655,499	414,128	317,018

Source: Official DoD military personnel records matched against VA healthcare data.

Notes: 1) The Pre-9/11 column represents the overall unique total. All other categories are sub-cohorts of the Pre-9/11 cohort; 2) All cohort data is as of FY09; and 3) Acronyms: AA = aid and attendance, FY = Fiscal Year, GMT = geographic means test, NSC = Nonservice-connected, POW = prisoner of war, and S/C = service-connected.

* Gulf War Era Veterans Report: Pre-9/11, February 2011

*Unknown records indicate no matches.

GW Veterans by VISN*

Table HC-14: Unique Veterans by VISN for All Cohorts – FY 2009

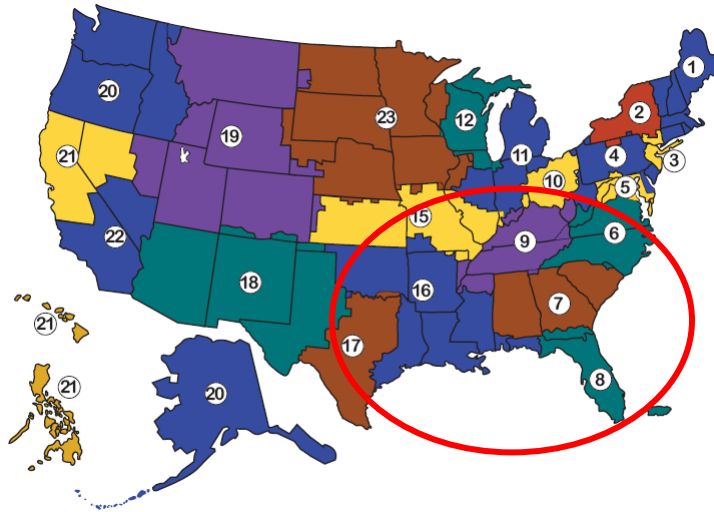
VISN	Pre-9/11	Deployed to Persian Gulf	Not Deployed to Persian Gulf	Gulf War	Stabilization Period	Desert Shield	Desert Storm	Post-Desert Storm	Al Jubayl	Non-Al Jubayl	Khamisiyah	Non-Khamisiyah
1	30,558	5,389	25,169	4,016	1,885	2,730	3,117	3,596	<10	3,114	898	2,698
2	20,300	3,903	16,397	3,025	1,259	2,106	2,380	2,762	<10	2,378	678	2,084
3	20,994	3,611	17,383	2,827	1,103	1,944	2,244	2,553	<10	2,241	647	1,906
4	38,485	7,883	30,602	6,169	2,521	4,206	4,874	5,553	<10	4,867	1,484	4,069
5	29,717	6,404	23,313	4,907	2,142	3,332	3,855	4,499	<10	3,852	1,220	3,279
6	67,784	19,713	48,071	15,951	5,583	12,116	13,031	14,483	49	12,982	3,727	10,756
7	83,756	22,176	61,580	18,432	5,713	13,941	15,375	16,901	67	15,308	5,431	11,470
8	80,003	17,784	62,219	13,523	6,230	9,416	10,364	12,241	12	10,352	2,984	9,257
9	49,658	12,889	36,769	10,856	3,043	7,862	8,983	10,037	48	8,935	3,149	6,888
10	27,635	6,098	21,537	4,745	1,971	3,390	3,752	4,284	<10	3,748	1,099	3,185
11	36,027	7,881	28,146	6,313	2,360	4,499	5,025	5,716	<10	5,018	1,418	4,298
12	32,068	6,822	25,246	5,174	2,328	3,661	4,092	4,681	<10	4,087	1,061	3,620
15	35,103	8,419	26,684	6,765	2,395	4,852	5,500	6,155	12	5,488	1,807	4,348
16	87,389	21,040	66,349	16,553	6,649	11,595	13,207	15,001	29	13,178	3,848	11,153
17	62,614	15,747	46,867	12,300	4,869	9,120	10,129	11,292	<10	10,123	4,070	7,222
18	48,582	12,139	36,443	8,750	4,821	6,030	6,950	7,918	<10	6,941	2,124	5,794
19	34,678	7,458	27,220	5,357	2,890	3,721	4,197	4,763	10	4,187	1,252	3,511
20	49,025	10,692	38,333	7,606	4,278	5,292	5,885	6,773	13	5,872	1,536	5,237
21	40,230	8,970	31,260	6,321	3,882	4,301	4,703	5,559	<10	4,694	981	4,578
22	54,909	15,014	39,895	9,563	7,823	6,681	6,916	8,011	28	6,888	863	7,148
23	41,845	8,439	33,406	6,354	2,874	4,563	5,139	5,688	16	5,123	1,484	4,204

Source: Official DoD military personnel records matched against VA healthcare data.

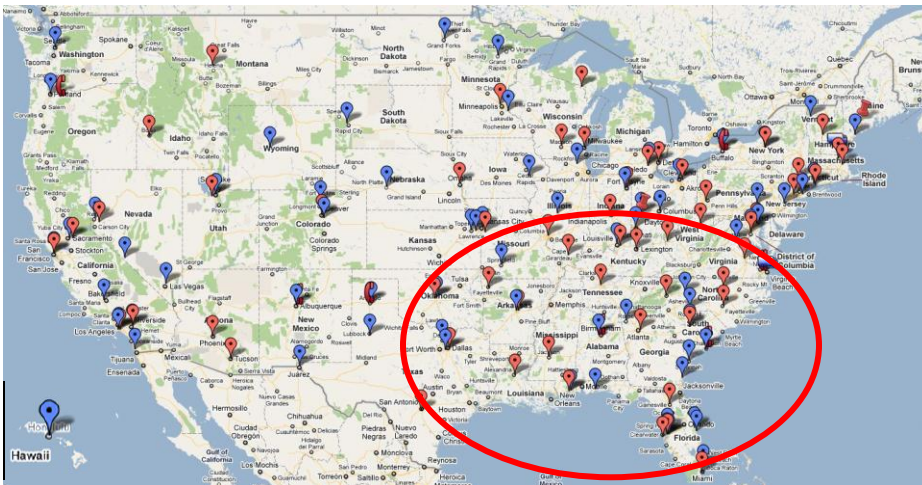
Notes: 1) The Pre-9/11 column represents the overall unique total. All other categories are sub-cohorts of the Pre-9/11 cohort; 2) Unique Veterans count at a VISN but can be counted in multiple VISNs; 3) All cohort data is as of FY09; and 4) Acronyms: FY = Fiscal Year, VISN = Veterans Integrated Service Network.

* Gulf War Era Veterans Report: Pre-9/11, February 2011

VA VISNs



VABBB National Tissue Recovery Network



Red markers – VA pathology department; Blue markers – non-VA diener

Research Tissue Needs of Investigators

- The value of postmortem CNS tissue had already been established via feedback from the RAC-GWVI 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 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-MAVERIC/Bedford VA
 - Operations and data coordinating center
 - Recruitment/enrollment/follow-up
 - Pager coverage/tissue recovery coordination
 - Medical informatics
 - Data management
 - Diagnostic neuropathology
- Tucson- SACTL
 - CNS tissue processing/storage
 - CSF processing/storage
 - Tissue data management

Recruitment

- Web site *
(www.research.va.gov/programs/tissue_banking/GWVIB.va.gov)
- Brochure
- Nationwide toll-free number- **855-561-7827** *
- Postings on GW Veteran web sites and newsletters
- Outreach to GW Veteran organizations

* Web site and toll-free number “go live” on 7/9/12

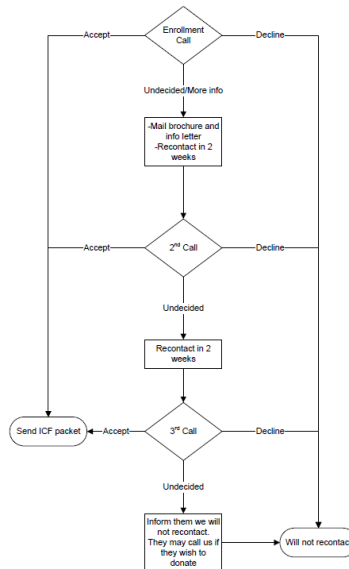
Web Site

The screenshot shows the website for the Gulf War Veterans' Illnesses Biorepository. At the top, it features the United States Department of Veterans Affairs logo and navigation links for VA Home, Veterans Services, Business, About VA, Media Room, Locations, and Contact Us. Below this is a search bar and a navigation menu for the Research & Development section, including links for Home, About, Programs, Research Making News, Outreach & Education, For Veterans, and For Researchers & Research Offices. The main content area is titled "Gulf War Veterans' Illnesses Biorepository" and includes a "What is the Gulf War Veterans' Illnesses Biorepository?" section, a "Resources" sidebar with links to FAQ and GWW Biorepository (408 KR, PCR), and a "Who can take part in this study?" section. A vertical strip of images on the right side of the page shows various military scenes, including a fighter jet, a soldier, and a tank.

Brochure

The brochure features a grid of six images: a soldier in a desert environment, soldiers in full chemical protection suits, a naval ship at sea, a fighter jet in flight, soldiers in a desert setting, and a tank. Below the images, the text reads "Gulf War Veterans' Illnesses Biorepository" and "Department of Veterans Affairs". At the bottom, it provides contact information: "For more information, contact 855-561-7827 | www.research.va.gov/programs/tissue_banking/GWVIB.va.gov" and the VA logo with the slogan "EXCELLENCE IN SERVICE".

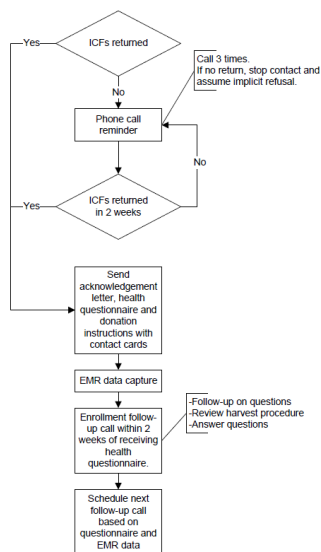
Recruitment



Informed Consent

- Purpose of study
- Broad based consent
- Ongoing data collection/recontact
- Permission to be contacted for other studies
- Use of results
- Confidentiality
- Next-of-kin consent

Enrollment



Data Acquisition

- Data collected at enrollment
 - Health history, GW symptom checklists (e.g., Kansas, Fukuda), military and occupational neurotoxicant exposures, etc. via mailed questionnaire
 - Medical history from VA electronic medical record if present
- Data collected during semi-annual or annual follow-up
 - Updated medical history and contact information via telephone and mailed questionnaires

Health Questionnaire

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

Tracking and Tissue Recovery

- Semi annual or annual follow-up to monitor health
- Portfolio development:
 - Contact VAMCs as primary tissue recovery site
 - Private hospitals, dieners, coroners, if VAMC unavailable
 - Employ funeral home for transport
 - Send specimen box to tissue recovery facility
- Brain, spinal cord & cerebrospinal fluid recovery
 - 24/7 coverage with delivery to Tucson by special door-to-door courier service

Tissue Processing and Storage

(Tucson and Boston)

Specimen Receipt (recording code #, age, gender, PMIs, cause of death)



Grossing (digital imaging, dry ice freezing, formalin fixation/FFPE blocks)



Tissue Monitoring (Luxol/H&E slides; QC: tissue pH, RNA integrity)



Storage (frozen, FFPE blocks, slides; barcode labeling, database input)



Neuropathology report (gross report; diagnostic)



Distribution (request review, inventory assessment, database tracking)

Tissue Matrix Data Storage

Donor

- Age, Ethnicity, Gender
- COD

Event

- i.e. Grossing
- pH, RIN, PMIs, reports, images

Sample

- Sample number/Storage location
- Anatomic region, FFPE, Frozen

Distribution of specimens

- Tissue request form
 - Description of review process for investigators
 - Specific aims, IRB approval, analyses to be conducted, tissue needed
- Review committee composition
 - Standing committee composed of members from all biorepository sites, VACO and outside experts
 - Membership is published
- Review procedures and criteria
 - Initial submissions checked for completeness and forwarded to committee
 - Monthly meeting by conference call to review submissions
 - Committee reviews and scores application
 - Investigator notification timeline
- Distribution procedures

VAB Staff

Boston

- Neil Kowall, M.D., Principal Investigator
- Christopher (Kit) Brady, Ph.D., Co-investigator
- Maxine Krengel, Ph.D., Co-investigator
- Shelley Amberg, M.P.H., Project Coordinator
- Sally Perkins, M.S., Project Manager
- Latease Guilderson, M.S.W., Research Assistant

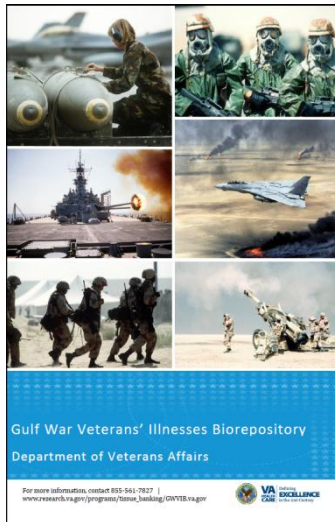
Bedford/Boston

- Ann McKee, M.D., Site PI and Chief Neuropathologist
- Thor Stein, M.D., Ph.D., Neuropathologist

Tucson

- Stephen Renner, M.D., Site PI
- Katrina Trevor, Ph.D., Co-investigator
- Jim Averill, Data Manager
- Sean Walker, Molecular Biology Specialist

Thank you!



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