Research Advisory Committee on Gulf War Veterans' Illnesses

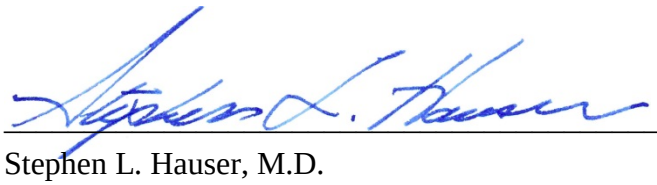
Committee Meeting Minutes
April 20–21, 2017

U.S. Department of Veterans Affairs
Washington, DC

Research Advisory Committee on Gulf War Veterans' Illnesses

Committee Meeting Minutes

I hereby certify the following minutes as being an accurate record of what transpired at the April 20–21, 2017, meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses.



Stephen L. Hauser, M.D.
Chair, Research Advisory Committee on Gulf War Veterans' Illnesses

Attendance Record

Members of the Committee:

Dr. Stephen Hauser, Chair
Ms. Kimberly Adams (Telephone)
Mr. James Bunker
Dr. Fiona Crawford
Ms. Marylyn Harris (Telephone)
Dr. Stephen Hunt
Dr. Nancy Klimas
Dr. Katherine McGlynn
Mr. Jeffrey Nast
Dr. Stephen Ondra (Absent)
Ms. Frances Perez-Wilhite
Dr. Scott Rauch
Dr. Caroline Tanner
Dr. Mitchell Wallin
Dr. Scott Young (Telephone)

Committee Staff:

Mr. Stanley Corpus
Mr. John Rukkila
Dr. Jon VanLeeuwen

Designated Federal Officer:

Dr. Victor Kalasinsky

Invited Speakers:

Dr. John Concato
Dr. Drew Helmer
Dr. Bertrand Huber
Dr. Victor Kalasinsky
Dr. Max Klein
Dr. Benjamin Kligler
Dr. Louise Oaklander
Dr. Daniel Perl
Dr. Dawn Provenzale

Others in Attendance:

Ms. Hanna Burris, Project Coordinator, VA Biorepository Brain Bank
Ms. LaTonya Small, Program Specialist, VA Advisory Committee Management Office
Mr. Gabriel Walt, Project Coordinator, VA Biorepository Brain Bank

Veterans:

Donna Miranda (wife of Wayne Miranda)
Wayne Miranda
Denise Nichols
Al Oakley
Venus Val-Tower

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

LOCATION: Revere Hotel Boston Common
200 Stuart Street, Boston, MA 02116

Call-in: 1-800-767-1750, access code 56978#
Watch Online: http://va-eerc-ees.adobeconnect.com/racgwvi_apr2017/

Agenda

Thursday, April 20, 2017

9:00 – 9:15	**Introductory Remarks**	**Dr. Stephen Hauser, Chair** **Res Adv Cmte on GW Veterans' Illnesses**
9:15 – 10:00	**Million Veteran Program**	**Dr. John Concato** **VA Connecticut Healthcare System, Clinical Epidemiology Research Center**
10:00 – 10:45	**Cooperative Studies Program #585: GW Era Cohort & Biorepository Project**	**Dr. Dawn Provenzale** **VA CSP Epidemiology Center - Durham**
10:45 – 11:00	**Break**	
11:00 – 11:45	**VA Biorepository and Brain Bank**	**Dr. Bertrand Huber** **VA Boston Healthcare System**
11:45 – 12:15	**Committee Discussion**	**Dr. Stephen Hauser, Chair** **Res Adv Cmte on GW Veterans' Illnesses**
12:15 – 1:15	**Lunch**	
1:15 – 2:00	**Small-fiber Neuropathy Causes Some Ill-defined Multisymptom Illnesses**	**Dr. Anne Louise Oaklander** **Mass. Gen. Hospital, Harvard Medical School**
2:00 – 2:45	**Round Table Discussion with Speakers and VA Representatives**	**Invited speakers, VA Representatives and Res Adv Cmte on GW Veterans' Illnesses**
2:45 – 3:15	**VA Update on Recommendations and Gulf War Research**	**Dr. Victor Kalasinsky** **VA Office of Research and Development**
3:15 – 3:30	**Break**	
3:30 – 4:00	**ORD Gulf War Research Strategic Plan Discussion**	**Dr. Victor Kalasinsky and** **Res Adv Cmte on GW Veterans' Illnesses**
4:00 – 4:30	**Committee Discussion**	**Dr. Stephen Hauser, Chair** **Res Adv Cmte on GW Veterans' Illnesses**
4:30 – 5:00	**Public Comment**	
5:00	**Adjourn**	

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Agenda

Thursday, April 21, 2017

8:45 – 9:00	**Introductory Remarks**	**Dr. Stephen Hauser, Chair** **Res Adv Cmte on GW Veterans' Illnesses**
9:00 – 9:45	**Research with Biorepositories: Blast Exposure and Neural Damage**	**Dr. Daniel Perl** **Uniformed Services Univ. of the Health Sciences**
9:45 – 10:30	**VA Integrative Health Strategy**	**Dr. Benjamin Kligler** **VA Integrative Health Coordinating Center**
10:30 – 10:45	**Break**	
10:45 – 11:30	**Committee Discussion**	**Dr. Stephen Hauser, Chair** **Res Adv Cmte on GW Veterans' Illnesses**
11:30 – 12:00	**Public Comment**	
12:00	**Adjourn**	

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
U.S. Department of Veterans Affairs

April 20, 2017
Boston, MA

Minutes

Introductory Remarks:

Dr. Stephen Hauser, Chair, Research Advisory Committee on Gulf War Veterans' Illnesses

Dr. Hauser noted a core feature in the 2016 RAC-GWVI Annual Report called for the VA to align basic research with applied clinical research and create a research program that brings to the fore chronic issues and Gulf War illness (GWI) and attempts to advance our understanding of these conditions through research with the best-possible, appropriately-sized cohorts. He noted that creating such a cohort for GWI would accelerate progress in identifying biomarkers and developing treatments and that the Committee would drive forward in conceptualizing a plan to make this possible. Dr. Hauser detailed the purpose of the meeting as to understand better the cohorts available, both within VA as well as outside of VA, that may assist in the proposed research. He reminded the Committee that they have an obligation to understand GWI deeply and, at the same time, they have an equal obligation to bring treatments to people who are suffering today.

Session 1: Presentation #1

Million Veteran Program

Dr. John Concato, VA Connecticut Healthcare System, Clinical Epidemiology Research Center

Dr. Concato briefly outlined the VA's Million Veteran Program (MVP), a large-scale research effort focused on collecting genomic data to better understand genetic influences on health and disease. MVP is a national, **voluntary** research program funded entirely by the VA's Office of Research and Development. The goal is to assemble a large, comprehensive database of one million Veterans that have contributed DNA samples for genetic sequencing that can be linked to health information. Over a half-million Veterans have provided consent forms and blood samples as of April 2017, making it one of the largest genetic databases in the world. The VA will use the data and infrastructure created by MVP to support multiple future research studies. Researchers will study diseases such as diabetes and cancer as well as military-related illnesses such as post-traumatic stress disorder. MVP enrollees are also being re-contacted to participate in new studies specifically looking at Gulf War-related chronic conditions.

Session 1: Presentation #2

CSP 2006: Genomics of Gulf War Illness in Veterans

Dr. Drew A. Helmer, Director of the WRIISC, VA New Jersey Health Care System

Dr. Helmer reviewed the CSP 2006 genome-wide association study (GWAS) of Gulf War illness among Gulf War Veterans. The study will analyze samples drawn from the Million Veteran Program (MVP) dataset, specifically the approximately 50,000 Veterans in the MVP program who were on active duty

during the Gulf War era with focus on the August 1990 to probably July 1991. The study will include samples from 7,500 individuals with Gulf War illness and 7,500 without Gulf War illness.

In a completed CSP 2006-pilot study, a questionnaire for the study was field-tested and used for initial phenotyping and to develop an algorithm to identify cases and controls. For this pilot study, 600 surveys were sent with 320 returned and 290 (48.3%) respondents were verified as having served during 1990–1991 Gulf War Era. The CSP 2006 project is proceeding with analysis of pilot data and writing of the study design, pending central IRB review and the required review by the Office of Management and Budget (6 to 12 months). Future directions include using the MVP platform to conduct a GWAS analysis and to explore novel approaches for phenotyping and defining Gulf War illness and identifying biomarkers.

Committee members inquired how the WRIISCs and other medical centers could be used to get people to sign up for studies when they come for an evaluation. It was suggested that recruitment materials should be shared to target people without having to have a VA investigator present. Committee members also discussed future applications or approaches. For example, Dr. Caroline Tanner suggested it would be very powerful to link phenotype and genetic information to exposure information. Dr. Helmer noted that as part of the Gulf War Module survey we already have standard exposure questions and the VA and DoD are also working on an Individual Lifetime Exposure Record to provide real-time exposure information.

Session 2:

Cooperative Studies Program #585: Gulf War Era Cohort and Biorepository Project Update

Dr. Dawn Provenzale, Director, VA Cooperative Studies Program Epidemiology Center, Durham. NC

Dr. Provenzale explained that the CSP 585 Gulf War Era Cohort and Biorepository (GWECB) project developed a cohort of U.S. Veterans who served in the military in 1990–1991. Participants provided samples, such as for genetic analysis, and agreed to be re-contacted about participating in future research studies investigating health conditions relevant to Gulf War Veterans. She noted the first phase of the CSP 585 (Sep. 2014 thru Aug. 2016) established the data and specimen repository and a request process so researchers can use this as a resource for their studies**.** Participants were mailed the Enrollment Coordinating Center consent form and a data survey, a similar process employed by MVP. A total of 1,276 Veterans were enrolled for 30.6% of the goal to enroll 3,000 Veterans, which is a lower than expected response rate. Despite challenges with recruitment and the low response rate, Dr. Provenzale stated important components of this project include agreements for data sharing activities and the ability to re-contact Veterans to participate in additional studies. VA/non-VA Medical Records and survey data as well as the collected blood specimen samples are available for research purposes.

The second phase of the project (June 2016 to present), Dr. Provenzale explained, initiated qualitative research interviews of Gulf War Era Veterans through focus groups and other activities to learn more about their perspectives on this and other Gulf War Era research projects. She noted conversations with Veterans, and lessons learned about barriers and facilitators of recruitment, will help improve Gulf War Era research projects and better serve Gulf War Era Veterans. When asked about hesitations for participating in research studies, Veterans noted distrust and dissatisfaction with VA and federal government for compromising of privacy and confidentiality and lack of research implementation follow-through. Conversely, Veterans answered they were motivated to participate in VA research to seek answers about exposures and health conditions, to help oneself, and to help other Veterans and service members. Dr. Provenzale suggested these findings could help researchers improve recruitment and more effectively address the needs and priorities of Gulf War Veterans, including those receiving care outside of VHA.

Dr. Provenzale pointed out the GWECB project has similarities to and collaborates with the MVP. A main difference she noted between GWECB and MVP is that MVP only includes VHA users, whereas GWECB includes both VHA and non-VHA users. Dr. Provenzale added for GWECB the process of collecting samples is similar to the MVP process and specimens collected go to Boston MAVERIC to be stored in the same freezer shelf but in different trays with totally different administrative access although a cooperative process similar to MVP allows sharing among interested investigators. During the discussion portion of the talk, Committee member Ms. Adams suggested using additional outreach to Veterans through VA Community Resource and Referral Centers to increase number of samples for GWECB.

Session 3:

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

Dr. Bertrand Huber, VA Boston Healthcare System

Dr. Huber explained the VA Biorepository and Brain Bank (VABBB) has grown since its initial development in 2006. Originally, it was created as a Gulf War amyotrophic lateral sclerosis brain bank, but the VABBB has now changed into a brain bank for any Veterans with ALS. At the same time, the Gulf War Veterans' Illnesses Biorepository (GWVIB) brain bank was created to serve the research tissue needs of investigators. GWVIB is open to all 1990–1991 Gulf War Veterans regardless of their illness or whether they receive care at VA. Dr. Huber reviewed the roles and responsibilities of different GWVIB sites in managing the brain banks and biorepositories. The Boston site has the operations and data coordinating center for recruitment, enrollment, and ongoing follow-up with all individuals enrolled. The Tucson site manages CNS tissue and CSF processing, storage, and diagnostic neuropathologic analysis as well as tissue requests and disbursements. The biorepository in Tucson holds postmortem CNS tissue pathology for research on neurodegenerative diseases, clinicopathological correlation, and development of therapeutics.

Dr. Huber noted the 15 Boston enrollees in the Gulf War illness study have had 21-mL blood samples collected and components related to blood are processed, stored in cryopreservation, and available, along with enrollment health data, but tissue is not yet available in the GWVIB. He explained Gulf War Veteran enrollment thus far has been disappointing and affected by difficulties recruiting Veterans to participate in VA research. He noted GWVIB longitudinal health data is useful now as well as years later for subsequent tissue donation that will be collected after death of the Veteran. Dr. Huber added that blood samples obtained and the history data can be used for other collaborating studies via data use and material transfer agreements.

Committee Discussion:

Dr. Stephen Hauser, Chairman, Research Advisory Committee on Gulf War Veterans' Illnesses

Presenters: Dr. John Concato, Dr. Drew Helmer, Dr. Dawn Provenzale, and Dr. Bertrand Huber.

Dr. Hauser asked the Committee how to link the kinds of cohorts being created within the VA system with deep phenotyping that will be needed. Dr. Helmer responded the first starting point already approved is to look at the medical records. For example, he noted the CSP 2006 participants will be VHA users and should have some medical record, because that is how the MVP is set up. The type, extent, and quality of evaluations will vary because they will have been done for clinical rather than research purposes. He added a next step might include add-on studies that would target some candidate genes and biomarkers of interest. Committee member Ms. Adams noted some Gulf War Veterans being evaluated will have more-standardized Registry Exams and some are eligible for the Airborne Hazards Registry exam that is more

clinically accessible. Dr. Provenzale pointed out that the CSP 585 and follow-up CSP 2006 study survey data are quite complementary. Dr. Concato shared lessons learned in MVP on the data side and the tools to go into data would be applicable to Gulf War and many other conditions and potentially include state-of-the-art machine learning techniques to go into the VA Corporate Data Warehouse.

Dr. Klimas reviewed how commercially available 23andMe platform technology is different from large-scale genomics research efforts led by the VA. Mr. Nast asked whether current studies will help in the treatment of Gulf War Veterans in the near future. Committee members and invited speakers spoke about how genomic research and other studies investigating the underlying biology of disease will help lead to more effective strategies for managing and treating diseases that affect Gulf War Veterans. Dr. McGlynn asked about availability of data from other VA or non-VA brain banks and biorepositories that could provide comparators when analyzing Gulf War Veterans' tissue samples. Dr. Huber answered that the VA Biorepository and Brain Bank connects to six other brain banks with many other tissues available for comparison. He noted results of genomic studies are often very powerful and will be guided by studies being done in the brain bank.

Session 4: Small-fiber Neuropathy Causes Some Ill-defined Multisymptom Illnesses

Dr. Anne Louise Oaklander, Massachusetts General Hospital, Harvard Medical School

Dr. Oaklander reviewed peripheral nerve disease and painful neuropathies with a focus on small-fiber neuropathy, which she thinks links, in part, to the cluster of Gulf War illness symptoms. She explained small fibers make up about 80 percent of our peripheral nervous system but are not picked up by the traditional neurological exam to detect peripheral neuropathy. She noted that small-fiber polyneuropathy (SFPN) presents with a plethora of symptoms and can cause multiple problems, such as unexplained chronic widespread pain with the muscles, shortness of breath, fatigue, and chronic headache.

Confirmation of SFPN, Dr. Oaklander explained, requires skin biopsies, usually from the lower leg, with analysis by complex immunohistochemical labeling specifically focused on bringing out the small fibers. Dr. Oaklander noted review of the skin biopsies with multi-variate regression allows very precise prediction of what would be the expected number of small fibers in a particular skin sample, given that person's sex, age, and race. Neuropathy, she added, is determined to be present if the biopsy has fewer nerve endings below an applied single cutoff threshold level.

Dr. Oaklander has found among Gulf War Veterans an elevated prevalence of abnormalities, compared to normal controls, in results of skin biopsy and Autonomic Function Testing for SFPN. She explained how subjects who have Gulf War illness have a substantially different pattern of more symptoms and higher pain scores as compared to Gulf War Veterans who are non-symptomatic. Comparison, she noted, of the abnormalities between Gulf War illness and fibromyalgia shows identical profiles where the symptomatic Veterans score very similarly to the fibromyalgia patients, as opposed to low scores in non-symptomatic Gulf War Veterans and normal controls. She noted that if there is an autoimmune component, there may be treatments already available. Dr. Oaklander speculated in the summary of her slide presentation that one-third to one-half of adults with unexplained chronic widespread pain and multi-organ symptoms of fibromyalgia or Gulf War illness may actually have undiagnosed SFPN. She went on to discuss that utilizing skin biopsies within Gulf War illness cohorts could help with diagnosing patients and discovering treatments.

Dr. Hauser asked whether skin biopsy would be the right phenotyping approach for the constellation of symptoms in patients with Gulf War illness, or would other biopsies—such as a gastrointestinal, bladder or pulmonary biopsy— also be needed? Dr. Oaklander stated skin biopsy is the gold standard for pathology studies of small-fiber neuropathy but for physiological studies it is not so clear. She noted these little nerve fibers weave through every organ of the body and data are still being collected from hundreds of study patients to determine what is needed to determine neuropathies and what is the normative data.

Session 5: Round Table Discussion with Speakers, VA Representatives, and RAC-GWVI

Chairman Dr. Stephen Hauser and Invited speakers Dr. John Concato, Dr. Drew Helmer, Dr. Dawn Provenzale, Dr. Bertrand Huber, Dr. Anne Louise Oaklander, Dr. Max Klein, Dr. Daniel Perl.

Chair Hauser inquired of the panel as to any advice they could provide to the Committee for steps moving forward to pull together a prospective, comprehensive study of Gulf War illness, for which the results could be utilized to advance research and improve patient care at VA Centers nationwide. Dr. Hauser summarized the challenge of pulling together a cohort study of Gulf War illness, and the need to link together efforts that are underway, and filling in pieces that are not there. Dr. Hauser noted that use of a hub-and-spoke model, we would have Centers of science and clinical research with linking to improved bedside care at every VA Center to harmonize what a Gulf War Study Program might be to explore biology and bring the clinical research to the forefront.

The Committee and panel members discussed how the hub-and-spoke model would positively augment development of VA Centers. It was noted the VA Centers could pull together to enhance and harmonize development of a definitive phenotyping study of Gulf War illness by pooling together resources as well as strengths of each organization. Considerations of how to augment development of VA Centers included discussion in the following areas: Compare and contrast in-person models versus telemedicine models, to define development; access the already established cohorts, i.e., MVP, CSP 585, etc., to expedite the recruitment process; capture comorbid events that continue to take place, to create a trajectory of the illnesses; digitize collected data to make it easily accessible by the clinician, as well as the patient; provide feedback for participants, in terms of current status of the research taking place, to ensure they feel engaged; eliminate the barriers of enrollment to engage Veteran participation in studies; differentiate between Gulf War Veterans and current combat Veterans, to define a control group, if one should exist between the two; receive ample tissue samples at the brain bank to perform the desired examinations; open lines of communication within VA to guarantee that all VA Centers are kept up-to-date on research projects taking place; request VA participation and encourage communication between VA and DoD, to allow for sharing of resources and funding for projects.

Session 6:

VA Update on Recommendations and Gulf War Research

Dr. Victor Kalasinsky, VA Office of Research and Development

Dr. Kalasinsky briefly gave an update on recommendations and Gulf War research that he had previously discussed in detail. He noted working groups continue to meet to review and update the Gulf War Research Strategic Plan. Dr. Kalasinsky indicated that the Secretary of the VA was briefed on and found favor with the proposed establishment of a hub-and-spoke coordinated system of Centers within the VA to better integrate research with clinical care. Review is ongoing to develop a case definition for Gulf War illness that would be satisfactory as a basis for an ICD-9 code.

Dr. Kalasinsky reviewed past recommendations from the Committee and provided an update on progress the VA has made related to each recommendation. He also summarized Gulf War-related research proposals that ORD received and reviewed for this year. Additionally, he discussed a joint pilot project between the VA and DoD called the Individual Longitudinal Exposure Record (ILER), which would provide a record of service members' environmental exposure data and health information that would be continuous across DoD and VA records.

Public Comment:

Public Comment review touched on the following topics: MVP collection of data, use of public radio programs for study recruiting, future site recommendations for RAC-GWVI meetings, documenting effects of Gulf War illness on Veteran families, effective use of Adobe Connect for the RAC-GWVI meetings, use and updating of the RAC-GWVI website, Veteran complaints about travel compensation to participate in VA studies and specialty clinics, dissemination of the findings of clinical research, getting the word out to Veterans to attend RAC-GWVI meetings and that they are open to the public.

Adjourn:

Dr. Hauser, RAC-GWVI Chair, adjourned the Committee meeting and noted continuation of the meeting on Friday, April 21st.

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
U.S. Department of Veterans Affairs

April 21, 2017
Boston, MA

Minutes

Introductory Remarks:

Dr. Stephen Hauser, Chair, Research Advisory Committee on Gulf War Veterans' Illnesses

Dr. Hauser called the Committee to order at 8:45 a.m. He reviewed the Agenda for the day.

Session 7:

Research with Biorepositories: Blast Exposure and Neural Damage

Dr. Daniel Perl, Center for Neuroscience and Regenerative Medicine, U.S. Department of Defense, Uniformed Services University of the Health Sciences.

Dr. Perl spoke about his 30-plus years of experience in research with biorepositories and noted that the value of a brain bank is judged by the number of samples it *distributes* and how many publications they generate. He stated that the better characterized the specimens (and the patients they are derived from), the more useful they are for research.

Dr. Perl reviewed best practices for tissue collection and noted that procedural issues and conditions need to be carefully documented, in particular post-mortem intervals for obtaining specimens. He noted careful and detailed neuropathology work-ups are critical. He stated a robust specimen inventory system is essential, and you cannot take the clinical diagnosis and assume that is what the patient actually suffered from and also that additional diagnoses were not present. He emphasized all brain bank dissection protocols are compromises. He explained, for instance, that using thawed frozen tissues that are then fixed does not produce results equivalent to use of fixed tissues.

Dr. Perl then discussed his recent research on blast injury and the surprising finding that it has a unique neuropathology. He shared how blast injury has its own neuropathology signature with common persistent symptoms in post-blast traumatic brain injury subjects include physical (e.g., headache, nausea, vomiting, dizziness, fatigue, blurred vision, sleep disturbance, sensitivity to light/noise, balance problems, hearing difficulties/loss, seizure), cognitive (e.g., impaired attention, concentration, recent memory, speed of processing, judgment, executive function), and behavioral/emotional (e.g., depression, anxiety, agitation, irritability, impulsivity, aggression) deficits.

No routine neuroimaging studies, Dr. Perl stated, have provided a consistent signal alteration to indicate the presence of pathologic lesions in the brains of post-blast TBI patients with significant persistent symptomatology. He emphasized that in the human brain after blast exposure, post-mortem case review revealed characterization of interface astroglial scarring in brains exposed to blast. He added scarring occurred at the interface of sites with differing densities (e.g., blood/brain, CSF/brain, gray matter/white matter); changes were not seen in cases of impact TBI, substance abuse, or CTE; and 2 of 5 chronic blast TBI cases with glial scarring also showed evidence of tau pathology, which may be indicative of early CTE.

Session 8:

VA Integrative Health Strategy

Dr. Benjamin Kligler, National Director, VA Integrative Health Coordinating Center (IHCC)

Dr. Kligler reviewed results of recent Complementary and Integrative Health (CIH) research among Veterans with Gulf War illness. He reviewed that Mindfulness-based Stress Reduction (MBSR) in addition to usual care led to improvements in pain, fatigue, and cognitive failures. MBSR sessions, he explained, were delivered in 8 weekly 2.5-hour sessions plus a single 7-hour weekend session. He noted that patients showed some impressive benefit from MBSR in a number of typical symptoms of Gulf War illness, including fatigue, cognitive failure, and pain. And after MBSR, Gulf War illness patients also experienced reductions in PTSD symptoms. Dr. Kligler also presented research showing that individualized acupuncture protocols were effective in treatment of Gulf War illness.

Dr. Kliger explained the VA's Integrative Health Coordinating Center (IHCC) implements CIH strategies in clinical activities, education, and research and has two major functions: the first to identify and remove barriers to providing CIH across the VHA system; the second to serve as a resource for clinical practices and education for both Veterans and clinicians. In promoting Whole Health System personal health planning, he noted, the IHCC partners with Veterans to discover their sense of meaning, aspiration, and purpose; promotes proactive healing environments through integrative wellbeing programs of CIH self-care, health coaching, and health partner support; and promotes healing relationships through integrative clinical care with health and disease management.

Dr. Kliger explained the IHCC provides guidance for CIH implementation and will initiate vetting process to integrate CIH services into VHA care. He noted CIH evidence-based therapies approved to date include acupuncture, tai chi, yoga, meditation, massage therapy, guided imagery, hypnosis, and biofeedback. Community care issues for CIH services include what CIH services to include, appropriate credentialing standards, proper documentation and communication with primary care teams, and collection of meaningful outcome data for encounters. The CARA Act (Comprehensive Addiction and Recovery Act), Dr. Kliger stated, is providing momentum for implementing CIH services in the VA.

During questions and comments from the Committee, Dr. Kligler addressed several issues including medical-legal partnership to the whole health approach, fidelity and standardization of care, necessity for integrative medicine physicians, and challenges with the Choice Program/Community Care Program.

Session 9:

Post-Infectious Myalgic Encephalomyelopathy/Chronic Fatigue Syndrome

Dr. Hauser and Dr. Nancy Klimas, Miami Veterans Affairs Medical Center and Nova Southeastern University, co-presented a PowerPoint slideshow created by Dr. Avindra "Avi" Nath, Director of the National Institute of Neurological Disorders and Stroke (NINDS) at the National Institutes of Health.

Dr. Nath from NINDS wasn't able to present the NIH protocol for deep phenotyping experiment now underway for chronic fatigue syndrome patients; however, Committee members Dr. Hauser and Dr. Klimas were able to review a slide presentation that Dr. Nath provided.

Dr. Hauser explained that chronic fatigue syndrome in some patients is triggered by a viral illness. He reviewed the NIH intramural program and protocol to investigate how immune dysregulation may contribute to the pathophysiology of CFS and whether immune therapy can alter the course of the illness in a subset of patients who have a clear infectious precipitation factor. Dr. Hauser said that understanding how Dr. Nath's NIH group approached a deep phenotyping study of CFS would be informative. He noted we find a number of similarities between the chronic conditions of Gulf War illness and chronic fatigue

syndrome, we really don't understand their biology, and we have no FDA-approved pharmaceuticals for these chronic conditions.

Drs. Hauser and Klimas, provided a summary of the NIH approach to studying post-infectious myalgic encephalomyelitis/chronic fatigue syndrome (PI-ME/CFS) triggered by a viral illness resulting in immune mediated brain dysfunction. The overall research program is proposed to consist of three phases. In Phase I, which is just beginning to get underway, the NIH will conduct a cross-sectional deep phenotyping of PI-ME/CFS to comprehensively characterize its pathophysiology in order to better define the condition and help harmonize future studies. Research Aims for Phase I include defining (1) clinical phenotype, (2) underlying pathophysiology, (3) abnormal immune and microbiome profiles, and (4) reproducibility of features in ex-vivo studies. Future directions will include implementation of follow-up Phase II—which will aim to validate select biomarkers—and Phase III, which aims to conduct an early phase intervention study to target biomarkers validated in Phase II. Patients for the study are recruited primarily from well-characterized ME/CFS cohorts.

Dr. Hauser noted, like Gulf War illness, chronic fatigue syndrome is a challenge that has important patient advocates, and congressional advocates. Committee members acknowledged the uniqueness of the NIH Clinical Research Center to do clinical research and that the world-class clinical and research resources available there would support a deep phenotyping study that could not be matched or recreated in the VA system. They also acknowledged possibly the only way VA might get to do something this in-depth in Gulf War illness would be to send VA study patients to NIH. The question was posed whether the VA should consider exploring "piggybacking" on the NIH study by pursuing a collaboration with the NIH. Committee members favorably received the idea of an NIH–VA partnership and that it would be a good use of VA research funds. Discussion continued that it would be worthwhile to pursue.

Although Committee members found favor with proposing the VA collaborate on the deep phenotyping study with NIH, more than one Committee member noted that the CFS sample size of the NIH study seemed to be relatively small. It was noted that the deep phenotyping study would not be the definitive study to characterize GWI and CFS and that follow-up studies would be needed, but this study has the potential to offer major advances in the field. There was additional discussion among the Committee related to timing, with the acknowledgement that establishing collaborations could take a long time to set-up. Despite the institutional challenges, there was agreement among Committee members that it was worth exploring how the VA and NIH might expeditiously partner to capitalize on this auspicious research opportunity.

Session 10:

ORD Gulf War Research Strategic Plan Discussion

Dr. Victor Kalasinsky, VA Office of Research and Development

Dr. Kalasinsky noted the current VA/ORD Gulf War Research Strategic Plan (2013–2017) is expiring and a newly structured Strategic Plan is under development for 2018–2022. He requested participation on the Writing Teams, presented a structure crosswalk between the old and new versions of the strategic plan, and reviewed a template to be used to facilitate writing of the new plan. He also reviewed a timeline for milestones that included drafting plan sections by June, reviewing sections at the August 2017 RAC-GWVI meeting, and finalizing by September 2017.

Dr. Kalasinsky discussed collaboration of the Committee with researchers, clinicians, and Gulf War Veterans. Committee members discussed including a section outside the Scientific Approach section of the strategic plan that would focus on communication and partnerships.

In reply to Dr. Kalasinsky asking Committee members for ideas on the strategic plan, Dr. Scott Rauch wondered whether there would be value for the Committee and the VA to emulate the approach taken by industry, which is to quickly identify research leads and then progress to actionable changes that enhance

the welfare of Veterans. He posed that it may be more appropriate to take a strategic approach similar to industry, rather than academia, by having objectives for VA-funded research efforts that lead to something actionable, rather than simply a publication.

Public Comment:

Public Commenters addressed the following issues and questions:

Committee member Kimberly Adams on the telephone line posed a question for a Veteran who asked whether the Gulf War Research Community considered using hyperbaric or pressure-chamber approaches to treating bacterial funguses that Veterans may have encountered, during Gulf War exposures. Committee members discussed various uses of hyperbaric therapy. Commenter Kurt Love requested that the Committee collect dental information and review the relation of dental disease to a variety of health problems, which prompted Committee discussion of mouth and oral organisms and dental complication issues. Commenter Ms. Nichols noted other Gulf War Veteran problems that include lack of dermatological research on skin rashes as well as vision changes and ringing in the ears connected with neurological-type chemical exposure. Ronald Brown from the National Gulf War Resource Center noted that the NGWRC is pursuing with the new VA Secretary the issue of brain cancer in Gulf War Veterans and trying to make this a presumptive condition for treatment by the VA. Committee member Kimberly Adams on the telephone line commented that due to Gulf War service many female Veterans are experiencing breast and gynecological cancers that need further research. Commenter Kurt Love described difficulties in getting a catalog of the 56,000 tissue samples from the original Armed Forces Institute of Pathology Gulf War Tissue Sample Repository.

Adjourn:

Dr. Hauser, Chair of the RAC-GWVI, adjourned the RAC Committee meeting and announced the Committee will meet again in August 2017 in San Francisco CA.