

Research Advisory Committee on Gulf War Veterans' Illnesses

Committee Meeting Minutes

September 21–22, 2022

U.S. Department of Veterans Affairs

Washington, D.C.

I hereby certify the following minutes as being an accurate record of what transpired at the September 21–22, 2022 meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses.

Lawrence Steinman

Lawrence Steinman, M.D.

Chair, Research Advisory Committee on Gulf War Veterans' Illnesses

Attendance Record	
Members of the Committee:	Special Guests:
Dr. Lawrence Steinman, Chair	Dr. Cheryl Walker
Dr. James Baraniuk	Dr. Kenneth Ramos
Mr. Ronald Brown	
Mr. Brent Casey	Invited Speakers:
Retired Col. Richard Gaard	Dr. J. Wesson Ashford
Dr. Drew Helmer	Dr. Katharine Bloeser
Mr. Thomas Mathers	Dr. Raymond Christian
Ms. Delphine Metcalf-Foster	Dr. Dane Cook
Dr. Carey Pope	Dr. Autumn Gallegos
Ms. Sonya Smith	Dr. Robert Haley
Dr. Elaine Symanski	Dr. Stephen Hunt
Ms. Jane Wasvick	Mr. Jason Johnson
Ms. Barbara Ward	Dr. W. Ian Lipkin
Mr. William Watts	Dr. Lisa McAndrew
Dr. James Woody	Dr. April Mohanty
	Dr. Avindra Nath
Designated Federal Officer:	Dr. Shannon Nugent
Dr. Karen Block	Dr. Peter Rumm
	Dr. Melissa Tursiella
Alternate DFO:	Dr. David Thompson
Marsha Turner	Dr. James Woody
Committee Staff:	Employee Education System (EES):
Mr. Stanley Corpus	Brian Peplinski
Ms. Marsha Turner	
Mr. Daniel Sloper	Attendance:
	September 21
RACGWVI Subcommittee Members:	In Person: 33
Dr. Lawrence Steinman	Online via Webex: 106
Dr. Karen Block	Telephone: 23
Retired Col. Richard Gaard	Subtotal: 162
Dr. Drew Helmer	September 22
Ms. Jane Wasvick	In Person: 26
Ms. Barbara Ward	Online via Webex: 134
Mr. William Watts	Telephone: 26
	Subtotal: 186
	Two Day Total = 348

**Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
(RACGWVI)**

Department of Veterans Affairs

LOCATION: Department of Veterans Affairs Washington, D.C.

810 Vermont Ave NW

Agenda

September 21–22, 2022

DAY 1 OF 2 Wednesday, September 21, 2022 9:00am – 4:00pm Eastern Time		
9:00am	Business	
9:00–9:30	Welcome, Introductions and Opening Remarks	Dr. Lawrence Steinman Committee Chair
9:30–9:40	Video Message from VA Secretary Denis McDonough	VA Senior Leadership
9:40-9:55	HOME Updates and the PACT Act and Gulf War Topics	Peter D. Rumm, MD, MPH, FACPM Director of Policy Health Outcomes Military Exposures (HOME), VHA, VA
9:55-10:15	RACGWVI 2022 Recommendations, VA Gulf War Research Program Updates	Karen Block, PhD RACGWVI Designated Federal Officer Senior Program Manager Gulf War Research VHA Office of Research & Development (ORD)
10:15-10:35	Congressionally Directed Medical Research Programs, Toxic Exposures Research Program Overview	Melissa (Missy) Tursiella, PhD Program Manager, Toxic Exposures Research Program, CDMRP
10:35-10:50	Break (15 minutes)	
10:50-11:20	Keynote Address: The Lived Experience of a Black American Gulf War Veteran	Raymond Christian, PhD 1990-91 Gulf War Veteran
11:20-11:40	Overview of the 1990-91 Gulf War Environment	James Woody, MD, PhD CAPT MC USN (Ret), Former Commanding Officer, Navy Medical Research and Development Command
11:40-12:10	Evaluation of a Gene–Environment Interaction of PON1 and Low-Level Nerve Agent Exposure with Gulf War Illness: A Prevalence Case–Control Study Drawn from the U.S. Military Health Survey’s National Population Sample	Robert W. Haley, MD Division of Epidemiology, Department of Internal Medicine, University of Texas Southwestern Medical Center Dallas, Texas
12:10-12:30	Gulf War Illness (GWI): Causation Considerations, Pathobiology versus Pathophysiology, Genes, Chemicals, Infectious Agents	J. Wesson Ashford, MD, PhD Director, VA Palo Alto War Related Illness and Injury Study Center, Clinical Professor of Psychiatry and Behavioral Sciences (affiliated), Stanford University
12:30-1:30	Lunch (60 minutes)	

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1:30-2:00	Post exertion malaise in GWI-Brain autonomic and behavioral interactions	Dane Cook, PhD Health Science Specialist/Research Physiologist, William S. Middleton Memorial Veterans Hospital, Madison WI
2:00-2:30	COVID-19 and the Nervous System	Avindra Nath, MD Clinical Director, Division of Intramural Research, Senior Investigator, Section of Infections of the Nervous System; National Institute of Neurological Disorders and Stroke, Bethesda MD
2:30-3:10	Fireside Chat	Committee and Invited Speakers
3:10-3:20	Break (10 minutes)	
3:20-3:30	VHA ORD Research Volunteer Registry	David A. Thompson, D.B.A. Director, VHA ORD Research Volunteer Program
3:30-4:00	Public Comment	Visitors and Invited Guests
4:00pm	Adjourn	DFO/Committee Chair
DAY 2 OF 2 Thursday, September 22, 2022 8:30am – Noon Eastern Time		
8:30am	Business	
8:30-8:40	Welcome/Opening Remarks	Lawrence Steinman, MD
8:40-8:50	Veteran Engagement Subcommittee Report	RACGWVI Subcommittee <ul style="list-style-type: none"> ▪ Dr. Larry Steinman ▪ Col. Richard Gaard ▪ Dr. Drew Helmer ▪ Ms. Barbara Ward ▪ Mrs. Jane Wasvick ▪ Mr. William Watts
8:50-9:00	Frustrations from a Gulf War Discarded Vet	Mr. Jason Johnson 1990-91 Gulf War Veteran
9:00-9:35	Insights into Gulf War Illness by Analogy to ME/CFS	W. Ian Lipkin, MD Director, Center of Infection and Immunity Mailman School of Public Health Columbia University, NY
9:35-10:00	<i>Gulf War Veteran Topic of Interest:</i> Clinical Guidelines for Chronic Multi-Symptom Illness	Stephen Hunt, MD Director, VA Post-Deployment Integrated Care Initiative
10:00 – 10:15	Break (15 minutes)	
10:15-10:25	Gulf War-Military Exposure Research Innovation Center (MERIC): Model for Implementing Evidence Based Practices: Overview	Lisa McAndrew, PhD Director of Research, Acting Director of Education NJ War Related Illness and Injury Center (WRIISC)

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10:25-10:35	GW-MERIC Project 1 Enhancing Quality of Care for Gulf War Illness through Clinician Awareness and Support	Shannon Nugent, PhD Core Investigator, VA Portland Healthcare System Assistant Professor, Oregon Health & Science Univ
10:35-10:45	GW-MERIC Project 2 Evaluation of VET-HOME	April Mohanty, MPH, PhD Research Health Scientist, VA Salt Lake City IDEAS Ctr; Assistant Professor, Dept of Internal Medicine, University of Utah
10:45-10:55	GW-MERIC Project 3 Concordant Care and Problem-Solving Treatment for Gulf War Illness	Autumn Gallegos, PhD Assistant Professor of Psychiatry, University of Rochester Medical Ctr, Rochester NY
10:55-11:05	GW-MERIC Project 4 Optimization of a web-based approach for treatment of GWI	Katharine Bloeser, MSW, PhD Research Scientist, NJ WRIISC; Assistant Professor, City University of New York – Hunter College;
11:05-11:10	Committee Business	Karen Block, PhD Designated Federal Officer
11:10-11:30	RACGWVI Insights and Closing Remarks	Larry Steinman, MD Zimmerman Chair of Pediatrics, Neurology and Neurological Sciences, Beckman Center for Molecular Medicine, Stanford University
11:30-Noon	Public Comment	Visitors and Invited Guests
Noon	Adjourn	DFO/Committee Chair

**Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
(RACGWVI)**

U.S. Department of Veterans Affairs (VA)

September 21–22, 2022

Committee Meeting Minutes

Welcome and Opening Remarks

— Karen Block, Ph.D., VA Office of Research & Development and Designated Federal Officer, RACGWVI

Dr. Block, Research Advisory Committee (RAC) Designated Federal Officer (DFO) and Director of the Office of Research and Development (ORD) Gulf War Research Program opened the meeting and confirmed a quorum was present. After several years of virtual only, this was the first hybrid (in-person and virtual) meeting of the RACGWVI. Those in attendance were asked to mute computers and phones; to introduce themselves when speaking; to be respectful of all people. A special thank you was given to the RACGWVI administrative staff for their hard work putting the meeting together and to all invited guests for taking the time to be part of the meeting. Dr. Block introduced Dr. Lawrence Steinman, RACGWVI Chairman.

Welcome, Introductions and Opening Remarks

— Lawrence Steinman, M.D., Chair, Research Advisory Committee on Gulf War Veterans' Illnesses.

Dr. Steinman thanked Karen for the introduction. He then asked the committee members to introduce themselves.

The committee members introduced themselves.

Dr. Steinman recognized Dr. Cheryl Walker as the new chair, and Dr. Kenneth Ramos as the vice-chair of the RACGWVI.

Dr. Steinman recognized Marsha Turner and asked for her and the RAC staff to introduce themselves.

Ms. Turner introduced herself as the committee manger and Alternate Designated Federal Officer (Alt-DFO) and introduced RAC operations manager Stan Corpus and RAC technical writer Dan Sloper.

Dr. Steinman thanked everyone for their introductions. He noted this was the first in-person meeting since 2020 in Decatur, Georgia and was excited that the RACGWVI would again be going out to meet and talk with Gulf War Veterans (GWV). Noting that the agenda was very busy he started the meeting with a video message from Secretary of Veterans Affairs (SECVA) Denis McDonough.

Session 1: Video Message

— VA Secretary Denis McDonough

The SECVA Denis McDonough addressed the committee via a prerecorded video message. In his address he congratulated all federal committees for their hard work and dedication to ensuring the VA is keeping its promise of support and care for Veterans.

Session 2: HOME Updates and the PACT Act and Gulf War Topics

— Peter D. Rumm, MD, MPH, FACPM, Director of Policy Health Outcomes Military Exposures (HOME), VHA, VA

Dr. Rumm presented information on The Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics Act of 2022 or PACT Act. The PACT Act, according to Dr. Rumm, gives over 20 toxic exposure-related presumptive conditions, increased healthcare eligibility, several rare cancers and increased education and websites (<https://www.va.gov/resources/the-pact-act-and-your-va-benefits/>). Dr. Rumm's group HOME will take the lead for section 509, Study on Veterans in Territories of the United States, of the PACT Act. He suggested the RACGWVI review section 405, improving compensation for disabilities occurring in Persian Gulf War Veterans. HOME is building a website to track all military exposures research funded by the federal government. The goal of the website is to be a one-stop-shop for GW research. Part of the education component of the PACT Act is a mandatory 90-minute training on military exposures, which must be completed by the end of 2022. Because of changes in disability claims, Dr. Rumm recommended the RACGWVI invite subject matter expert Keith Hancock of the VA compensation service to speak to the group. Dr. Rumm briefly spoke of several other points to include: modification of the Kansas definition by Dr. Reinhard (Matthew J. Reinhard, PsyD, Director of D.C. War Related Illness and Injury Center (WRIISC)); further refinement of GWI symptoms between deployed/non-deployed GWV by Dr. Erin Dursa, HOME; establishment of a telehealth method for registry exams by Dr. Anisa Moore (Director, Veterans Exposure Team (VET) VET-HOME); establishment of an educational/certificate program in military exposures, Military Exposures Training (MET), through the American College of Preventive Medicine; HOME will establish a toxicology center under senior toxicologist Dr. Terra Vincent and an Occupational and Environmental Medicine center under Dr. Eric Shuping (Director of Operations, HOME).

Questions:

Mr. Mathers: What is the plan to have physicians complete the MET, and does the Gulf War Registry collect genetic information?

Dr. Rumm: Collecting genetic information—No. Regarding education, the process/course is still being developed, any suggestions will be considered.

Mr. Brown: Will the VA share the new presumptive procedure with the committee? Will the VA pay for Veterans to travel to testing centers? Is the physicians' toxic exposure training mandatory or voluntary?

Dr. Rumm: Some MET training is still voluntary; however, the Level 1 is mandatory for all providers. The committee can contact Dr. Patricia Hastings, Chief Consultant, HOME, regarding sharing new presumptive process materials. The testing will be virtual, with referrals to local providers being made as needed.

Sonya Smith: Will considerations be made for Veterans in rural areas that lack internet access?

Dr. Rumm: Dr. Anisa Moore is working on that situation.

Col. Rich Gaard: Will support staff and non-physicians be allowed to take MET?

Dr. Rumm: Yes. The MET is free of charge for everyone.

GWV: Will the burn pit registry include 1992-93 Somalia Veterans?

Dr. Rumm: Not at this time; may change due to PACT ACT.

Dr. Block: What will the HOME toxicology center do?

Dr. Rumm: Besides GW and other battlefield toxic exposures, the center will also investigate military toxic exposures while in garrison at places such as Camp Lejeune, Fort McClellan, Fort Ord and others.

Session 3: RACGWVI 2022 Recommendations, VA Gulf War Research Program Updates
— Karen Block, PhD, RACGWVI Designated Federal Officer, Senior Program Manager
Gulf War Research, VHA Office of Research & Development (ORD)

Dr. Block addressed the committee regarding the four research-based recommendations presented to SECVA by the RACGWVI, all of which received VA concurrence. The first recommendation was to fund research into key focus areas of basic and clinical research, to support the diagnostics and treatment of Gulf War Illness. The second recommendation was the establishment of a Gulf War Military Exposure Research Innovation Center (GW-MERIC) purposed to expedite and implement evidence-based clinical treatment and diagnostic research for GWV with GWI. Recommendation three was to initiate research on the relationship between COVID-19, long-haul COVID-19 and their impact on GWI. Recommendation four was to continue the RACGWVI subcommittee Veteran Engagement Sessions (VES). The SECVA reviewed and approved all four recommendations.

Dr. Block updated the committee on the joint VA-NIH (National Institutes of Health) Project In-Depth, which is a deep phenotyping study of GWI, also looking at similarities and differences between ME/CFS and GWI and how the symptoms overlap.

Session 4: Congressionally Directed Medical Research Programs, Toxic Exposures Research Program Overview

— Melissa Tursiella, PhD Program Manager, Toxic Exposures Research Program, CDMRP

Dr. Tursiella introduced herself as the program manager for the Congressionally Directed Medical Research Program, otherwise known as CDMRP, and the newest program, the Toxic Exposures Research Program (TERP) with a mission of supporting hypothesis-driven, meritorious, impactful scientific research that will have a maximum benefit to service members, Veterans and the American public. The mission of the CDMRP is to transform healthcare through innovative and impactful research by responsibly managing collaborative research that discovers, develops, and delivers healthcare solutions. The CDMRP is not a funding agency, it is an execution management agency, which means it implements and manages funding for biomedical research programs directly from Congress and supports additional Department of Defense (DoD) medical research programs. All projects go through a two-tier scientific peer-review process to determine research merit and funding recommendation. Research projects for 2022 include multiple cancer studies, including rare cancers, various neurologic studies such as Alzheimer's, Parkinson's and chronic pain research. The previous Gulf War Illness Research Program (GWIRP), to include its website and information, has been brought under the TERP program. Also, under TERP is the Neurotoxin Exposure Treatment Parkinson's Research Program (NETPRP), an environmental health portfolio which includes studies on burn pits and metal toxicology. Previously supported research included awards focused on phase II/III clinical trials. The focus of the new program to improve scientific understanding and pathology from toxic exposures and increased efficiency in assessing comorbidities and speeding development of preventions, treatments and cures. The current TERP budget is 30 million dollars that directly supports four major research areas GWI, burn pits and other airborne hazards, non-toxic exposures and other military toxic exposures in general (e.g., prophylactic medications, pesticides, industrial chemicals). Congress's directional language is to improve scientific understanding pathobiology and exposure, efficiently assess comorbidities and develop treatments, cures, and preventions for the four major research areas.

Questions:

Mr. Watts: Will CDMRP continue funding research for 1990-91 GWV?

Dr. Tursiella: Yes.

Session 5: Keynote Address: The Lived Experience of a Black American Gulf War Veteran
— Raymond Christian, PhD 1990-91 Gulf War Veteran

Dr. Christian provided a narrative of his life and experiences from childhood and growing up in a ghetto, joining the military and serving in the 1990-91 Gulf War, to returning home and learning to adjust to a civilian life while suffering from post-traumatic stress disorder (PTSD) and the other emotional and physical consequences of being combat Veteran. The committee and invited guests were all emotionally moved by his presentation.

Session 6: Overview of the 1990-91 Gulf War Environment

— James Woody, MD, PhD CAPT MC USN (Ret), Former Commanding Officer, Navy Medical Research and Development Command

Dr. Woody introduced himself as a retired Naval Medical Officer who served in the 1990-91 Gulf War as an investigator monitoring for use of chemical and/or biological weapons. Dr. Woody presented details on his background in the detection, surveillance and treatments for various infectious agents and weapons throughout the Middle East. In his presentation Dr. Woody spoke of unconfirmed reports that Saddam Hussein had biological weapons, so the U.S. military aircraft routinely monitored air samples over the region testing for any use of the weapons; none were detected or found. General illness encountered by troops in the field included enterotoxigenic E. Coli (ETEC) food/diet/hygiene related diarrhea and sandfly fever; all cases were treatable with standard pharmaceuticals and antibiotics. Dr. Woody commented that his surveillance team collected samples from a thousand U.S. Marines before and after deployment, but he is unsure what happened to those samples and feels it would be worth the effort to locate them. To his best knowledge there is no identifying and/or unifying etiology for GWI; however, there are many environmental stressors and toxins that may provide an explanation and those are now being studied, results published and effective therapies being developed.

Questions:

Mr. Brown: Is PTSD in GWV more psychological based rather than physiological for actual GWI?

Dr. Woody: I cannot address that question.

Session 7: Evaluation of a Gene–Environment Interaction of PON1 and Low-Level Nerve Agent Exposure with Gulf War Illness: A Prevalence Case–Control Study Drawn from the U.S. Military Health Survey’s National Population Sample

— Robert W. Haley, MD Division of Epidemiology, Department of Internal Medicine, University of Texas Southwestern Medical Center Dallas, Texas

Dr. Haley introduced himself as a former RACGWVI member from 2002-08. His research was funded by the U.S. Army and the VA/CDMRP. The hypothesis of the study was to look for a gene-environment interaction component to GWI. If that were found, then it would prove an important etiology of GWI. The hypothesis-framing studies were based on the sounding of M8A1 chemical alarms, the times the alarms sounded, location(s) of the activated alarms and weather patterns; each of those studies were presented and demonstrated how they contributed to the conclusion(s) that a chemical nerve agent, in this case sarin, exposure along with advanced side effects caused by pyridostigmine bromide (PB) tablets, were a leading cause of GWI. Further cell/tissue and animal studies were conducted to determine variations in level of severity of GWI among GWV. For human studies a population of GWV were statistically selected based on the Defense Manpower Data Center (DMDC) on responses to a study interview. Those results supported a genetic component, specifically the Q192R polymorphism of the paraoxonase (PON1) gene, which allows the body more effectively breakdown/eliminate sarin. The severity of GWI caused

by sarin exposure is dependent on the expression of the PON1 gene; higher the expression, lower the damage. In summary, the gene-environment interaction between presumed nerve agent exposure and the PON1 gene offers strong support that there is a true causal effect at work. It further partly supports why some GWV who were presumably exposed to toxins like nerve agents suffer from GWI and some do not.

Questions:

Male Voice: If you have a weak PON1 gene and possibly exposed to nerve agents your chance of developing GWI is higher than a person with a strong PON1 gene?

Dr. Haley: Yes

Mr. Mathers: The M8A1 alarms only sounded when a threshold limit was reached which meant if a person was in the vicinity of an alarm they were exposed? Furthermore, were any studies similar to yours conducted on the sarin terrorist attack in Japan?

Dr. Haley: Regarding the alarms, yes; regarding the attack in Japan, only in very limited ways.

Dr. Block: Does the PON3 gene play a similar role as PON1?

Dr. Haley: PON3 has no activity against organophosphates, in this case sarin.

Mr. Brown: The DoD has dismissed all the chemical alarms soundings as false alarms caused by dust. Did your study use the cumulative dose exposures that the DoD created in your study for different units?

Dr. Haley: The mentioned alarms were in response to the Khamisiyah Plume exposures. That was the quantitative or semi-quantitative data; any evidence of chemical weapons released from Khamisiyah is tenuous and was not as pronounced when compared to exposure from the initial bombing.

Session 8: Gulf War Illness (GWI): Causation Considerations, Pathobiology versus Pathophysiology, Genes, Chemicals, Infectious Agents

— J. Wesson Ashford, MD, PhD Director, VA Palo Alto War Related Illness and Injury Study Center (WRIISC), Clinical Professor of Psychiatry and Behavioral Sciences (affiliated), Stanford University

Dr. Ashford introduced himself as a researcher at WRIISC since 2007 and a previous speaker/presenter for the RACGWVI. He is employed and funded by the VA; however, the information he presented does not officially represent the VA or VA policy. Dr. Ashford explained of approximately 700,000 GWV, 30 to 40 percent of them have GWI. GWI was initially thought by medical doctors to be psychological while psychiatrists thought it was medical; Dr. Ashford explained GWI is both. The initial symptoms were introduced in 1997 by the Iowa Persian Gulf Study Group. According to that study GWV were reporting chronic pain, chronic fatigue, impaired cognitive function and PTSD. Dr. Ashford presented studies involving the brain stem, because it controls the autonomic nervous system (e.g., energy, feelings, motivation, sleep/wake cycles, appetite, digestion, blood flow, etc.) and could be the source for the body disfunction/symptoms of GWI. Dr. Ashford explained how the brain stem besides being responsible for regulating bodily functions plays a role in basic memory and brain function. Dr. Ashford presented MRI results from GWV showing normal and abnormal brain blood flow. The abnormal blood flow brains showed holes where the blood flow was not normal, those data came from GWV complaining of GWI symptoms. The abnormal brain stem function is termed dysautonomia, which is common in GWV suffering with fibromyalgia, chronic fatigue syndrome (CFS) and irritable bowel syndrome (IBS). However, Dr. Ashford stated the majority of GWV did not start showing signs of GWI until after they returned to the U.S. That evidence led him to consider that GWI could be caused autoimmune dysregulation and/or an immune response to a chronic infection, such as Long-COVID,

and in the case of GWI, may possibly be connected to a camel disease, Middle East Respiratory Syndrome (MERS). Presented evidence supporting a chronic infection hypothesis included aches and pains, respiratory problems, difficulty concentrating, headaches, IBS those reported in Long-COVID symptoms overlap with GWI. The immune response/chronic infection situation is termed tardive dysautonomia and WRIISC has several studies on that topic currently.

Questions:

Mr. Brown: Did your presented study consider that some GWV were forced to leave military service because of developing GWI-related problems, such as respiratory, and no longer being able to meet physical requirements?

Dr. Ashford: GWI doesn't require the Veteran to immediately develop the problem, it can happen several years later.

Male Voice: Has there been brain volumetric data correlated with GWI and isoenzyme activity, such as PON1R?

Dr. Ashford: Yes, there were some studies conducted and evidence did support a correlation.

Session 9: Post exertion malaise in GWI-Brain autonomic and behavioral interactions
— Dane Cook, PhD Health Science Specialist/Research Physiologist, William S. Middleton Memorial Veterans Hospital, Madison WI

Dr. Cook introduced himself. His presented research was merit-review funded grant and a multi-site collaboration between the Madison, Wisconsin VA and the New Jersey WRIISC. Dr. Cook defined post-exertional malaise (PEM) as a worsening of symptoms, such as pain, fatigue and problems with cognition post-exertion. It is an understudied aspect of GWI, and its symptoms type, severity, and time course are not well established; however, understanding PEM is critical towards understanding the pathophysiology. The study enrolled 124 deployed GWV, 73 GWV with GWI and 51 healthy controls; all pre-study comorbidities were recorded, the test subjects selected were of statistically similar body mass index, age and physical capabilities. To determine baseline brain function individuals were exposed to pain and fatiguing tasks; the autonomic nervous system by exposure to orthostatic challenges; heart rate, blood pressure, and brain blood flow by exposure to cold presser challenges. Those systems were then challenged with acute exercise to measure response. The study aim was to look at interaction among those systems to determine if they can predict severity of GWI in addition to explaining PEM because a single system cannot explain GWI or if exercise can be an effective multidisciplinary treatment. At the end of the challenges a blood sample was taken for genetic testing of 13 genes of interest based on previous myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) studies. Study results demonstrated a large change in both PEM and several target genes in GWV with GWI when statistically compared to the healthy controls. However, there was some variability in the response time, some subjects reported none or few immediate post-testing PEM symptoms then developing severe symptoms several days later, while some subjects immediately experienced symptoms. Intensity of symptoms also varied among test subjects. Conclusions show that gene expression and PEM symptoms occur in GWV with GWI compared to healthy controls. The study supported the hypothesis that a single system or a single predictor of GWI is not working, instead a model looking at multiple physiological systems and how those systems interact, may be necessary to explain both GWI and PEM.

Questions:

Dr. Baraniuk: There was a decrease in gene expression for the adrenergic receptors after exercise?

Dr. Cook: Opposite.

Dr. Baraniuk: Did you do any CFS studies?

Dr. Cook: Yes, but we did not see an adrenergic increase, only the genes IL10 and NR3C1.

Dr. Baraniuk: You actually measured systemic hyperalgesia pain?

Dr. Cook: Yes.

Ms. Smith: How many women were in the study?

Dr. Cook: About 10 percent; there were few volunteers.

Male Voice: Are your studies concluded?

Dr. Cook: There are two ongoing studies.

Mr. Mathers: How did you get a homogeneous pool of test subjects?

Dr. Cook: The study looked at GWV with GWI-related wide-spread pain, then categorizing for other study-based characteristics such as fatigue.

Male Voice: How does your study impact CFS?

Dr. Cook: By understanding the stressors that cause PEM and CE/CFS doctors will be better able to develop an exercise program that will not trigger those conditions.

Dr. Block: What about cortisol?

Dr. Cook: No difference was noted.

Session 10: COVID-19 and the Nervous System

— Avindra Nath, MD Clinical Director, Division of Intramural Research, Senior Investigator, Section of Infections of the Nervous System; National Institute of Neurological Disorders and Stroke, Bethesda MD

Dr. Nath introduced himself as GWI researcher whom, due to the COVID-19/coronavirus pandemic, has shifted study focus to acute COVID-19 infection, long-COVID and how those symptoms overlap with GWI. Dr. Nath explained people who develop COVID-19 can be divided into two groups; severe symptoms at onset of infection, but then recover, and mild symptoms at onset, but develop new symptoms weeks or months later. Any virus that attacks the respiratory system will have an impact on the rest of the body due to its impact on oxygen/blood flow. Furthermore, neurological complications can occur before the manifestation of respiratory symptoms. This suggests neurological manifestations can be the presenting symptoms, many days before the start of respiratory symptoms and those individuals could develop cardiovascular or cerebrovascular issues because of the virus. Dr. Nath stated all coronaviruses cause neurological manifestations and complications. With COVID-19 many patients reported neuropathic pain, paresthesia (unexplained tingling), dysautonomia, which can disrupt breathing and circulation, and cognitive dysfunction and fatigue. Those symptoms are very common to CE/CFS and those Veterans suffering with GWI; however, in the case of COVID-19 the primary cause of the problem is known. Which could lead to the question of, is GWI a secondary problem caused by an initial viral infection and/or immune system challenge? The brain/central nervous system and immune system are very connected, and when studying a disease, such as COVID, both systems need equal consideration. MRI analysis of the brain from people who died of COVID found perivascular fibrinogen leakage indicating vascular injury, and that platelets were activated and formed clots in small blood vessels which could cause strokes. However, no virus has been found in the brain, but large amounts of virus were aggregated around major nerves linked to the brain.

Those study data formulated the hypothesis that viral proteins may be the cause of the immune-mediated damage. The concluding hypothesis is direct invasion of the brain by the COVID-19/corona virus is rare and does not explain the neurological complications. Neuroimmune dysfunction is driven by activation of innate immune exhaustion and antibody-mediated phenomenon. Endothelial cell damage by immune complexes is the prime pathophysiological process in neurological COVID, and neuroinflammation may accelerate protein aggregation and lead to neurodegenerative diseases.

Questions:

Dr. Steinman: Based on your research and the similarities between COVID-19 and GWI symptoms, are there any COVID-19 therapeutic targets that will help with GWI?

Dr. Nath: Not yet as the clinical trials have not been conducted.

Session 11: Fireside Chat

— Invited Speakers and Committee

During this section the committee and invited speakers discussed the presented information and how that knowledge can advance the study of, and development of treatments for GWI. The consensus was that there is a large body of scientific and medical research on GWI, however, the problems with developing effective treatments are understanding the root cause of GWI, identifying disease biomarkers for targeted and effective treatments and the initiation of clinical trials.

Session 12: VHA ORD Research Volunteer Registry

— David A. Thompson, D.B.A. Director, VHA ORD Research Volunteer Program

Dr. Thompson introduced himself as the director of the Research Volunteer Program (RVP) and a GWV who served 30 years in the U.S. Air Force. The purpose of the RVP and the Research Volunteer Registry (RVR) is to increase awareness of VA clinical trials and provide a comprehensive website for clinical trial research information. By doing this the group hopes to enhance volunteer recruitment, increase Veteran access and awareness and provide information on current VA clinical research and overcome the challenges of the current enrollment process due to privacy laws. The RVP looks to enroll not just Veterans, but also their family members and/or caregivers. By enrolling at the website, those individuals are consenting to be contacted for a future study, or to participate in an ongoing study that needs additional participation. The website, besides being a source of information for the Veterans, will also be a resource for researchers. They will be able to quickly identify the number applicable volunteers for a specific study and build research proposals and grant requests based on that information. Dr. Thompson stated that initially only volunteer numbers are noted, no personal information is included on the website. The researcher(s) only receive that information after the RVP receives the approved permission from the study committee and Institutional Review Board (IRB)—Protection of Veteran personal information is paramount. Dr. Thompson said his group is developing the website based on feedback from stakeholders and Veterans to ensure it will be user-friendly. The current timeline for the launch of the full website will be spring of 2023. He concluded by providing the RVP email address if anyone wanted to contact his office (researchvolunteer@VA.gov).

Questions:

Male Voice: How often will the information be updated?

Dr. Thompson: Every six to 12 months.

Male Voice: Will your website link to other websites so consenting Veterans don't have to keep filling in forms?

Dr. Thompson: Yes, we link to as many VA approved/appropriate websites as possible.

Session 13: Public Comment

— Visitors and Invited Guests

The committee opened the meeting for questions and comments from the public audience. Those questions and comments were moderated by Mr. Bill Watts.

Gulf War Babies & Parents United: This group contacted the RACGWVI several days before the meeting and asked permission to address the committee, longer than the three to five minutes, regarding the birth defects in children and grandchildren of GWV. The group would like further research on generational effects of GWI and for the inclusion of children of GWV suffering from birth defects caused by parental GWI/battlefield toxic exposure to receive healthcare benefits.

Male GWV: The Veteran asked if there was any research or information on nocturnal tonic clonic seizures?

Dr. Steinman responds: Seizures have been and continue to be studied. They tie into other potential brain injuries related to GWI.

Meeting Adjourned.

Day 2

Session 1: Veteran Engagement Subcommittee Report

— RACGWVI Subcommittee: Dr. Drew Helmer Presenting

Dr. Helmer addressed the RACGWVI on behalf of the subcommittee. Over the past year the subcommittee held two VES. Despite being virtual-only, the first one had a total attendance of 243 GWV, the second a total of 909. The top three concerns voiced by GWV were the sharing of information, denial, cover up, and concealment of GWI and compensation and disability claims. The overall conclusion is for the VES to continue as they are valuable forums for hearing the concerns of GWV and generating ideas for discussion at the full committee meetings.

Session 2: Frustrations from a Gulf War Discarded Vet

— Mr. Jason Johnson, 1990-91 Gulf War Veteran

Mr. Johnson came to the attention of the RACGWVI at a subcommittee Veterans Engagement Session. His raw and honest story emotionally touched all the attending GWV and the subcommittee members and he was asked to speak at this meeting. Mr. Johnson spoke at length of the not just his personal difficulties, but of the struggles of all GWV dealing with GWI. His honest and open description of the problems GWV struggle with each day as they deal with not just their declining physical and mental health, but the seeming apathy and reluctance of the VA healthcare system to provide any form of treatment and/or benefits, the lack of GWI education and awareness provided to VA healthcare providers, and the general feeling of being a forgotten GWV.

Session 3: Insights into Gulf War Illness by Analogy to ME/CFS

— W. Ian Lipkin, MD Director, Center of Infection and Immunity Mailman School of Public Health Columbia University, NY

Dr. Lipkin introduced himself. In his research the focus was to highlight similarities between GWI and ME/CFS. Common symptoms between GWI, ME/CFS, and post-COVID are fatigue, muscle/joint pain and headache. Inflammation pathways had the highest similarities when comparing GWI and ME/CFS. The study looked at 24 hours post-exercise changes in inflammation pathways between the two diseases. The study design used plasma collected before, immediately after and 24 hours post-exercise in test subjects and controls. Those results

showed differences in protein levels between test subjects and controls at each time point. In both cases there were significant similarities in plasma proteomic profiles between GWI and ME/CFS subjects at study baseline and 24 hours post-exercise. Those abnormalities are found in pathways associated with inflammation, mitochondria, peroxisomes and neural signaling. The results have shown important findings for future research using the same experimental method. Those studies would look at RNA levels, metabolomic and transcriptomic data. Further peripheral studies to be conducted would look at large DNA viruses, adenoviruses, herpes viruses and endogenous retroviruses.

Questions:

Dr. Helmer: How do alleles relate to some of the metabolic markers?

Dr. Lipkin: The markers for inflammation, abnormalities and neuronal signaling were reexamined in GWI and ME/CFS test subjects and they were all consistent.

Male Voice: Your study did not see clinical recovery after 24 hours in GWI and ME/CFS test subjects?

Dr. Lipkin: Sorry, our study only looked at the biochemistry. Our group had no direct interaction with the patients so I cannot answer that question.

Dr. Block: Did the study measure lactic acid or anything about anaerobic glycolysis?

Dr. Lipkin: The study did not see any significant differences in lactic acid, but we did not specifically measure for it.

Session 4: Gulf War Veteran Topic of Interest: Clinical Guidelines for Chronic Multi-Symptom Illness

— Stephen Hunt, MD Director, VA Post-Deployment Integrated Care Initiative

Dr. Hunt introduced himself as a former member of the RACGWVI. He immediately addressed the question of, how does the VA take better care of GWV? Dr. Hunt introduced three parts to improving VA care: clinical practice guidelines, the PACT Act and a toxic exposure screening process which can be utilized for any future military conflicts/deployments. The clinical practice guideline will be an evidence-based, systematic approach to care and provide decision support for GWV healthcare providers. The guidelines will help standardize treatment, provide recommendations, help diagnose the condition that is present and provide treatments known to work. The PACT Act expands eligibility in the presumptive conditions, enhanced claims processing and screening of every Veteran. If a GWV enters a clinic with concerns about GWI their information is entered into the registry and they can submit a claim. When Veterans come for a screening five actions will be done. The first step will be to acknowledge the Veterans exposure concerns, and that the Veteran will be provided the needed support. The Veteran will be educated about the presumptive conditions and how to submit a claim. The Veteran will be given a document with all the information being explained to them, including resource websites and how to download the related apps. There must also be a rebuilding of trust with the Veterans. And, the most important aspect, is to stay engaged in ongoing, good healthcare with providers and ensure they remain educated on toxic exposures so they can give the best treatment possible.

Questions:

Dr. Block: Can the RACGWVI have the information to hand out at VES?

Dr. Hunt: Yes.

Session 5: Gulf War-Military Exposure Research Innovation Center (MERIC): Model for Implementing Evidence Based Practices: Overview

— Lisa McAndrew, PhD Director of Research, Acting Director of Education NJ War Related Illness and Injury Center (WRIISC)

Dr. McAndrew introduced herself as the Action Director of Education at the New Jersey WRIISC and would be speaking about the implementation of the GW-Military Exposure Research Innovation Center (GW-MERIC). The mission of the GWI-MERIC is to generate knowledge on how to accelerate the translation of evidence-based research into clinical care, and ensure all Veterans receive evidence-based, informed, and prompt care for GWI at all VA clinics/hospitals. Those changes will be addressed by four research projects seeking to understand how to address barriers at the clinician and the treatment level. Several specific problems being addressed are to accelerate the translation of evidence-based practices into clinical care, to increase GWI education and awareness in VA healthcare providers and improve GWI care from a general primary healthcare approach to a specialized one. To ensure the changes happen the GW-MERIC have partnered with VA program offices such as HOME, WRIISC, Office of Primary Care (OPC) and others, and talking with Veterans and VA clinicians to listen to their needs. The changes being initiated by GW-MERIC are in direct response to the RACGWVI recommendations to the VA Secretary to expedite and implement evidence-based clinical treatment for GWI. The goal of the GW-MERIC is to ensure a GWV with GWI is never again told, “it is all in your head.”

Session 6: GW-MERIC Project 1 Enhancing Quality of Care for Gulf War Illness through Clinician Awareness and Support

— Shannon Nugent, PhD Core Investigator, VA Portland Healthcare System Assistant Professor, Oregon Health & Science Univ

Dr. Nugent introduced herself as a research investigator at the VA Portland Healthcare System, Center to improve Veteran Involvement in Care and leader of GW-MERIC Project 1. The mission of the project is to ensure every VA clinician is aware of and can identify GWI, and knows what resources are available to manage GWI. To accomplish that mission a multi-disciplinary team comprised of methodologic and content experts partnered with several VA offices, include the OPC, Patient Centered Care and Cultural Transformation (PCCCT) and WRIISC and they are working to enhance recognition of GWI in the VA clinics and improve the quality of care provided. The process will be three parts: clinical engagement in communication strategy development to aid in dissemination of awareness and education; marketing and clinician GWI pocket card; public-facing GWI resources website with updated research and national efforts. This initiative is being conducted at eight VA hospitals, four that received the initiative, four that did not. Results from the study will be used to guide the team in bring GWI awareness to all VA healthcare centers to improve the healthcare of GWV.

Session 7: GW-MERIC Project 2 Evaluation of VET-HOME

— April Mohanty, MPH, PhD Research Health Scientist, VA Salt Lake City IDEAS Ctr; Assistant Professor, Dept of Internal Medicine, University of Utah

Dr. Mohanty introduced herself as a core investigator at the Salt Lake City Informatics Decision Enhancement and Analytics Science Center (IDEAS) and assistant professor at the University of Utah. Project 2 focuses on improving the quality and equity of health and healthcare as it relates to chronic diseases, including chronic multisymptom illness. The project aim is to improve the awareness, recognition and knowledge surrounding GWI and military exposures by building on the success of the Veterans' Exposure Team Health Outcomes (VET-HOME).

The project will assess if VET-HOME increased registry enrollment of eligible GWV and if registry enrollment increased GWV engagement in VA care. The VA is improving recognition of GWV and GWI through several military exposure registries managed by HOME. VET-HOME is a national program with a centralized approach to improving the process and consistency of registry exam participation, and to serve as a central hub for exposure-relevant information, care and resources. Processes are being developed for continuous improvement in training of staff, military exposure health clinicians and work-flow design and tailoring as needed. VET-HOME is the opportunity to ensure that Veterans maximally benefit from VA care and improving the experiences of Veterans with high exposure concerns.

Session 8: GW-MERIC Project 3 Concordant Care and Problem-Solving Treatment for Gulf War Illness

— Autumn Gallegos, PhD Assistant Professor of Psychiatry, University of Rochester Medical Ctr, Rochester NY

Dr. Gallegos introduced herself as an assistant professor at the University of Rochester Medical Center and the leader for Project 3. Project 3 partners are OPC, Office of Mental Health and Suicide Prevention (OMHSP) and WRIISC. The research team included experts in clinical trial design, quantitative and qualitative methods and GWI treatment and research. The aim of Project 3 was to ensure behavioral health clinicians receive GWI education and are trained in evidence-based practices that could be used when dealing with GWV GWI-induced mental health concerns, not GWI itself. The focus would be on not just anxiety or depression, but on cognitive difficulties, problems with memory and attention and feelings of invalidation. They will also receive training on helping to rebuild confidence and trust with the GWV regarding VA care and treatment of their GWI. The concordant care process has three steps: validation of the GWV GWI, develop shared understanding of the medical condition and working with the GWV to develop a reasonable treatment plan. Project 3 has already been tested with 300 clinicians with overwhelmingly positive results with the next step to expand it further.

Session 9: GW-MERIC Project 4 Optimization of a web-based approach for treatment of GWI

— Katharine Bloeser, MSW, PhD Research Scientist, NJ WRIISC; Assistant Professor, City University of New York – Hunter College

Dr. McAndrew re-introduced herself and apologized for Dr. Bloeser, whom due to technical difficulties was unable to virtually present Project 4. Project co-investigators were from the New Jersey WRIISC, Iowa State University, the Bedford VA and Rutgers University. The goal of Project 4 is to ensure every GWV benefits from the VA research on treatments for GWI. However, some GWI treatments, such as a low-glutamate diet or exercise plans can become complex. To help with these the VA developed a web-based approach, an app called “My Best Self.” The app was designed to ensure it fit with GWV experiences and will be a tool GWV will want to continually use to help with the treatment plan they developed with their healthcare provider. My Best Self is essentially a health coach app that is specifically tailored to GWV with GWI that will help them navigate their care plan by setting weekly goals, giving reminders, and encouraging them to speak with their healthcare provider if they feel the need.

Questions:

Male Voice: Is the app specifically designed for 1990-91 GWV or for all the various wars in the Middle East?

Dr. McAndrew: Currently, only 1990-91 GWV.

Session 10: Committee Business

— Karen Block, PhD Designated Federal Officer

Dr. Block thanked all the speakers for their informative presentations and continuing support of GWV and GWI research. She then officially informed everyone that this was the last meeting with Dr. Larry Steinman as chair of the RACGWVI. The new chair of the RACGWVI is Dr. Cheryl Walker and vice-chair Dr. Kenneth Ramos. Dr. Block addressed Dr. Steinman's accomplishments during his four-year tenure as chair. He started the VES which have provided direct information, experiences, concerns and feedback from GWV. The RACGWVI increased GWV participation in its meetings to over a thousand. Based on Dr. Steinman's research recommendations deep phenotyping and biomarker research has increased and helped with prognostic and diagnostic codes. Dr. Block pointed out, that during two of those years there was a pandemic and everyone on the RACGWVI was meeting virtually but they were still able to get all that work accomplished.

Dr. Steinman thanked everyone, the committee and staff who made his work seem easy. He was proud of the VES. Commenting on how listening to someone tell you their concerns can be therapeutic for both people, especially for something as tremendous as GWI. "Thank you to everyone."

Session 11: RACGWVI Insights and Closing Remarks

— Larry Steinman, MD Zimmerman Chair of Pediatrics, Neurology and Neurological Sciences, Beckman Center for Molecular Medicine, Stanford University

Dr. Steinman addressed the committee, invited guests and the Veterans listening to the meeting. He thanked them for the privilege of being the chair of the RACGWVI. He was honored to have worked with so many people dedicated to helping and caring for GWV. He wished everyone the best and said he would continue to support and be a resource for the RACGWVI and GWI.

Session 12: Public Comment

— Visitors and Invited Guests

The committee opened the meeting for questions and comments from the public audience. Those questions and comments were moderated by Mr. Bill Watts.

Daughter of GWV: She said that her father's medical record is incomplete and has no information in it concerning GWI despite her father having participated in GWI studies and qualifying for several of the presumptive conditions. She further commented the VA seems to lack any consistent standard of care and treatment for GWV, a lack of compassion for her father's condition and situation and the VA needs to have better documentation retention and record keeping.

Denise Nichols GWV: Ms. Nichols address the audience and thanked them for letting her speak. She addressed her history as a military nurse, working with and testifying to congress in both the House of Representatives and the Senate. Stating that 32 years after the 1990-91 Gulf War and GWV are still battling the VA for claims and getting the VA to acknowledge GWI. She encouraged all the GWV to enroll in the GW registries and to talk with each other via internet platforms such as Facebook.

Male GWV: The Veteran spoke of the experimental vaccines given to the GWV and how those vaccines were never documented in medical records. He would like the committee to explore further on the topic.

Dr. Steinman responds: In previous sessions the RACGWVI invited a DoD spokesman to address the topic but there was no response.

Male GWV: What is being done to ensure when GWV go to exams the medical professionals have been properly trained?

Wife of GWV: She cares for her 51-year-old husband who suffers from GWI. She speaks of lack of care for and understand about GWI at the VA. How her husband's GWI has impacted their family. It was only after registering on the Open Burn Pit registry they finally received any type of help. She encouraged all the GWV to enroll in the registries.

Jim Bunker GWV: Mr. Bunker addressed the committee and thanked them for their hard work and all the presenters for their informative presentations. He asked if in the future a representative from the Veterans Benefit Administration (VBA) could address the committee. With all the changes in the VA including the PACT Act, a VBA representative could help GWV understand the changes and how to navigate the process.

Meeting adjourned.

Acronym List

This list contains all acronyms from the September 21–22, 2022, RACGWVI Committee Meeting.

<u>Acronym</u>	<u>Name</u>
Alt-DFO	Alternate Designated Federal Officer
CDMRP	Congressionally Directed Medical Research Program
CFS	Chronic Fatigue Syndrome
COVID-19	Coronavirus Disease Of 2019
DFO	Designated Federal Officer
DMDC	Defense Manpower Data Center
DNA	Deoxyribose Nucleic Acid
DoD	Department of Defense
EES	Employee Education System
ETEC	Enterotoxigenic E. Coli
GW	Gulf War
GWI	Gulf War Illness
GWV	Gulf War Veteran(s)
GWIRP	Gulf War Illness Research Program
GW-MERIC	Gulf War-Military Exposure Research Innovation Center
HOME	Health Outcomes & Military Exposures
IBS	Irritable Bowel Syndrome
IDEAS	Infomatics Decision Enhancement and Analytics Science
IRB	Institutional Review Board

ME/CFS	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
MERIC	Military Exposure Research Innovation Center
MERS	Middle East Respiratory Syndrome
MET	Military Exposure Training
NETPRP	Neurotoxin Exposure Treatment Parkinson's Research Program
NIH	National Institutes of Health
OMHSP	Office of Mental Health and Suicide Prevention
OPC	Office of Primary Care
ORD	Office of Research and Development
PACT Act	The Sergeant First Class Heath Robinson Honoring our Promise to Address Comprehensive Toxics Act of 2022
PCCCT	Patient Centered Care and Cultural Transformation
PEM	Post-Exertional Malaise
PB	Pyridostigmine Bromide
PON1	Human Paraoxonase Gene
PTSD	Post-Traumatic Stress Disorder
RAC	Research Advisory Committee
RACGWVI	Research Advisory Committee on Gulf War Veterans' Illnesses
RVP	Research Volunteer Program
RVR	Research Volunteer Registry
SECVA	Secretary of the VA
TERP	Toxic Exposures Research Program

U.S.	United States
VA	Veterans Affairs
VBA	Veterans Benefit Administration
VES	Veterans Engagement Session
VET	Veteran Exposure Team
VET-HOME	Veterans' Exposure Team Health Outcomes
VHA	Veterans Health Administration
WRIISC	War Related Illness and Injury Study Center