Research Advisory Committee on Gulf War Veterans' Illnesses

June 28-29, 2010, Committee Meeting Minutes

Department of Veterans' Affairs
Washington, DC

Research Advisory Committee on Gulf War Veterans' Illnesses
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I hereby certify the following minutes as being an accurate record of what transpired at the June 29-30, 2009 meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses.

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/signed/
James H. Binns
Chairman
Research Advisory Committee on Gulf War Veterans' Illnesses

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Attendance Record

Members of the Committee
James Binns, Chairman
* Roberta White, Scientific Director
Floyd Bloom
Beatrice Golomb
Joel Graves
Anthony Hardie
Marguerite Knox
William Meggs
James O'Callaghan
Lea Steele
Adam Such

Committee Staff
Kimberly Sullivan
Sadie Richards

Designated Federal Officer
Bill Goldberg

Other Members of VA Central Offices
John Gingrich, VA Chief of Staff
Joel Kupersmith, VA Chief Research and Development Officer

Guest Speakers
Fiona Crawford
Apostolos Georgopoulos
Ronnie Horner
Michael Mullan
Col. Jonathan Newmark
Ashok Shetty
Alvin Terry
Michael Weiner
Melissa Kaime

* participated by phone

Abbreviations

ALS – Amyotrophic Lateral Sclerosis

CDC – Center for Disease Control

CDMRP – Congressionally Directed Medical Research Programs

CPT – Continuous Performance Test

CSP – Cooperative Studies Program

DFO – Designated Federal Officer

DFP – Diisopropyl Fluorophosphate

DoD – Department of Defense

EEG – Electroencephalogram

GABA – γ-Aminobutyric Acid

GWI – Gulf War Illness

IED – Improvised Explosive Device

IOM – Institute of Medicine

IRB – Institutional Review Board

MCS – Multiple Chemical Sensitivity

MEG – Magneto-encephalography

MRI – Magnetic Resonance Imaging

MRS – Magnetic Resonance Spectroscopy

MS – Multiple Sclerosis

NAA – N-acetyl-aspartate

NGF – Nerve Growth Factor

OPs – Organophosphates

ORD – Office of Research and Development

PB – Pyridostigmine Bromide

PER – Permethrin

PTSD – Post-Traumatic Stress Disorder

RFA – Request for Application

SNI – Synchronous Neural Interactions

TrkA – Tyrosine Kinese Receptor

UCS – Unpredictable Chronic Stress

VA – Department of Veterans' Affairs

VBA – Veterans Benefits Administration

VHA – Veterans Health Administration

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
June 28-29, 2010

Department of Veterans Affairs, 810 Vermont Avenue, Room 230, Washington, DC

Agenda
Monday, June 28, 2010

8:00 – 8:30	**Informal gathering, coffee**	
8:30 – 8:35	**Welcome, introductory remarks**	**Mr. Jim Binns, Chairman** **Res Adv Cmte Gulf War Illnesses**
8:35 – 9:30	**Case report: long-term cognitive sequelae of sarin exposure**	**COL Jonathan Newmark** **Joint Program Executive Office for Chemical/Biological Defense** **Department of Defense**
9:30 – 10:15	**Effects of military service on the brain**	**Dr. Michael Weiner** **San Francisco VA Medical Center**
10:15 – 10:30	**Break**	
10:30 – 11:15	**Organophosphate exposure and cognition: Novel mechanisms of neurotoxicity**	**Dr. Alvin Terry** **Medical College of Georgia**
11:15 – 12:00	**Neural Stem cell dysfunction and its implications on memory and mood in a rat model of Gulf-War illness**	**Dr. Ashok Shetty** **Durham VA Medical Center**
12:00 – 12:45	**Proteomic analysis of cellular response to Biological warfare agents and cognitive function in animal models**	**Dr. Fiona Crawford** **Tampa VA Medical Center** **Dr. Michael Mullan** **Roskamp Institute**
12:45 - 1:45	**Lunch**	
1:45 - 2:30	**ALS rates in Gulf War veterans**	**Dr. Ronnie Horner** **University of Cincinnati**
2:30 – 3:15	**Magneto-encephalography (MEG) patterns in neurological diseases**	**Dr. Apostolos Georgopoulos** **Minneapolis VA Medical Center**
3:15 – 3:30	**Break**	
3:30 - 4:30	**Committee Discussion: VA Gulf War Task Force Report**	**Mr. Jim Binns, Chairman** **Dr. Kimberly Sullivan** **Res Adv Cmte Gulf War Illnesses**
4:30 – 5:00	**Public comment**	

Meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses
June 29, 2010

Department of Veterans Affairs, 810 Vermont Avenue, Room 230, Washington, DC

Agenda
Tuesday, June 29, 2010

8:00 – 8:30	**Informal gathering, coffee**	
8:30 – 9:15	**CDMRP Gulf War program update**	**CAPT Melissa Kaime** **Congressionally Directed Medical Research Program**
9:15 –9:45	**VA Gulf War Task Force Report**	**Mr. John Gingrich** **Chief of Staff** **Dept. of Veterans Affairs**
9:45 – 10:30	**Update of VA Gulf War research RFAs**	**Dr. William Goldberg** **VA Office of Research and Development**
10:30 – 10:45	**Break**	
10:45 – 11:30	**Federal Advisory Committee Ethics Training**	**Mr. Jonathan Gurland** **VA Office of General Counsel**
11:30 – 12:00	**VA Gulf War research program development**	**Dr. Joel Kupersmith** **Chief Research and Development Officer** **Dept. of Veterans Affairs**
12:00 – 12:45	**Committee discussion: Institute of Medicine (IOM) Gulf War report**	**Mr. Jim Binns, Chairman** **Res. Advisory Cmte Gulf War Illnesses**
12:45 – 1:15	**Public comment**	
1:15	**Adjourn**	

DAY 1

The June 28-29, 2010 meeting of the Research Advisory Committee on Gulf War Veterans' Illnesses (hereinafter referred to as the Committee) was held in Room 230 at the Department of Veterans' Affairs, 810 Vermont Avenue, NW, Washington, D.C.

Welcome, Introductions & Opening Remarks

Mr. James Binns, Committee Chairman
Dr. Kimberly Sullivan, Scientific Coordinator

Chairman James Binns called the meeting to order at 8:30am. After welcoming everyone, Chairman Binns expressed his enthusiasm regarding the Institute of Medicine's (IOM's) new report which called for an integrated and well-managed Gulf War Illness research program. He commended Dr. Steven Hauser and his committee (none of whom were present at the meeting) for their major contribution to Gulf War illness research. Chairman Binns then remarked that Dr. White would be absent from this meeting due to illness.

Dr. Kimberly Sullivan then remarked that the annual report was still being prepared before introducing Col. Jonathan Newmark.

Case Report: Long-Term Cognitive Sequelae of Sarin Exposure

COL Jonathan Newmark, Department of Defense

COL Newmark, speaking as a clinician rather than a representative of any agencies with which he is affiliated, provided an update on a patient he had seen who had been exposed to liquid and vapor sarin that was found to be leaking from an improvised explosive device (IED) that he had been responsible for deactivating and transporting in the back of a vehicle in Iraq in 2004 (see Appendix A – Presentation 1). He described the circumstances of the patient's exposure to sarin vapor and remarked that neurocognitive abnormalities were documented 8 months after exposure. He explained that the patient had been examined again in 2006 but that the neurobehavioral test was invalid (the report noted that the patient had poor effort on the validation tests and the neuropsychologist who performed the tests stated that he appeared to have functional complaints but no neurobehavioral abnormalities). COL Newmark explained that the patient redeployed to Iraq, has been promoted and received a physical prior to entering airborne school in May 2010. COL Newmark spoke to the patient and his doctor in May 2010, and that his doctor had expressed confidence that the patient would succeed in airborne school. In addition, COL Newmark reported that the patient reported that his symptoms had recently waned. COL Newmark reminded the Committee that unlike many of the Gulf War veterans, this patient had not been exposed to oil well fires, DEET, permethrin, or pyridostigmine bromide (PB). COL Newmark concluded by stating that he thought the neurotoxicity of sarin and possibly the stress of the exposure contributed to the patient's symptoms, which appear to have resolved over time.

Dr. Beatrice Golomb, a member of the Committee, then briefly remarked on what she described as an analogous experience of a post Gulf War sarin vapor exposure in a patient whose wife corroborated his assertions that he has experienced chronic personality changes, neurocognitive

problems, and severe changes in physical function since his reportedly repeated, several second exposures in a nerve agent training center. She then asked if COL Newmark could confirm whether sarin is currently used in nerve agent training centers.

COL Newmark replied that the only live agent training in the United States military that he is aware of occurs at Ft. Leonard Wood, Missouri. He stated that to his knowledge all other centers use tear gas.

Dr. William Meggs, a member of the Committee, then pointed out that poor effort on neuropsychological and neurobehavioral testing does not rule out real pathology, and may even be part of the neurobehavioral abnormality.

COL Newmark agreed with Dr. Meggs that absence of proof is not proof of absence, but commented that it also is not proof of presence.

Dr. Meggs then remarked that the clinical experience with both encephalopathy and peripheral neuropathy is that some people experience temporary dysfunction then gradually improve, while others end up with fixed deficit that never goes away. He commented that this patient was obviously in a high degree of functionality but that he may still be impaired in some ways that have not been detected.

COL Newmark replied that his understanding was that encephalopathy and peripheral neuropathy have not been linked to the type of exposure to sarin that this patient had.

Mr. Anthony Hardie, a member of the Committee, asked if COL Newmark had experience with patients exposed to mustard gas, stating that he has strong reason to believe that he was exposed to lewisite and mustard in Northern Kuwait. He said that he has been following the studies of Iranian veterans of the Iran-Iraq war, including a cohort of 30-40,000 individuals who are currently being tracked. Mr. Hardie expressed his belief in the roles that PB, pesticides and sarin play in causing illnesses in Gulf War veterans, but he thinks other factors may well be contributing and asked COL Newmark what he had seen in patients exposed to mustard gas.

COL Newmark replied that he had only seen two cases and both were documented exposures to liquid, resulting in severe surface burns in both patients. He had not seen any patients exposed to mustard gas as a vapor, such as Mr. Hardie suspects he was exposed to.

Dr. Lea Steele, a member of the Committee, asked COL Newmark what happened to the driver of the vehicle in which the two soldiers were exposed.

COL Newmark replied that he went off duty for three weeks following the exposure but did not complain of symptoms or go in for evaluation in 2005. COL Newmark believed that the driver was medically retired from the Army around 2006 or 2007, with a diagnosis of bipolar disorder. COL Newmark was not aware of whether this individual has ever sought care under the VA.

Chairman Binns asked COL Newmark if there was anything he believed that this patient might have done that may have facilitated his recovery to the extent that he has actually recovered.

COL Newmark replied that he did not know, but stated that he had spoken to the newly appointed medical informatics consultant to the Surgeon General (who is also the chief medical informatics officer for the Army Surgeon General) in preparation for his presentation to the Committee. In that conversation COL Newmark made the suggestion that a tracking mechanism be built into the longitudinal medical record system. He was told that this request had been put in for individuals suffering from brain trauma, and COL Newmark said he would put in a request to add in the module for tracking other unusual patients as well. He stated that doing so could help build what General Shinseki has referred to as a seamless medical records system.

Chairman Binns and Dr. Sullivan then thanked COL Newmark for his presentation. Dr. Sullivan commented on the importance of understanding the single exposures, as they shed light on the individual impacts of the more complex exposures experienced by many Gulf War veterans.

Dr. Sullivan then introduced Dr. Michael Weiner.

Effects of military service on the brain

Dr. Michael Weiner, San Francisco VA Medical Center

Dr. Weiner presented findings from research he has done using magnetic resonance spectroscopy (MRS), including studies of the neuronal marker N-acetyl-aspartate (NAA) in the basal ganglia of veterans with Gulf War illness, research into the effects of sarin exposure, studies of chronic multisymptom illness and some data on post-traumatic stress disorder (PTSD) (see Appendix A – Presentation 2). Using Dr. Robert Haley's criteria to identify Gulf War veterans with "Syndrome 2," Dr. Weiner did not replicate Dr. Haley's findings of reduced NAA-creatine ratio in the basal ganglia. He also found no relationship between sarin exposure and any of the Haley syndromes, but did find reduced hippocampal volume and total gray matter volume in sarin exposed versus unexposed Gulf War veterans (based on the Khamisiyah plume model) using a 1.5 Tesla scanner. In a separate group of Gulf War veterans with "Syndrome 2" studied with a 4 Tesla scanner, Dr. Weiner found a slight elevation of NAA-creatine ratio in the basal ganglia. Further studies with the 4 Tesla scanner found no statistical difference in hippocampal volume between exposed and unexposed Gulf War veterans, but white matter was reduced in highly exposed veterans compared to moderately exposed veterans. The latter finding replicated findings of Heaton et al. but was only seen on the 4 Tesla (not the 1.5 Tesla) scanner. Futher 4 Tesla research into differences in certain subfields of the hippocampus is currently being done.

Dr. Weiner also reported findings related to reductions in the volume of specific subareas of the hippocampus in patients with PTSD.

At the conclusion of Dr. Weiner's presentation Dr. Sullivan asked him to speak to the comments he had made in his recent paper regarding the possibility that differences between his findings and those of Dr. Heaton regarding decreased white vs. decreased gray matter in the brains of sarin exposed Gulf War veterans were due to differences in boundary identification (of white vs. gray matter regions of the brain). She specifically asked whether the better visualization on the 4 Tesla (4T) MRI compared to the 1.5 Tesla could have had something to do with the boundary issue. Dr. Weiner replied that he perceived the small sample sizes studied to be the fundamental problem. He

added that he saw value in conducting a longitudinal imaging study in subjects who were exposed to sarin, to see if their brains change over time.

Dr. Golomb then remarked on the methodology used by White et al. to track each veteran's proximity to the Khamisiyah plume (rather than simply categorizing veterans by whether they had received a letter notifying them of their potential exposure to the plume). Dr. Weiner responded by clarifying that this was the same approach he took, using the same exposure level data provided by the Department of Defense (DoD). Dr. Golomb then cautioned against using veterans' Khamisiyah exposure status as a proxy for Gulf War theater exposure, noting that exposure to oxidative stressors and other acetylcholinesterase inhibitors could not be accounted for in that way. She also referenced a finding by Mackness et al. that reported reduced paraoxonase activity in Gulf War veterans compared to those deployed elsewhere. Dr. Weiner replied that his study compared veterans who were deployed to the Gulf War with veterans who were on active duty at the time of the Gulf War but who remained in the United States.

Dr. Golomb then asked if Dr. Weiner excluded Gulf War veterans who met the criteria for PTSD in any of his analyses. He replied that he effectively had, in that he statistically covaried for PTSD in all of his analyses, including the hippocampal measurements.

Dr. Golomb made another comment about the wide prevalence of sleep apnea that she had seen in veterans, noting that certain sleep disturbances associated with PTSD in common test batteries are also sequelae of sleep apnea. Dr. Weiner acknowledged the importance of this consideration, stating that he had published a paper with Thomas Neylan on the association between sleep disorders and changes in a subfield of the hippocampus known as the CA3/dentate gyrus.

Dr. Meggs then asked why NAA was originally looked at by Dr. Weiner. Dr. Weiner replied that Dr. Haley would be able to answer that question, since he was the one to do the original study. He went on to explain that NAA is an amino acid that is unique to neurons in the brain which is a sensitive marker of neuronal injury. Dr. Weiner remarked that his research set out to replicate Dr. Haley's findings but that he found no serious biological change in the subjects with Gulf War illness (syndrome 2 symptoms).

Dr. Sullivan then asked whether Dr. Weiner had included questions about veterans' exposure to pesticides or PB in his research, since it is known that Gulf War veterans were exposed to 15 different types of pesticides. Dr. Weiner replied that he had considered it but ultimately decided that the data gathered from such questions would not be sufficiently reliable to merit their inclusion in his study design.

Dr. Steele then expressed concern about Dr. Weiner's study design, and asked whether he had the data that would allow him to look at subgroups, including people with and without PTSD. She then asked if he had controlled for PTSD in the context of different exposure levels to sarin. Dr. Steele also asked if it would be possible to look at the other exposure subgroups. She remarked that even self-reported exposures to pyridostigmine bromide and pesticides provide a type of proxy for whether people took a lot of PB, some PB or no PB. Dr. Steele noted that studies which look at these exposure subgroups really inform researchers of what's going on. Dr. Weiner replied that the primary objective of this study was simply to replicate Dr. Haley's findings and determine whether

or not they were robust. He added that at the time the study was designed people were not talking about PB, and that his protocol underwent peer review. He said that although he had no data on PB exposure, he encouraged researchers to contact him to run analyses on the extensive amount of data that he did collect.

Dr. Steele then expressed her interest in Dr. Weiner's finding that the NAA-choline ratio was elevated in the Syndrome 2 patients. Dr. Weiner replied that those findings had not been corrected for multiple comparisons. He explained that if he started correcting for multiple comparisons that he ended up with no significance at all. Thus, he explained, the finding that the NAA-choline ratio was elevated was not significant. Rather, the major finding was that there was not a reduction in NAA.

Dr. Steele continued with her inquiry, and asked Dr. Weiner what the implications were (in humans or animal models) of having elevated NAA, or if those findings were not often seen. Dr. Weiner replied that elevated NAA is not commonly found.

Mr. Hardie then asked Dr. Weiner what he meant by "changes" when he referred to seeing neuropsychological changes. Dr. Weiner replied that subjects who reported severe Gulf War illness symptoms did not differ significantly in their performance on a challenging battery of neuropsychological tests compared to Gulf War era veterans who were not deployed. Mr. Hardie then pointed out that the percentage of veterans recruited to the Army just prior to and during the Gulf War who had high school diplomas was close to 100%, and that this was the peak period for the Army in its recruiting of highly educated individuals. He remarked that the veterans serving during the Gulf War era were the best and the brightest that the military has ever had, which he suggested may have had an impact on the neuropsychological test results.

Mr. Hardie then commented on the value of pre-deployment neuropsychological testing, followed by post-deployment testing for all members of the military, since this would enable individuals to be tested against themselves rather than against their peers. Dr. Weiner remarked that introducing pre-deployment testing would likely cause the liability consequences to the government to increase astronomically. Mr. Hardie noted that he had undergone robust testing before deploying, and that his post-deployment tests have shown consistent deficits that have remained over time.

Dr. Meggs then remarked that the overlap between PTSD and chemical exposures may be akin to what Hans Selye observed when his research on rodent models found that psychological stress could induce the same illness as toxins did. Dr. Weiner replied that when he was a young student Selye had been one of his heroes. He noted that Selye's main point was that the body has a set of systems which adapt to stress, and that those systems are activated no matter what the stress is.

Dr. O'Callaghan then asked if Dr. Weiner knew of other studies in which hippocampal volume reversals were seen. Dr. Weiner replied that this was demonstrated in a famous study of London taxi drivers that showed larger hippocampal volumes in taxi drivers taking the certification exam compared to those who had not taken the exam. Dr. Weiner explained that this was one example of evidence for plasticity – where certain areas of the brain can expand as new synapses are generated through particular activities involving the release of growth hormones. He noted that in certain diseases, such as Alzheimer's disease, hippocampal atrophy occurs. He explained that it is very unclear how the hippocampal atrophy story interacts with the symptomatology of PTSD. He said

that the only obvious connection is that the hippocampus is involved with learning, and PTSD is a disorder of learning. Dr. Golomb then asked about the study design of the taxi driver research and Dr. Weiner said that there were other studies more relevant to PTSD and Gulf War illness (in which pre- and post-testing of the same individuals had been done).

Dr. Steele then asked if Dr. Weiner was planning to study GABA (γ-Aminobutyric Acid) in the brains of Gulf War veterans. Dr. Weiner replied that he was, adding that no specific protocols had been developed yet, but that they would be over the next few months.

Dr. Meggs asked if Dr. Weiner's neuroimaging techniques could be used to assess whether or not any low-grade neuroinflammation (glial cell activation) was going on in the brains of Gulf War veterans. Dr. Weiner replied that he was not a neurologist, but that the best way he knew of was to do a lumbar puncture and see whether or not there are inflammatory markers in the cerebrospinal fluid. He acknowledged the existence of a PET scanning ligand that uses benzodiazepine receptors which is claimed to detect activation of glial cells, but he stated that he wasn't sure how sensitive or robust that technique was.

Chairman Binns then asked Dr. Weiner if he felt that the DoD's Office of Force Health Protection and Readiness' characterization of the IOM report was accurate, with specific regard to their finding that Gulf War service caused PTSD and by implication the symptoms of Gulf War veterans were related to PTSD. Dr. Weiner replied that he had not read the recent IOM report, but that his research found that among the subjects he studied who seemed to have Gulf War illness symptoms either defined by the CDC criteria or by the Haley factor analysis, there was a considerable overlap with DSM-IV diagnosis of PTSD. He thought the fairest thing to say was that people going into battle are exposed to a wide variety of stressors, and that some of them come out with impairments as a result of the combination of stressors they were exposed to in combat. He added that each individual was unique in this regard, which makes scientific research on the population difficult. He stated that he supported a treatment-based approach, ideally by using biological markers to identify which individuals would respond to different treatments.

Chairman Binns then urged Dr. Weiner to read the IOM report, remarking that it concluded that the excess of unexplained medical symptoms reported by deployed Gulf War veterans cannot be reliably ascribed to any known psychiatric disorder. Dr. Weiner agreed with that, reiterating that a substantial minority of the subjects he studied who had Gulf War illness symptoms met the criteria for PTSD DSM-IV, but the majority did not, so he could not ascribe a psychological cause for their symptoms.

Mr. Hardie, who in addition to being a member of the Committee is a Gulf War veterans who sits on the Congressionally Directed Medical Research Programs' (CDMRP) panel then told Dr. Weiner that he was pleased to hear that Dr. Weiner was moving toward focusing on treatments with his research.

Chairman Binns then thanked Dr. Weiner for his presentation. Dr. Sullivan added that she and the Committee members were looking forward to reading his paper on the 4 Tesla MRI study. Chairman Binns then called for a short break. At 11:00am, after the break, Dr. Sullivan introduced the next speaker, Dr. Alvin Terry.

Organophosphate exposure and cognition: Novel mechanisms of neurotoxicity

Dr. Alvin Terry, Medical College of Georgia

Dr. Terry began his presentation with an overview of the basal forebrain cholinergic system, then reviewed organophosphate (OP) pesticides before presenting findings from his animal studies investigating the consequences of subacute/subthreshold exposures to organophophates on various domains of cognitive function (See Appendix A – Presentation 3). Dr. Terry explained that the goal of his research was to identify biomarkers and then targets for drug development to ultimately treat any deficits found. Among other findings, Dr. Terry's in vitro research has contributed to a growing pool of evidence suggesting that OPs interfere with axonal transport. Dr. Terry's subacute chlorpyrifos exposure studies also found impairments in spatial learning, impaired prepulse inhibition of the auditory startle response, and decreased expressions of a variety of cholinergic markers. Dr. Terry's recent and ongoing research has also revealed that rodents exposed to repeated, subacute doses of chlorpyrifos exhibited increased premature responding and decreased accuracy in their responses to an animal model of the Continuous Performance Test (CPT) compared to controls. Additional research currently underway in Dr. Terry's lab involves looking at the effect of chlorpyrifos on axonal transport of mitochondria. Dr. Terry also discussed some of his research using diisopropyl fluorophosphates (DFP) which is structurally similar to sarin and soman (See Appendix A – Presentation 3 for more detailed findings).

At the conclusion of Dr. Terry's presentation, Dr. Sullivan remarked that Dr. Terry's research appeared to agree with those in one of her studies which found that the CPT was significantly different in the higher exposed pesticide applicators compared to lower exposed veterans. Dr. Sullivan also asked if Dr. Terry had seen the paper recently published by Dr. Marc Weisskopf at Harvard University looking at urinary metabolites of OPs, higher levels of which were found to be associated with attention deficit disorder (ADD) in the children studied. Dr. Terry replied that he had seen that and other similar papers.

Dr. Steele asked Dr. Terry to clarify whether his lab was carrying out research on mitochondrial transport, and whether it was in vitro or in vivo. He replied that he was in the early stages of that research, which utilizes rat cortical neurons in vitro. She followed up by asking if any findings had been made regarding the duration of the effects seen and Dr. Terry replied that this would be the focus of future research. Dr. Steele asked if any research was being done on this transport in humans. Dr. Terry replied that most axonal research is post-mortem, but that other "real-time" techniques are being developed.

Chairman Binns then asked if Dr. Terry could explain whether the effects on axonal transport would relate to effects on the autonomic nervous system, since that is an area that has been seen to be affected in ill Gulf War veterans. Dr. Terry replied that axonal transport is important in all neurons – including those in the central and peripheral nervous systems. Chairman Binns then asked if Dr. Terry had any preliminary thoughts on targets for treatment. Dr. Terry replied that he had not yet tested any of the compounds his lab has in development for cognitive disorders in the OP context, but that there are a series of choline analogs that might prove to be promising.

Dr. Steele then asked what Dr. Terry's general sense was about the duration of the behavioral effects that were seen in his animal models after OP exposure. Dr. Terry replied that his current research was looking into these long-term and permanent changes.

Chairman Binns then thanked Dr. Terry for his presentation before Dr. Sullivan introduced the next speaker, Dr. Ashok Shetty.

Neural Stem cell dysfunction and its implications on memory and mood in a rat model of Gulf War illness

Dr. Ashok Shetty, Durham VA Medical Center

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Dr. Shetty presented his research on neural stem cell dysfunction and its implications on memory and mood in a rat model of Gulf-War illness (See Appendix A – Presentation 4). He began by explaining that his rat model involves exposure to low doses of pyridostigmine bromide (PB) and pesticides that were used in the Gulf War (including DEET and permethrin). Dr. Shetty then gave a brief introduction to hippocampal neurogenesis and neurogenic regions in the brain before discussing the specifics of his experiments. One main conclusion from his research was that that 28 days exposure to a combination of Gulf War illness-related chemicals diminishes hippocampal neurogenesis in the immediate post-exposure period and for prolonged periods after exposure, as evidenced after a four month follow-up period. He also found that reduced hippocampal neurogenesis was associated with impaired learning, memory and mood functions. In a subsequent study, Dr. Shetty found that predictable chronic mild stress alone has beneficial effects which include increased neurogenesis, as well as improved mood and memory function. However, Dr. Shetty then studied predictable chronic mild stress in combination with the chemicals investigated above and found that the addition of mild stress exacerbates the deleterious effects of Gulf War illness related chemicals on hippocampal neurogenesis and on cognitive functions such as learning, memory, and mood. Based on these findings, Dr. Shetty believes that stem cell dysfunction in the hippocampus likely underlies the cognitive and mood impairments observed in this Gulf War illness model. Dr. Shetty then discussed preliminary results of his ongoing immunostaining study which focuses on neuroinflammation and microglial cells. He added that exposure to a combination of these chemicals appears to have a specific effect on hippocampus stem cell function, because this exposure did not induce widespread hippocampal neurodegeneration or inflammation. Furthermore, exposure to each of the chemicals alone did not elicit the results seen when chemicals are administered in combination.

At the conclusion of Dr. Shetty's presentation, Dr. Meggs asked what the significance of Dr. Shetty's use of the word "widespread" was. Dr. Shetty replied that what he meant was that activated microglial cells were isolated and not seen in every section through the hippocampus.

Dr. Golomb then asked if Dr. Shetty had run experiments where individual exposures were coupled with restraint stress. Dr. Shetty replied that those tests had not been run yet, but there was interest in doing so. Dr. Golomb then commented on Dr. Shetty's use of the first swim test as a model of depression, but cautioned him against interpreting increased floating (vs. swimming) time as a central nervous system (CNS) effect since there is evidence suggesting that the chemicals used in Dr. Shetty's experiments can cause peripheral myopathy, thus muscle weakness could actually be the cause of increased time spent floating vs. swimming. Dr. Shetty agreed with Dr. Golomb, stating

that he had run a test to determine that swimming speed was not decreased, and that motor functioning seemed normal. He also agreed that further depression tests would be a good idea going forward. Dr. Golomb suggested that additional tests of motor fatigability be included as well.

Chairman Binns then asked Dr. Shetty if he thought neurogenesis might be increased in rats that were exposed to a swim test subsequent to their chemical exposures. Dr. Shetty replied that it could be possible because the cognitive training actually enhances neurogenesis. He added that he had just started another experiment where immediately after the chemical exposure researchers give the rats anti-depressants. The results suggest that this reduces the decline in neurogenesis to some extent.

Dr. O'Callaghan asked if Dr. Shetty had any evidence for the extent of immunosuppression that is associated with his model of mild stress. Dr. Shetty said that he has not studied that but that other research has measured cortical steroid levels and found that the stress hormone level is elevated only in the initial few days, then adaptation occurs and returns levels to normal.

Dr. Sullivan then asked if Dr. Shetty would expect overall hippocampal volume to be lower given the reductions seen in particular areas. Dr. Shetty replied affirmatively, with particularly significant reductions expected to be seen in the dentate gyrus.

Dr. Steele asked if there was any literature on the benefits of mild stressors on some of the measures Dr. Shetty looked at in his studies. Dr. Shetty replied that his results were totally unexpected (and by implication contributed to the filed of knowledge in that regard). Dr. Steele then asked if Dr. Shetty planned to look at the long-term effects of chemical and stress exposure in animals whose immediate post-exposure assessments were normal. Dr. Shetty said that he would be looking at the long-term effects in all animals.

Miss Debbie Hunter, a member of the audience from the Senate Committee on Veterans Affairs, asked if the slides would be available publicly. Dr. Sullivan replied that the slides would be put up on the Committee's website.

Chairman Binns then thanked Dr. Shetty for his presentation, and Dr. Sullivan introduced the next speaker, Dr. Fiona Crawford.

Proteomic analysis of cellular response to biological warfare agents and cognitive function in animal models

Dr. Fiona Crawford, Tampa VA Medical Center
Dr. Michael Mullan, Tampa VA Medical Center

Dr. Crawford first presented findings from her and Dr. Michael Mullan's neuronal cell culture research, which is focused on genomic and proteomic analyses, then discussed cognitive and proteomic findings from research they have conducted in animal models (see Appendix A – Presentation 5). Drs. Crawford and Mullan have focused on the effects of the insecticide Permethrin, PB, and the insect repellent DEET (collectively referred to as Gulf War agents) in their research, with the aim of identifying biomarkers and pathogenic mechanisms of Gulf War illness. Dr. Crawford presented data suggesting that genomic and proteomic analyses support the

feasibility of the identification of molecular targets that could potentially be modulated to mitigate the effects of Gulf War agent exposure. Dr. Crawford also reported that plasma proteomic analyses demonstrate significantly modulated plasma proteins at 145 days post-exposure in a mouse model and thus support the pursuit of Gulf War Illness (GWI) biomarkers specific to particular clinical presentations.

At the end of Dr. Crawford's presentation Rev. Joel Graves, a member of the Committee, asked what the dysregulation in amyloid processing and signaling that Dr. Crawford has discussed might suggest in regards to clinical treatment. Dr. Crawford replied that currently the results are just raw data, but that once standard molecular biological approaches had been applied to tease out some of the mechanisms involved, progress toward treatment methodologies would be made. She praised proteomic analyses for their ability to capture temporal effects following animal model exposures.
Dr. Sullivan then remarked on the delayed impairments seen only 80+ days out on the Morris water maze experiment, and asked if Dr. Crawford had any hypothesis for the underlying mechanism. Dr. Crawford replied that she did not know, but was intrigued by the neurogenesis research presented by Dr. Shetty, and wondered if it might be relevant to the results of her studies. Dr. Sullivan asked if Dr. Crawford would plan to look at this in future research and she said that she would.

Chairman Binns mentioned hearing of the value of proteomic and genomic analysis when he and Dr. Golomb visited the Lawrence Livermore National Laboratory in 2003, and he asked Dr. Crawford how she would structure a program that was designed to try to in the most efficient way possible move the process forward (given that 7 years had passed since he had heard those techniques promulgated). Dr. Crawford replied that she had been communicating with Dr. Golomb about the possibility of translation to human plasma samples in terms of the biomarker studies. Dr. Crawford stated that, from that aspect, she thought it would be important to develop a range of different animal models, showing different aspects of Gulf War illness symptomatology, to identify biomarkers from those, and then to go into the clinical population. She explained that the population is too diverse to propose any sort of proteomic approach in the human plasma, but that animal models could be used to look for biomarkers correlating to cognitive dysfunction (for example), from which potential biomarkers of interest in humans could be extrapolated and studied in patients with Gulf War Illness suffering from cognitive dysfunction. Dr. Crawford also called for the identification of good preclinical models in order to move forward with potential therapeutic treatment in clinical trials.

Chairman Binns then thanked Dr. Crawford before adjourning the meeting for lunch.

At 1:49pm the meeting recommenced with an introduction by Dr. Sullivan of the next speaker, Dr. Ronnie Horner.

Amyotrophic Lateral Sclerosis rates in Gulf War veterans

Dr. Ronnie Horner, University of Cincinnati

Dr. Horner began his presentation by reviewing the current understanding of Amyotrophic Lateral Sclerosis (ALS) epidemiology among Gulf War veterans before discussing the emerging evidence relevant to the etiology of the outbreak (See Appendix A – Presentation 6). Dr. Horner's review focused on the finding that there is a 2-fold higher risk of ALS among 1991 Gulf War Veterans.

Based on his analysis of the literature, Dr. Horner believes that elevated risk probably can't be explained by methodological biases and that etiology remains uncertain. He postulated that exposures immediately prior to or during deployment may be involved, and suggested that it might be more useful to focus on mechanism vs. specific etiologic agent(s).

At the completion of Dr. Horner's presentation, Dr. Golomb made the suggestion that OPs be included in the list of potential mechanisms being investigated, in light of the association between OP exposure and Parkinson's disease. Dr. Horner replied that they probably should, but that the focus should perhaps be more on what's happening in the neurons in Parkinson's and related diseases rather than on what's killing these neurons. He emphasized the importance of therapy and prevention-based approaches.

Dr. Meggs then described an ALS patient he had seen years ago who was suffering from muscle atrophy and was referred to the toxicology clinic because his job for most of his life had involved changing the fluids in transformers and in servicing transformers for a utility company. Dr. Meggs then noted that when this patient went out on disability the progression of his lower motor neuron disease went into remission. He asked if Dr. Horner or anyone else present had any insight regarding this type of scenario. Dr. Horner replied that he had never heard of anyone recovering. Dr. Golomb said there were a few cases of recovery in the literature, suggesting that it could be the variation in mechanism that was important. She remarked that she thought Vitamin D deficiency was something that every once in awhile is identified to be a factor in motor neuron disease, and correction sometimes seems to reverse the problem.

Dr. Steele then asked if any interesting findings ever arose from the questionnaires distributed to patients or their family members in an attempt to determine their exposure histories. Dr. Horner replied that he was not aware of any major findings, and remarked that looking for causative agents would not necessarily be a fruitful endeavor – and that he felt mechanism-based, therapy-oriented approaches offered greater promise. Dr. Steele then asked if understanding the etiology would help elucidate the mechanism. Dr. Horner replied that it could, but that epidemiology could be deceptively simple.

Dr. Steele then commented on the fact that higher rates of ALS were found in the Air Force Gulf War veterans, and that previous research showed that when veterans self-reported whether or not they had been to the Gulf different results were seen than if the DoD records of whether or not they had been to the Gulf were used. She continued, mentioning that she had done an epidemiological study of Kansas Gulf War veterans and found that it was predominantly Air Force veterans who had ben misidentified by the DoD as not having been in the Gulf when in fact they were. She concluded her point by stating that she had always found these higher rates seen through self reported Gulf War service and the higher rates in Air Force to be important. Dr. Horner replied in agreement – that using self report yielded higher risk ratios than using DoD data, noting that during times of war records are not always precise.

Dr. Steele then referenced the Weiskopf study, remarking that it did not disaggregate the study subjects by whether they deployed to the Gulf or not, whereas Dr. Horner's study did. Dr. Horner explained that Dr. Weiskopf's study did not use rates (relative risk) like his study did, adding that, in his opinion, the control group should be non-deployed military, not the general population.

Miss Hunter then expressed her interest in any relevant research related to Vitamin D deficiency with regard to Gulf War illness. Dr. Golomb responded that she would, for the third year in a row, be proposing a randomized control trial looking at Vitamin D deficiency in this population. She added that relatively little research has looked at environmental exposures and Vitamin D, but that one rodent study actually showed exposure of rodents to depleted uranium depresses Vitamin D concentrations. Dr. Golomb further remarked that Vitamin D has been shown in a range of randomized control trials to improve muscle strength, reduce pain and improve depression.

Mr. Hardie then asked Dr. Horner when the other peak in the ALS outbreak had occurred (in addition to one in 1996). Dr. Horner replied that it appeared to be in 1991 just after the conflict. He explained that there was a sudden spike and then it dropped; but cautioned that it could have just been a statistical artifact due to small numbers.

Dr. Steele then asked if Dr. Horner has looked at comparisons between this outbreak and any other identified clusters of ALS to see what may be similar, noting that she thought she had heard athletes might have higher rates of ALS. Dr. Horner replied that very vigorous exercise has been suggested as being associated with higher rates of ALS. Dr. Golomb added that a possible confounding factor in those studies could be herbicides applied to the athletic fields.

Dr. Sullivan then asked Dr. Horner to reiterate the point he made on one of his early slides regarding the consistently elevated rates of ALS found by different researchers in deployed vs. non-deployed Gulf War veterans. Dr. Golomb asked if any of the listed studies had been conducted by Dr. Robert Haley. Dr. Horner replied that Dr. Haley's studies were case-control (not population studies). Dr. Sullivan then asked if the studies on this slide had been validated by VA physicians. Dr. Horner replied that two neurologists who were experts in ALS independently looked at the medical records (all that were available) to make a determination of diagnosis.

Chairman Binns then asked Dr. Horner if he could provide any further information on the protein that he had referred to which he thinks might help ALS patients. Dr. Horner replied that he has been trying to work with a pharmaceutical company because he thinks that metallothioneins may offer a potential therapy. He explained that they have been linked to anti-inflammation and anti-oxidative developments as well as with neuro-detoxification, especially of metals. He remarked that metallothioneins are also associated with anti-apoptosis effects. He added that these proteins cross the blood-brain barrier and are taken up by the neurons in mice injected with them. In addition, excess metallothioneins are excreted in the urine. He cautioned that human studies had not yet been conducted, so this was just a hypothesis that remains to be tested.

Dr. Sullivan and Chairman Binns then thanked Dr. Horner for his presentation before Dr. Sullivan introduced the next speaker, Dr. Apostolos Georgopoulos.

Magneto-encephalography (MEG) patterns in neurological diseases

Dr. Apostolos Georgopoulos, Minneapolis VA Medical Center

Dr. Georgopoulos discussed current approaches for evaluating brain status, as well as the need for assessing dynamic brain function, before going into detail about the Synchronous Neural

Interactions (SNI) test that he has developed (See Appendix A – Presentation 7). After elaborating on the SNI test, Dr. Georgopoulos remarked that he believes it has the prospect of becoming the first routine test for assessing dynamic brain function, aiding in differential diagnosis, monitoring disease progression, and evaluating the effects of interventions by using magneto-encephalography (MEG).

At the conclusion of Dr. Georgopoulos' presentation, Dr. Sullivan asked him to talk about the differences that might be expected to be seen in the SNI tests of individuals who were medicated vs. non-medicated. Dr. Georgopoulos replied that of 18 non-medicated subjects only 1 was misclassified. He added that the outcome is only as good as the sample, which he has carefully been selecting. He added that null TBI subjects could be differentiated from subjects with PTSD using his SNI test. In addition, Dr. Georgopoulos remarked that recovered PTSD subjects (i.e. those who had undergone successful therapy interventions) presented similar patterns on the SNI test as subjects still suffering from PTSD. He added that the notable difference was that the recovered subjects had attenuated patterns (exhibiting far less deviation from the control/lower strength of response) compared to those subjects still experiencing PTSD.

Dr. Sullivan followed up by asking whether Dr. Georgopoulos thought that he could assess treatment evaluations. He replied affirmatively, remarking that this was one strength of the SNI test. He emphasized the importance of close and immediate post-treatment monitoring. He also replied that some diseases, unlike PTSD, present differently (on the SNI test images) in each individual. He said that even in these diseases careful monitoring still reveals deviations from controls, as well as changes in these deviations over time. He expressed optimism that this approach could be used by knowledgeable individuals to study individuals with Gulf War Illness.

Dr. Golomb then asked when Dr. Georgopoulos expected to have results for Gulf War veterans. He replied that he should have some by the end of the year. He said that he was about to begin a pilot study comparing 50 asymptomatic GW veterans with 50 symptomatic GW veterans. He said that if differences were detected he would then stratify the symptomatic groups and expand the cohort.

Dr. Georgopoulos then remarked that he felt his SNI test was just one tool, and that other techniques such as urine and blood testing were complementary and important in this research.

Dr. Bloom then remarked that he found Dr. Georgopoulos' SNI test to be one of the greatest demonstrations of comparing diseased brains to "normal" brains that he had ever seen. He then asked if the patterns observed in MS patients experiencing remission reverted to normal. Dr. Georgopoulos replied that he had not yet conducted a study to look at that, but that PTSD remission was observed.

Chairman Binns then asked if the breakthrough in this SNI test approach was rooted in the concept of subtracting noise using a software program. Dr. Georgopoulos replied that it was not, rather, he had developed the mechanisms underlying the test. Dr. Georgopoulos then explained that his approach is unique in that he knows how to look at the data rather than simply take time series and correlate them, which can obscure the true underlying relationships.

Dr. Steele then asked if Dr. Georgopoulos was able to tell what brain regions were affected by looking at the SNI test patterns (or "signature"). Dr. Georgopoulos replied that to localize anything using MEG one has to do many repetitions in order to derive a model. He remarked that his approach samples at very high frequencies (e.g. 1 Kilohertz), which means that each sensor has a relatively localized source. By doing this, Dr. Georgopoulos stated that he is able to detect very small changes in these integrated synaptic activities that are very much in the vicinity of each sensor. He went on to describe the affected regions observed in his PTSD subjects, noting that the signatures noticed did not necessarily reflect all brain changes associated with the disease, rather just those involving the cortex. He also expressed optimism that the SNI test could lead to successful interventions using biofeedback for some diseases, including PTSD.

Dr. Sullivan then remarked that she had heard of researchers using MRI with electroencephalogram (EEG) to obtain similar images. She asked what Dr. Georgopoulos to give his opinion on this approach. Dr. Georgopoulos replied that, as a cortical electrophysiologist, he felt MRI and fMRI were good for studying certain brain phenomena, and could be used, but that SNI test using MEG gives the best signal. He elaborated by noting that fMRI uses low frequencies (compared to the high frequencies used in the SNI test) and that EEG does not have the power comparable the SNI test due to distortion.

Dr. Sullivan and Chairman Binns then thanked Dr. Georgopoulos for his presentation before Chairman Binns called for a brief break.

The meeting reconvened at 4:00pm.

Committee Discussion: VA Gulf War Task Force Report

Chairman James Binns, Research Advisory Committee on Gulf War Veterans' Illnesses

At the beginning of this session, Chairman Binns reviewed several specific recommendations made in the draft report of the VA Task Force on Gulf War Veterans' Illnesses, hereafter referred to as the Task Force (see Appendix A – Presentation 8). Chairman Binns focused on recommendations 3A and 4A of the March 29, 2010 Task Force report draft, commenting on these recommendations with relation to those that the Committee has issued in the past.

His first request was that if the revised VA clinician training materials for treating ill Gulf War veterans (part of recommendation 3A) hadn't already been developed or printed and disseminated, that a recommendation be added to the Task Force report calling for these materials and all aspects of the proposed training program to be submitted to the Committee's Scientific Director and Staff for advisory review regarding its content as to what scientific research has shown regarding the health problems of Gulf War veterans. He acknowledged that such review would have no official standing, since it would not be reviewed by the entire Committee, but that the process would be valuable in developing the clinician training program.

Dr. Goldberg then stated that he did not know the status of the training program's development because it was being handled by another office (Clinical Care, not the Office of Research and Development).

Rev. Graves asked if someone from that office would be able to speak to the Committee in the next few days. Dr. Goldberg replied that it might be, but that he could not be sure. He added that Dr. Cassano would be the one to ask about the status of the training program, and stated that he would contact her that evening to inquire.

Chairman Binns then clarified that the background information (on Gulf War Illness) in the previous physician training program had not been current, and that this was the main concern he would like to revise in the new program. He then asked for additional comments regarding whether his proposed recommendation should be made.

Dr. Steele remarked that she was one of the individuals who had expressed concern about the previous training program, and how it did not accurate reflect the science. She supported Chairman Binns' suggestion but asked Chairman Binns to clarify who the Committee's Scientific Director and Staff (namely Drs. White and Sullivan) should issue their comments/recommendations to following their review of the materials if given the chance to look them over. Chairman Binns replied that if they had sufficient concerns they could bring them to the Committee at a public forum in order to make official recommendations, but that this would still leave open the fate of any recommendations made. Dr. Sullivan agreed that it could go to the full Committee, but remarked that this would delay the training implementation of those recommendations. She expressed interest in discussion options with Dr. Cassano if she would be willing to talk to the Committee.

Mr. Hardie then commented that although he likes the overall revisions made to the VA website he would also like to see the old clinical training guide taken down until the revisions area made because the version that is currently posted is outdated and does not reflect the recommendations made.

Dr. Golomb commented that she completely concurred, and that she would rather see no training manual than a training program that is not reflective of the evidence and therefore damaging. She then asked if anyone present knew how the personnel who were to design the new training manual were selected. Chairman Binns replied that all that was known about the process was written in the Task Force report draft, and that essentially all that was said therein was that a group had met regarding the training revisions.

Mr. Hardie expressed his support for the process Chairman Binns had laid out, emphasizing that the less lengthy and less complex it was the better.

Dr. O'Callaghan made a request that the date of the Committee's previous recommendation be specified so as to avoid ambiguity. Chairman Binns agreed that it should be more clear, adding that the Committee had discussed the issue at the November 2006 meeting and issued the recommendation several months later after fine-tuning the language.

Chairman Binns then discussed recommendation 4A from the Task Force report draft, and requested that the contract referred to therein and any other future IOM Gulf War reports be modified to specify that the IOM report be performed in accordance with the underlying 1998 statute (see Appendix A – Presentation 8). He further added that he was confident that the IOM

would do so, and was pleased that they are conducting a new study on pyridostigmine bromide and pesticides.

Dr. Steele then expressed her support for Chairman Binns' suggested changes. Chairman Binns then called for any other comments regarding the task force report before thanking the VA for soliciting and the Committee for previously submitting their comments.

Dr. Goldberg then remarked that the comments were still being processed and responded to, and that he hoped to have all of these responses and resulting changes completed by the end of the month. At Chairman Binns' request, he then offered to share with the Committee the link where all comments had been publicly posted.

Chairman Binns then called on the first contributor signed in for the Public Comments period.

Public Comment

Mr. Jim Bunker, President of the National Gulf War Resource Center, announced his organization's upcoming Health & Educational Fair for Veterans of Southwest Asia, to be held in Dallas, TX August 5-8, 2010. He remarked that Col. Gingrich would be speaking about the Task Force report on Saturday, Aug. 7, and that anyone could register and attend the meeting. Mr. Bunker then spoke about the sarin exposed veterans from the Iraq war, noting that they did not have the multiple chemical exposures that the Gulf War veterans did (namely PB, pesticides and oil well fire smoke). He also spoke about the importance of having a standard case definition for Gulf War Illness so that researchers' findings can be compared. He said that after supporting Dr. Steele's definition for several years he had decided that the standard definition should be the one used in the CFR 3.317 which defines what a sick Gulf War veteran is. He distinguished this definition as unique in that it defined GWI as lasting 6 or more months. Mr. Bunker requested that the Committee make a recommendation to ensure that any research going forward uses the exact same definitions for GWI as the CFR 3.317 (which is what veterans must meet in order to be considered for compensation). Mr. Bunker then spoke about his frustration with fighting the VA system to not skew Gulf War illness and physical ailments as psychiatric in origin or due to PTSD.

Chairman Binns then thanked Mr. Bunker and asked him to briefly discuss the specifics of the meeting in Dallas. Mr. Bunker said that speakers would include Col. Gingrich, Ross Perot, Dr. Robert Haley, Dr. Lea Steele and others. He added that further details could be found on his organization's website: www.ngwrc.org. Chairman Binns then called on Maj. Denise Nichols to speak.

Maj. Nichols, a Gulf War veteran, nurse, and member of the audience, spoke about the disconnect between the clinicians and researchers. She encouraged the VA to work harder to get information out on current research being done as findings emerge. She also called for more case reports from VA doctors, suggesting that the Committee make a recommendation that emphasizes the importance of case reports in Gulf War Illness research. Maj. Nichols suggested that an electronic bulletin board be created that would be accessible to clinicians and researchers within and outside of the VA system who are working with or treating Gulf War veterans. She

ended her comment with a memorial to a recently deceased general who had helped veterans with ALS get service connection from the VA.

Chairman Binns took the opportunity to also acknowledge the passing of Senator Byrd, who he noted had contributed a great deal to the Gulf War veterans' cause by authoring the 1998 legislation that set up the Committee and also the IOM reviews.

Ms. Alison Johnson then spoke about a case of a man she knew had survived 15 years with ALS. She remarked that he was chemically sensitive and had been living a "relatively pristine life" near the ocean, spending much of his time outdoors. She postulated that Vitamin D could be part of the reason for his prolonged survival, and said she also wondered if avoidance of further chemical exposures may have contributed to his diminished degeneration. Ms. Johnson then thanked the Committee for all the contributions they had made to the field of Multiple Chemical Sensitivity (MCS) in the past ten years. She also said that she had copies of her book to give to Committee members if they did not already receive one, and recommended that people read the chapter on the Exxon-Valdez oil spill, given the current conditions in the Gulf of Mexico. She added that unlike many of the unprotected workers sent to clean up that spill, many of the individuals cleaning up the Gulf of Mexico would already have faced exposures to oil and/or formaldehyde from FEMA trailers (both resulting from Hurricane Katrina). These previous exposures would likely put them at risk for having chemical sensitivity.

Chairman Binns then concluded the day's proceedings at 4:39pm.

DAY 2

At 8:35am Dr. Sullivan began the meeting by introducing the first speaker of the day, Captain Melissa Kaime.

CDMRP Gulf War Illness Research Program Update

CAPT Melissa Kaime, Congressionally Directed Medical Research Program

CAPT Kaime began her presentation by providing an overview of the Congressionally Directed Medical Research Programs (CDMRP), then discussed the Gulf War Illness Research Program (GWIRP) funding history, and concluded with a summary of the FY06-FY10 CDMRP management and request for proposals from investigators present at the meeting and their colleagues (See Appendix A – Presentation 9).

At the conclusion of CAPT Kaime's presentation Dr. Sullivan and Chairman Binns thanked CAPT Kaime, and Chairman Binns expressed appreciation for CAPT Kaime's encouragement of new researchers to enter the field and apply for CDMRP funding.

Mr. Hardie, who in addition to being a Committee member has been a Consumer Reviewer on the integration panel for the last few years, then thanked CAPT Kaime and her team- including other consumer reviewers and scientists who sit on the CDMRP scientific merit review board, for the work they have put into the CDMRP on behalf of Gulf War veterans. CAPT Kaime thanked Mr.

Hardie for his gratitude, and in turn expressed appreciation for all that Dr. Melissa Forsythe, Director of the GWIRP, has done as well.

Chairman Binns theen thanked CAPT Kaime once more before calling for a brief break prior to the arrival of VA Chief of Staff John Gingrich, who Chairman Binns introduced at 9:12am.

VA Gulf War Task Force Report

Mr. John Gingrich, Chief of Staff of the Department of Veterans Affairs

Mr. Gingrich began his presentation by encouraging VA clinicians and others working with veterans to take on a mindset of advocacy and compassion for the experiences each veteran carries. He then reviewed the April 1st release of the Task Force report draft and consequent feedback, remarking that he thought it garnered the largest amount of public comment the VA had received to any posted proposal to date. Mr. Gingrich estimated that during the public comment period (April 1-May 3) the VA had received 150 formal comments, with 28 written responses submitted, in addition to 300 voice web comments and 2,100 votes on the different items. He added that he had personally read every comment that had come in, and was in the process of going through to read each submission a second time. Mr. Gingrich emphasized that the current version of the report is not the final version, but that he would expect the final report to be submitted to the Secretary in August.

Mr. Gingrich then spoke about the IOM Volume 8 report on Gulf War Health, remarking that it had been received, the Secretary of the VA had made his determination within the 60 day deadline, and that the VA was currently in the process of making notifications internally in anticipation of the full 120 day deadline by which the VA has to make an announcement as to where they are headed with regard to the Volume 8 report. Mr. Gingrich then remarked that he was pleased that the Volume 8 report publicly (though not officially) stated that undiagnosed and unexplained illnesses were real. He also expressed appreciation that, in his opinion, the Volume 8 report substantiated what the VA was doing with regard to PTSD – namely that veterans should receive service connected benefits for PTSD triggered by service-related stressors beyond the realm of combat. Mr. Gingrich expressed his belief that the Volume 8 report would be released in the next 60-90 days.

Mr. Gingrich then mentioned the upcoming testimony on Gulf War Illness, remarking that he and the other members of the panel plan to focus on how to provide the necessary care and services to ill veterans. He also remarked that the VA had agreed to attend the August 2010 Gulf War reunion in Dallas, and that he would be there with a team of people who will be able to help veterans learn about and register for benefits. Mr. Gingrich then spoke about the Secretary's assertion that by 2015 no veteran's benefits claims will exceed 125 days, with a 98% accuracy rate. He then announced that later that day the VA would be releasing a pilot program whereby veterans who walk into one of three regional offices with their complete claims papers will be able to walk out that same day with their claim processed. He added that later in the week the VA would also be announcing a contract for a totally automated claim processing procedure to be piloted for ill veterans affected by Agent Orange that will allow veterans to go to a website, fill out an application, access an electronic medical form for one of the presumptive conditions, and get a doctor (including doctors outside the VA system) to fill out and submit that electronic medical form (or do so in hard copy). He stated that this would create a totally electronic claims process with a turnaround time of less than 60 days.

Mr. Gingrich explained that this was just one of 28 new initiatives being piloted in the VA system. He then opened the floor for questions.

Chairman Binns thanked Mr. Gingrich and then expressed his appreciation for Mr. Gingrich's request to be personally briefed by Dr. Stephen Hauser, the chair of the committee that wrote the IOM report, on the Volume 8 report findings. Chairman Binns then remarked that he had been encouraged by a conversation he had recently had with Dr. Hauser, who had told him that he believed research into Gulf War Illness was not only important work, but that answers could likely be found.

Col. Marguerite Knox, a member of the Committee who is also a nurse practitioner in the South Carolina Army National Guard, thanked Mr. Gingrich for his efforts working with the VA. Mr. Gingrich replied that he is just part of a larger system of people who are all trying to come together to streamline the process between the Veterans Health Administration (VHA), Veterans Benefits Administration (VBA), General Counsel and the Board of Veterans Appeals. He explained that the VA had already begun pilot programs on three service connected illnesses for the automated claims process he described (Parkinson's disease, ischemic heart disease and hairy cell leukemia), and that the goal was to expand this to 67 illnesses by the end of the year. Another change Mr. Gingrich said had recently gone through was that physical exams of veterans no longer required two clinicians' signatures (just one would be sufficient).

Mr. Hardie then thanked Mr. Gingrich for his efforts to improve communication and collaboration between the different branches of the VA. He also asked if Gulf War Illness, as an undiagnosed condition, would be one of the 67 illnesses for which Mr. Gingrich hopes to have automated claims processing up and running by the end of the year. Mr. Gingrich replied that he did not know but that he hoped so and would look into it. He added that certain conditions (such as PTSD) could not be done in this way because of the inability to use a simple checklist for the claim process.

Mr. Hardie then expressed his concern with the service connection benefits associated with some of the combinations of conditions common to ill Gulf War veterans – namely fibromyalgia, irritable bowel syndrome and chronic fatigue syndrome. He explained that veterans with chronic fatigue syndrome could receive up to 100% disability, but that the maximum for irritable bowel syndrome is 30%, and for fibromyalgia it is 40%. Mr. Hardie continued, remarking that fibromyalgia preempts chronic fatigue syndrome in the Oklahoma VA system for veterans diagnosed with both conditions, meaning that veterans in this region (such as himself) only receive 40% service connection instead of 100%. Mr. Gingrich replied that this did not make sense to him, and Mr. Hardie agreed. Mr. Bunker then commented that the level of service connection varied across the regional offices. From his experience working with veterans all over the country he attested that while some regional offices lump everything together under fibromyalgia, as Mr. Hardie has experienced, others give 40% for fibromyalgia and another 40-60% for chronic fatigue.

Mr. Gingrich then explained that he is working on clarifying the understanding of the language of undiagnosed illness, and understanding the service connection breakdown for veterans with multiple illnesses that each have different service connections. He emphasized that he feels strongly that the VA needs to make sure it doesn't disadvantage the veterans. Mr. Hardie replied that the problem did not have to do with the VA formula, and that the Social Security Administration had approved his

claim, adding that the issue was larger than just his personal case. Mr. Gingrich replied that he would get to the bottom of it, and that by working through Mr. Hardie's case he and the VA staff would learn things that could be applied universally to improve the system.

Rev. Graves then thanked Mr. Gingrich for his efforts, particularly his willingness to work with doctors and veterans to figure out all of the different service connections that exist among the ill Gulf War veterans, many of whom suffer from overlapping undiagnosed and neurological diseases which manifest differently in different people (thus making assigning levels of service connection a challenge). Mr. Gingrich thanked Rev. Graves and explained that the veteran must be kept at the center of the focus and that the VA would continue to work on the challenging issues he mentioned.

Maj. Nichols then thanked Mr. Gingrich for all that he is doing, before requesting that the VA recognize the importance of working on providing in-home aid for the many ill Gulf War veterans who are in need of such services. She also re-emphasized the importance of improved means of electronic communication between clinicians and researchers. She requested that a short piece of Mr. Gingrich's Committee briefings be shown on the VA weekly news address in order to show other vets that there is a movement forward which they can be a part of. Mr. Gingrich then explained that the VA is working on adding a data field to Vista that will allow veterans to electronically self-identify the conflicts in which they were involved in their electronic medical records, which would be accessible to clinicians. He noted that this program would be tested first in the Desert Shield/Desert Storm veterans.

Mr. Bunker then commented on the issue of service connection that he and Mr. Hardie had presented to Mr. Gingrich earlier. Mr. Bunker stated that he felt it was time for the VA to do as the Social Security Administration had recently done and upgrade the fibromyalgia service connection percentage to 100%.

Ms. Angela McLamb, a Gulf War veteran from the audience, then asked Mr. Gingrich when the clinicians would be trained regarding current Gulf War illness research. She noted that her 2 doctors had asked her when and how they could receive training from the VA. Mr. Gingrich replied that the process would start this summer, beginning with environmental exposure training at conferences and training events. He then asked Dr. Victoria Cassano to provide the details. Dr. Cassano explained that at the end of July exposure evaluation training would be done with primary care doctors, environmental health clinicians and other interested individuals in Indianapolis, IN and then Portland, OR. She explained that the training would not only involve issues of burn pits and sand storms, but also sodium dichromate and several other issues. She also stated that the VA hoped to repeat the training four times next year.

Mr. Hardie then asked if Mr. Gingrich had a staff person that Ms. McLamb might be able to talk to about a significant personal issue that she needed to have addressed. Mr. Gingrich recommended that she speak to several of his staff members who were present in order to get the issue worked out. Mr . Hardie thanked Mr. Gingrich, then Chairman Binns asked everyone to join him in thanking Mr. Gingrich as he had to leave for another meeting. Before departing, Mr. Gingrich acknowledged the 300,000 employees and 800,000 volunteers that were working to make the VA more of an advocacy organization for veterans. Chairman Binns then introduced the next speaker, Dr. William Goldberg.

Update of VA Gulf War Research RFAs

Dr. William Goldberg, VA Office of Research and Development (ORD)

Dr. Goldberg began by telling the Committee that the 13 submissions to the VA Request for Applications (RFAs) had been reviewed the previous week, and that funding decisions had been made, though formal results of the reviewing process had not been released, and none of the investigators had been notified of whether they had been selected for funding. He told the Committee that the VA planned to probably fund three of the 13 submissions (a 23% funding rate). He mentioned that a fourth proposal was highly scientifically valid but that it did not meet the criteria for funding any of the 3 RFAs, so would be recommended for resubmittal to a different RFA. Of the 3 proposals that were approved for funding, two were small clinical trials for new treatments, and the other was an animal study focused on developing new treatments – thus it was a pre-clinical new treatment trial. Dr. Goldberg also stated that the RFAs would be reissued, virtually unchanged except for the textual changes recommended by the Committee in March. He said that once they were ready the reissued RFAs would be posted to the ORD website and sent directly to all VA research offices with instructions that they be disseminated to individual investigators, as usual.

Dr. Goldberg's presentation was accompanied by several handouts (See Appendix B), including a roster of the committee that reviewed the 13 proposals (Appendix B – Document 1). He commented that many of the individuals on that committee have published in the Gulf War literature, and that the VA was very careful to ensure that there was good representation on the committee so that proposals could be chosen on the basis of their relevance to Gulf War veterans' health research, not just whether they posed interesting scientific questions. Other documents that Dr. Goldberg circulated included the 2009 and 2010 currently funded Gulf War research portfolio (See Appendix B – Documents 2-3). He remarked that in addition to the studies listed therein, Dr. Georgopoulos had a pilot project that was not yet included on the list. He expressed hope that the 3 new projects that had just been reviewed could be started this fiscal year. As such, he expected to be seeing several new projects added to the portfolio list for 2010.

Regarding the 2009 portfolio, Dr. Goldberg mentioned that there was close to $7 million on the books for the ongoing approved projects contracted to University of Texas Southwestern (UTSW). He explained that at least another $650,000 would likely be spent on the UTSW contracts due to the significant amount of closeout costs for finalizing, data management and data transfer of all their findings. As such, Dr. Goldberg explained that none of the previously approved projects under contract with UTSW were terminated early, rather, he stated, the VA had simply stopped accepting new task orders.

The last document Dr. Goldberg addressed was a page from the draft Task Force report that accounts for all historical funding, in order to put each annual funding expenditure into perspective (see Appendix B – Document 4). Dr. Goldberg then opened the floor to questions.

Mr. Hardie thanked Dr. Goldberg, specifically for listening to the Committee's previous requests and changing the funding listed under Gulf War for Dr. Weiner's 4 Tesla Magnetic Resonance Imaging (MRI) system such that only $5 million of the total $11 million in funding for the

equipment was slotted under "Gulf War" funding. He remarked that despite this improvement, $5 million was still the preponderance of the total $7.4 million funding for the year.

Dr. Goldberg responded that this change had been finalized and would not be changed again. He added that the VA would monitor and ensure that Dr. Weiner was using that portion of his time to research new Gulf War projects. Dr. Golomb then expressed her doubt that Dr. Weiner's Gulf War projects would amount to $5 million worth of time. Dr. Goldberg then asserted that more service-directed projects would be coming on board for the 2010 budget, mentioning that Dr. Bloom currently was sitting on a planning committee for one such project. Chairman Binns then asked Dr. Goldberg to elaborate on that project, if possible. Dr. Goldberg explained that Dr. Bloom was participating in the planning committee for a new Cooperative Studies Program (CSP) project that will marry the genome-wide association study with the next surveillance study, thereby creating what he thought would be the largest national cohort for research purposes.

Mr. Hardie then asked to continue his question. He stated that he had some significant concerns about the methodology Dr. Weiner was using to select veterans who were exposed to sarin versus those who were not. He also expressed concern that Dr. Weiner's results at the lower imaging level (1.5 Tesla) did not reproduce the results of the higher level (4.0 Tesla). As such, Mr. Hardie requested that the VA ORD exert close oversight of Dr. Weiner's methodology.

Mr. Hardie also expressed discontent with inclusion of Dr. Dane Cook's study in the Gulf War research category since it had included veterans of the current Iraq war (not just the 1991 Gulf War veterans). He explained that this has been an issue of concern to the Gulf War veterans which he has consistently raised questions about. Mr. Hardie then clarified that he agrees with the importance of the research that Dr. Cook was doing, but that he felt trouble with recruitment was at the heart of the matter. Mr. Hardie explained that he wanted to be sure recruitment was being done correctly, and that he or others could possibly help with developing a "how to" list on how to recruit study participants (as he had in the past when he was still working with the state veterans agency). Dr. Goldberg replied that the trouble with recruitment usually stemmed from Institutional Review Board (IRB) restrictions. Dr. Goldberg explained that veterans interested in getting involved in research should go to clinicaltrials.gov, where all government-funded clinical trials were listed, noting that they were open for recruitment.

Dr. Golomb then commented that she is currently working on a write-up of her recruitment experience for Gulf War veterans (including obstacles and solutions) and she expressed great interest in working with Mr. Hardie to get his input in order to create a product that could be widely disseminated to anyone interested in recruiting Gulf War veterans. Dr. Goldberg expressed support for this initiative, adding that one of the things he hopes will come out of the genome-wide association study is a national cohort that will hopefully be able to be tapped into by investigators in future sub-studies. Dr. Goldberg also remarked on the difficulty of researchers returning again and again to the same small cohort of individuals, noting that often the response rate from veterans will decrease over time. Mr. Hardie then commented on an approach that had worked in a study which he had participated in. As an ill Gulf War veteran participating in the study, he had voluntarily agreed to be interviewed by the media, to discuss the study and give information about how other interested veterans could get involved. Mr. Hardie encouraged Dr. Goldberg to consider working with Public Affairs on that type of approach.

Chairman Binns then suggested that the new IOM report may offer a chance to re-energize both the research community and the veteran participants. He stated that he was alerting members of Congress who were involved in funding CDMRP about this, noting that it was an urgent need that fulfills a national mission.

Dr. Goldberg then remarked that he had one more update for the group. He said that he had conversed with Dr. Fiore the previous week and that discussions with their IRB about opening and announcing the brain bank operation for Gulf War veterans had begun. Dr. Goldberg expressed hope that by the next meeting (in November) there would have been some movement on that front.

Dr. Sullivan then remarked that she believes that she and her colleagues in Boston have had success recruiting Gulf War veterans in Boston over the years largely due to the personal touch they had kept with the veterans over time.

Dr. Steele then asked Dr. Goldberg to talk a bit about the planning group that Dr. Bloom is on, and whether the cohort to be recruited would all be Gulf War veterans, and how the study/studies of the cohort would be directed. Dr. Goldberg replied that the cohort would consist completely of Gulf War veterans, and that Dr. Bloom could explain further. Dr. Bloom then described the group as a cooperative study planning program, with one of the investigators in Florida taking the lead as the "principal proponent." He explained that it was still in the planning stages, and that he was brought in as a critic, and that since making comments three and a half weeks previously he had not seen any further drafts, which left him uncertain of when and how the planning process would be completed. He explained that one of the main goals was to develop a large cohort which could be used, among other things, by the principal proponent to develop a genomic and proteomic analysis that might distinguish causative or adaptive features of Gulf War Illness that might possibly lead to the development of treatments. Dr. Bloom added that the program was still in its preliminary stages, and that the cadre of investigators who would participate hadn't been identified.

Chairman Binns expressed his support for Dr. Bloom's involvement, and also mentioned that he also hoped the 2,000 blood samples from the UTSW program which Dr. Bloom had helped review would not go to waste.

Maj. Nichols then recommended to Dr. Goldberg that a mechanism be created by which the Gulf War veterans who participate in studies such as Dr. Cook's could provide feedback as part of the evaluation process going forward.

Chairman Binns closed then remarked on how many of the researchers who had presented to the Committee the previous day had been funded by the VA through the 2005 RFA, which was the first year that Dr. Goldberg was involved in the process. Dr. Sullivan then expressed her support for the Gulf War brain bank. Dr. Goldberg then apologized that it had taken so long to expand the brain bank beyond ALS patients, and that efforts were currently being made to be able to expand it to include other organs. He added that the VA would be monitoring the process very closely. Dr. Sullivan added that she felt the investment in neuroimaging alongside brain banking would shed a lot of light on the whole field. Mr. Binns then thanked Dr. Goldberg and called for a break. The meeting resumed at 10:44am with the annual federal advisory committee ethics training.

Federal Advisory Committee Ethics Training

Mr. Jimmy Dubois, VA Office of General Counsel
Ms. Ann Kopley, VA Office of General Counsel

Mr. Dubois provided the ethics training, which included briefing on conflicts of interest, representational activities, gifts, misuse of position, teaching, speaking and writing activities, fundraising, political activities and rules that may apply after individuals have left the Committee. At the conclusion of the ethics training Chairman Binns welcomed Dr. Joel Kupersmith to present on the progress of the VA Gulf War Research Program.

VA Gulf War Research Program Development

Dr. Joel Kupersmith, Chief Research and Development Officer, Dept. of Veterans Affairs

Dr. Kupersmith began by providing an overview of the members and recent organizational meeting of the Gulf War research program steering committee, of which Dr. Max Buja of UT Houston is the chair (See Appendix C – Documents 1-2). He explained that four of the steering committee's members were chosen by the VA and the other four were selected by the Committee. Dr. Kupersmith explained that the steering committee would report through the Gulf War Research Advisory Committee, as well as the National Research Advisory Council, and that it would look into matters related to integration of Gulf War research programs, and conduct analyses and develop reports as necessary. Dr. Kupersmith explained that the recent steering committee meeting involved a review by Dr. O'Leary of the recent Gulf War publications, the IOM report, the Committee's 2008 report, and some other reports, as well as time spent discussing the CSP cohort. Dr. Kupersmith said that the steering committee's next meeting would be in the fall, then opened the floor to questions.

Chairman Binns explained that Dr. O'Callaghan, who also sits on the steering committee, had needed to leave 15 minutes ago due to an emergency, but that he had informally mentioned that he thought the preliminary meeting had been good. Dr. Kupersmith then remarked that a hearing was also coming up. Chairman Binns expressed his appreciation for Dr. Bloom's inclusion on the planning committee for the new CSP program. Dr. Kupersmith asked if the roster for that planning committee had been discussed already and Dr. Goldberg replied that it had not. Dr. Kupersmith then expressed his belief that official steering committee coordination with CDMRP and others would be an important consideration. Dr. Kupersmith asked Chairman Binns to reflect on that. Chairman Binns said that informally the Committee has accomplished that by having two people that currently sit on both review bodies – Dr. White and Mr. Hardie. He added that the Committee had wanted someone on the steering committee who had a background in genetics and that Dr. Christiani filled that role nicely, as he is an expert in the genetic aspects of environmental and occupational health issues.

Mr. Hardie then thanked Dr. Kupersmith and recommended that he include an article in the next Gulf War Review about the creation of the steering committee, for the sake of transparency for the stakeholders. He also asked if their might be some means for Gulf War veterans to contact or

submit comments to the steering committee. Dr. Kupersmith said that additional suggestions from the veterans would be welcomed.

Dr. Sullivan then asked if Dr. Kupersmith could provide additional details about the expansion of the brain bank beyond ALS patients. Dr. Kupersmith said that he didn't have the information with him, but that he felt the steering committee should be thinking about that. Dr. Sullivan agreed, remarking that the established cohorts of Gulf War veterans would be an easy place to start recruiting from for the longitudinal cohorts.

Chairman Binns asked if Dr. Kupersmith could elaborate on the plans to bring in a program manager, and how that person would interface with or within ORD. Dr. Kupersmith explained that this person would be in ORD, reporting directly to himself and Dr. O'Leary. He added that this individual would be a toxicologist who would be hired through the normal VA hiring procedure. Dr. Goldberg then explained that he would likely continue on as the Designated Federal Officer (DFO) for this committee, but that the new toxicologist to be hired would hopefully take on the duties of managing the portfolio. Dr. Kupersmith added that eventually the new toxicologist might be the DFO. Dr. Goldberg added that any such transition would be a slow and gradual one. Dr. Kupersmith then stated that he saw the main parts of the job to be the management of the portfolio and the interaction with the steering committee, as well as interaction with the CSP project planning committee. He added that it would not just be for Gulf War but for exposures in general, including Iraq war exposures. The floor was then opened to questions from the audience.

Ms. Alison Johnson asked if Dr. Kupersmith was looking into the exposures that the National Guard troops were facing in the current Gulf of Mexico oil spill. Dr. Kupersmith replied that he had not thought about it but that it was worth thinking about for the future.

Chairman Binns said that he was delighted to hear that the managerial person would have a broad focus. Dr. Kupersmith remarked that he believed this was on the mind of the IOM when they wrote their recommendations, and that Gulf War veterans would provide a cohort that enables it to be studied, but that its implications were broader.

Miss Hunter stated that she thought there would be value in researching the chemical exposures occurring among members of the military and others cleaning up the oil from the beaches in the Gulf of Mexico. Dr. Kupersmith agreed that there could be value in studying those exposures. Maj. Nichols commented that many of the National Guard were capable of using the VA system, and that the lesson learned from the Gulf War about getting baseline information from individuals involved in the cleanup should be applied. Dr. Kupersmith replied that that would need to happen at the state level. Maj. Nichols said that there needed to be some high level coordination.

Chairman Binns then thanked Dr. Kupersmith for coming to speak to the Committee before beginning his presentation on the new IOM report.

Committee discussion: Institute of Medicine (IOM) Gulf War report

Mr. Jim Binns, Chairman, Res. Advisory Cmte Gulf War Illnesses

Chairman Binns presented several key findings from the Volume 8 IOM report, which was still in draft form at the time of the meeting (See Appendix A – Presentation 10). After reviewing these excerpts, Chairman Binns remarked that he found it reassuring that a group of people assembled by the IOM would so strongly be advocating a national program that included but also extended beyond VA investigators to tap into the best researchers available.

Dr. Meggs then remarked that he applauded many parts of the IOM report, but that he felt the evidence supporting the role of organophosphates and PB in Gulf War illness should have been recognized by the IOM committee. Chairman Binns asked if Dr. Steele had any thoughts on the matter. Dr. Steele responded that she had not read that section of the report but that she did not see the basis on which the IOM committee was not agreeing with the Committee's causality findings. She further commented that it was very difficult for the IOM to ever assign causality to anything, especially because they base such findings only on human studies, whereas the Committee teased out the conflicting findings from the human studies and integrated these with all the other kinds of evidence. She further remarked that the IOM wasn't charged to look at the exposures and their association, so they had not given it much space. She said that she did not know why the IOM committee did not agree with the strong association between Gulf War illness and exposure to pesticides and PB, but that she was aware that the VA had commissioned a new report specifically to look at that issue.

Dr. Sullivan then remarked that the Committee had been working hard to have people come to talk about this issue and educate everyone about the host of literature on these topics, which she hoped the IOM committee would look at in detail.

Dr. White then asked if Dr. Steele thought that part of the reason may have been that the IOM committee was very critical of the size of the cohorts for the epidemiological studies of chemical exposure relationships. Dr. Steele asked if the IOM committee had said that specifically, since some of the cohorts were large. Dr. White replied that, to her surprise, the IOM committee had said that the cohorts weren't representative of the whole – of all of the deployed forces – rather that they were representative of sub-groups. Dr. Sullivan commented that it seemed to her that the rules governing the IOM committee were such that they can only state causation when it is essentially obvious, whereas the Committee could come to a conclusion regarding causation that was not restricted by such stringent criteria. Dr. Golomb then remarked that she had been one of the early proponents of acetylcholinesterase inhibitors as a potential causal factor, but that she was not persuaded that they were the only factor.

Mr. Hardie then commented that is appears to him that the IOM report is a review of the published literature, whereas the Committee also reviews current research studies that have not yet been published, and asked whether this was an accurate interpretation. Dr. Steele agreed with Mr. Hardie's distinction. Dr. Sullivan added that there can be significant lag time between when research is conducted and when it is published, and that the Committee tries to get researchers to come present as early as possible following their discovery of relevant results. Dr. Steele added that the reason to only look at published research was that it had been through peer review. She

explained that the Committee's strategy had been to see if all the different kinds of research hung together, so that they would never rely on unpublished research. Dr. Sullivan explained that the growing body of evidence (compared to the vacuum of information in general when the Committee first began its work) was encouraging.

Chairman Binns then remarked that the Committee could decide whether they felt it would be worth writing a small piece to distinguish the differences between their 2008 report and the IOM's recent (volume 8) report, after Dr. Steele had a chance to read the IOM report more deeply. Dr. Steele said she found Chairman Binns' summary of some of the IOM report's key findings (see Appendix A – Presentation 10) very compatible with the history of what the Committee has found about Gulf War Illness. Chairman Binns responded that when Dr. Hauser gave his summary and briefing of the IOM's recent report those were the points that he emphasized.

Before beginning the public comment period Chairman Binns asked if Dr. White, who was participating by phone, had any additional comments she wished to add, but she did not.

Public Comment

Ms. McLamb, a member of the Army National Guard for 22 years, began the public comment session by describing her personal experience of getting ill a week and a half after receiving the anthrax vaccine in Saudi Arabia, at the time when the nerve agent plume from Khamisiyah was in the air, from which point on she claimed her health had never been the same. She explained that the only diagnosis her doctors could give her was chronic fatigue syndrome. Ms. McLamb then expressed her frustration at the inaccuracies in the DoD records, which do not have her unit's correct location at the time of the Khamisiyah plume. She also remarked that she had suffered from PTSD due to trauma experienced while she was on duty in 1981, prior to the Gulf War, and that her illnesses during and following the Gulf War were not due to PTSD. Ms. McLamb also made the recommendation that clinicians need to receive more training on Gulf War illness – and be notified in advance when training is going to be available, and that clinicians should remember to treat Gulf War veterans with respect. Ms. McLamb also recommended to other ill veterans that they keep notes between their doctor's visits that they can type up and bring to their clinicians. She said that her doctors had been appreciative of this, and had recommended that she advise other veterans to do the same. Ms. McLamb also brought up the need for increased research into women's health issues in the context of the Gulf War. Ms. McLamb concluded by thanking the Committee for all that they do.

Ms. Johnson then commented on the importance of keeping the issue of multiple chemical sensitivity (MCS) in mind when considering Gulf War Illness and other exposure-related illnesses. She explained that it was not uncommon for individuals with MCS to feel violent or suicidal when re-exposed to certain chemicals. Ms. Johnson also recommended that close follow-up be done on individuals who had undergone the doxycycline trial because doctors (she cited Dr. Chaney) had claimed that anyone taking an antibiotic like doxycycline for 6 months would be "a gut cripple for the rest of their life." She recommended looking into this in the cases of irritable bowel syndrome that were arising in Gulf War veterans. Ms. Johnson concluded by speaking about a Center for Disease Control (CDC) document that had been leaked which

mandated a fragrance-free workplace for all of the CDCs in the country, plus control of pesticides and cleaning products. She explained that this might enable many ill Gulf War veterans (with MCS) to keep their jobs, simply by having the CDC document on hand to show their employers. Dr. Golomb responded by saying that it might be a good recommendation for VA hospitals to also become fragrance free. Ms. Johnson agreed, adding that the CDC's 13 page policy document could be found on her Chemical Sensitivity Foundation website under Fragrance Issues. Dr. Golomb then commented that there is evidence from one study suggesting that Gulf War veterans who were exposed to pesticides have a twelve-fold increased risk of multiple chemical sensitivity. Dr. Golomb then recounted a case she was aware of where a woman had been exposed to pesticides after her home had been treated twice for pests, after which she had experienced severe weakness, muscle frasciculations and a range of neurological problems – in addition to violent suicidal ideation (which she had never had in her life prior to that exposure to pesticides).

Maj. Nichols then thanked the Committee for their continued dedication to the Gulf War veterans, and called on the Gulf War veterans present and listening in to keep their faith and to keep fighting for themselves and their comrades.

Chairman Binns then thanked Maj. Nichols and the other members of the audience for their comments. Dr. Sullivan then thanked the invited speakers for taking the time to come share their findings, especially those who had not yet published the research they spoke about to the Committee. Mr. Hardie took a moment to acknowledge the activists in the audience – namely Maj. Nichols, Mr. Steve Robinson, Mr. Donald Overton, and Mr. Jim Bunker for their continued participation and advocacy. Mr. Bunker then remarked on Mr. Gingrich's dedication to the veterans, and also thanked the members of the Committee for their hard work. Chairman Binns then brought the meeting to a close at 12:32pm.

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