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6/16/2003 → 4/20/2015

PUBLIC COMMENT SUBMITTED TO THE

VA RESEARCH ADVISORY COMMITTEE ON GULF WAR VETERANS' ILLNESSES

I request that this committee make it a priority to review the published findings and current status of VA-funded research into the role of:

1) <u>MULTIPLE CHEMICAL SENSITIVITY</u> (MCS) in Gulf War Syndrome, and the degree to which VA has incorporated these research findings into its programs for education of Gulf War veterans and physicians, medical care and compensation.

If you do so, you will find that FIVE years after VA researchers (Kang et al) first announced at the 1998 International CFS Conference in Boston that MCS was the single most common diagnosis among deployed Gulf War (1) veterans (afflicting 15%, over 100,000), the VA has not yet expanded its MCS research and has not yet begun to diagnosis, treat, code or even screen Gulf War veterans for MCS in its Gulf War Registry or other clinical programs. VA also has never explained its neglect of MCS. But more than neglect is involved: Gulf War vets given an MCS diagnosis by non-VA physicians still find that VA denies their requests for MCS treatment and compensation. Please ask the VA why!

In comparison, the VA has recognized both by CFS and Fibromyalgia as Gulf War service related since 1998 (and thus compensable based on disability), even though their COMBINED prevalence among Gulf War veterans is less than that of MCS.

2) <u>CARBON MONOXIDE POISONING</u> (CO) in Gulf War Syndrome, and the degree to which VA has incorporated these research findings into its programs for education of Gulf War veterans and physicians, medical care and compensation.

If you do so, you will find that the VA has not funded any studies on either the CO levels or CO health effects that Gulf War veterans may have encountered from various types of CO exposure in the Gulf. CO levels in various military occupations could be easily measured by winder for having troops wear small datalogging CO detectors –they cost under \$600 while conducting live fire exercises (especially from inside ships and vehicles), driving vehicles, sleeping inside heated but unvented tents, etc. Such CO exposures were ubiquitous in the first Gulf War. The failure to consider CO is astounding given that all the reported symptoms of GWS are all also symptoms of CO poisoning, including MCS and particularly multi-sensory sensitivity (to previously tolerated levels of smell, light, sound, flavors, hot weather, and touch), which is a CO hallmark. Even though oxygen is the standard treatment for CO poisoning, and even though VA has funded studies showing veterans have impaired oxygenation of their brains and blood, VA has never researched or offered O2 treatments to Gulf War vets with CO symptoms. Please ask the VA why!

Reviews written by VA researchers of literature on similar post war syndromes prior also never mention CO, but CO was first associated with shell shock and neurasthenia in The Lancet in 1916 (Feb 12, 331-8), and acknowledged there as a significant battlefield toxin by no less an authority than the director of the British Army's Trench Warfare Department.

Note that of all VA researchers, only Dr. Virginia White of the Boston VA Environmental Hazards Research Center has published on both MCS (in Gulf War veterans) and CO poisoning (in civilians) but only separately, without acknowledging any connection between them.

Please ask her why!

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1 paper in PubMed discusses Carbon Monoxide exposure as a possible cause of Gulf War Syndrome (2004)

Emmerova M1, Jirava F., Med Confl Surviv. 2004 Jul-Sep;20(3):209-17. Is Gulf War Syndrome really a mystery? Since the end of the 1991 Gulf War about 20,000 United States veterans and similar proportions of troops from other allied contingents have been affected by a variety of symptoms which have collectively become known as 'Gulf War Syndrome'. Similar symptoms have been reported in Iraqi civilians including children. Despite extensive investigations no agreement has been reached on whether there is an underlying cause or causes. In this article, the principal features of the illness are summarized and some of the proposed causes discussed. It is proposed that the common cause is the toxic smoke from incomplete combustion of oil from burning wells, and this hypothesis is related to the known toxicology of two likely combustion products, nitric oxide and carbon monoxide. The effect of this proposal on possible investigations and treatment is considered.

15 papers in PubMed discuss high prevalence of Multiple Chemical Sensitivity in Gulf War veterans (1996-2008)

- 1. Ciccone DS1, Weissman L, Natelson BH. J Health Psychol. 2008 May;13(4):529-36. doi: 10.1177/1359105308088525. Chronic fatigue syndrome in male Gulf war veterans and civilians: a further test of the single syndrome hypothesis.

 Different modes of fatigue onset in male Gulf War veterans versus male civilians raise the possibility that chronic fatigue syndrome (CFS) may not be a single disease entity. We addressed this issue by comparing 45 male veterans with CFS to 84 male civilians who satisfied identical case criteria. All were evaluated for fibromyalgia (FM), multiple chemical sensitivity and psychiatric comorbidity. CFS was more likely to present in a sudden flu-like manner in civilians than veterans (p < .01) and comorbid FM was more prevalent in civilians (p < .01). These findings question the assumption that all patients with CFS suffer from the same underlying disorder
- 26. Systematic review of multi-symptom conditions in Gulf War veterans.

 BACKGROUND: Gulf War veterans have a number of health complaints. We therefore decided to carry out a systematic review to identify and summarize the findings from studies that have assessed multi-symptom conditions in Gulf War veterans and in an unexposed comparison group. METHOD: Studies published between January 1990 and May 2004 were identified by searching a large number of electronic databases. Reference lists and websites were also searched and key researchers were contacted. Studies were included if they compared the prevalence of chronic fatigue syndrome, multiple chemical sensitivity, CDC-defined chronic multi-symptom illness, fibromyalgia, or symptoms of either fatigue or numbness and tingling in Gulf War veterans and non-Gulf veterans. A total of 2401 abstracts were independently reviewed by two authors. RESULTS: Twenty-three publications fulfilled the inclusion criteria. Gulf deployment was most strongly associated with chronic fatigue syndrome (OR 3.8, 95% Cl 2.2-6.7). Gulf War veterans were also approximately three and a half times more likely than non-Gulf veterans to report multiple chemical sensitivity or chronic multi-symptom illness as defined by CDC. The methodological quality of the studies varied but the later and larger studies were of a high methodological standard with robust sampling strategies, adequate response rates and good adjustment for confounders. CONCLUSIONS:The results support the hypothesis that deployment to the Gulf War is associated with greater reporting of multi-symptom conditions
- 3. Fiedler N1, Giardino N, Natelson B, Ottenweller JE, Weisel C, Lioy P, Lehrer P, Ohman-Strickland P, Kelly-McNeil K,Kipen H. Psychosom Med. 2004 Jul-Aug;66(4):588-98. Responses to controlled diesel vapor exposure among chemically sensitive Gulf War veterans.

OBJECTIVE:A significant proportion of Gulf War veterans (GWVs) report chemical sensitivity, fatigue, and unexplained symptoms resulting in ongoing disability. GWVs frequently recall an association between diesel and petrochemical fume exposure and symptoms during service. The purpose of the present study among GWVs was to evaluate the immediate health effects of acute exposure to chemicals (diesel vapors with acetaldehyde) with and without stress. METHODS:In a single, controlled exposure to 5 parts per million (ppm) diesel vapors, symptoms, odor ratings, neurobehavioral performance, and psychophysiologic responses of 12 ill GWVs (GWV-I) were compared with 19 age- and gender-matched healthy GWVs (GWV-H). RESULTS:Relative to baseline and to GWV-H, GWV-I reported significantly increased symptoms such as disorientation and dizziness and displayed significantly reduced end-tidal CO(2) just after the onset of exposure. As exposure increased over time, GWV-I relative to GWV-H reported significantly increased symptoms of respiratory discomfort and general malaise. GWV-I were also physiologically hyporeactive in response to behavioral tasks administered during but not before exposure. CONCLUSIONS:Current symptoms among GWV-I may be exacerbated by ongoing environmental chemical exposures reminiscent of the Gulf War. Both psychologic and physiologic mechanisms contribute to current symptomatic responses of GWV-I.

4 . Gray GC1, Reed RJ, Kaiser KS, Smith TC, Gastañaga VM. Am J Epidemiol. 2002 Jun 1;155(11):1033-44. Self-reported symptoms and medical conditions among 11,868 Gulf War-era veterans: the Seabee Health Study. Erratum in Am J Epidemiol. 2005 Feb 1;161(3):302.

US Navy Seabees have been among the most symptomatic Gulf War veterans. Beginning in May 1997, the authors mailed Gulf War-era Seabees a health survey in serial mailings. As of July 1, 1999, 68.6% of 17,559 Seabees contacted had returned the questionnaire. Compared with other Seabees, Gulf War Seabees reported poorer general health, a higher prevalence of all 33 medical problems assessed, more cognition difficulties, and a higher prevalence of four physician-diagnosed multisymptom conditions: chronic fatigue

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syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel syndrome. Because the four multisymptom conditions were highly associated with one another, the authors aggregated them into a working case definition of Gulf War illness. Among the 3,831 (22% cases) Gulf War Seabee participants, multivariable modeling revealed that female, Reserve, and enlisted personnel and participants belonging to either of two particular Seabee units were most likely to meet the case definition. Twelve of 34 self-reported Gulf War exposures were mildly associated with meeting the definition of Gulf War illness, with exposure to fumes from munitions having the highest odds ratio (odds ratio = 1.9, 95% confidence interval: 1.5, 2.4). While these data do not implicate a specific etiologic exposure, they demonstrate a strong association and a high prevalence of self-reported multisymptom conditions in a large group of symptomatic Gulf War veterans.

5. Reid S1, Hotopf M, Hull L, Ismail K, Unwin C, Wessely S. Occup Environ Med. 2002 Mar;59(3):196-8. Reported chemical sensitivities in a health survey of United Kingdom military personnel.

OBJECTIVE: To report the prevalence of self reported chemical sensitivities in three cohorts of United Kingdom service personnel. METHOD: Cross sectional postal survey of three cohorts of United Kingdom military personnel comprising Gulf veterans (n=3531), those who had served in Bosnia (n=2050), and those serving during the Gulf war but not deployed there (Era cohort, n=2614). RESULTS: Sensitivity to at least one everyday chemical was reported by a considerable proportion of all three cohorts, and particularly by veterans of the Gulf war (Era: 14%; Bosnia: 13%; Gulf: 28%). CONCLUSION: Reported chemical sensitivities were common in all three military cohorts. Our understanding of chemical sensitivities remains limited and objective evidence for a causal link between low level exposures to chemicals and reported symptoms is lacking. Given their frequency in the population, further work in this area is necessary.

6. Reid S1, Hotopf M, Hull L, Ismail K, Unwin C, Wessely S. Am J Epidemiol. 2001 Mar 15;153(6):604-9. Multiple chemical sensitivity and chronic fatigue syndrome in British Gulf War veterans.

The objective of this study was to measure the prevalence of multiple chemical sensitivity (MCS) and chronic fatigue syndrome (CFS) in British Gulf War veterans and to investigate their association with reported exposures and psychologic morbidity. In 1997--1998, the authors undertook a cross-sectional survey of three cohorts of British military personnel comprising Gulf veterans (n = 3,531), those who had served in Bosnia (n = 2,050), and those serving during the Gulf War but not deployed there (Era cohort, n = 2,614). MCS and CFS were defined according to operational criteria. The prevalence of MCS in the Gulf, Bosnia, and Era cohorts was 1.3%, 0.3%, and 0.2%, respectively. For CFS, the prevalence was 2.1% (Gulf cohort), 0.7% (Bosnia cohort), and 1.8% (Era cohort). In Gulf veterans, MCS was strongly associated with exposure to pesticides (adjusted odds ratio = 12.3, 95% confidence interval: 5.1, 30.0). Both syndromes were associated with high levels of psychologic morbidity. These findings suggest that CFS and MCS account for some of the medically unexplained illnesses reported by veterans after deployment to the Gulf. MCS was particularly associated with Gulf deployment and self-reported exposure to pesticides, findings that merit further exploration given the controversial status of this diagnosis and the potential for recall bias in a questionnaire survey.

- 7. Proctor SP1 Occup Med. 2000 Jul-Sep;15(3):587-99. Chemical sensitivity and gulf war veterans' illnesses.

 Dr. Proctor summarizes the current research literature describing Gulf War (GW) veterans' health issues, particularly as they pertain to chemical sensitivity (CS) and multiple chemical sensitivity (MCS) syndrome. In several studies of GW veterans, using differing criteria and varying assessment measures for CS and MCS, the prevalence rates for CS are reported to be 36-86% in Department of Veterans' Affairs patient populations and 0.8-20% in general cohorts of GW veterans. The [general population] rates of MCS are 2-6%. Targeted research is needed to adequately evaluate GW veterans' health concerns and MCS.
- Black DW1, Doebbeling BN, Voelker MD, Clarke WR, Woolson RF, Barrett DH, Schwartz DA. Arch Intern Med. 2000 Apr 24;160(8):1169-76. Multiple chemical sensitivity syndrome: symptom prevalence and risk factors in a military population. OBJECTIVE: To assess the prevalence of and risk factors for self-reported symptoms suggestive of multiple chemical sensitivities/idiopathic environmental intolerance (MCS/IEI) in Persian Gulf War (PGW) veterans from Iowa and a comparison group of PGW-era military personnel. METHODS:A population-based sample of lowa military personnel was surveyed using a cross-sectional telephone interview. Study participants were randomly drawn from 1 of 4 domains; PGW active duty, PGW National Guard/Reserve. non-PGW active duty, and non-PGW National Guard/Reserve. A complex sample survey design was used selecting participants from the following substrata: age, sex, race, rank, and military branch. The criteria for MCS/IEI were developed using expert consensus and the medical literature. RESULTS:A total of 3695 study participants (76% of those eligible) completed the telephone survey. The prevalence of symptoms suggestive of MCS/IEI in all participants was 3.4%. Veterans of the PGW reported a significantly higher prevalence of symptoms suggestive of MCS/IEI than did non-PGW military personnel (5.4% vs 2.6%); greater sensitivity to organic chemicals, vehicle exhaust, cosmetics, and smog; and more lifestyle changes. The following risk factors for MCS/IEI were identified with univariate analysis: deployment to the Persian Gulf, age (>25 years), female sex, receiving a physician diagnosis of MCS, previous professional psychiatric treatment, previous psychotropic medication use, current psychiatric illness, and a low level of preparedness. Multiple logistic regression analysis identified several independent risk factors for MCS/IEI, including deployment to the Persian Gulf. age, sex, rank, branch of service, previous professional psychiatric treatment, and current mental illness. CONCLUSIONS:Self-reported symptoms suggestive of MCS/IEI are relatively frequent in a military population and are more common among PGW veterans than comparable controls. Reported chemical sensitivities and accompanying behavioral changes were also frequent. After adjusting for age,

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deployment) showed a robust association with symptoms suggestive of MCS.

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sex, and training preparedness, previous professional psychiatric treatment and previous psychotropic medication use (before

9. Black DW1, Doebbeling BN, Voelker MD, Clarke WR, Woolson RF, Barrett DH, Schwartz DA. J Occup Environ Med. 1999 Oct;41(10):928-33. Quality of life and health-services utilization in a population-based sample of military personnel reporting multiple chemical sensitivities.

We sought to assess quality of life and health-services utilization variables in persons with symptoms suggestive of multiple chemical sensitivity/idiopathic environmental intolerance (MCS/IEI) among military personnel. We conducted a cross-sectional telephone survey of a population-based sample of Persian Gulf War (PGW) veterans from Iowa and a comparison group of PGW-era military personnel. A complex sample survey design was used, selecting subjects from four domains: PGW active duly, PGW National Guard/Reserve, non-PGW active duty, and non-PGW National Guard/Reserve. Each domain was substratified by age, gender, race, rank, and military branch. The criteria for MCS/IEI were developed by expert consensus and from the medical literature. In the total sample, 169 subjects (4.6%) of the 3695 who participated (76% of those eligible) met our criteria for MCS/IEI. Persons who met the criteria for MCS/IEI more often reported the following than did other subjects: more than 12 days in bed due to disability, Veteran's Affairs disability status, Veteran's Affairs disability compensation, medical disability, and unemployment. MCS/IEI cases also had higher outpatient rates of physician visits, emergency department visits, and inpatient hospital stays. Subjects who met the criteria for MCS/IEI more often reported impaired functioning on each Medical Outcomes Study 36-Item Short Form subscale, compared with those who did not meet the criteria. We concluded that although the diagnosis of MCS/IEI remains controversial, the persons who met our criteria for the disorder are functionally impaired.

10. Kipen HM1, Hallman W, Kang H, Fiedler N, Natelson BH. Arch Environ Health. 1999 Sep-Oct;54(5):313-8. Prevalence of chronic fatigue and chemical sensitivities in Gulf Registry Veterans.

More than 68000 of the 700000 veterans of the Gulf War have become members of the Veteran Affairs' Gulf War Registry. In 1995, we undertook a questionnaire study of the symptoms and medical histories reported by a randomly selected subsample of 1935 of these veterans to characterize their complaints. All results reported were based on questionnaire responses without face-to-face evaluation or physical examinations. Inasmuch as initial registry symptoms overlapped those of Chronic Fatigue Syndrome and Multiple Chemical Sensitivities, we also included standard questions for these syndromes in the questionnaire. A total of 1161 (60%) individuals responded, and there were no major demographic biases; therefore, 15.7% of registry veterans qualified for Chronic Fatigue Syndrome in accordance with the 1994 Centers for Disease Control definition. In addition, 13.1% qualified for multiple chemical sensitivities in accordance with a widely used definition, and 3.3% of the respondents had both conditions. There were no effects of gender, race, branch, duty status (active or reserve), or rank, although Multiple Chemical Sensitivities was somewhat more prevalent in women and African Americans. The data gleaned in this study suggested that the unexplained symptom syndromes of Chronic Fatigue and Multiple Chemical Sensitivities may characterize an appreciable portion of the complaints of those who volunteered for the Veterans Affairs' Gulf War Registry, and further investigation is warranted.

- Bartha et al, Arch Environ Health. 1999 May-Jun;54(3):147-9. Multiple chemical sensitivity: a 1999 consensus. 11. Consensus criteria for the definition of multiple chemical sensitivity (MCS) were first identified in a 1989 multidisciplinary survey of 89 clinicians and researchers with extensive experience in, but widely differing views of, MCS. A decade later, their top 5 consensus criteria (i.e., defining MCS as [1] a chronic condition [2] with symptoms that recur reproducibly [3] in response to low levels of exposure [4] to multiple unrelated chemicals and [5] improve or resolve when incitants are removed) are still unrefuted in published literature. Along with a 6th criterion that we now propose adding (i.e., requiring that symptoms occur in multiple organ systems), these criteria are all commonly encompassed by research definitions of MCS. Nonetheless, their standardized use in clinical settings is still lacking, long overdue, and greatly needed-especially in light of government studies in the United States, United Kingdom, and Canada that revealed 2-4 times as many cases of chemical sensitivity among Gulf War veterans than undeployed controls. In addition, state health department surveys of civilians in New Mexico and California showed that 2-6%, respectively, already had been diagnosed with MCS and that 16% of the civilians reported an "unusual sensitivity" to common everyday chemicals. Given this high prevalence, as well as the 1994 consensus of the American Lung Association, American Medical Association, U.S. Environmental Protection Agency, and the U.S. Consumer Product Safety Commission that "complaints [of MCS] should not be dismissed as psychogenic, and a thorough workup is essential," we recommend that MCS be formally diagnosed--in addition to any other disorders that may be present--in all cases in which the 6 aforementioned consensus criteria are met and no single other organic disorder (e.g., mastocytosis) can account for all the signs and symptoms associated with chemical exposure. The millions of civilians and tens of thousands of Gulf War veterans who suffer from chemical sensitivity should not be kept waiting any longer for a standardized diagnosis while medical research continues to investigate the etiology of their signs and symptoms.
- 12. Miller CS1, Prihoda TJ., Toxicol Ind Health. 1999 Apr-Jun;15(3-4):386-97. A controlled comparison of symptoms and chemical intolerances reported by Gulf War veterans, implant recipients and persons with multiple chemical sensitivity. Using the Environmental Exposure and Sensitivity Inventory (EESI), a standardized instrument for measuring chemical sensitivity, we obtained and compared ratings of symptoms, chemical (inhalant) intolerances, other intolerances (e.g., drugs, caffeine, alcohol, skin contactants), lifeimpact, and masking (ongoing exposures) in five populations: multiple chemical sensitivity (MCS) patients who did (n =

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96) or did not (n = 90) attribute onset of their illness to a specific exposure event, patients with implanted devices (n = 87), Gulf War veterans (n = 72), and controls (n = 76). For each patient group, mean scores on the first four scales were significantly greater than for controls. MCS patients reported avoiding more chemical exposures (were less masked) than the other groups. Across groups, for a given level of symptoms, as masking increased, mean scores on the Chemical Intolerance Scale decreased. In contrast, mean scores on the Other Intolerance Scale appeared to be less affected by masking. These findings suggest that some patients with antecedent chemical exposures, whether exogenous (chemical spill, pesticide application, indoor air contaminants) or endogenous (implant). develop new chemical, food, and drug intolerances. Reports of new caffeine, alcohol, medication, food, or other intolerances by patients may signal exposure-related illness. Masking may reduce individuals' awareness of chemical intolerances, and, to a lesser degree, other intolerances.

- Pollet C1, Natelson BH, Lange G, Tiersky Ľ, DeLuca J, Policastro T, Desai P, Ottenweller JE, Korn L, Fiedler N, Kipen 13. H., J Med. 1998;29(3-4):101-13. Medical evaluation of Persian Gulf veterans with fatigue and/or chemical sensitivity. The purpose of this study was to determine if Gulf War veterans with complaints of severe fatigue and/or chemical sensitivity (n = 72) fulfill case definitions for chronic fatigue syndrome (CFS) and/or multiple chemical sensitivity (MCS) and to compare the characteristics of those veterans who received a diagnosis of CFS (n = 24) to a group of non-veterans diagnosed with CFS (n = 95). Thirty-three veterans received a diagnosis of CFS with 14 having MCS concurrently; an additional six had MCS but did not fulfill a case definition for CFS. The group of fatigued veterans receiving a diagnosis of CFS was comprised of significantly fewer women and fewer Caucasians than the civilian group, and significantly fewer veterans reported a sudden onset to their illness. Veterans with CFS had a milder form of the illness than their civilian counterparts based on medical examiner assessment of the severity of the symptoms, reported days of reduced activity, and ability to work. Since CFS in veterans seems less severe than that seen in civilians, the prognosis for recovery of veterans with this disorder may be better.
- 14. Bell IR1, Warg-Damiani L, Baldwin CM, Walsh ME, Schwartz GE., Mil Med. 1998 Nov;163(11):725-32. Self-reported chemical sensitivity and wartime chemical exposures in Gulf War veterans with and without decreased global health ratings. This cross-sectional telephone survey study assessed prevalence rates of current chemical sensitivity, frequency of chemical odor intolerance, and self-reported Persian Gulf chemical exposures among 41 randomly sampled Department of Veterans Affairs outpatients who were Persian Gulf War (PGW) and PGW-era veterans. The participants were drawn from an initial random list of 100 veterans, of whom 28 PGW and 20 era veterans had correct telephone data on file. Of those contacted, 86% of PGW veterans (24/28) and 85% of era veterans (17/20) agreed to participate. Significantly more PGW veterans with poorer global health after military service reported considering themselves now "especially sensitive to certain chemicals" (86%, 12/14) than did the PGW veterans or era veterans in stable health (both comparison groups 30%, 3/10). Among PGW veterans, the subset with worse health associated with marked increases in chemical odor intolerance since their military service had a significantly higher odds ratio for exposure to multiple chemicals, notably wartime pesticides and insect repellent, than did comparison groups. The high rate of chemical sensitivity of PGW veterans with deteriorated health is almost three times that in PGW-era veterans and in elderly primary care outpatient veterans at the same Department of Veterans Affairs medical center and in community-based civilian samples (i.e., 30%). These preliminary findings suggest the need for further study of chemical sensitivity, including tests for acquired increases in neural sensitizability to multiple low-level chemicals, in ill PGW veterans.

15. Fiedler N1, Kipen H, Natelson B, Ottenweller J. Regul Tox Pharm. 1996 Aug;24(1 Pt 2):S129-38. Chemical sensitivities and the Gulf War: Department of Veterans Affairs Research Center in basic and clinical science studies of environmental hazards.

The purpose of the New Jersey Center for Environmental Hazards Research is to define the illness referred to as Persian Gulf Syndrome (PGS). Our preliminary data indicated that more than half of the Persian Gulf Registry (PGR) veterans reported illness characterized by severe fatigue and symptoms consistent with chemical sensitivities. Therefore, our research approach focuses on investigations of veterans with chronic fatigue syndrome (CFS) and multiple chemical sensitivities (MCS). Project 1 is an epidemiological study of 2800 PGR veterans. Symptoms, indices of Chronic Fatigue (CF) and Chemical Sensitivity (CS), and risk factors will be surveyed with mailed questionnaires. Risk factors include demographics, past medical history, psychosocial variables, Gulf War experiences such as prophylactic medication use, occupational and environmental exposures, and pesticide exposures. Symptoms will be clustered to define Gulf War Syndromes. Significant associations between risk factors and these symptom clusters will also be investigated Subjects identified as CF, CS, or both will be recruited into Projects 2 and 3. In Project 2, healthy veterans will be compared to veterans with CF, CS, and CF concurrent with CS. Veterans will undergo four studies: (1) viral-immunological, (2) psychiatric, psychological, behavioral, and neuropsychological, (3) autonomic dysregulation, and (4) marker of P4501A2 induction resulting from exposure to combusting material. The purpose of Project 3 is to test the autonomic, immunologic, neuropsychologic, and psychologic responses of veterans with CS or CF to two stressors: controlled chemical exposure and exercise. CS subjects will undergo chemical exposures in our Controlled Environment Facility (CEF) to assess their biologic and psychologic response to low-level exposure. CF subjects will undergo a maximal treadmill exercise test. Circadian patterns of catecholamines and axillary temperature, viral burden, and cardiovascular and endocrine reactivity will be measured in response to this physical stressor. Project 4 is an animal study evaluating the interaction between stress and pathology/physiology when rats are predisposed to disease by exposure to Soman or to Dioxin. Two strains of rats that differ in stress reactivity will be used to determine the interaction of hereditary factors and chemical exposure.

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Appendix C Screening fon Garbon Mo	mavido Dojeonina			-21, 2015
	sulting Toxicologist and Environmental H	lealth Engineer.		6 page7 9 of 1 410-889-6666
	Gender: ⊔ M ⊔ F Aç	_		
Screening Date:/	Screened by: ☐ self ☐ other			
Ib. If CO poisoning is known and how ma Ic. Source(s) of CO Poisonin Home Appliances: ☐ Oven ☐ Wood/Pellet Stove ☐ Ge Id. Highest CO levels measu ☐ In Arterial Blood _ Ie. Dates Treated: ☐ Normal a	Unknown ☐ Yes, First known poisoning thow many others were exposed? # any now have similar symptoms? # g: ☐ Vehicle ☐ Boat ☐ Fire ☐ Explost/Range ☐ Furnace ☐ Boiler ☐ Water Harrator ☐ Lawn Mower ☐ Leaf or Snowned: ☐ In Air= ppm on/_ ☐ and/ or ☐ Hyperbaric oxygen for harrans began within months of CO explants.	Siblings Siblings of the sibling of	or Children, # Adults or Children, # Fireplan or Children, # Price Fireplan or Children, # Price Fireplan or Children, # Price Fireplan or Children, # Adults or Children, # _	nethane ce
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	Other CO-Related Disorders (check is 8 or more began within one year, pos		• • •	• •

Check <u>Current Disorders</u> below but <u>only</u> if symptoms of the disorder (=Sx) have been experienced in last week	Year or Age Sx Began	Severity = Low, Med, Hi	Check <u>Current Disorders</u> below but <u>only</u> if symptoms of the disorder have been experienced in last week	Year or Age Sx Began	Severity = Low, Med, Hi
☐ Alzheimer's or short-term memory loss		LMH	⊔ Irritable Bowel Syndrome		LMH
☐ Attention Deficit Disorder or ADHD		LMH	⊔Low metabolic rate (temp below 98 F)		LMH
☐ Anemia or Hemochromatosis		LMH	⊔Lupus		L M H
⊔ Asthma		LMH	⊔ Mitral Valve Prolapse		LMH
☐ Autism, Asperger's, or PDD of any type		LMH	⊔ Migraines or Throbbing Headaches		LMH
☐ Bipolar Disorder, aka Manic Depression		LMH	⊔ Multiple Sclerosis		LMH
⊔ Blurred Vision		LMH	⊔ Myofascial Pain Syndrome		LMH
☐ Chronic Fatigue Syndrome/CFIDS or ME		LMH	☐ Panic Attacks or Disabling Anxiety		LMH
☐ Depression of any kind		LMH	⊔ Parkinson's Disease or Parkinsonism		LMH
☐ Dermatitis, especially red rashes		LMH	⊔ Pre-menstrual Dysphoric Disorder		LMH
⊔ Diabetes, type 2		LMH	⊔ Psychosis or Schizophrenia		LMH
☐ Dysautonomia (sweats and/or chills)		LMH	⊔ Scleroderma or CREST		LMH
⊔ Epilepsy of any kind		LMH	⊔ Temporomandibular Joint Disorder		LMH
⊔ Fibromyalgia or Chronic Muscle Pain		LMH	⊔ Tinnitus or other sounds inside ears		LMH
⊔ Heart Disease or Angina Chest Pain		LMH	⊔ Other:		LMH

Screening Results: Score each question above as indicated. If Question 2 scores >5 and Question 4 scores >7, unresolved CO poisoning is probable even if answer to Question 1 is unknown. If Question 3 scores A, B, C or D, this adds greatly to the suspicion, but only if facial asymmetry is <u>not evident</u> in photos taken <u>before onset</u> of sensory symptoms.

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Appendix C

Testing to Confirm Suspected Carbon Monoxide Poisoning

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TESTING FOR CO IN BLOOD

The standard test for CO in blood is carboxyhemoglobin [COHb], which measures the amount of CO bound to hemoglobin. This is normally measured only in arterial <u>or</u> venous blood based on the mistaken assumption that arterial and venous COHb are either always equal or only insignificantly different.

Post-mortem studies of CO poisoning victims, however, show the arterial-venous difference (or gap) in COHb in the heart may be anywhere +14% to -18% [Blackmore 1970] and gaps in other organs may be even more [Levine 2002]. In comparison, the normal a-v COHb gap in healthy smokers and non-smokers is just 0 to +1%. [Meyer 1988]

The a-v COHb gap is much larger than +1% during CO poisoning, when more CO is being absorbed than excreted. But it is consistently negative after CO poisoning until all the CO absorbed into blood and tissues during exposure is exhaled, which may take years or even decades unless and until accelerated by appropriate treatment (see TREATMENT OF CONFIRMED CO POISONING, below).

The appropriate blood tests to confirm CO poisoning, therefore, include both arterial and venous COHb drawn from the same elbow while seated at rest. Venous should be done first since it is less painful. A negative art-ven COHb gap is evidence that the tissues contain a higher than healthy level of CO which is slowly diffusing into venous blood. This excess CO may be from previously inhaled exogenous CO and/or increased production of endogenous CO from heme catabolism occurring beyond the lungs as part of the physiology of various conditions such as arthritis, diabetes, PMS and pregnancy.

COHb Results for:	Testing Date: / Lab:
Venous COHb=	%, drawn first from ⊔Left or ⊔Right elbow; Arterial COHb= % from the same elbow
A-V COHb gap=	= % If negative: abnormally high CO in tissues from exog and/or endog sources
If zero: in stable e	equilibrium with air; If positive ≤1: healthy; If positive >1: recent CO exposure from air and/or lungs

TESTING FOR CO IN BREATH

The standard test for CO in breath requires people to hold their breath for 20-25 seconds before exhaling an end-tidal sample into a breath CO analyzer. Studies show that this breathholding time results in ppm measurements of CO that closely correlate with the percent venous COHb. A patent-pending method developed by Albert Donnay yields an arterial measure after 5 seconds of breathholding and the average of all tissues after 35 seconds.

Any small professional CO detector that displays in ppm accurately from true zero can be used for breath testing. The least expensive suitable device is currently the T40 Rattler by Industrial Scientific. This is sold in USA by Zoro Tools (855-289-9676) for \$176, and in Canada by Acklands Grainger (905-731-5516) for \$156. Both prices including shipping.

DONNAY INSTRUCTIONS FOR BREATH CO TESTING (=bCO)

- 1. Sit in a comfortable chair with a clear plastic vegetable bag and your CO detector turned ON.
- 2. Wait until detector displays zero, then place it in the bottom of bag.
- 3. Twist bag from bottom to top to force out as much air as possible.
- 4. Hold bag loosely in one your fist about half-way up the twisted length and then fold the top of the bag back over your fist. Under your fist, untwist the bag so it is ready to inflate.
- 5. While continuing to hold bag in your fist, breathe in and hold your breath for 5 seconds.
- 6. Exhale as fast and as fully as possible. When almost done exhaling, raise your fist to your mouth, put your lips tightly over the bag, relax your grip slightly, and blow the last 1 to 2 seconds of your exhalation into the bag.
- 7. Tighten your grip again and twist the bag several times under your fist to keep your breath from leaking out
- 8. Wait 30 seconds and record the CO level displayed through the bag.
- 9. Open the bag, remove the detector and wait for the display to return to zero.
- 10. Repeat from step 2, but this time holding your breath for 20 seconds, and then repeat a third time after holding your breath for 35 seconds.

Breath CO Results for:	Testing Date:	11	Device:	
Arterial bCO after 5 sec= ppm,	, Venous bCO after 20 sec= p	pm, Net Tissu	e bCO after 35 sec= _	_ ppm
Interpretation: bCO results confirm	current exogenous CO poisonin	ıg IF Arterial >	> Venous, regardless o	f Tissue
hne	prior or endogenous CO Poison	ing IF Tissue	> Venous > Arterial	