Reader Feedback

The "Reality" of Gulf War Illness

We believe Dr. Orme's recent discussion[1] of the Research Advisory Committee on Gulf War Veterans' Illnesses (RAC-GWVI) 2008 report[2] reflects an unfortunate misunderstanding of the findings in the report and a limited familiarity with the broad research related to Gulf War illness (GWI). In recent years, the breadth and consistency of evidence has led to substantial agreement among government agencies and independent review panels regarding the existence and serious nature of the undiagnosed illness affecting 1991 Gulf War veterans.[2–8] Findings in the RAC-GWVI 2008 report, for example, overlap considerably with those of a recent Institute of Medicine (IOM) report.[3] Both reports indicate that Gulf War multisymptom illness affects a significant number of Gulf War veterans—approximately 25% to 33% of the nearly 700,000 U.S. veterans who served—and is not explained by psychiatric causes or disorders.[2,3]

Dr. Orme's view that GWI might not be "real" or that it is primarily a psychiatric disorder was a common opinion in the decade following the Gulf War, when studies evaluating this problem were limited. We now know that veterans of this war have relatively low rates of psychiatric disorders,[9–12] including somatization disorders and posttraumatic stress disorder (PTSD), compared with veterans of other wars.[2] Furthermore, although studies show that the subgroup of Gulf War veterans who experienced combat and related stressors are at increased risk for PTSD, such stressors are not significant risk factors for GWI, when other deployment factors are taken into account.[2,13,14]

Dr. Orme's detailed presentation is limited by the selection of studies he considers, his misinterpretation of the RAC-GWVI findings, and the framework he creates for assessing the "reality" of GWI. For example, he speculates that ill Gulf War veterans suffer from a somatic syndrome, but he seems unaware of the many Gulf War studies, which provide data on somatic and other psychiatric disorders, as well as conditions he identifies as functional somatic syndromes, but do not support his view.[2,3] His line of reasoning conflates veterans' memory complaints with GWI more generally, and fails to differentiate the RAC-GWVI's observations on self-reported memory symptoms from evidence related to measured deficits on neuropsychological tests. There is no evidence, and the RAC-GWVI report does not suggest, that veterans' memory complaints are the cardinal symptom of GWI. The committee specifically points out that many veterans who report cognitive difficulties do *not* exhibit measurable neuropsychological deficits when tested. However, as indicated by the RAC-GWVI and other scientific panels, studies comparing symptomatic Gulf War veterans with healthy veterans consistently identify significant group differences on a variety of neurocognitive measures.[2,3,15]

More importantly, Dr. Orme's catalogue of results related to memory testing misses the larger point: Both the existence and characteristics of GWI are well documented by numerous epidemiologic and clinical studies of these veterans. The hallmark of GWI is a complex of multiple, often debilitating, symptoms that affect several biological systems and are not explained by well-established diagnoses. As detailed by the RAC-GWVI 2008 report, studies also have identified significant alterations in brain structure and function, as well as immune, autonomic, and neuroendocrine measures that objectively distinguish *groups* of symptomatic Gulf War veterans from healthy controls.[2] Currently, however, no clinical tests are able to diagnose GWI.

In light of current research, we believe the existence of GWI is no

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longer in question. Remaining differences between independent scientific reviews primarily relate to the question of etiology. Although both the RAC-GWVI and the IOM consider it likely that GWI resulted from an interplay of environmental and genetic factors, the RAC-GWVI found that neurotoxic exposures during deployment were causally associated with GWI,[2] while the IOM panel concluded there was insufficient evidence to pinpoint specific causes.[3] Considerable work remains to adequately address this problem, however. Both the RAC-GWVI and IOM have called for a dedicated federal research effort focused on identifying useful diagnostic tests and effective treatments for the many veterans who continue to suffer from GWI.

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Additional Reader Feedback

Contrary to the assertion of Dr. Orme in the November issue of *Federal Practitioner*,[1] current scientific evidence demonstrates that the chronic multisymptom illness reported by at least one-fourth of Gulf War veterans is a serious medical condition not of psychosomatic origin. These conclusions in the Research Advisory Committee on Gulf War Veterans' Illnesses (RAC-GWVI) 2008 report[2] have been subsequently corroborated by the VA and the Institute of Medicine (IOM).

Dr. Orme's basic contention is that the inconsistency of measured memory deficits on neuropsychological testing (in selectively chosen studies) is reason to conclude that there is no such thing as Gulf War illness (GWI) and that it likely represents a somatic disorder. We believe his view—that the lack of objective markers for 1 of many symptoms of GWI negates the "reality" of the entire illness—is ill founded and illogical. In fact, GWI is characterized by many other symptoms, including dysfunction in other cognitive domains (for example, attention, executive system, visuospatial, and psychomotor), as well as concurrent symptoms of fatigue, headaches, chronic pain, gastrointestinal problems, and other chronic abnormalities. Despite the many symptoms associated with GWI, studies show that few Gulf War veterans (< 1%) have diagnosed somatization disorders.[3,4]

Dr. Orme's presentation of neurocognitive findings in Gulf War veterans misrepresents the literature in this area. He speculates that the studies showing significant neuropsychological differences between veteran groups are not valid because of "methodological problems," including malingering or "lack of effort" on the part of Gulf War veterans. In fact, these studies did account for potential motivation problems among participants[5,6] and demonstrated that diminished motivation or frank malingering are not significant problems in this veteran population.[6–8] For example, Barrash and colleagues reported that 1% of Gulf War veterans displayed questionable performance on neuropsychological assessments and they were not significantly more likely to show reduced performance effort than nondeployed veterans of the same era. Similar findings have been reported in

2 other independent studies of a different cohort.[6,8]

The RAC-GWVI report states that memory is a commonly reported symptom of GWI and that neuropsychological testing does not always show objective measures of differences in individual veterans within the specific cognitive domains tested. This pattern is not uncommon in disorders that cause subtle cognitive dysfunction, such as in subclinical encephalopathy.[9] A more careful review of the RAC-GWVI report would have shown that it was never suggested that Gulf War veterans were displaying a clear amnestic syndrome, but, rather, a pattern of functioning that appeared to reflect a slowing of response speed that could affect mental flexibility across multiple cognitive domains.[2] It also is not uncommon for individuals to report memory difficulties when, in fact, they may be showing mild attention or executive system dysfunction (which has been reported in studies of Gulf War veterans).

The RAC-GWVI report also indicates that although veterans' symptoms are the most obvious and consistent indicators of GWI, many studies have identified objective measures that significantly distinguish veterans with GWI from healthy controls. Specific differences relate to structure and function of the brain, function of the autonomic nervous system, neuroendocrine and immune alterations, and variability in enzymes that protect the body from neurotoxic chemicals. These findings soon may be used to identify objective diagnostic tests for GWI.

A major study published by VA investigators in 2009[10] found that multisymptom illness is the most prevalent health problem among Gulf War veterans, affecting 25% of those who served—a rate higher than that found in veterans of the same era who did not deploy. Correspondingly, a 2010 IOM report on Gulf War and health[11] concluded that multisymptom illness is associated with Gulf War service, affects 1 in 3 Gulf War veterans, and cannot be explained by any known psychiatric condition. Rather, the IOM proposes it is likely the result of multiple environmental and genetic factors. The IOM report calls for a major national research program to identify treatments for the illness, echoing a comparable recommendation by the RAC-GWVI. The evidence from several independent panels agree that a significant proportion of Gulf War veterans are ill with a chronic multisymptom illness.[2,11] It is important to note that each panel was made up of independent researchers who are experts in their respective fields.

We were disappointed by the lack of depth and breadth reflected in Dr. Orme's consideration of the literature on the health of Gulf War veterans. We were especially concerned that a clinician at the VA who evaluates ill veterans continues to suggest that GWI is a somatoform disorder, despite consistent evidence to the contrary. It has been difficult enough for clinicians to identify helpful treatments for symptomatic veterans during the 20 years following the Gulf War. Unfortunately, it has been even more difficult for Gulf War veterans who, coping with their own illness, must rely on care provided by clinicians who believe their condition to be psychosomatic and/or malingering.

In light of the broad and consistent evidence now available, we believe the time for debating the "reality" of GWI is over. It is now time to find effective treatments to improve the health of these ailing veterans.

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The author responds:

I appreciate the comments from members of the Research Advisory Committee on Gulf War Veterans' Illnesses (RAC-GWVI) and the concern of all that there is a reasoned approach to the difficult issue of Gulf War illness (GWI). Such an approach requires careful review of the literature, on which, significant and influential conclusions are based. I believe the original article[1] does that. The studies I reviewed are the same that the RAC-GWVI referenced in support of their claims of neurocognitive deficits in "symptomatic" veterans and associated with toxins.[2] My review of the studies suggests conclusions considerably different from those offered by the RAC-GWVI, which is discussed in the body of my article. However, given conflicting opinions, readers are encouraged to examine the data in the original article[1] and to consult the referenced articles in order to form their own conclusions.

The RAC-GWVI members noted that veterans claiming GWI do not, in general, have diagnosable somatoform disorder. I do not disagree on this point. But there appears to be confusion regarding the difference between somatoform disorders and mass psychogenic illness or functional somatic syndromes (the latter 2 terms are used interchangeably here). Somatoform disorders are psychiatric conditions that are diagnosed through clinical interview; symptoms may be evident on psychometric tests. Mass psychogenic illness, on the other hand, is a sociological event, not a psychiatric disorder, and is not amenable to psychometric assessment.[3,4] This is described in some detail in my article. The proposal then, is not that individuals who report symptoms of GWI have psychiatric disorders, as the RAC-GWVI members correctly defend against, but that some veterans may have been influenced by media attention, other sources of information, or aspects of the work environment, innocently misconstruing cause-and-effect related to normal symptoms (of particular relevance to this discussion, normal everyday forgetfulness). GWI then, may be an example of mass psychogenic illness. This remains a viable area for research.

My article suggests it is premature to state with confidence that GWI is "real," results in memory problems, and is caused by toxins. This remains the case.[5–8] The Institute of Medicine (IOM) stated there is "inadequate/insufficient evidence to determine whether an association exists between deployment to the Gulf War and neurocognitive and neurobehavioral performance."[9] Also, as the RAC-GWVI members noted, the IOM stated there is sufficient evidence of an association between "multisystem illness" and deployment to the Gulf War; however, this is simply the substitution of one vague and poorly understood entity that is strongly associated with psychological variables with another.[10]

Our military members and veterans deserve the best medical care available based on research efforts that do not rest until no stone is left unturned in the search for medical understanding. Neurocognitive concerns associated with GWI are not at that point and this remains a puzzle. Therefore, I believe all etiologic considerations, including mass psychogenic illness, should remain on the table.

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