

Unexplained Symptoms After Terrorism and War: An Expert Consensus Statement

Daniel J. Clauw, MD
Charles C. Engel, Jr., MD, MPH
Robert Aronowitz, MD
Edgar Jones, DPhil, PhD
Howard M. Kipen, MD, MPH
Kurt Kroenke, MD
Scott Ratzan, MD, MPA, MA
Michael Sharpe, MD
Simon Wessely, MD

Learning Objectives

- Describe the characteristics of unexplained post-exposure symptoms that favor a causal association with a catastrophic event such as war or a terrorist act.
- Suggest possible ways in which pre-event interventions might prevent or minimize post-exposure symptoms.
- What measures might be taken during or after a catastrophic event to lessen or eliminate post-event symptoms?

Abstract

Twelve years of concern regarding a possible “Gulf War syndrome” has now given way to societal concerns of a “World Trade Center syndrome” and efforts to prevent unexplained symptoms following the most recent war in Iraq. These events serve to remind us that unexplained symptoms frequently occur after war and are likely after terrorist attacks. An important social priority is to recognize, define, prevent, and care for individuals with unexplained symptoms after war and related events (eg, terrorism, natural or industrial disasters). An international, multidisciplinary, and multiinstitutional consensus project was completed to summarize current knowledge on unexplained symptoms after terrorism and war. (J Occup Environ Med. 2003;45:1040–1048)

From the Department of Medicine, University of Michigan School of Medicine (Dr Clauw); the Department of Psychiatry (Dr Engel), Uniformed Services University of the Health Sciences; History and Sociology of Science (Dr Aronowitz), Family Practice and Community Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; King’s College School of Medicine (Dr Jones), London; the Department of Occupational Health (Dr Kipen), Environmental and Occupational Health Sciences Institute (EOHSI), University of Medicine & Dentistry of New Jersey, Robert Wood Johnson Medical School; the Department of Medicine (Dr Kroenke), Regenstrief Institute for Health Care, Indiana University School of Medicine; the University of Edinburgh (Dr Sharpe); and the Department of Epidemiological & Liaison Psychiatry (Dr Wessely), King’s College School of Medicine, London.

The ideas expressed in this article are the private views of the authors and do not reflect the official policy or position of Uniformed Services University, Department of the Army, Department of Defense, or the U.S. Government.

Charles C. Engel has no commercial interest related to this article.

Address correspondence to: Charles C. Engel, Jr., MD, MPH, Associate Professor of Psychiatry, Department of Psychiatry, Uniformed Services University School of Medicine, Bethesda, MD 20814-4799; E-mail: cengel@usuhs.mil.

Copyright © by American College of Occupational and Environmental Medicine

DOI: 10.1097/01.jom.0000091693.43121.2f

The resulting consensus statement finds that divergent yet overlapping constellations of unexplained symptoms occur after war and can also occur after terrorism. These symptoms constitute valid illness, although elucidating pathogenesis is fraught with scientific peril, and sometimes perspective and preconception overwhelms a priori hypothesis formation and testing. At present, there is little scientific basis for future prevention and care of unexplained symptoms after war or terrorism, although evidence suggests that some well-intended strategies are potentially harmful. Research is needed into appropriate responses given the near certainty of unexplained symptoms after future wars and terrorist acts. Consensus statement conclusions are limited to illness in the absence of disease.

Nearly 12 years have elapsed since the end of the Gulf War, and concerns persist of a unique Gulf War syndrome involving a wide range of unexplained symptoms, reminding us that military personnel returning from wars have regularly described disabling symptoms.¹ After September 11, 2001, there have been many reports in the news media about ailments and symptoms among first-responders and people in or around the World Trade Center (WTC).² Research suggests respiratory ailments occurred among many who were not directly exposed to dust and other irritants but experienced psychosocial or emotional precipitants.³

Research into these public health challenges continues, and meanwhile, society must seek lessons and

successfully apply them to prevent future episodes of unexplained symptoms. Indeed, the return of U.S. and British forces to Iraq highlights the need to better understand, prevent, and manage unexplained symptoms after war and terrorism. This article contains an expert consensus statement that addresses issues pertaining to medically unexplained symptoms after war and terrorist attacks.

Medically Unexplained Symptoms Defined

One of the main obstacles to understanding medically unexplained symptoms is the confusing terminology applied to them. For clarity, this statement adopts a consistent terminology. “Unexplained symptoms” or “medically unexplained symptoms” are used to describe physical symptoms that provoke care-seeking but have no clinically determined pathogenesis after an appropriately thorough diagnostic evaluation.⁴ Clinicians, scientists, symptomatic individuals, the media, employers, or other groups apply labels to unexplained symptoms for divergent purposes, and sometimes, like in the case of low-level chemical sensitivities (toxic) and fibromyalgia (rheumatologic), these labels communicate an implied pathogenesis. This statement relies on the more generic “medically unexplained symptoms” or “unexplained symptoms” to describe diagnoses or conditions characterized by symptoms rather than objective clinical evidence (ie, laboratory findings or signs on examination) of an underlying pathophysiological process.

Historical examples of terms used to describe unexplained symptoms after war include “soldier’s heart,” “shell shock,” “effort syndrome,” and “Gulf War syndrome.”^{1,5} Similar illnesses characterized by unexplained symptoms include fibromyalgia, chronic fatigue syndrome, somatization disorder, and multiple chemical sensitivity.^{6–10}

Disease and illness are terms often applied inexactly. For consistency, this consensus statement will use the term “disease” to describe a clinically identified pathophysiological process (ie, objective signs on physical examination or valid laboratory evidence).^{11–15} The statement will use the term “illness” to refer to a subjective lack of wellness that is inferred through words and behavior. Illnesses encompass a wide range of physical and mental symptoms and associated suffering and disability.^{11,12,16} The conclusions outlined in this consensus statement address the circumstance of illness in the absence of disease (ie, symptoms and suffering without objective signs or valid laboratory evidence obtained on clinical examination).

The Consensus Development Process

This consensus statement emphasizes prevention of unexplained symptoms and related disability occurring after terrorism and war. Explicit steps were taken to balance the diverse perspectives of interested stakeholders. The project’s planning committee was international in composition and included physicians, nurses, policymakers, epidemiologists, and war veterans. Agencies supporting various planning committee members included a U.S. veteran service organization, nonprofit organizations, academia, and the U.S. Departments of Defense, Veterans Affairs, and Health and Human Services. The planning committee nominated people to serve on the consensus committee and charged the consensus committee to develop this consensus statement. The planning committee developed 3 questions to focus the effort. The questions were:

1. What is the strength of the epidemiologic and scientific evidence that war and terrorism or similar catastrophic events cause unexplained symptoms?
2. What epidemiologic and scientific evidence is necessary to con-

clude that an exposed population suffering from unexplained symptoms has a new and unique illness?

3. What is the strength of the evidence that unexplained symptoms after war or terrorism can be prevented or mitigated using population and/or healthcare-based strategies, especially strategies involving communication and education?

The consensus committee was charged with reviewing pertinent evidence and deriving concise, reasoned, and, to the extent possible, evidence-based responses to these questions. The consensus committee consisted of 8 internationally recognized scholars covering the areas of occupational medicine and toxicology, rheumatology, psychiatry, epidemiology, general medicine, medical history, medical sociology, medical ethics, and health communication. These scholars have conducted research on unexplained symptoms and related syndromes, including chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities; and their research has helped clarify the epidemiology, definition, mechanisms, and management of unexplained symptoms. Federal government employees were not considered for consensus committee membership to preserve impartiality.

The consensus committee adhered to an explicit process involving review and synthesis of existing scientific evidence. In addition to relying on their own knowledge of relevant scientific literature, these scholars read nearly 300 articles on 7 topics related to the consensus statement questions (annotated bibliography available on request). These topics were: 1) relationship of symptoms to extreme exposures and events; 2) epidemiology of unexplained symptoms; 3) defining a disease or syndrome; 4) prevention and care of symptoms and disability; 5) exposures of past concern; 6) health risk communication; and 7) the limits of

science and epidemiology. The Thirteenth Conference on Military Medicine, held in May 1999 on the campus of the Uniformed Services University of the Health Sciences in Bethesda, Maryland, served as a public consensus committee meeting. During that 3-day open meeting (agenda and transcripts available on request), the consensus committee listened to Federal, public, industrial, and private experts, and they moderated discussions related to unexplained symptoms after terrorism and war. Two closed committee meetings occurred later to refine the consensus statement. The planning committee reviewed a near-final draft of the consensus statement, offered comments, and the consensus committee had the option of revising the statement accordingly. The goal of this effort is to review evidence from diverse sources and reach broad-based conclusions regarding a topic that has become a complex, multidisciplinary inquiry.

1. What is the strength of the epidemiologic and scientific evidence that war and terrorism or similar catastrophic events cause unexplained symptoms?

Consistent historical and epidemiologic evidence suggests that war veterans are at an increased risk of unexplained symptoms and illness.^{1,17} Although clusters of unexplained symptoms have received various diagnostic labels, studies show extensive overlap across these syndromes.¹⁸ Veterans' unexplained symptoms have included fatigue, dizziness, musculoskeletal pain and stiffness, breathlessness, headache, difficulty sleeping, chest pain, gastrointestinal symptoms, depression, persistent anxiety, and a sense of being distant or "cut off" from others. Similar overlapping illnesses occur commonly in the civilian population too, suggesting war is only one of several potential precipitating factors.^{7,19}

In recent years, posttraumatic stress disorder (PTSD) has received extensive public, clinical, and scientific attention and has often been invoked to explain otherwise unexplained symptoms occurring after war. PTSD can occur after any catastrophic or life-threatening event and was first defined in its modern form in the *Diagnostic and Statistical Manual for Mental Disorders*, Third Edition. PTSD was originally called "post-Vietnam syndrome" because of the large number of veterans of that conflict who reported these symptoms. The symptoms considered most characteristic of PTSD are emotional and include recurrent and intrusive recollections of the inciting event, distressing dreams, flashbacks, and avoidance of thoughts and activities associated with the trauma. However, physical symptoms are common in PTSD, including difficulty with sleep, impaired concentration, and hypervigilance. Surveys of military medical records from World War I occasionally reveal clusters of symptoms similar to those of modern PTSD descriptions.⁵ Arguably, however, physicians of the time could have been more alert to the physical rather than psychosocial manifestations of illness. During World War II, some of these same symptoms were again described in the medical records of U.K. servicemen, although they were not then viewed as constituting a discrete illness.⁵

A second overlapping pattern of illness after war includes unexplained physical symptoms. Historical and clinical research suggests that unexplained physical symptoms occur with greater frequency among war veterans than among comparable individuals groups who are not war veterans.^{5,20-24} In contrast to the situation after war, the studies investigating whether natural disasters or terrorism increase one's risk of unexplained physical symptoms offer conflicting results. Numerous cross-sectional studies confirm a link between natural disaster and unexplained physical symptoms.²²⁻²⁸

However, the link is only inconsistently confirmed in longitudinal studies.^{22,27,28} Reasons can include methodologic problems (eg, use of measures that are insensitive to change) or varying disaster characteristics.

Technologic accidents, manmade disasters often associated with the fear of toxic exposures, are correlated with heightened perceptions of health risk.²⁹ These events tend to involve controversy and public debate, heightened fear, anticipation of unpredictable and affect laden health consequences (eg, cancer, reproductive abnormalities, or risk to child health), and a perceived loss of control within communities near the accident. Powerful outside interests such as industry or government agencies are frequently involved and offer an easily identifiable focus for blame and outrage.³⁰

In the final analysis, physical versus psychologic distinctions regarding unexplained symptoms might rest on preconception and perspective rather than a priori hypothesis testing. Historically, observers of syndromes of unexplained symptoms have often drawn differing conclusions from like presentations. Whereas some observers have preferred to see a common physiological mechanism that explains symptoms, others have postulated common psychologic traumas ranging from childhood abuse to current stressors. Still others have invoked the tendency for some individuals to seek relief from social predicaments and for some clinicians and scientists to derive novel illnesses that accommodate them.^{31,32}

2. What epidemiologic and scientific evidence is necessary to conclude that an exposed population suffering from unexplained symptoms has a new and unique illness?

To distinguish a new illness, several elements should be present. First, the illness must be clinically

relevant and recognizable. Methods used to define illness from symptoms include consensus opinion and statistical approaches such as factor analysis. All methods have limitations, and the best approach relies on more than one method. For example, Fukuda and colleagues found agreement between the views of expert clinicians and factor analysis when defining chronic multisymptom illness.³³ Agreement across multiple methods increases confidence that a valid illness has been defined. The sole use of a statistical method like factor analysis is associated with significant limitations. Of note, factor analyses performed on large samples will generate clustering even within a set of random numbers. It is therefore important that statistical approaches involve replication in an independent sample and that appropriate control groups are used to investigate whether identified symptom syndromes occur at an increased prevalence or incidence in populations thought to be at greatest risk. Symptom clustering identified using statistical techniques can be highly dependent on the manner in which data is collected (eg, an algorithmic symptom interview can introduce artifactual symptom clustering because the questions are asked in clusters). Similarly, syndromes identified statistically might not make clinical or pathophysiological sense, could be awkward to implement in practice, or could be the result of confounding.³⁴

Symptoms alone are particularly problematic for use as an indicator of disease. Unexplained symptoms occur frequently in the absence of characteristic signs or laboratory abnormalities. Research suggests that at least one third of symptoms in both clinical and population-based studies are medically unexplained.³⁵ It is therefore difficult to identify a new illness “signal” against the backdrop of competing symptom “noise” in a population of interest. This problem increases the likelihood that a novel disease could go unrecognized. Therefore, when societal suspicion is

high, numerous epidemiologic studies of exposed and unexposed samples (eg, silicone breast implants) are often completed before a scientific and societal consensus is reached that a novel disease is unlikely.³⁶ In the interim, public speculation (eg, media, political, or scientific debates) surrounding the suspected health effects can increase healthcare use and symptom reporting in the same populations thought to be most at risk of illness.^{37–39} This rise in healthcare use can cause some observers to draw erroneous or premature conclusions regarding the presence of an emerging disease.

Because an emerging disease manifesting only symptoms can be difficult to distinguish from overlapping clusters of unexplained symptoms like fibromyalgia and chronic fatigue syndrome, identification of a *cause* is useful for establishing the presence of disease. Bradford Hill was among the first to establish criteria for estimating the strength of a causal inference, and these “Hill Criteria,” although refined over time, have long served as a cornerstone for drawing causal inferences. These criteria are used to assess a collection of studies addressing the same causal hypothesis. Important factors to consider when assessing evidence regarding potential causal links are:

1. Presence of association (the strength and consistency of association across available studies of differing methodology).
2. Appropriate temporal sequence between putative exposure and illness (exposure must precede illness onset to be considered as a causal agent). If the illness subsides on removal of exposure and recurs with rechallenge, a causal link is more likely. An unpredictable, latent, or varying interval between exposure and illness usually decreases the likelihood that an association represents a causal link, although carcinogenic exposures and exposures to radi-

ation typically cause disease after a latent period.

3. Presence of a “dose-response” relationship between exposure and illness. If it can be shown that increasing dose of exposure leads to increasing risk or severity of illness, then the likelihood that an association represents a causal link is higher.
4. Biologic plausibility of a causal exposure–illness link. The less plausible the putative causal mechanism, the greater is the probability an association is the result of chance or confounding.

Simply finding a physiological correlate of an illness does not establish the illness as a disease or the association as causal, because causality can run in either direction: the physiological abnormality can be a cause, effect, or marker of symptoms. For example, electroencephalographic changes associated with pain can be a marker of an underlying cause, a nervous system response to pain, or a nervous system response to previous treatments administered for the pain. Technologic capacity to assess physiological parameters has increased dramatically in recent years, whereas ability to discern the clinical significance of these physiological changes has often lagged further behind. Early etiologic hypotheses based on laboratory assays often later prove to be the result of chance or the absence of adequate controls (eg, so-called “chronic Epstein-Barr virus” syndrome). Similarly, nascent statistical, imaging, or measurement approaches need careful validation and clinical correlation before applying them to the study of symptom-based illnesses or results are likely to raise more questions rather than insights. A detailed review of sampling and measurement issues germane to symptoms research has been recently published.³⁵

Our understanding of illnesses, particularly those based on symptoms alone, is shaped by prevailing

culture, ideas, and beliefs. The etiologic void that accompanies syndromes based on medically unexplained symptoms amplifies these influences. Social and historical factors have influenced the name (eg, “soldier’s heart,” neurasthenia, chronic fatigue immune dysfunction syndrome, hysteria), theoretical underpinnings (eg, psychologic repression, chronic infection, environmental toxicities, immunologic dysfunction), populations at risk (eg, “yuppie flu,” Gulf War syndrome), and fashionable treatments (psychoanalysis, corticosteroids, exercise, low-level toxin avoidance) of medically unexplained symptoms. These factors influence what symptoms are considered the prominent ones, what clinical specialists are sanctioned to treat an illness, and what types of clinical and scientific investigations are completed to understand an illness.

Although history shows that new diseases are occasionally recognized, there are many more examples of comparable symptoms clusters that receive different names and identities because of the different historical and medical contexts in which they occurred. During World War I, for example, medically unexplained symptoms were commonly interpreted and treated as a cardiac problem (“disordered action of the heart”) or as a neurologic problem caused by microscopic hemorrhaging (“shell shock”). Similar symptoms after the Gulf War have been explained as low-level environmental toxicities. Some have suggested that even PTSD is the product of potent cultural determinants characteristic of the unique period in which the illness was defined.⁴⁰ Feinstein and others have suggested that illnesses should not adopt names that presume a cause (eg, PTSD, Gulf War illnesses) because this causal presumption gradually becomes reified rather than systematically examined.^{41,42}

3. What is the strength of the evidence that unexplained symptoms after war or terrorism can be prevented or mitigated using population or healthcare-based strategies, especially strategies involving communication and education?

Like in many areas of science and medicine, we know more about what does not work than what works for medically unexplained symptoms after war or terrorism. After every major conflict since the World War I, there have been important inquiries into the management of subsequent unexplained symptoms. These inquiries have usually concluded that selection is significant, that training and unit cohesiveness are protectors against such disorders, and that once in combat, the intensity of battle is an important variable leading to “breakdown.”^{43,44} Despite this accumulated expertise, new wars continue to produce large numbers of veterans experiencing unexplained symptoms.^{45,46} Nonetheless, available research allows speculation on what preventive and clinical factors might be helpful.

Pre-event Screening. Evidence of the feasibility and efficacy of predeployment screening programs designed to differentiate individuals based on vulnerability to unexplained symptoms after war is lacking. Severe psychiatric risk factors are likely to be recognized within present military systems (eg, screening for severe diseases or psychiatric illness). Screening for modest risk factors (eg, those with a remote history of psychiatric illness) yield gains that are too small to achieve practical use. For example, after World War II, it was concluded that rigorous screening would effectively remove most of those at high risk of breakdown but only at the expense of removing many who would have excelled.⁴⁷ Given the heterogeneous nature of unexplained symptoms, the same dilemma is likely to hold.

Pre-event Intervention. This is also an area that has received little systematic study. It is possible that psychosocial efforts to prepare all or subgroups of individuals for war or terrorist exposures can offer benefits. Cognitive-behavioral theory holds that expectations and beliefs determine emotional and behavioral responses to external events.⁴⁸ Cognitive-behavioral interventions that prepare military personnel or first-responders to the realities of wartime and terrorist events can lead to more adaptive behavioral and emotional responses to these events. These approaches applied in predeployment training can help prevent unexplained symptoms after war or terrorism. For example, studies from World War II indicate that troops with a realistic idea of what war involved before they entered battle were less likely to suffer breakdowns than those holding distorted or glamorized views.⁴⁹

Research in both humans and animals suggests that when several stressors are closely linked in time or when an animal is exposed to multiple stressors, the effects are more prolonged than if the same exposures occur over a longer period of time.⁵⁰ Hence, it might be optimal to expose troops to necessary perturbations well in advance of deployment to minimize the burden on them once war or terrorism is inevitable.

Intervention During the Event. War and terrorism are events fraught with multiple biologic, psychologic, and social stressors. Stress research suggests that the nature and intensity of a stressor might not be as important a determinant of physiological response as the environment and context in which the stressor occurs. Studies in animals and humans have demonstrated that the adverse consequences of physiological stressors are pronounced when individuals lack: 1) control; 2) predictability; 3) direction; and 4) social support.⁵⁰ Observations from war usually, but not always, find that higher-ranking soldiers and those from units with

higher *esprit de corps* have lower rates of illness, and that support troops, often isolated and in small groups, tend to have higher illness rates even though they were exposed to less intense levels of fighting.⁵¹ The importance of social support as a buffer against the emergence of somatic symptoms was also demonstrated in a population-based survey after the terrorist attack on the WTC.²⁶ Interventions aimed at improving cohesion among military units and first-response teams, providing appropriate direction and high-quality leadership, building a sense of individual responsibility and control, and reducing uncertainty under inherently chaotic circumstances are most likely to improve performance and to maximize health outcomes.

Postevent Population-Based Interventions. A point of considerable importance regarding postdeployment intervention is that well-intended approaches can often create more harm than benefit. The majority of individuals exposed to war, terrorism, or other major life stressors gets better spontaneously and does not develop unexplained symptoms. For example, there is essentially no systematic evidence that routine “critical incident debriefing” improves health outcomes, and what evidence there is suggests debriefing occasionally does more harm than good.⁵² Debriefings are also costly and difficult to implement successfully on any large scale. However, evidence suggests identifying smaller numbers of high-risk people (eg, those with acute stress disorders) and providing them with several sessions of cognitive-behavioral therapy delivered by a skilled therapist can prevent PTSD.⁵³

Future planning for terrorist activity and postwar circumstances should routinely anticipate that several issues are likely to arise after any event involving possible exposures that are popularly but not scientifically associated with adverse health outcomes. Even when science

fails to support a relationship between an exposure and an illness, the average person can still perceive significant risk. Normative ways people infer causality rely mainly on beliefs and perceptions rather than logic or science.^{30,54} Common perceptions regarding exposures were previously addressed. For example, any perception of possible radiation exposure can lead to fear, outrage, and the presumption of exposure and of future illnesses, even if scientific estimates of exposure suggest it is insignificant or nonexistent.

Survey evidence suggests the public mistrusts industry and government to respond scrupulously.^{55,56} Consequently, after war or terrorism, government response agencies must employ appropriate expertise to facilitate communication between government representatives and affected individuals, their families, and their advocates. If opportunities to communicate are missed or mishandled, public distress and mistrust can worsen, and many with unrelated but otherwise unexplained physical symptoms might attribute their symptoms to war or terrorism-related exposures. The general public might be more likely to perceive government or industrial agencies as perpetrators and those with health concerns as victims deserving of remuneration, extending and exacerbating reduced functioning.

Education programs for those affected after war or terrorism are a logical and practical postevent strategy. For example, the most common injuries and illnesses suffered after exposure to war or terrorism are self-limited symptoms. Public health messages reminding people that symptoms are likely to resolve with time can reduce morbidity and unneeded medical care. These public messages need to avoid stigmatizing the sufferers of unexplained symptoms or to unwittingly trivialize them as “the worried well.” Public health officials should not fan the flames of a social “contest” in which the stigmatized group feels they must prove

the validity of their symptoms, leading to escalating controversy, symptoms, disability, and litigation. Compassionate health messages that separate the reality of individual suffering from what is known or unknown about an alleged health threat are crucial.

From a policy perspective, the large role that social factors play in every aspect of unexplained symptoms after war, terrorism, or other related events suggests that public statements, research practices, and clinical care should be formulated with direct input from the different groups and individuals who have a stake in the outcome (eg, affected individuals, advocacy groups). Policies must be communicated openly and with full disclosure, because past mistakes are well documented (eg, destroyed or lost files, cover-ups). The power of the media to amplify mistakes must be recognized. Therefore, careful procedures for providing the media with accurate information that is compassionate and respectful of those the public perceives as victims becomes a matter of public health rather than simply good public relations.

Postevent Health Care. Once an individual has developed medically unexplained symptoms after war or terrorism and seeks care for them, some treatments can help and others will exacerbate or perpetuate problems. The focus of constructive treatment for unexplained symptoms is on symptom management and efforts to restore or enhance functioning. Aggressive efforts to identify objective clinical findings and establish a “hard diagnosis” are usually inappropriate, can result in increased adverse effects from medical care and diagnostics, and can perpetuate patients’ disability.⁵⁷ First and foremost, clinicians must handle patient concerns respectfully, viewing them as legitimate from the outset. This is particularly important when the patient mistrusts the clinician, as is frequently the case in military or workplace settings.

Well-intentioned care involving exhaustive diagnostic testing can create the impression that the likelihood of a serious undiagnosed disease is high, even when it is not. Diagnostic testing performs best when clinical suspicion is high, and even the best tests produce a high proportion of false-positive findings when clinical suspicion is low. Unnecessary diagnostic tests seldom benefit patients, and they do not provide lasting reassurance when they are negative.^{58,59}

Clinical interventions must be connected to appropriate programs that assist affected individuals in transitions back into military, civilian, workplace, and family life. The effects of chronic unexplained symptoms can take time to reverse and require incremental return to work strategies. “All-or-nothing” return to work approaches easily overwhelm affected individuals and result in high failure rates. Both nonpharmacologic (eg, cognitive behavioral therapy, aerobic exercise) and pharmacologic (nonnarcotic analgesics, tricyclic drugs, antidepressants) treatments are useful for managing unexplained symptoms and supported by evidence from clinical trials.⁶⁰ Early, optimally primary care, intervention is important, because unexplained symptoms can become increasingly treatment-refractory the longer they have lasted.^{61,62} Many important perpetuating factors exist and often become more prominent with time.⁴ An evidence-based approach to evaluating and managing unexplained symptoms is detailed elsewhere.⁶³

Conclusions

The conclusions outlined in this consensus statement are specifically limited to situations involving illness in the absence of disease (ie, patient-reported symptoms and observable disability or suffering that occurs in the absence of objective signs or valid laboratory evidence of structural pathology on clinical examination).

Question 1. What is the strength of the epidemiologic and scientific evidence that war and terrorism or similar catastrophic events cause unexplained symptoms?

Consistent evidence suggests an excess of symptoms and illness among war veterans. To a lesser extent, the findings are similar among individuals exposed to other catastrophic events. These unexplained symptom syndromes go by a variety of names. Most of them are difficult to defend as discrete or unique diseases, but that does not invalidate the illness that affected individuals report.

Question 2. What epidemiologic and scientific evidence is necessary to conclude that an exposed population suffering from unexplained symptoms has a new and unique illness?

It is rare that an apparently novel illness based solely on unexplained symptoms can be shown to result from unique environmental exposures or disease processes. This practical reality is balanced by the likelihood that medically unexplained symptoms are sometimes caused by environmental exposures or disease processes. However, the chance of scientific errors when investigating illnesses defined on the basis of unexplained symptoms is great given the absence of consistent examination, laboratory, or imaging characteristics on which to base the case definition. Consequently, broader opportunities can exist for social and historical context to influence the illness recognition process. The identification of novel or specific mechanisms for such illnesses is an infrequent event, requiring replicated epidemiologic studies and societal, clinical, and scientific consensus. Given these realities, it might be best to start with existing case definitions for overlapping illnesses in the civilian population (eg, fibromyalgia, chronic fatigue syndrome, chronic multisymptom illness) rather than with a novel name and definition that reifies speculative mechanisms be-

fore scientific evidence and medical consensus supports them.

Question 3. What is the strength of the evidence that unexplained symptoms after war or terrorism can be prevented or mitigated using population or healthcare-based strategies, especially strategies involving communication and education?

There is little systematic research on which to base strong and unequivocal recommendations regarding population-based or healthcare-based interventions that are proven to prevent or mitigate postwar syndromes. Further studies are necessary. Research should examine both physiological and psychosocial factors that can portend a higher baseline risk of unexplained symptoms after war or terrorism, pre-event strategies to prevent adverse health outcomes, and postevent interventions that can improve the health of individuals who already experience unexplained symptoms.

Acknowledgments

The consensus committee wishes to acknowledge the contributions and arrangements made by members of the Unexplained Symptoms After Terrorism & War Consensus Project Planning Committee. Members of the planning committee include Charles Engel, MD, MPH (Uniformed Services University); Patricia Collins, RN (Office of the Assistant Secretary of Defense for Health Affairs, Tri-care Management Activity); Howard Fauver, MD (Uniformed Services University); Gary Gackstetter, DVM, MPH, PhD (Uniformed Services University); Kenneth Hyams, MD, MPH (Navy Medical Research Center); Michael E. Kilpatrick, MD, (Office of the Special Assistant for Gulf War Illnesses, Department of Defense); Larry Laughlin, MD, PhD (Uniformed Services University); Craig Llewellyn, MD, MPH (Uniformed Services University); Peter Mazzella, MSW (Department of Health & Human Services); Frances Murphy, MD, MPH (Department of Veterans Affairs); CAPT Laura Omer, NC, USN (Uniformed Services University); Matthew Puglisi (The American Legion); James Riddle, DVM, MPH (Office of the Assistant Secretary of Defense for Health Affairs); Bryce Reddington, PhD (Henry M. Jackson Foundation for the Advancement of Military Medicine); Michael Roy, MD, MPH (Uniformed Services University); David Trump, MD, MPH (Office

of the Assistant Secretary of Defense for Health Affairs); Jay Shapiro, MD (Johns Hopkins University School of Medicine); and Col John Graham (British Ministry of Defence Liaison Officer, Gulf Health).

References

- Hyams KC, Wignall FS, Roswell R. War syndrome and their evaluation: from the U.S. Civil War to the Persian Gulf War. *Ann Intern Med.* 1996;125:398–405.
- France D. Now, WTC syndrome? *Newsweek.* November 5, 2001.
- Centers for Disease Control and Prevention. Self-reported increase in asthma severity after the September 11 attacks on the World Trade Center, Manhattan, New York, 2001. *MMWR Morb Mortal Wkly Rep.* 2002;51:781–784.
- Engel CC Jr, Katon WJ. Population and need-based prevention of unexplained symptoms in the community. In: Institute of Medicine. *Strategies to Protect Health of Deployed U. S. Forces: Medical Surveillance, Record Keeping, and Risk Reduction.* Washington, DC: National Academy Press; 1999:173–212.
- Jones E, Hodgins VR, McCarthy H, et al. Post-combat syndromes from the Boer war to the Gulf war: a cluster analysis of their nature and attribution. *BMJ.* 2002;324:321–324.
- Clauw DJ, Chrousos GP. Chronic pain and fatigue syndromes: overlapping clinical and neuroendocrine features and potential pathogenic mechanisms. *Neuroimmunomodulation.* 1997;4:134–153.
- Aaron LA, Buchwald D. A review of the evidence for overlap among unexplained clinical conditions. *Ann Intern Med.* 2001;134:868–881.
- Kipen H, Fiedler N. Invited commentary: sensitivities to chemicals: context and implications. *Am J Epidemiol.* 1999;150:13–16.
- Barsky AJ, Borus JF. Functional somatic syndromes. *Ann Intern Med.* 1999;130:910–921.
- Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet.* 1999;354:936–939.
- Mayou R, Sharpe M. Diagnosis, illness and disease. *Quart J Med.* 1995;88:827–831.
- Susser M. Disease, illness, sickness: impairment, disability and handicap. *Psychol Med.* 1990;20:471–473.
- Burkett GL. Culture, illness, and the biopsychosocial model. *Fam Med.* 1991;23:287–291.
- Engel GL. The need for a new medical model: a challenge for biomedicine. *Science.* 1977;196:129–136.
- Kleinman A, Eisenberg L, Good B. Culture, illness and care: clinical lessons from anthropologic and cross-cultural research. *Ann Intern Med.* 1978;88:251–258.
- Jennings D. The confusion between disease and illness in clinical medicine. *Can Med Assoc J.* 1986;135:865–870.
- Jones E, Wessely S. A case of chronic fatigue syndrome after the Crimean War and Indian Mutiny. *BMJ.* 1999;2:1645–1647.
- Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities. *Arch Intern Med.* 1994;154:2049–2053.
- Gardner JW, Gibbons RV, Hooper TI, et al. Identifying new diseases and their causes: the dilemma of illnesses in Gulf War veterans. *Mil Med.* 2003;168:186–193.
- Feudtner C. 'Minds the dead have ravished': shell shock, history and the ecology of disease-systems. *History of Science.* 2000;31:377–420.
- Bourke J. *Dismembering the Male: Men's Bodies, Britain and the Great War.* Chicago: University of Chicago Press; 1996.
- Solomon Z, Mikulincer M, Habershaim N. Life-events, coping strategies, social resources, and somatic complaints among combat stress reaction casualties. *Br J Med Psychol.* 1990;63:137–148.
- Davidson JR, Hughes D, Blazer DG, et al. Post-traumatic stress disorder in the community: an epidemiological study. *Psychol Med.* 1991;21:713–721.
- Engel CC Jr, Liu X, McCarthy BD, et al. Relationship of physical symptoms to posttraumatic stress disorder among veterans seeking care for Gulf war-related health concerns. *Psychosom Med.* 2000;62:739–745.
- McFarlane AC, Atchison M, Rafalowicz E, et al. Physical symptoms in post-traumatic stress disorder. *J Psychosom Res.* 1994;38:715–726.
- Galea S, Ahern J, Resnick H, et al. Psychological sequelae of the September 11 terrorist attacks in New York City. *N Engl J Med.* 2002;346:982–987.
- Andreski P, Chilcoat H, Breslau N. Post-traumatic stress disorder and somatization symptoms: a prospective study. *Psychiatry Res.* 1998;79:131–138.
- Smith EM, North CS, McCool RE, et al. Acute postdisaster psychiatric disorders: identification of persons at risk. *Am J Psychiatry.* 1990;147:202–206.
- Renn O. Health impacts of large release of radionuclides. Mental health, stress and risk perception: insights from psychological research. *CIBA Foundation Symposium.* 1997;203:205–231.
- Bennett P. Understanding responses to risk: some basic findings. In: Bennett P, Calman K, eds. *Risk Communication and Public Health.* Oxford: Oxford Medical Publications; 1999:3–19.
- Arpino C. The rise and fall of the psychosomatic hypothesis in ulcerative colitis. In: *Making Sense of Illness: Science, Society and Disease* (RA Aronowitz, editor). Cambridge: Cambridge University Press; 1998:39–56.
- Aronowitz R. From myalgic encephalitis to yuppie flu. In: *Making Sense of Illness: Science, Society, and Disease* (RA Aronowitz, editor). Cambridge: Cambridge University Press; 1998:19–38.
- Fukuda K, Nisenbaum R, Stewart G, et al. Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *JAMA.* 1998;280:981–988.
- Wegman D, Woods NF, Bailar J. Invited commentary: how would we know a Gulf War syndrome if we saw one? *Am J Epidemiol.* 1997;146:704–711.
- Kroenke K. Studying symptoms: sampling and measurement issues. *Ann Intern Med.* 2001;134:844–855.
- Angell M. Do breast implants cause systemic disease? Science in the courtroom. *N Engl J Med.* 1994;330:1748–1749.
- Hopwood D, Guidotti T. Recall bias in exposed subjects following a toxic exposure incident. *Arch Environ Health.* 1988;43:234–237.
- Decoufle P, Holmgren P, Boyle C, et al. Self-reported health status of Vietnam veterans in relation to perceived exposure to herbicides and combat. *Am J Epidemiol.* 1992;135:312–323.
- Neutra R, Lipscomb J, Satin K, et al. Hypotheses to explain the higher symptom rates observed around hazardous waste sites. *Environ Health Perspect.* 1991;94:31–38.
- Young A. *The Harmony of Illusions, Inventing Post-Traumatic Stress Disorder.* Princeton: Princeton University Press; 1995.
- Feinstein AR. *Nosologic Challenges of Diagnostic Criteria for a 'New Illness.'* Conference on Federally Sponsored Gulf War Veteran's Illnesses Research; Pentagon City, VA; June 1998.
- Scadding G. Essentialism and nominalism in medicine: logic of diagnosis in disease terminology. *Lancet.* 1996;348:594–596.
- Belenky GL, Noy S, Solomon Z. Battle stress: the Israeli experience. *Military Review.* 1985;65:28–33.
- Belenky GL, Noy S, Solomon Z. Battle stress, morale, cohesion, combat effec-

- tiveness, heroism, and psychiatric casualties: the Israeli experience. In: *Contemporary Studies in Combat Psychiatry* (G. Belenky, editor). Westport, CT: Greenwood Press; 1987.
45. Jones E, Palmer I. Army psychiatry in the Korean War: the experience of 1 commonwealth division. *Mil Med.* 2000;165:256–260.
 46. Unwin C, Blatchley N, Coker W, et al. Health of UK servicemen who served in the Persian Gulf War. *Lancet.* 1999;353:169–178.
 47. Ingraham L, Manning F, Gabriel RA. *Military Psychiatry: A Comparative Perspective*. Westport, CT: Greenwood Press; 1986:61–75.
 48. Beck AT. Cognition, affect, and psychopathology. *Arch Gen Psychiatry.* 1971;24:495–500.
 49. Stafford-Clark D. Morale and flying experience: results of a wartime study. *Journal of Mental Science.* 1949;95:16–17-27–29.
 50. Seeman TE, McEwen BS. Impact of social environment characteristics on neuroendocrine regulation. *Psychosom Med.* 1996;58:459–471.
 51. Gal R, Jones FD. *A Psychological Model of Combat Stress*. Washington, DC: Office of the Surgeon General, US Army; 1999.
 52. Wessely S, Rose S, Bisson J. Brief psychological interventions ('debriefing') for treating immediate trauma-related symptoms and the prevention of post-traumatic stress disorder (Cochrane Review). In: *The Cochrane Library*. Oxford: Update Software; 1999.
 53. Bryant R, Sackville T, Dang S, et al. Treating acute stress disorder: an evaluation of cognitive behavior therapy and supportive counselling techniques. *Am J Psychiatry.* 1999;156:1780–1786.
 54. Tversky A, Kahneman D. Judgment under uncertainty; heuristics and biases. *Science.* 1974;185:1124–1131.
 55. Lipset SM, Schneider W. The decline of confidence in American institutions. *Political Science Quarterly.* 1983;98:379–402.
 56. Harris L, et al. Confidence in leadership. *Harris Poll Number 9* (http://www.harrisinteractive.com/harris_poll/printerfriendlyindex) 1999.
 57. Hadler NM. Fibromyalgia, chronic fatigue, and other iatrogenic diagnostic algorithms. Do some labels escalate illness in vulnerable patients? *Postgrad Med J.* 1997;102:61–177.
 58. Howard L-M, Wessely S. Reappraising reassurance: the role of investigation. *J Psychosom Res.* 1996;41:307–311.
 59. Coia P, Morley S. Medical reassurance and patients' responses. *J Psychosom Res.* 1999;45:377–386.
 60. Kroenke K, Swindle R. Cognitive-behavioral therapy for somatization and symptom syndromes: a critical review of controlled clinical trials. *Psychother Psychosom.* 2000;69:205–215.
 61. Bombardier CH, Buchwald D. Outcome and prognosis of patients with chronic fatigue vs. chronic fatigue syndrome. *Arch Intern Med.* 1995;155:2105–2110.
 62. Kroenke K, Jackson JL. Outcome in general medical patients presenting with common symptoms: a prospective study with a 2-week and a 3-month follow-up. *Fam Pract.* 1998;15:398–403.
 63. Kroenke K. Patients presenting with somatic complaints: epidemiology, psychiatric comorbidity, and management. *Int J Methods Psychiatric Res.* 2003;12:34–43.