Contract No. IOM-2794-04-001
The National Academies

SUPPLEMENT:

HEALTH EFFECTS OF PERCEIVED EXPOSURE TO BIOCHEMICAL WARFARE AGENTS

Prepared for the National Academies
by
The Center for Research Information, Inc.
9300 Brookville Rd
Silver Spring, MD 20910
http:// www.medresearchnow.com
(301) 346-6501
cri@ix.netcom.com

April, 2004

ACKNOWLEDGMENTS

Submitted to Dr.William Page, The National Academies, Institute of Medicine, Program Officer, Advisory Panel for the Study of Long-term Health Effects of Participation in Project SHAD (Shipboard Hazard and Defense).

The supplement addresses and describes a growing body of health effects research and interest centered upon the psychogenic sequelae of the trauma that may arise from perceived exposure to chemical and biological weaponry, or related agents.

This supplement is incorporated by reference into the health effects report of each agent reviewed by the Center for Research Information under National Academies Contract No. IOM-2794-04-001.

The Center for Research Information recognizes its ethical and contractual obligation to update, revise, or otherwise amend this supplement if new or necessary information on its subject matter should arise, be requested, or be ascertained during the contract period.

The Principal Investigator wishes to thank Matthew Hogan, Linda Roberts, Lawrence Callahan, and Emnet Tilahun for research assistance, editorial content assistance, and project input.

Principal Investigator: Victor Miller

Text Draft & Editing: Victor Miller & Matthew Hogan
Project Manager: Matthew Hogan
Administration: Linda Roberts

SPECIAL NOTE ON CITATIONS AND AUTHORITIES

Reference to particular works shall be by the name of the principal author (or editor, where appropriate). It will appear appended inside parentheses to the sentence or paragraph which references the information or quotation from that particular work or authority. If, however, the source is already cited or identified within the text, it will not appear at the end of the sentence or paragraph.

The year of publication may be appended to clarify which of several sources by the same principal author/editor is being cited, or if otherwise appropriate for clarity.

Citations will be to an authority listed in the Bibliography at the end of this report. Worldwide web references may include URL's.

TABLE OF CONTENTS

PREFACE

Medical scholarship is increasingly accepting the idea that the simple awareness of being exposed to agents of chemical or biological warfare can pose significant health effects for an individual. "The threat or perceived exposure to chemical warfare agents has been shown to have a lasting and adverse impact on human health," write Col. James Riddle and his co-authors in a study published in the August 2003 issue of *Military Medicine*. The trauma of a perception of exposure may be sufficient to elicit stress-induced debilitation. "The [mere] belief that chemical weapons were being used," they observe, "may cause or exacerbate illness because of . . . maladaptive stress response." (Riddle)

The authors of the study, whose affiliations span the Pentagon's Health Affairs office, the Department of Veterans Affairs, the Naval Research Center, and the U.S. Army Medical Research Institute of Chemical Defense, came to this determination after finding that mysterious poor health conditions of certain Persian Gulf War (1990-1991) veterans did not correlate with any demonstrated actual exposure to weapons of mass destruction, but nevertheless did seem to correlate with a subjective belief on the part of the veterans that they had in fact been so exposed. "Feelings of helplessness in the face of a ubiquitous and unseen killer can be overwhelming," Riddle et al. explain.

Psychogenic effects can be short and long term. "The psychological impact of a potential or actual chemical attack can result in immediate casualties from acute stress disorder, grief, anger, scapegoating, and somatization disorders. Longer term effects include phobias, sleep disorders, post-traumatic stress disorder, substance abuse, and major depression." Specific studies on veterans who have undergone mustard-gas exposure in military tests compel the conclusion that psychogenic effects of the subjective awareness of exposure to biochemical weaponry are a major set of health effects. "The life threat inherent in . . . exposure," one such study concludes, "suggests that experimental mustard-gas exposure is a traumatic event that meets the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed. DSM-IV) A.1 criterion for a diagnosis of PTSD [Post-traumatic stress disorder]." (Schnurr 2000)

Authoritative acceptance of the existence of purely psychogenic health effects of perceived exposure appears to be increasingly firm. "The IOM [Institute of Medicine] Committee [on Health Effects Associated with Exposures during the Gulf War] recognized the impact on health from the threat of or perceived exposure to chemical and biological warfare agents," Riddle and his colleagues report. An IOM committee in 1993, also evaluating the effects on veterans of mustard-gas testing from five decades earlier, determined in a similar vein that "the best available evidence indicates a causal relation between the experiences of the subjects . . . and the development of psychological effects." (IOM)

The Riddle study and review further argues that greater study of the psychogenic effects of perceived exposure needs to be a key concern for veterans' health. In a statement directed primarily at the studies of the health condition of Persian Gulf War veterans but

which clearly possesses validity in regard to the health effects of all veterans who have felt exposed to biochemical weapons, the authors express a consensus that "the Department of Veterans Affairs and IOM should examine the health impact from . . . the perceived exposure to chemical warfare agents as an important health concern and cause of morbidity among . . . veterans." The practical importance is driven home in studies examining the psychological effects on military personnel of biochemical warfare agent testing. These studies consistently note significantly higher levels of long-term health problems and long-term medical services use by veterans who have experienced psychogenic effects from perceived chemical weapons exposure. (Schnurr 2000, Schnurr 1996, Friedman 1994)

The area remains problematic, however, because questions persist as to how easily and authoritatively researchers and diagnosticians can distinguish psychogenic effects from pathogenic or toxicological ones. "The psychological trauma of experiencing a potential or real attack from chemical warfare agents," Riddle et al. note, "presents a confounding factor in evaluating the health effects of actual exposures." The possible confounding of psychogenic health effects of exposure with the physical effects induced by a chemical or biological agent is an area not fully studied. "[F]urther research is ongoing," state the researchers, as to "whether there are synergistic effects among various agents, including [the action of] psychological stressors. . . ."

This supplement has been prepared to address in a concentrated and extended fashion the new, evolving, and important issues of psychogenic health effects arising from awareness of biochemical agent exposure. Precisely because it is a new, evolving, and difficult field, with research and publication actively in progress, this supplement may be further amended or developed over the contract period as new data and scholarship may arise, or as further inquiry is requested.

I. EXECUTIVE SUMMARY

This report constitutes a general supplement by the Center for Research Information for each of its individual reviews of the human health effects of exposure to select biological and chemical warfare agents (and related simulants and tracers) used in the Department of Defense's Project SHAD (Shipboard Hazard and Defense) program of the 1960s. This supplement's purpose is to provide information regarding the psychogenic health effects evoked by a mere subjective awareness of having been exposed to one or more of such agents. It should be added for the sake of clarity that any issues related to psychological or neuropsychiatric effects arising from the physiological harm induced by a specific agent are not included in this supplement, but are treated separately in the health effects report for the respective agent.

Biological and chemical weapons function as more than simply agents of direct harm to life and bodily integrity. They are also psychological weapons. Their insidious mode of operation, and the lack of certainty about their presence and persistence, combine to create an unusual level of fear and stress among those believing themselves exposed to them. Studies which have assessed subjective reactions to incidents of the use of biochemical weapons in intentional attacks, accidental releases, and controlled experiments suggest that psychological harm arising resulting from awareness or perception of the use of such agents may result in a number of cases of psychological harm comparable to or even far exceeding the number of cases suffering persistent physiological harm.

Of course, as noted in the preface, precisely distinguishing psychogenic effects from physiologically-induced ones remains a challenge in research. A related problem is the possible presence of co-morbidities of a psychological nature (e.g., substance abuse, depression) in victims which might also confound an etiological determination. Nevertheless, with the increasing study and medical acceptance over the past few decades of the existence and nature of psychiatric conditions like post-traumatic stress disorder, as well as with increasing study of incidents of biochemical weapons exposure, certain effects likely to be of psychogenic origin have been observed and studied in association with perceived exposure to biochemical warfare agents.

Although there have been other effects and co-morbidities observed, the most common and most studied type of psychogenic effect of perceived exposure to biochemical weaponry is post-traumatic stress disorder (PTSD), which is characterized by a complex set of psychiatric syndromes. Formerly known as "shell shock" or "combat fatigue," its formal description by the American Psychiatric Association is a set of psychiatric manifestations elicited by "an extreme traumatic stressor" usually involving a direct experience of an event in which the life, physical safety, or physical integrity of oneself (or a person in one's physical presence) is seriously harmed or threatened. It can also involve learning of such a trauma to a close associate (e.g. family member).

PTSD normally manifests in one of three courses: acute (resolving before 3 months), chronic (lasting more than 3 months), and delayed onset (commencing 6 months after the stressor incident). The prevalence of PTSD in the general population appears to be around 8%. Military veterans face a much higher risk, usually arising from combat experience, but in the case of veterans who have undergone chemical weapons exposure testing with mustard-gas, an authoritative study has turned up a rate of 32%, with another 10% manifesting some clinical signs of PTSD. This level of incidence is comparable to that of veterans who underwent the trauma of a prisoner of war experience.

The issues of the duration of the PTSD and the nature of the symptom manifestations are especially complicated in the case of perceived exposure to biological or chemical weapons agents. That is because of the unusual type of stressor experience it involves, which is called a "contamination stressor". In contamination stressors, the initial trauma may be information about the existence of an uncertain possible future threat rather than, or in addition to, the actual physical experience of the threat. This unusual situation invests a future-looking orientation into the trauma in which the victim stresses over unknown consequences yet to manifest. This is different from the more traditional understanding of PTSD in which there is cognitive preoccupation with a trauma from the past. In contamination stressors, revelations about the full nature of the exposure may occur more slowly and much later than the actual exposure incident (e.g. progressive declassification of the fact and nature of exposure and other related information). Therefore, establishing the precise traumatic origin of the stress disorder and the progress of its psychogenic effects may also be problematic. There may even be two or more stressors where experience of the exposure and further information about the contamination are separated in time and progress.

Typically, the presenting symptoms of PTSD are grouped into symptom clusters: "re-experiencing", "avoidance" and "numbness". The first cluster includes "flashbacks," the experiencing of physical sensations from the traumatic event, agitation accompanying traumatic event reminders, recurrent dreams and nightmares, other sleep disturbances, feelings of danger or panic with a need to escape with no danger present, and problems with anger and emotional control. A classic manifestation is the exaggerated startle response, which includes tachycardia, breathing difficulties, shaking, and sweating after being startled. "Avoidance" symptoms are efforts by the PTSD sufferer to evade reminders and memories of the trauma, and can include partial amnesia and full social withdrawal. "Numbness" symptoms are the loss of emotion and the dissociation from outside events. Strange physical sensations, a general surreal or disconnected feeling, absence of pain or sensation, and a loss of interest in enjoyable activities are the common manifestations of "numbness". Nonspecific symptoms of PTSD include episodes of dizziness, headache, gastrointestinal disorders, immune system problems, chest pain, body discomforts, and difficulty concentrating.

PTSD may also manifest with secondary symptoms. These are effects which arise from the direct behavioral symptoms of PTSD. Some of these symptoms coincide with primary PTSD manifestations, or with common PTSD co-morbidities. What determines

them to be secondary effects is if they arose from the consequences of a PTSD primary manifestation rather than as a primary manifestation itself. Commonly, these secondary manifestations are depression with related loss of interest in previously enjoyed activities, despair, loss of one's existing belief system, social isolation, aggressive behavior, self-blame, guilt, scapegoating, relationship problems, feeling dislocated, engaging in frequent arguments and fights, identity and self-esteem problems, feeling permanently damaged, and suffering from other physical health problems arising from the neglect of health that may be engendered by PTSD avoidance symptoms.

Risk factors for PTSD have been studied for the general population and for military personnel and veterans. In the latter cases, studies have been made specifically in the context of stress from chemical warfare agent testing. In the work of Paula Schnurr and colleagues, the PTSD risk factors for veterans who had undergone testing of biochemical weaponry (mustard-gas) were a veteran's Hispanic ethnicity (probably related to the generally observed higher risk of PTSD for nonwhite veterans arising from the lack of social support attributable to lingering racism), a lack of volunteering for the exposure testing, a lack of preparation for the testing, the number of exposures to the agent, the appearance of physical symptoms of agent exposure during the testing experience, the witnessing of the distress of other participants, the existence of a prohibition on discussing or disclosing the experience, and delays in discussing/disclosing the experience. A sense of betrayal and secrecy are hypothesized as aggravating factors for PTSD incidence. The age of the participants in the testing, however, was not correlated to PTSD in the mustard-gas tests.

Other general risk factors for PTSD in veterans are prisoner of war experience, war-related injury or disability, combat experience, and a younger age of original entry into the military. Female gender and membership in a non-white minority are also associated with PTSD higher risk in the military, factors (as noted previously) attributed to the damaging persistence of racism and sexism. In the general population, observed PTSD risk factors include the nature of the event and its specific meaning for an individual, the lack of a social support system, economic deprivation in childhood, childhood trauma or abuse, lower educational attainment, a pre-existing personal psychiatric disorder, a family history of psychiatric disorder, diminished individual coping skills, and female gender.

Neurobiologically, PTSD appears to involve a deficiency in the functional interaction of the amygdala, the hippocampus, and the medial frontal cortex, among which emotions and stress reactions are mediated and regulated. Commonly noted biologic effects of PTSD include increased heart rate and blood pressure when the patient is reminded of the stressor event, increased urinary dopamine, altered sleep functions (presumed to be related to altered pontine function/noradrenergic dysregulation) including increased phasic rapid eye movement (REM) sleep, and peripheral sympathetic signs – skin conductivity, and electromyographic activity of the frontalis. Physiologic opiate production may also be enhanced, which is believed to induce the "numbness" symptomatology.

Other psychogenic co-morbidities, general non-specific effects of stress, and atypical reactions to the trauma induced by perceived exposure to biological or chemical weapons have been observed. Some of these effects may be identical with or coincide with the primary and secondary effects of PTSD, but they also may exist independently. Common short-term stress-related responses to perceived exposure to biochemical weaponry have included Acute Stress Disorder, grief, anger, scapegoating, guilt, anxiety, acute intense fear, panic, somatization including contagious somatization (e.g. mass fainting spells on reports of gas in the area). The Iraqi Scud attacks on Israel, initially feared to have included chemical weapons, engendered psychogenic breathing difficulties, tremors, sweating, anxiety, and labile mood. A more atypical reaction to the same attacks was "Saddam Syndrome", an acute delusional paranoid psychosis among a small group of studied individuals.

Longer-term general psychogenic and psychosocial effects of stress from public disasters which may mimic reaction to biochemical warfare agent exposure, include sleep disorders (not attributable to PTSD), substance abuse, major depression, phobias, and loss of dignity (in situations involving community life disruption, e.g. evacuation). The Three Mile Island nuclear reactor leak led to the following effects noted in the local community after 18 months: persistent severe demoralization, significantly elevated emotional stress, greater level of somatic complaints, and greater levels of anxiety and alienation. Substance abuse, depression, and anxiety disorders are noted co-morbidities of PTSD; they can also lead to harmful psychosocial impairments of marital, vocational, and other social relationships .

Outcomes for veterans with PTSD traced to perceived exposure to biochemical warfare agents during exposure testing included greater use of medical services, including outpatient VA facilities, poorer overall physical health, a higher likelihood of acquiring chronic illnesses and disability, along with greater functional impairment overall. Treatment of PTSD usually involves a complex psychotherapeutic regimen combining cognitive elements and pharmacotherapy. The aim is the stabilization of symptoms, the processing of traumatic perceptions, and the integration of the trauma into the patient's worldview. There is no single pharmaceutical therapy for PTSD; such therapy is usually geared towards alleviation of individual symptoms (anxiety, depression, etc.). Non-pharmacological therapy includes cognitive-behavioral therapy, particularly "exposure therapy" aimed at re-imagining the trauma and controlling reactions. Dynamic psychotherapy, group therapy among trauma victims, and novel eye movement and touch therapies designed to ease the stress of trauma recollection are also common therapeutic avenues.

Finally, it is noted that the published advisory information from the federal government on the health effects of Project SHAD agents (and which are aimed at assisting clinicians who interact with SHAD veterans) appears to contain only one discussion of the possibility of PTSD symptoms resulting from exposure to biological or chemical warfare agents, simulants, and tracers. That reference is limited in scope. It addresses the narrow issue of the possibility of PTSD as a long-term effect resulting from physically harmful exposure to sarin, as demonstrated by the victim's having experienced actual acute

physical effects from the exposure. (The PTSD-related health effect information in that context is deduced greatly from studies of individuals exposed to sarin during sarin terror attacks by a religious sect in Japan in the 1990s.) There appears, however, to be no discussion of the more general risk of adverse psychogenic health effects solely from the awareness/perception of exposure to biological and chemical agents, nor a discussion of the observed high rate of PTSD found among military veterans who perceived such exposure as a result of actual participation in military testing of biochemical weaponry.

II. PSYCHOLOGICAL ASPECTS OF BIOCHEMCIAL WEAPONRY

Interest in and data regarding the psychogenic effects of perceived exposure to biological and chemical agents have grown over the past decade or two as a result of several factors: 1) increasing study and acceptance of the existence of psychological disorders such as post-traumatic stress disorder, 2) greater accumulated systematic study of persons exposed to biochemical warfare agents, and 3) examinations of psychogenic effects of exposure resulting from observations of a series of experimental, accidental, and willful events involving exposures to weapons of mass destruction. Those latter events have included the deliberate terroristic releases into the public of sarin gas by a Japanese cult in the middle 1990s, the feared development and use of biochemical weapons by Iraq, especially during the Persian Gulf War, and studies of veterans and soldiers involved over the years in actual or possible war-related, experimental, and accidental exposures of these substances. (See e.g., Schnurr 2000, Tochigi, Yokoyama, Page, Kawana, Rose, IOM, Fullerton) It may be fair to speculate that concerns following the September 11, 2001 attacks, the ensuing war on terrorism, the subsequent anthrax scare, and the allegations of the possession of weapons of mass destruction by Saddam Hussein's regime in Iraq prior to the March 2003 American invasion may serve to propel continuing and further interest and study. (Artenstein)

Biological and chemical warfare agents, in addition to their direct destructive harm, form a subset of "psychological warfare, whether [an] attack is real or a . . . hoax, and whether it is initiated by a lone sociopath, by a group of domestic or foreign terrorists, or a nation." (DiGiovanni) Artenstein in the 2004 edition of Cohen's comprehensive text *Infectious Diseases* specifically cites psychosocial health effects as a vital area of growing interest in the study of the consequences of biowarfare.

Based on the published literature, it is conceivable, if not probable, that deleterious psychogenic health effects of perceived exposure to biological or chemical weaponry (or their simulants) may be more likely to happen than actual serious physiological harm from the agents used. A high level of psychological reaction to biochemical warfare agents has been observed in many incidents. During World War I, more soldiers were hospitalized during one mustard gas attack for a psychogenic "gas mania" than for physical symptoms of gas toxicity. (DiGiovanni) In one of the sarin terror attacks in Japan, about two-thirds of those who sought emergency medical care manifested little or no toxic harm. (DiGiovanni) Psychogenic reactions characterized about 40% of impact vicinity residents after Iraq's first missile attack on Israel in the Persian Gulf War, at a time when the use of chemical weapons in such an attack was most widely anticipated. (Talmon, Kark) Mustard gas testing during World War II yielded a 32% prevalence rate of post-traumatic stress disorder five decades later. (Schnurr 2000)

The reasons for the psychological impact of perceived exposure are most likely found in the insidious and unfamiliar pathogenesis of biological and chemical weapons, especially the biological weapons. "A chemical, or even more so, biological incident poses a

sudden, unanticipated, and unfamiliar threat to health that lacks sensory cues, is prolonged or recurrent, perhaps is contagious, and produces casualties that are observed by others." (DiGiovanni) (This type of psychological stressor is called a "contamination stressor" and is treated in more detail in section IIIA, below.) (See also Schnurr 2000)

III. PREVALENT EFFECT: POST-TRAUMATIC STRESS DISORDER

A. General

The most likely psychogenic response to perceived exposure to a chemical or biological agent is post-traumatic stress disorder (PTSD). According to the *Diagnostic & Statistical Manual of Mental Disorder (DSM-IV)* of the American Psychiatric Association, PTSD results from "an extreme traumatic stressor involving direct personal experience of an event that involves actual or threatened death or serious injury, or other threat to one's physical integrity; or witnessing an event that involves death, injury, or a threat to the physical integrity of another person; or a threat to the physical integrity of another person; or learning about unexpected or violent death, serious harm, or threat of death or injury experienced by a family member or other close associate." (Miller)

Prevalence

It is estimated that up to 8% of the general population may succumb to PTSD at some point in their lives. (Carlson, NIMH) Veterans are particularly subject to PTSD because of combat experiences, a fact reflected in the historic names for PTSD syndromes ("shell shock", "combat fatigue", etc.). (Carlson, Friedman) In a study specifically addressing effects of biochemical weapons agent exposure in military testing, Schnurr (2000) found 32% prevalence of PTSD in a veteran cohort that had been subject to mustard-gas/lewisite experiments. An additional 10% manifested partial symptoms. The risk of PTSD in the whole group was greater than that of combat veterans and equivalent to the PTSD incidence among former prisoners of war.

Duration of disorder

PTSD is divided into acute, chronic, and delayed onset diagnostic categories. Formal criteria describe them as follows:

Acute PTSD lasts less than 3 months after the traumatic stressor event.

Chronic PTSD lasts more than 3 months, but manifests within 6 months of the stressor event.

Delayed onset PTSD is PTSD that does not manifest until after 6 months of the stressor event. (Miller)

Contamination stressors and onset timing

In situations where one may learn of a traumatic threat long after the experience of the threat has happened, as may occur in cases of secret biochemical weapons testing, defining the time of the traumatic stressor event may be problematic. Stressors of this type are called "contamination stressors," where information about a harmful contaminant

is the stimulus of the trauma rather than, or in addition to, the experience of the direct threat of exposure. These events have a unique cognitive focus that is future-oriented, contemplating the emergence of future harm from the past contamination, rather than merely recollecting a past trauma, which is more typical of PTSD. Multiple stressor incidents might also exist: the exposure to the biochemical warfare agents, discoveries of new information about the stressor, and experiences of anticipated harm. (Schnurr 2000, IOM)

B. PTSD Symptomatology

Non-specific symptoms of PTSD

Dizziness, headache, gastrointestinal disorders, immune system problems, chest pain, body discomforts are commonly associated with PTSD. Difficulty concentrating is another noted effect of PTSD. (Carlson, NIMH, Miller)

Main symptom clusters

The symptoms of post-traumatic stress disorder are usually categorized under the following broad clusters (Carlson, NIMH, Miller):

Re-Experiencing symptoms
Avoidance symptoms
Numbness symptoms

Re-experiencing symptoms typically include "flashbacks" to the traumatic event, seeing images of the event, experiencing physical sensations of the event, becoming agitated or upset at reminders of the event, bad dreams, nightmares, "microawakening", and other sleep disturbances (e.g. difficulty falling or staying asleep), feeling in danger or experiencing panic or a need to escape without a present threat existing, having difficulty in emotional control, including episodes of extreme anger and aggressive ideation. (Carlson, NIMH, Miller, Bremner)

One of the more commonly observed phenomena in PTSD patients is the "exaggerated startle response". Tachycardia, breathing difficulties, shaking and sweating can accompany the ordinary experience of being startled. (Carlson, NIMH, Miller, Bremner)

Avoidance symptoms reflect the patient's desire to escape reminders of the traumatic event. The PTSD sufferer will often go to great extent to avoid trauma reminders and memories. This can give rise to a partial amnesia in which the patient has difficulty remembering parts of the traumatic event. The PTSD sufferer may progress to full social withdrawal. (Carlson, NIMH, Miller, Bremner)

Numbness symptoms are those in which PTSD sufferers become less emotional and more dissociated with outside events. The numbness symptoms tend to manifest as a surreal or disconnected feeling, strange physical sensations, literal numbness in physical sensation

(no pain or feeling), and a loss of interest in activities that one normally enjoys. (Carlson, NIMH, Miller, Bremner)

Biologic Etiology & Findings

The mechanism of PTSD's etiology is generally attributed to biologic as well cognitive sources. Current theorizing centers on interaction of three CNS-brain regions: the amygdala, the hippocampus, and the medial frontal cortex. The amygdala mediates arousal and distress states, and it is believed that the hippocampus and medial frontal cortex fail to dampen those levels of distress and arousal to levels consistent with normal functioning. (Bremner)

The following biologic manifestations are commonly observed in PTSD patients (Bremner):

Increased heart rate and blood pressure when reminded of the stressor event
Increased urinary dopamine
Altered sleep functions (presumed to be related to altered pontine function/noradrenergic dysregulation), including increased phasic rapid eye movement (REM) sleep. (See Ross)
Peripheral sympathetic signs – skin conductivity, electromyographic activity of the frontalis

Secondary effects

Secondary symptoms result from the primary effects, particularly the avoidance symptoms. A PTSD sufferer may withdraw from normal activities and relationships and experience from that withdrawal additional psychological and psychosocial sequelae. Some of these symptoms may coincide with other direct symptoms, co-morbidities, or other possible direct and acute effects of perceived exposure to biological and chemical warfare agents. In this context, however, secondary effects describe conditions arising subsequent to and as a result of the behavior engendered specifically by primary PTSD symptomatology. (Carlson, NIMH)

Secondary effects typically include depression with related loss of interest in activities, despair, loss of existing one's belief system, social isolation, aggressive behavior, self-blame, guilt, scapegoating, relationship problems, feeling dislocated, engaging in frequent arguments and fights, identity and self-esteem problems, feeling permanently damaged, and general suffering from physical health problems arising from the neglect of health that may be engendered by PTSD avoidance symptoms. (Carlson, NIMH)

Associated Symptoms

"Associated symptoms" of PTSD is the term that described the physical symptoms resulting directly from the trauma that gave rise to the post-traumatic stress disorder. In

the case of exposure to biological or chemical weapons, such symptoms would be the actual physical health effects of those agents (which, in the context of this supplement, are treated in the individual health effects report for the respective agent). It is stressed again that clear distinction between neuropsychiatric impact of specific agent pathology and the psychogenic effects of perceived contact may be difficult to establish. (Tochigi, Nishiwaki, Riddle)

C. Predictive Factors

Risk factors for acquiring PTSD have been studied in the context of both general population risk and of veterans' risk. The latter receives much emphasis because of the traumatic nature of warfare. (Friedman, NIMH) Most relevant to this report, however, has been the examination of the risk factors for PTSD among veterans who have had perceived exposures to biochemical warfare agents as a result of participation in mustard-gas/lewisite tests during the Second World War.

Observed risk factors for actually exposed military personnel

Paula Schnurr and her colleagues (2000) found several factors to be significantly correlated with PTSD morbidity among veterans who had participated in chamber and field-testing of mustard-gas and lewisite in a secret program during World War II aiming to determine protective measures against attack by those vesicant agents:

Ethnicity. Military personnel of non-white ethnicity have been determined in general to be more susceptible to PTSD. This is generally traced to the existence of racism and its legacy, including a resultant lack of social support for those afflicted. (Friedman) Schnurr (2000) reports that Hispanic participants in the vesicant testing showed a higher rate of PTSD than other test participants.

Involuntariness and lack of preparation for participation. Involuntary participation in the testing and an absence of preparation for the testing engendered a higher likelihood of PTSD occurrence. (Schnurr 2000)

(The correlation of PTSD with the lack of volunteering and protective training for participation in biochemical warfare agent testing may suggest a supplemental or alternative explanation for a finding in one study on the health effects of exposure certain nerve agents. In Page's study for the IOM of the Army's Edgewood anticholinesterase agent testing, there were found to be statistically significant higher psychological morbidity outcomes for those survey respondents who reported having had an additional uncontrolled exposure to toxic agents at some point. While this finding was hypothesized as reflecting recall bias (i.e., that sicker individuals were more likely to recall non-experimental exposure), it may be suggested that the finding can also reflect the possibility implied by Schnurr's conclusions that the less voluntary and formally supervised an exposure is to a harmful agent, the more likely it is that the victim will develop psychogenic or psychiatric health problems from the awareness of that involuntary and unprepared exposure. (Page 2003))

Number of exposures. The greater the number of exposures the subject had to the tested chemical agent was positively correlated with PTSD. (The type of exposure – whether in chamber or in the field – showed no correlation to PTSD risk.)

Manifestation of symptoms. Those who experienced acute effects of the agents during the testing showed significantly higher risk for PTSD.

Witnessing distress of other participants. Those who witnessed others undergoing distress while the tests were performed were more likely to manifest PTSD.

Prohibition of disclosure. Because the tests were secret, some participants were compelled to take an oath of secrecy and were subject to criminal prosecution if they disclosed their participation. Such participants had a higher rate of PTSD. This was hypothesized to result from the absence of "emotional processing of fear information" considered vital for trauma recovery. (Secrecy has also been theorized as an aggravating factor in the failure of some individuals to recover from the stress of childhood trauma or abuse.)

Delay in disclosure. Study participants delayed disclosure not only from secrecy obligations but also because full information about the nature of the tests was withheld. Those who disclosed first in the 1990s appear to have a higher incidence of PTSD than other participants who discussed the incidents earlier. One emotional factor hypothesized as an aggravating factor in stress disorders is a sense of betrayal, and the authors of the study theorize that a sense of government betrayal over the hazards of the testing may have contributed to PTSD morbidity.

The study authors found to their surprise that the age of the veteran at the time of the testing was not a significant factor in PTSD morbidity.

Special PTSD risk factors for veterans generally

Prisoner of war status, war-related injury or disability, and combat experience correlate most closely with PTSD in veterans. Earlier age of entry into the military has been shown to be a risk factor, though age was irrelevant in the mustard-gas testing discussed above. Female gender and membership in a non-white minority are also associated with higher risk; these factors attributed to the presence of racism and sexism. (Friedman, Carlson, Schnurr 2000, IOM)

Circumstantial risk factors

The younger that one is at the time of entry into the military, the higher the likelihood one has of being afflicted with PTSD after a traumatic stressor. (But note that that did not apply in the mustard-gas/lewisite testing subjects, see above this section.) The nature of the event and the specific meaning it may have for an individual are factors which can

affect susceptibility. The lack of a social support system may exacerbate the risk of PTSD. (Friedman, NIMH, Carlson)

General population risk factors

Certain characteristics appear to be positively associated with PTSD risk in the general population. These include economic deprivation in childhood, childhood trauma or abuse, lower educational attainment, a pre-existing personal psychiatric disorder, a family history of psychiatric disorder, diminished individual coping skills, and female gender. (Friedman, NIMH, Carlson, Miller)

IV. ADDITIONAL PSYCHOLOGICAL SYMPTOMS OF PERCEIVED EXPOSURE TO BIOLOGICAL AND CHEMICAL WEAPONRY

PTSD is not the only psychogenic effect observed after traumas involving perceived exposures to biological and chemical warfare agents. Co-morbidities to PTSD, general non-specific effects of trauma, and atypical reactions to the trauma related to perceived exposure to biological or chemical weapons have been observed. This section presents possible psychogenic sequelae in addition to PTSD from perceived exposure to biological and chemical warfare agents. Some of these effects may be identical with or coincide with the primary and secondary effects of PTSD, but they have been observed independently.

A. Short-Term

Short-term effects are typically Acute Stress Disorder, grief, anger, scapegoating, guilt, anxiety, acute intense fear, panic, somatization, and contagious somatization (e.g. mass fainting spells on reports of gas in the area). (DiGiovanni) Acute psychogenic presentations after initial Iraqi Scud attacks with feared chemical weapons in Israel included breathing difficulties, tremors, sweating, anxiety, and labile mood. (DiGiovanni)

An atypical reaction in Israel was "Saddam Syndrome" in which a very small number of persons developed an acute delusional paranoid psychosis after the first Scud attacks on the nation by Iraq in the Persian Gulf War. The outcomes, however, were generally favorable and rapid. Two of the affected, however, who had suffered from pre-existing cognitive disorder, did not recover fully. (Talmon)

B. Long-term

The following are long-term general psychogenic and psychosocial effects of stress from public disasters in which exposure to toxic or pathogenic agents was feared. (DiGiovanni, Wolfe, NIMH, Carlson, Evans, Fullerton)

Sleep Disorders (other than PTSD disturbances)
Substance abuse
Major depression,
Phobias
Loss of dignity (usually in traumatic situations involving community life disruptions, e.g. evacuations)

Eighteen months after the Three Mile Island nuclear reactor leak in the late 1970s, the following effects were noted in the community after 18 months (DiGiovanni):

Persistent severe demoralization
Significantly elevated emotional stress
Greater level of somatic complaints
Greater level of anxiety and alienation

C. Co-morbidities of PTSD

The following co-morbidities often lead to secondary psychosocial problems, particularly impairment of marital, vocational, and social function. (Friedman 1994, Wolfe, Carlson, NIMH)

Depression
Anxiety disorders
Phobias
Alcohol/substance abuse.

V. OUTCOMES & TREATMENT

A. Outcomes

Psychological trauma experienced by military subjects of biochemical warfare testing show poorer overall physical health, higher likelihood of medical services use (including VA outpatient treatment), higher likelihood of chronic illnesses and disability, and greater functional impairment overall than other veterans. (Schnurr 2000, Friedman 1994)

B. Treatments of PTSD

A complex psychotherapeutic regimen combined with some pharmacotherapy is the standard approach. The progressive aims of treatment are the stabilization of symptoms, the processing of traumatic perceptions, and the integration of the trauma into the patient's worldview. (Miller) The target of therapy is symptomatic and no curative process is known yet to exist. (NIMH, Carlson) Therefore, many different types of therapeutic treatment for PTSD exist.

This section addresses the common therapeutic methods used. These include cognitive-behavioral therapy, pharmacotherapy, group therapy, dynamic psychotherapy, and an innovative attention-controlling technique involving eye movement. (Carlson) A discussion of each follows.

Cognitive-Behavioral Therapies

Cognitive-behavioral therapy (CBT) methods emphasize "exposure therapy," in which a controlled re-imagining of the trauma is performed in order for the patient to learn to control the distress from the trauma. CBT for trauma also can include (Carlson, NIMH):

Learning skills for coping with anxiety (such as breathing retraining or biofeedback) and negative thoughts ("cognitive restructuring"),

Anger management

Preparing for stress reactions, a process known as "stress inoculation" and especially useful for handling future trauma symptoms,

Addressing urges to use alcohol or drugs when trauma symptoms occur ("relapse prevention")

Social skills, marital therapy aimed at learning effective communication and relationship skills

Pharmacotherapy

Pharmacotherapy is aimed also at PTSD symptoms. Anxiety, depression, and insomnia reduction are the frequent targets of treatment. Relieving distress and emotional numbness are also common targets for pharmacotherapy. Antidepressant drugs have

shown some positive results in PTSD treatment. Nevertheless, there is no definitive pharmacological treatment for PTSD. (Carlson, NIMH)

Group therapy

Group therapy is also employed to allow trauma survivors to be able to share traumatic experiences within the sympathetic environment of fellow sufferers. Coping mechanisms are discussed among the patients to help each other in dealing with such effects as shame, guilt, rage, fear, doubt, and self-condemnation. "Trauma narratives" are shared as well with the aim of helping patients confront their difficulties. Retelling of the trauma narrative to a psychotherapist is another feature of PTSD treatment. This allows for development of coping mechanisms under professional guidance. Self-esteem, emotional control, and identification of trauma reminders are cultivated. (Carlson, NIMH)

New densitization therapy

Another type of therapy is a new technique called Eye Movement Desensitization and Reprocessing (EMDR). In this regimen, exposure therapy and other cognitive-behavioral therapies are combined with certain body actions, usually eye movements, hand taps, and sounds, which cause the patient to shift attention. This is believed to help evoke memories of the trauma in a controlled fashion enabling better coping with the trauma and it symptoms. (Carlson, NIMH)

VI. PSYCHOGENIC HEALTH EFFECTS IN OFFICIAL ADVISORIES

The materials issued by the Department of Defense and the Department of Veterans Affairs are compiled and linked at http://www1.va.gov/shad. None of the materials, several of which are designed to assist clinicians in treating Project SHAD veterans, note the realistic possibility of PTSD or other stress symptoms resulting generally from the perception of exposure to biochemical warfare agents.

A reference to PTSD as a possible long-term effect of exposure to sarin appears in the Under Secretary for Health's [Department of Veterans Affairs] Letter IL 10-2001-015 of December 31, 2001. (http://www.va.gov/publ/direc/health/infolet/10200115.pdf.) It also appears in an earlier version of the same letter of December 1, 2000. (http://www.va.gov/publ/direc/health/infolet/10200112.pdf.)

The reference in those letters is to observed symptoms of PTSD following actual exposure to sarin (with subsequent acute effects) among victims of the sarin terror attacks in Japan in the 1990s. This is the sole case we can find in official advisories on the subject of Project SHAD which discuss the association of long-term psychological symptoms with exposures to the type of agents used in Project SHAD. The general but likely possibility (based on the data and research cited herein) of psychogenic health effects arising from the perceived exposure to biochemical warfare agents in an experimental military project context appears to remain ill-addressed in the official federal government advisories as best as we can determine to this time.

VII. CHART OF POSSIBLE PSYCHOGENIC HEALTH EFFECTS OF PERCEIVED EXPOSURE TO BIOLOGICAL AND CHEMICAL WEAPONS

A. BASIC CONSIDERATIONS

- Biological and chemical weapons are also psychological weapons
- Increasing awareness exists that perception of exposure likely to trigger psychogenic effects
- Conceivably, psychogenic health effects may be among most common from exposure experience

Problems:

- Precisely distinguishing psychogenic effects from physiological ones
- Presence of co-morbidities of a psychological nature (substance abuse, depression alongside post-traumatic stress disorder, etc.)

B. MOST COMMON PSYCHOGENIC EFFECT: PTSD

- Post-traumatic stress disorder (PTSD) is the most observed and studied psychological consequence of perceived or actual exposure
- PTSD is a complex set of psychiatric syndromes.
- Its formal diagnostic description encompasses:
  -- "an extreme traumatic stressor"
  -- involving a direct experience of an event in which the life, physical safety, or physical integrity of oneself or a person in one's physical presence is seriously harmed or threatened.
  -- a stressor may also be learning of a such a harm or threat to a close associate (e.g. family member)
- PTSD prevalence in the general population 8%.
- Veterans generally at higher risk, usually arising from combat experience
- Veterans in WWII mustard-gas tests had prevalence rate of 32% with another 10% also manifesting some clinical signs of PTSD
- Mustard-gas testees manifest PTSD rate comparable to prisoner of war experience.

C. PTSD: COURSE, SYMPTOMATOLOGY, AND RISK

Three Courses of PTSD:

:

- Acute (resolving before 3 months)
- Chronic (lasting more than 3 months)
- Delayed onset (commencing 6 months after the stressor incident).

"Contamination stressor":

- Unusual stressor type for PTSD, but relevant to perceived exposure to biochemical warfare agents
- Initial trauma may merely be *information* about the existence of an uncertain possible serious threat, rather than, or in addition to, the actual physical experience of the threat.
- There may even be two or more stressors since traumatic information or sets of information and the contamination itself may occur at different times

Atypical "future-looking" PTSD orientation in which one stresses over future unknown consequences; different from the more traditional understanding of PTSD as resulting from trauma from the past.

Symptom clusters:

- Non-specific
- Re-experiencing
- Avoidance
- Numbness

Nonspecific symptoms:

- episodes of dizziness,
- headache,
- gastrointestinal disorders
- immune system problems,
- chest pain
- body discomforts
- difficulty concentrating
- exaggerated startle response (which includes tachycardia, breathing difficulties, shaking and sweating after being startled)

"Re-experiencing" symptoms**:**

- "flashbacks"
- experiencing physical sensations from the traumatic event
- agitation accompanying traumatic event reminders
- nightmares
- sleep disturbances
- feelings of danger or panic with a need to escape though no danger present
- problems with anger and emotional control

.
"Avoidance" symptoms:

- evading reminders and memories of the trauma
- partial amnesia of the traumatic event
- full social withdrawal

"Numbness" symptoms:.

- loss of emotion
- dissociation from outside events.
- strange physical sensations
- a general surreal or disconnected feeling
- absence of pain or sensation,
- a loss of interest in enjoyable activities.

Secondary Symptoms:

- These are secondary consequences of the direct behavioral symptoms of PTSD

- depression with related loss of interest in activities
- despair
- loss of one's existing belief system
- social isolation
- aggressive behavior
- self-blame
- guiilt

- scapegoating
- relationship problems
- feeling dislocated
- engaging in frequent arguments and fights
- identity and self-esteem problems
- feeling permanently damaged
- physical health problems arising from the neglect of health engendered by PTSD avoidance symptoms.

Biologic Effects & Findings

- PTSD: believed to be dysfunction in interaction of amygdala, the hippocampus, and the medial frontal cortex

Biologic effects of PTSD:

- increased heart rate (during trauma reminders)
- blood pressure (during trauma reminders)
- increased urinary dopamine
- altered sleep functions (presumed to be related to altered pontine function/noradrenergic dysregulation)
  -- increased phasic rapid eye movement (REM) sleep
- peripheral sympathetic signs
  -- skin conductivity, and electromyographic activity of the frontalis.
- physiologic opiate production may be enhanced, (induces? the "numbness" symptomatology)

Risk factors for PTSD:

Veterans of biochemical weaponry (mustard-gas/lewisite) testing --

- Hispanic ethnicity (consequence of racism inhibiting social support system)
- lack of volunteering for the test
- lack of preparation for the test
- number of exposures to the agent
- appearance of symptoms of agent exposure during the testing experience
- witnessing of the distress of other participants
- existence of a prohibition on discussing or disclosing the experience
- delays in discussing/disclosing the experience

Note:

- A sense of betrayal and secrecy are hypothesized as aggravating factors for PTSD incidence
- The age of the participants in the testing was *not* correlated to PTSD in the mustard-gas tests

Risk factors for PTSD in veterans generally --

- past prisoner of war status
- war-related injury or disability
- combat experience
- and an earlier age of entry into the military.
- Female gender and membership in a non-white minority factors attributed to the damaging persistence of racism and sexism

PTSD risk factors for the general population --

- the nature of the event and its specific meaning for an individual

- lack of a social support system
- economic deprivation in childhood
- childhood trauma or abuse
- lower educational attainment
- a pre-existing personal psychiatric disorder
- a family history of psychiatric disorder
- diminished individual coping skills
- female gender.

D. ADDITIONAL PSYCHOGENIC EFFECTS OF PERCEIVED EXPOSURE

(Co-morbidities, general non-specific effects of stress, and atypical reactions to the trauma induced by perceived exposure to biological or chemical weapons)

- May be identical with or coincide with the primary and secondary effects of PTSD, but they also may manifest independently

Short-term stress-related responses

- Acute stress disorder
- grief
- anger
- scapegoating
- guilt
- anxiety
- acute intense fear
- panic
- somatization, including contagious somatization (e.g. mass fainting spells on reports of gas in the area).

Initial Effects of Scud Attacks on Israel (with perception of chemical weapons risk):

- breathing difficulties
- tremors
- sweating
- anxiety
- labile mood.
- "Saddam Syndrome", atypical acute delusional paranoid psychosis.

Long-term effects of trauma

General:

- sleep disorders (not attributable to PTSD)
- substance abuse
- major depression
- phobias
- loss of dignity (e.g. in evacuation situations)

Effects on residents, 18 months after The Three Mile Island nuclear reactor leak:

- persistent severe demoralization
- significantly elevated emotional stress
- greater level of somatic complaints
- greater levels of anxiety and alienation

PTSD Co-morbidities:

- substance abuse

- depression
- anxiety disorders
- consequent psychosocial impairments: marital, vocational, and other social relationship dysfunction

E. OUTCOMES

For veterans with PTSD:

- greater use of medical services, including outpatient VA facilities
- poorer overall physical health
- higher likelihood of acquiring chronic illnesses and disability
- greater functional impairment overall

F. TREATMENT

- usually complex psychotherapeutic regimen combining cognitive elements and pharmacotherapy
- treatment is targeted at alleviation of symptoms

Aims of treatment:

- stabilization of symptoms
- processing of traumatic perceptions
- integration of the trauma into the patient's worldview

Pharmacotherapy:

- no single pharmaceutical therapy for PTSD
- alleviation of individual symptoms (anxiety, depression, etc.) is goal

Other Therapies:

- cognitive-behavioral therapy:
  -- "exposure therapy" (re-imagining the trauma and controlling reactions),
- dynamic psychotherapy
- group therapy among trauma victims
- novel eye movement and touch therapies designed to ease the stress of trauma recollection

VIII. BIBLIOGRAPHY WITH ABSTRACTS

Artenstein. 2004. Bioterrorism and biodefense. In Cohen et al ed. *Infectious Diseases*. Edinburgh, NY; Mosby.

Astin et al. 1994. Posttraumatic stress disorder in victimization-related trauma. *New Dir.Ment.Health Serv.* (64)(64): 39-51.
Symptom manifestations of posttraumatic stress disorder (PTSD) are explained in light of current research findings. Assessment methods for evaluating PTSD and trauma exposure are presented and implications for treatment are discussed.

Beckett. **2002.** Post-traumatic stress disorder. *N.Engl.J.Med.* 346(19): 1495-8; author reply 1495-8.

Benedek et al. 2002. Emergency mental health management in bioterrorism events. *Emerg.Med.Clin.North Am.* 20(2): 393-407.
The United States has not suffered significant psychosocial or medical consequences from the use of biological weapons within its territories. This has contributed to a "natural" state of denial at the community level. This denial could amplify the sense of crisis, anxiety, fear, chaos, and disorder that would accompany such a bioterrorist event. A key part of primary prevention involves counteracting this possibility before an incident occurs. Doing so will require realistic information regarding the bioterrorism threat followed by the development of a planned response and regular practice of that response. Unlike in natural disasters or other situations resulting in mass casualties, emergency department physicians or nurses and primary care physicians (working in concert with epidemiologic agencies), rather than police, firemen, or ambulance personnel, will be most likely to first identify the unfolding disaster associated with a biological attack. Like community leaders, this group of medical responders must be aware of its own susceptibility to mental health sequelae and performance decrement as the increasing demands of disaster response outpace the availability of necessary resources. A bioterrorist attack will necessitate treatment of casualties who experience neuropsychiatric symptoms and syndromes. Although symptoms may result from exposure to infection with specific biological agents, similar symptoms may result from the mere perception of exposure or arousal precipitated by fear of infection, disease, suffering, and death. Conservative use of psychotropic medications may reduce symptoms in exposed and uninfected individuals, as may cognitive-behavioral interventions. Clear, consistent, accessible, reliable, and redundant information (received from trusted sources) will diminish public uncertainty about the cause of symptoms that might otherwise prompt persons to seek unnecessary treatment. Training and preparation for contingencies experienced in an attack have the potential to enhance delivery of care. Initiating supportive social, psychotherapeutic, and psychopharmacologic treatments judiciously for symptoms and syndromes known to accompany the traumatic stress response can aid the efficient treatment of some patients and reduce long-term morbidity in affected individuals. Preventive strategies and planning must take into account the idea that specific groups within the population are at higher risk for psychiatric morbidity.

First responders comprise one group at psychologic risk in this situation, and healthcare providers comprise another. These and other high-risk groups will benefit from the same supportive interventions developed for the community as a whole.

Bleich et al. 1991. Israeli psychological casualties of the Persian Gulf war: characteristics, therapy, and selected issues. *Isr.J.Med.Sci.* 27(11-12): 673-676.
The Persian Gulf war in 1991 presented Israel with its first experience of a threat of chemical attack on the home front. Ground-to-ground missiles were aimed directly at civilian populations, threatening death and destruction over a period of several weeks. Uncertainty as to time, place, and nature of the missile attacks affected the civilian population psychologically. The psychological responses of the population were the result of the continuous nature of the emergency which affected the entire population, and the destruction, injury, and displacement which affected those who were the targets of the attacks. The primary psychological effects of the emergency were investigated in several ways: surveys of samples of civilian and rear-echelon military populations, studies of the military personnel who asked for ambulatory psychological treatment as a result of the war, and studies of the specific populations that bore the brunt of the actual physical attacks were conducted. These studies show a high level of distress in the samples, with considerable differentiation between the populations. Levels of functioning generally remained intact even among the displaced or injured. Interventions were based on experience gained in the treatment of combat stress reaction. The issues of evacuation of psychological casualties to hospitals, psychiatric aspects of chemical attacks, and secondary traumatization of therapeutic and other staff are emphasized.

Bremner et al. 1999. "The Neurobiology of Posttraumatic Stress Disorder" in Saigh et al. ed. *Posttraumatic Stress Disorder: A Comprehensive Text*. Allyn & Bacon. Boston: 103.

Breslau. 2002. Epidemiologic Studies of Trauma, Posttraumatic Stress Disorder, and Other Psychiatric Disorders. *Can J Psychiatry.* 47(1): 923-9.

This paper reviews recent epidemiolgic studies of posttraumatic stress disorder (PTSD) in the general population. Risk factors for PTSD in adults vary across studies. Most community residents have experienced 1 or more PTSD-level traumas in their lifetime, but only a few succumb to PTSD.

Brown et al. 1984. The anxiety disorders. *Ann.Intern.Med.* 100(4): 558-564.
Anxiety commonly accompanies serious illness. However, in some patients anxiety is the primary manifestation of illness. Diagnostic criteria for these "primary" anxiety disorders have been redefined in the most recent revision of the American Psychiatric Association's Diagnostic and Statistical Manual. We discuss these new diagnostic categories; review

the theoretical basis for the psychodynamic, behavioral, and physiologic manifestations of each of these disorders; and critically examine the treatments offered for each.

Carlson et al. 2004. in National Center for PTSD. Treatment of PTSD. http://www.ncptsd.org/facts/treatment/fs_treatment.html (March 15, 2004).

Clauw et al. 2003. Unexplained symptoms after terrorism and war: an expert consensus statement. *J.Occup.Environ.Med.* 45(10): 1040-1048.
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.

Cote. **1996.** [The vulnerability factors and the psychodynamic stakes in post-traumatic reactions]. *Sante Ment.Que.* 21(1): 209-227.
Some people react to collective trauma with clinical manifestations which often become a clinical syndrome. How can these different reactions be explained? Inspired by clinical research in the literature review, and divided according to the fragilizing aspects of the triad of vulnerability (trans-traumatic, pre-traumatic and posttraumatic), the author brings a psychoanalytical explanation to those different reactions.

Curtis et al. 1988. Neuroendocrine findings in anxiety disorders. *Endocrinol.Metab.Clin.North Am.* 17(1): 131-148.
Anxiety disorders are newly defined syndromes in which inappropriate state anxiety is the sole or primary symptom. Hormonal manifestations of acute stress are usually minimal or absent in these disorders. A number of findings suggest receptor down-regulation or enzyme induction of sorts that would be expected to mute or dampen these responses.

DiGiovanni. **1999.** Domestic terrorism with chemical or biological agents: psychiatric aspects. *Am.J.Psychiatry.* 156(10): 1500-1505.
OBJECTIVE: This article highlights the mental health consequences of a domestic terrorist incident involving chemical or biological weapons. METHOD: The author reviews the literature on the neuropsychiatric effects of selected chemical and biological

weapon agents, on the psychological sequelae of mass disasters, and on approaches to crisis intervention. RESULTS: Disturbances of behavior, affect, and cognition can result directly from the pharmacological actions of some chemical and biological weapon agents. In addition, an incident involving these agents can have considerable psychological effects on individuals and the community. In either case, some disorders are acute and others are prolonged or delayed in onset. Effective therapeutic intervention involves a broad range of clinical, social, and administrative actions. CONCLUSIONS: Psychiatrists have an important role in the management of a chemical or biological terrorist incident and, along with their other medical colleagues, should train and prepare for it.

Evans. **2002.** Bioterrorism watch. Traumatized health care providers may need stress counseling in horrific aftermath of bioterror attack. *Hosp.Peer Rev.* 27(5): suppl 1-3.

Foa et al. 1992. Uncontrollability and unpredictability in post-traumatic stress disorder: an animal model. *Psychol.Bull.* 112(2): 218-238.
The disturbances observed in animals subjected to unpredictable and uncontrollable aversive events resemble post-traumatic stress disorder (PTSD) symptoms and thus may constitute an animal model of this disorder. It is argued that the similarity between animals' symptoms and those of trauma victims may reflect common etiological factors. Relevant experiments in which animals exhibit generalized fear and arousal, discrete fear of a conditioned stimulus (CS), analgesia, and avoidance are reviewed with the view that these manifestations may be analogous to the PTSD symptom clusters of persistent arousal, reexperiencing, numbing, and avoidance, respectively. Finally, animal paradigms are suggested to test the validity of the model and specific hypotheses are derived from the animal literature regarding trauma variables that are predictive of particular PTSD symptom clusters.

Friedman et al. 1994. Post-traumatic stress disorder in the military veteran. *Psychiatr.Clin.North Am.* 17(2): 265-277.
1. Military personnel exposed to war-zone trauma are at risk for developing PTSD. Those at greatest risk are those exposed to the highest levels of war-zone stress, those wounded in action, those incarcerated as prisoners of war, and those who manifest acute war-zone reactions, such as CSR. 2. In addition to problems directly attributable to PTSD symptoms per se, individuals with this disorder frequently suffer from other comorbid psychiatric disorders, such as depression, other anxiety disorders, and alcohol or substance abuse/dependence. The resulting constellation of psychiatric symptoms frequently impairs marital, vocational, and social function. 3. The likelihood of developing chronic PTSD depends on premilitary and postmilitary factors in addition to features of the trauma itself. Premilitary factors include negative environmental factors in childhood, economic deprivation, family psychiatric history, age of entry into the military, premilitary educational attainment, and personality characteristics. Postmilitary

factors include social support and the veteran's coping skills. 4. Among American military personnel, there are three populations at risk for unique problems that may amplify the psychological impact of war-zone stress. They are women whose war-zone experiences may be complicated by sexual assault and harassment; nonwhite ethnic minority individuals whose premilitary, postmilitary, and military experience is affected by the many manifestations of racism; and those with war-related physical disabilities, whose PTSD and medical problems often exacerbate each other. 5. The longitudinal course of PTSD is quite variable. Some trauma survivors may achieve complete recovery, whereas others may develop a persistent mental disorder in which they are severely and chronically incapacitated. Other patterns include delayed, chronic, and intermittent PTSD. 6. Theoretically primary preventive measures might include prevention of war or screening out vulnerable military recruits. In practice, primary preventive measures have included psychoeducational and inoculation approaches. Secondary prevention has been attempted through critical incident stress debriefing administered according to the principles of proximity, immediacy, expectancy, and simplicity. Tertiary prevention has included psychotherapy, pharmacotherapy, dual diagnosis approaches, peer counseling, and inpatient treatment. Few treatments have been rigorously evaluated. 7. There are both theoretical reasons and empirical findings to suggest that military veterans with PTSD are at greater risk for more physical health problems, poorer health status, and more medical service usage. Much more research is needed on this matter. 8. Despite the potential adverse impact of war-zone exposure on mental and physical health, there is also evidence that trauma can sometimes have salutary effects on personality and overall function.

Fullerton et al. 1990. Behavioral and psychological responses to chemical and biological warfare. *Mil.Med.* 155(2): 54-59.
Understanding the behavioral and psychological responses in a chemical environment is critical to individual health and unit functioning. Reports of incidents of acute nerve agent and other organophosphate exposures and of repeated low-dose toxic exposures can provide information about psychiatric symptomatology, performance disruption, and recovery. This paper presents a review of the literature on the longer term consequences of acute and chronic exposure to nerve agents and other organophosphates. In addition, reports on psychological responses during chemical warfare training are reanalyzed to identify behavioral and psychological casualties attributed to the unique stressors of the CBW environment.

Grauer et al. 2000. Stress does not enable pyridostigmine to inhibit brain cholinesterase after parenteral administration. *Toxicol.Appl.Pharmacol.* 164(3): 301-304.
The peripherally acting cholinesterase inhibitor pyridostigmine was widely used during the Gulf War as a pretreatment against possible chemical warfare attack. Following consistent reports on long-term illness among Gulf War veterans, pyridostigmine was examined for its possible long-term effects. These effects were suggested to be induced by the combination of pyridostigmine administration and stress exposure that allowed

this quaternary compound to enter the brain through stress induced changes in blood-brain barrier (BBB) permeability. Recently, pyridostigmine administration was demonstrated to inhibit brain cholinesterase following acute stress in mice. However, the effect was not replicated under similar conditions in guinea pigs. Because of the significant implication of these findings, we tested brain cholinesterase (ChE) inhibition following the administration of pyridostigmine, or the tertiary carbamate physostigmine, with or without stress in mice. Different experiments were performed to examine the contribution of gender, age (young and adults), stress (type and intensity), or strain (CD-1 and FVB/n) parameters. No inhibition of brain ChE was detected in any of these experiments. At the same time, physostigmine induced the expected decrease in brain ChE in all the experiments. Thus, we could not replicate the findings that suggest pyridostigmine can affect brain cholinesterase following stress.

Horowitz. **1999.** *Essential papers on posttraumatic stress disorder*. 548.

Hsu et al. 2002. Posttraumatic stress disorder among adolescent earthquake victims in Taiwan. *J.Am.Acad.Child Adolesc.Psychiatry.* 41(7): 875-881.
OBJECTIVE: To assess the exposure experience and prevalence of posttraumatic stress disorder (PTSD) among adolescent victims in the worst-affected region (Chungliao) near the epicenter of a severe earthquake (7.3 on the Richter scale) that occurred on September 21, 1999, in Taiwan. METHOD: The experience of exposure to the earthquake and subjective symptoms of junior high school students aged 12 to 14 who remained in the area were assessed with self-rated questionnaires. Psychiatrists made independent diagnoses for PTSD by using the Children's Interview for Psychiatric Syndromes. RESULTS: Six weeks after the earthquake, 21.7% of 323 students demonstrated PTSD. Those with PTSD showed significantly more psychiatric symptoms than did those without PTSD. Being physically injured and experiencing the death of a close family member with whom they had lived were the 2 major risk factors for PTSD. CONCLUSIONS: This study demonstrates that PTSD among adolescent victims of a severe earthquake in Taiwan is not as high as that reported in other studies. Methodological differences in the investigations are discussed, along with differences in symptom manifestations. However, long-term follow-up of these victims is recommended to prevent the development of other psychiatric complications.

[IOM] Institute of Medicine. 1993. "Relationship of Mustard Agent and Lewisite Exposure to Psychological Dysfunction" in Rall et al. ed. *Veterans at Risk: The Health Effects of Mustard Gas and Lewisite*: 199-213. National Academies Press, Washington, D.C.

Kark et al. 1995. Iraqi missile attacks on Israel. The association of mortality with a life-threatening stressor. *JAMA.* 273(15): 1208-1210.
OBJECTIVE--The imminent deadline for the 1991 Persian Gulf War and, subsequently, the 18 missile attacks by Iraq on Israel represented an unusual, short-term, life-threatening stressor for an entire nation. We studied mortality in Israel in January and February 1991 to determine whether excess deaths were precipitated on days of missile attacks. DESIGN--A time-series mortality study. SETTING--The state of Israel.

PARTICIPANTS--All Israelis aged 25 years and older. MAIN OUTCOME MEASURE--Daily mortality by sex, age, region, underlying cause, and place of death. RESULTS--On January 18, 1991, the day of the first strike on Israeli cities, a 58% increment in total mortality occurred in the Israeli population (95% confidence interval [CI], 34% to 86%; P < .0001), a 77% excess (95% CI, 40% to 120%) in women and a 41% excess (95% CI, 10% to 79%) in men. This excess mortality occurred largely in the targeted Tel Aviv-central coastal plain and Haifa regions from cardiovascular causes and mainly out of hospital, significantly more so (P < .01) in women than men. Subsequently, on 16 attack days no overall excess was noted, yet a 10% increase in out-of-hospital deaths occurred. CONCLUSIONS--Likely explanations for the initial increase in mortality include acute emotional stress coupled with breathing difficulties induced by gas masks and extended stay in sealed rooms with resultant hypoxia in susceptible individuals. Women were more vulnerable than men. The absence of elevated total mortality in the subsequent attacks suggests a rapid adaptation to the circumstances surrounding the war. The policy of an unventilated sealed room may have been detrimental.

Kawana et al. 2001. Psycho-physiological effects of the terrorist sarin attack on the Tokyo subway system. *Mil.Med.* 166(12 Suppl): 23-26.
The investigation describes the follow-up of the victims of the 1995 Tokyo sarin attack who were followed by a team at the St. Luke's International Hospital. A symptom questionnaire ("St. Luke's Questionnaire") was developed and given 2, 3, and 5 years following the sarin attack. Somatic and psychological symptoms have continued for 5 years after the incident. New post-traumatic stress disorder diagnostic criteria, which include physical symptoms, were developed and applied for assessment of the outcomes. The St. Luke's cohort was also compared with other Japanese sarin attack cohorts. Interventions, including counseling, medical treatments, and support group activities, were associated with fewer symptoms among the victims.

Mayne et al. 1999. Research review on anger in psychotherapy. *J.Clin.Psychol.* 55(3): 353-363.
This article selectively reviews clinically relevant research on the theory and treatment of anger. Anger is first defined, within the context of emotion theory, as the cognitive, behavioral, physiological, experiential, and social manifestations of a central nervous system process. The theories and techniques used to treat anger from several theoretical perspectives are then evaluated, making conceptual links to a basic affective model. We then review research on the treatment of anger in clinical populations (aggressive adults and children, clients with post-traumatic stress disorder, and clients with cardiovascular disease). We conclude with a discussion of anger suppression and inhibition.

Miller. 2000. Post-Traumatic Stress Disorder in Primary Care Practice. *J Am Acad Nurse Practitioners.* 12(11): 475-82.

PURPOSE: To provide clinicians in primary care settings with guidelines on evaluation, diagnosis and management of post-traumatic stress disorder (PTSD).

Mellman. **1997.** Psychobiology of sleep disturbances in posttraumatic stress disorder. *Ann.N.Y.Acad.Sci.* 821(142-149.
Sleep disturbances are prominent complaints of PTSD patients. Some, but not all, of the polysomnographic studies support the occurrence of sleep disruption. The main dimensions of sleep disturbance in the disorder relate to arousal regulation and REM-related functions of dreaming and memory processing. Both of these issues are relevant to the pathogenesis of PTSD and manifestations of the disorder during wake states. Studies elucidating the effects of treatment on sleep parameters are an important direction for future research.

Murburg. **1994.** Catecholamine function in posttraumatic stress disorder : emerging concepts. 42(371.

NIMH [National Institute of Mental Health]. 2004. Facts About Post-Traumatic Stress Disorder. http://www.nimh.nih.gov/anxiety/ptsdfacts.cfm (March 20, 2004)

Nishiwaki et al. 2001. Effects of sarin on the nervous system in rescue team staff members and police officers 3 years after the Tokyo subway sarin attack. *Environ.Health Perspect.* 109(11): 1169-1173.
Although the clinical manifestations of acute sarin poisoning have been reported in detail, no comprehensive study of the chronic physical and psychiatric effects of acute sarin poisoning has been carried out. To clarify the chronic effects of sarin on the nervous system, a cross-sectional epidemiologic study was conducted 3 years after the Tokyo subway sarin attack. Subjects consisted of the rescue team staff members and police officers who had worked at the disaster site. Subjects consisted of 56 male exposed subjects and 52 referent subjects matched for age and occupation. A neurobehavioral test, stabilometry, and measurement of vibration perception thresholds were performed, as well as psychometric tests to assess traumatic stress symptoms. The exposed group performed less well in the backward digit span test than the referent group in a dose-effect manner. This result was the same after controlling for possible confounding factors and was independent of traumatic stress symptoms. In other tests of memory function, except for the Benton visual retention test (mean correct answers), effects related to exposure were also suggested, although they were not statistically significant. In contrast, the dose-effect relationships observed in the neurobehavioral tests (psychomotor function) were unclear. None of the stabilometry and vibration perception threshold parameters had any relation to exposure. Our findings suggest the chronic decline of memory function 2 years and 10 months to 3 years and 9 months after exposure to sarin in the Tokyo subway attack, and further study is needed.

Page. **2003.** Long-term health effects of exposure to sarin and other anticholinesterase chemical warfare agents. *Mil.Med.* 168(3): 239-245.
In a telephone survey of 4,022 military volunteers for a 1955-1975 program of experimental exposures to chemical agents at Edgewood, Maryland, the current health of those exposed to anticholinesterase agents was compared with that of men exposed to no active chemicals (no chemical test) and to two or more other types of chemical agents (other chemical tests). The survey posed questions about general health and about neurological and psychological deficits. There were only two statistically significant differences: volunteers in anticholinesterase agent tests reported fewer attention problems than those in other chemical tests and greater sleep disturbance than those in no chemical tests. In contrast, volunteers who reported exposure to civilian or military chemical agents outside of their participation in the Edgewood program reported many statistically significant adverse neurological and psychological effects, regardless of their experimental exposure. In this study, the health effects of self-reported, nonexperimental exposure, which are subject to recall bias, were greater than the health effects of experimental exposure.

Platman. **1999.** Psychopharmacology and posttraumatic stress disorder. *Int.J.Emerg.Ment.Health.* 1(3): 195-199.
Posttraumatic Stress Disorder (PTSD) is a complex and challenging psychiatric disorder. Its more severe manifestations will require psychopharmacologic intervention. This paper offers guidance in the psychopharmacologic management of PTSD.

Proctor et al. 1998. Health status of Persian Gulf War veterans: self-reported symptoms, environmental exposures and the effect of stress. *Int.J.Epidemiol.* 27(6): 1000-1010.
BACKGROUND: Most US troops returned home from the Persian Gulf War (PGW) by Spring 1991 and many began reporting increased health symptoms and medical problems soon after. This investigation examines the relationships between several Gulf-service environmental exposures and health symptom reporting, and the role of traumatic psychological stress on the exposure-health symptom relationships. METHODS: Stratified, random samples of two cohorts of PGW veterans, from the New England area (n = 220) and from the New Orleans area (n = 71), were selected from larger cohorts being followed longitudinally since arrival home from the Gulf. A group of PGW-era veterans deployed to Germany (n = 50) served as a comparison group. The study protocol included questionnaires, a neuropsychological test battery, an environmental interview, and psychological diagnostic interviews. This report focuses on self-reported health symptoms and exposures of participants who completed a 52-item health symptom checklist and a checklist of environmental exposures. RESULTS: The prevalence of reported symptoms was greater in both Persian Gulf-deployed cohorts compared to the Germany cohort. Analyses of the body-system symptom scores (BSS), weighted to

account for sampling design, and adjusted by age, sex, and education, indicated that Persian Gulf-deployed veterans were more likely to report neurological, pulmonary, gastrointestinal, cardiac, dermatological, musculoskeletal, psychological and neuropsychological system symptoms than Germany veterans. Using a priori hypotheses about the toxicant effects of exposure to specific toxicants, the relationships between self-reported exposures and body-system symptom groupings were examined through multiple regression analyses, controlling for war-zone exposure and post-traumatic stress disorder (PTSD). Self-reported exposures to pesticides, debris from Scuds, chemical and biological warfare (CBW) agents, and smoke from tent heaters each were significantly related to increased reporting of specific predicted BSS groupings. CONCLUSIONS: Veterans deployed to the Persian Gulf have higher self-reported prevalence of health symptoms compared to PGW veterans who were deployed only as far as Germany. Several Gulf-service environmental exposures are associated with increased health symptom reporting involving predicted body-systems, after adjusting for war-zone stressor exposures and PTSD.

Rosen. **2004.** Posttraumatic stress disorder : issues and controversies.

Ross et al. 1989. Sleep disturbance as the hallmark of posttraumatic stress disorder. *Am.J.Psychiatry.* 146(6): 697-707.
The reexperiencing of a traumatic event in the form of repetitive dreams, memories, or flashbacks is one of the cardinal manifestations of posttraumatic stress disorder (PTSD). The dream disturbance associated with PTSD may be relatively specific for this disorder, and dysfunctional REM sleep mechanisms may be involved in the pathogenesis of the posttraumatic anxiety dream. Furthermore, the results of neurophysiological studies in animals suggest that CNS processes generating REM sleep may participate in the control of the classical startle response, which may be akin to the startle behavior commonly described in PTSD patients. Speculating that PTSD may be fundamentally a disorder of REM sleep mechanisms, the authors suggest several strategies for future research.

Scaer. **2001.** The neurophysiology of dissociation and chronic disease. *Appl.Psychophysiol.Biofeedback.* 26(1): 73-91.
Dissociation as a clinical psychiatric condition has been defined primarily in terms of the fragmentation and splitting of the mind, and perception of the self and the body. Its clinical manifestations include altered perceptions and behavior, including derealization, depersonalization, distortions of perception of time, space, and body, and conversion hysteria. Using examples of animal models, and the clinical features of the whiplash syndrome, we have developed a model of dissociation linked to the phenomenon of freeze/immobility. Also employing current concepts of the psychobiology of posttraumatic stress disorder (PTSD), we propose a model of PTSD linked to cyclical autonomic dysfunction, triggered and maintained by the laboratory model of kindling, and perpetuated by increasingly profound dorsal vagal tone and endorphinergic reward systems. These physiologic events in turn contribute to the clinical state of dissociation.

The resulting autonomic dysregulation is presented as the substrate for a diverse group of chronic diseases of unknown origin.

Smith et al. 2000. Bioterrorism. A new threat with psychological and social sequelae. *N.C.Med.J.* 61(3): 150-163.

Stewart et al. 1998. Functional associations among trauma, PTSD, and substance-related disorders. *Addict.Behav.* 23(6): 797-812.
This review article presents several potential functional pathways which may explain the frequent co-occurrence of PTSD and substance abuse disorders in traumatized individuals. Emerging empirical studies which have examined these potential pathways are reviewed, including studies on relative order of onset, PTSD patients' perceptions of various drug effects, comparisons of PTSD patients with and without comorbid substance use disorders, and correlational studies examining the relations between severity of specific PTSD symptom clusters and substance disorder symptoms. Research on the acute and chronic effects of alcohol and other drugs on cognitive and physiological variables relevant to PTSD intrusion and arousal symptoms is reviewed to highlight ways in which these two sets of PTSD symptoms might be functionally interrelated with substance abuse. Finally, based on these findings, recommendations are made for the treatment of individuals with comorbid PTSD-substance use disorders.

Strous et al. 2004. Reactions of Psychiatric Inpatients to the Threat of Biological and Chemical Warfare in Israel. *J.Nerv.Ment.Dis.* 192(4): 318-323.
In the months before the Second Gulf War, the threat of biological and chemical warfare led many Israelis to experience significant stress and mood changes. In this study, we investigated whether this threat affected the subjective mood and behavior of inpatients with schizophrenia and compared the results with effects noted in their clinical staff. Subjects were evaluated at two points in time-2 months before the war and on day 1 of the war-with a specially designed questionnaire and with the Spielberger Scale for Trait Anxiety. Although the responses of the two groups did not differ radically before the war, on the first day of war, significant differences were noted, with patients demonstrating increases in anxiety and level of concern. Both groups reported similar effects on their mood. Patients were more concerned about the potential for the outbreak of World War III, whereas staff were more concerned about economic effects. Female subjects in both groups demonstrated greater anxiety and mood changes after the outbreak of war compared with before the war. Effects observed on the patients may be related to the decreased coping threshold resulting from their illness, which renders psychotic patients more vulnerable to any acute stressor; however, effects on the staff members should not be ignored.

Talmon et al. 1992. ["Saddam syndrome": acute psychotic reactions during the Gulf War--renewal of concept of brief reactive psychosis]. *Harefuah.* 123(7-8): 237-40, 308.
6 patients came to our psychiatric emergency room during the first 2 weeks of the Gulf War presenting the clinical picture of acute delusional paranoid psychosis (4 women and 2 men between the ages of 30-77). 4 were without previously known psychopathology, while the other 2 were known to have had some nonpsychotic cognitive impairment. The first 4 recovered completely within a short time while the other 2 continued to have psychopathological symptoms. We discuss psychogenic or reactive psychosis, and the concept of reactivation when cumulative trauma exceed the individual's personal threshold, as may occur during a war. Different phenomenological syndromes may follow.

Tochigi et al. 2002. Serum cholesterol, uric acid and cholinesterase in victims of the Tokyo subway sarin poisoning: A relation with post-traumatic disorder. *Neuroscience Research*. 44: 267-72.

Ursano. **2002.** Post-traumatic stress disorder. *N.Engl.J.Med.* 346(2): 130-132.

Voiculescu. **1983.** Neuropsychiatric implications of the state of war. *Physiologie.* 20(4): 283-285.

Wagner et al. 2000. An investigation of the impact of posttraumatic stress disorder on physical health. *J.Trauma.Stress.* 13(1): 41-55.
In a large sample of Gulf War veterans (N = 2301) we examined the relations between PTSD symptoms assessed immediately upon returning from the Gulf War and self-reported health problems assessed 18-24 months later. PTSD symptomatology was predictive of self-reported health problems over time for both men and women veterans, even after the effects of combat exposure were removed from the analysis. Female veterans reported significantly more health problems than male veterans, however, there was no interactive effect of gender and PTSD on health problems. These findings provide further support for the theory that psychological response to stressors impacts health outcome.

Wolfe et al. 1999. Relationship of psychiatric status to Gulf War veterans' health problems. *Psychosom.Med.* 61(4): 532-540.
OBJECTIVE: A growing body of research has shown that there are important links between certain psychiatric disorders and health symptom reporting. Two disorders in particular (posttraumatic stress disorder (PTSD) and major depression) have been the

most widely implicated to date, and this association has sometimes been used to explain the occurrence of ill-defined medical problems and increased somatic symptoms in certain groups, most recently Gulf War veterans. METHODS: Structured psychiatric diagnostic interviews were used to examine the presence of major psychiatric (axis I) disorders and their relation to health symptom reporting in a well-characterized, stratified subset of Gulf War veterans and a non-Gulf-deployed veteran comparison group. RESULTS: Rates of most psychiatric disorders were substantially lower than national comorbidity estimates, consistent with prior studies showing heightened physical and emotional well-being among active-duty military personnel. Rates of PTSD and major depression, however, were significantly elevated relative to the veteran comparison group. The diagnosis of PTSD showed a small but significant association with increased health symptom reports. However, nearly two-thirds of Gulf participants reporting moderate to high health symptoms had no axis I psychiatric diagnosis. CONCLUSIONS: Results suggest that rates of psychiatric illness were generally low with the exception of PTSD and major depression. Although PTSD was associated with higher rates of reported health problems, this disorder did not entirely account for symptoms reported by participants. Factors other than psychiatric status may play a role in Gulf War health problems.

Yehuda et al. 1993. Criteria for rationally evaluating animal models of posttraumatic stress disorder. *Biol.Psychiatry.* 33(7): 479-486.
Animal models of stress have the potential to provide information about the course and etiology of posttraumatic stress disorder (PTSD). To date, however, there have been no systematic approaches for evaluating the relevance of animal models of stress to PTSD. It has been established in the animal literature that different types of stress paradigms lead to different biobehavioral consequences and that many different factors contribute to differential responsivity to stress. It becomes important therefore to differentiate between factors that are essential to the induction of PTSD-like symptoms and those that influence their manifestations. In the present commentary, we present five criteria that must be fulfilled by animal models of stress for them to be useful to understanding the induction of PTSD. We then evaluate two potential animal models of stress--inescapable shock-learned helplessness and time-dependent sensitization--to illustrate how to more successfully pair animal models of stress with the specific clinical syndrome of PTSD.