13 Psychological Factors in Chemical Warfare and Terrorism*

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I. INTRODUCTION

The early 21st century is faced with a significant health threat in the form of chemical weapons. These have been used more frequently and in more diverse settings since they were first used on World War I (WWI) battlefields. The potential to cause large numbers of serious casualties among deployed and deploying military forces and among civilian populations provides a stark reminder to medical planners of the limits of both military and civilian medicine. However, medical countermeasures to these chemical warfare (CW) agents have been, and continue to be, developed. These CW agents, their countermeasures, and the health care implications of their use are described in this chapter. We suggest likely psychological, physiological, and neurological effects that will be encountered should these agents be employed against, or their countermeasures used by, U.S. forces and citizens on the battlefield or in the homeland. We further suggest that these pharmacologic and toxicologic actions will occur in the broad context of a nuclear, biological, chemical (NBC) environment with its attendant confounding variables. For example, recent studies point to potential increased difficulty in the differential diagnosis of stress reaction vis-à-vis organophosphate (OP)-induced organic brain syndromes. Knowledge of the

*The opinions or assertions contained herein are the private views of the authors, and are not to be construed as reflecting the view of the Department of the Army or the Department of Defense.

behavioral effects of the CW agents and of their medical countermeasures is imperative for military and civilian medical and mental health planners as they prepare to deal with possible incidents involving battlefield CW agent use or chemical terrorism.

II. CHEMICAL WARFARE (CW) AGENTS AND PERFORMANCE

The early 21st century is faced with a significant health threat in the form of chemical weapons. These have been used more frequently and in more diverse settings since they were first used on World War I (WWI) battlefields. Traditionally, U.S. Armed Forces have been concerned with four classes of CW agents: (a) choking (e.g., phosgene [CG] and chlorine, which were employed simultaneously during WWI), (b) blood (e.g., cyanide [CN]), (c) blister (e.g., sulfur mustard [HD]), and (d) nerve agents (e.g., sarin [GB]). These agents differ in terms of their rapidity of action, lethality, and the requirement for prompt and/or sustained medical care. The accompanying tables provide a summary of the major CW agents of concern, including their historical mortality/morbidity, principal target tissue, current/proposed countermeasures, and principal behavioral effects of the CW agents and their countermeasures. The CW agents' potential to cause large numbers of serious casualties provides a stark reminder to medical planners of the limits of both military and civilian medicine. The purpose of this review is to describe likely psychological, physiological, or neurological effects that will be encountered should these agents be used on the integrated battlefield or against homeland facilities and personnel, with emphasis on their psychological or behavioral effects. Defense of the homeland against potential terrorist use of CW agents is clearly an emerging requirement for both our military and civilian medical response systems.[1–5]

Choking and blood agents were first used on the battlefield early in WWI. Although several choking agents (e.g., phosgene and chlorine) were employed simultaneously, it has been determined that the choking agent phosgene produced a large number of casualties requiring extensive hospitalization.[6] The primary clinical effect of phosgene is a pulmonary edema following a clinical latent period of variable length. The latent period is dependent primarily on the intensity of exposure (viz., the Ct, or concentration $\times$ time). The latency period is also partly dependent on the physical activity of the exposed individual with higher activity levels found to be more detrimental. For a review of phosgene's effects, see Sciuto.[6] He suggests that the primary effects of phosgene upon military performance would undoubtedly be the result of its capacity to produce deep lung injury. In addition, Sciuto cites evidence that phosgene may produce a toxic encephalopathy in man.[6] Phosgene exposure and subsequent intoxication almost certainly would cause decreased O_2 delivery to the central nervous system (CNS) and to other body systems, with accompanying behavioral and functional deficits under conditions in which continuous mental and/or physical performance is demanded.

Blood agents appeared on WWI battlefields within weeks after the initial use of choking agents and were employed in an effort to rapidly produce lethal casualties.

The principal blood agent is cyanide (CN), a biochemical poison that has a marked CNS toxicity.[7] Acute, sublethal poisoning is associated with a Parkinson-like syndrome, to include a selective neurodegeneration in experimental animals.[8] In man, Utti et al. reported a delayed onset Parkinsonism developing over a 2-year period post-intoxication.[9] Gradients of CNS effects can be observed either after exposure to lower concentrations or following exposure to lethal amounts via the oral or percutaneous routes.[10] Initial signs of CNS excitement, including anxiety and agitation, may progress to signs of CNS depression, such as coma and dilated, unresponsive pupils. Correspondingly, in animals, pathological studies from WWI and WWII indicate that residual cyanide lesions are significant only in the case of animals receiving a narrow range of exposures just below the lethal dose. As reported by Moore and Gates, recovering animals show residual neurological damage, principally in the cerebrum and cerebellum.[7] Kanthasamy et al. demonstrated a correlation between loss of dopaminergic neurons and locomotor dysfunction following CN intoxication.[11] Thus, cyanide should be regarded as a CNS-active CW agent with potential to produce residual CNS or neurobehavioral effects. However, no studies or casualty figures exist to suggest that cyanide is effective in producing militarily significant casualty rates in a trained and protected force. It is believed by some to have been used against unprotected populations and remains a threat to armed forces and civilians in both conventional and unconventional conflicts.

The most effective agent at producing casualties in WWI was the so-called "mustard gas," or HD. Smith points out that mustard produced hundreds of thousands of casualties, many of whom required extensive hospitalization, even more casualties than were seen with phosgene.[12] The pernicious nature of mustard was reinforced in the mid-1980s in the Iran-Iraq War, in which it produced an estimated 45,000 chemical casualties. The major clinical effects of exposure to HD are significant skin, eye, and pulmonary lesions, which are usually nonfatal. The length of hospitalization following these injuries was estimated to be 42 days per casualty during WWI and up to 70 days during the Iran-Iraq War.[13–15] Reports of neuropsychiatric effects, such as severe apathy, impaired concentration, and diminished libido have appeared in the literature, generally in the form of case reports rather than experimental studies.[16,17] However, in general, the psychological and behavioral effects observed after HD exposure are attributable to post-traumatic stress disorder (PTSD).[18] Lohs reported that chemical munitions workers manifested specific neurological sequelae such as impaired concentration, diminished libido, and sensory hypersensitivity.[17] Unfortunately, for many of these workers, additional or co-exposures were noted, which confound our ability to identify relationships between HD exposure and effects. Examination of the literature also reveals a paucity of long-term follow-up in the area of psychiatric sequelae linked to HD exposure.

Other potential blister agents include lewisite and phosgene oxime (CG). Lewisite was synthesized during the late stage of WWI, but there are no reports of its battlefield use. Its antidote, British Anti-lewisite, finds medicinal use today as a heavy metal chelator. Although classified as a vesicant, CG is a corrosive urticant for which, like lewisite, there are no reports of battlefield use. There are also no reports of CNS effects following intoxication with these agents.

Following WWI, work in Germany to develop organophosphorus (OP) insecticides led to the identification of a new class of CW agent compounds of extreme toxicity, the nerve agents (GA [Tabun], GB [Sarin], GD [Soman], etc.). As highly active CNS agents, sublethal exposures to this type of CW agent can be expected to produce prominent deficits in behavior and performance. McDonough provided a review emphasizing human reports of the toxicological and neurobehavioral effects of exposure to nerve agents and their medical countermeasures.[19] A considerable body of literature exists on this topic, and the interested reader is encouraged to use McDonough's review as well as Longo's, Karczmar's, and McDonough and Shih's as useful starting points.[19–22]

Earlier studies using nerve agents were often carried out in doses that produced depressed cholinesterase levels or overt signs of intoxication in animals or symptoms of cholinergic poisoning in man. Animal studies have explored the effects of nerve agents on learning, long-term or short-term memory, nociception, general activity levels, or propioception.[23–28] Occasionally, these studies were designed to demonstrate pharmacologic and behavioral antagonism with anticholinergic drugs such as atropine or antidotal combinations of atropine and oximes.[13,21,29,30] Some human experimental studies have appeared in the literature, with the U.S. Army military volunteer test program ending in the 1970s.[13] These human studies are supplemented by reports of behavioral effects of exposures to other OP compounds, those in widespread use as pesticides. According to McDonough, the behavioral effects of OP in man can be divided into three classes: (1) effects on cognitive processes, (2) effects on mood/affect, and (3) disturbances of sleep/wakefulness.[19] The intensity and duration of these behavioral effects of acute OP exposure are generally related to the magnitude of blood ChE inhibition.[29] In fact, based on his review, McDonough concluded that behavioral CNS symptoms of OP exposure have not been seen at levels of ChE inhibition less than 50% and are more typically seen when inhibition reaches 70–80% of control levels.[19] Somewhat less effort has been given to characterizing the effects of "low-level" exposures to nerve CW agent, perhaps due to the steepness of their toxicity curves and the resultant difficulty in determination of low-level dosages.[26] Recent concern over the possible sublethal exposure of members of the U.S. Armed Forces to the nerve agent GB during and following the Gulf War has led to a renewed study of this problem. The reader can identify pertinent on-going studies and review their annual reports and abstracts on the Internet at http://www.va.gov/resdev/pgrpt97.htm.[31]

Much of the data regarding long-term neurological sequelae to exposures to cholinesterase inhibitors in man have been gathered following accidental exposures to OP pesticides. In one of the major studies, Savage et al. found significant deficits on several cognitive tests of memory and abstraction, without apparent effect on the EEG or neurological examinations.[32] Steenland et al. found deficits in vibrotactile sensitivity and sustained attention among previously intoxicated subjects vs. controls; however, as with the previous study, nerve conduction tests and neurologic examinations were negative.[33] In a follow-up of humans suffering moderate to severe exposure to the CW agent GB, a deficit in the Digit Symbol Substitution Test unrelated to post-traumatic stress was observed by Yokoyama et al.[34] The Digit Symbol

Substitution Test of the WAIS (Webster Adult Intelligence Scale; Japanese version) was described as measuring "motor persistence, sustained attention, response speed, and visuomotor coordination." The decrease in Digit Symbol test scores was found 6 to 8 months after acute poisoning, at a time when ChE levels had returned to normal. The WAIS deficit was also unrelated to the level of ChE inhibition on the day of poisoning. The authors suggested that acute ChE inhibition might not be a good predictor of the chronic effects of GB on psychomotor performance.

For chronic, subclinical exposures to OP, the data are less consistent, but some authors have reported subclinical effects on the CNS and peripheral nervous system (PNS). On the other hand, Ames et al. surveyed 45 pesticide applicators, each of whom had at least one documented episode of asymptomatic AChE exposures.[35] He reported no CNS or PNS effects. For example, Stephens et al., studying a population of 146 sheep dippers with an average of 15 years of potential exposure to several OP (diazinon, propetamphos, chlorfenvinphos) found significant changes in sustained attention and speed of information processing.[36] These authors found no effects on memory or learning. Duffy et al. reported EEG changes in CW agent chemical plant workers that persisted for more than 1 year after accidental exposure to GB, but they suggested that the functional significance of these changes was unclear.[37] A review of the literature by a National Academy of Sciences (NAS) expert panel also indicated they were unable to clearly identify a functional correlate of the observed EEG changes.[38]

We believe that studies to determine the potential long-term psychologic/neurologic sequelae following OP intoxication are confounded by factors such as low response rates, possible selection and follow-up biases (loss to follow-up of the most severe cases), compensatory psychologic response, possible co-exposures, and the like. For this reason, the recent national investment into additional research in this area is well founded. The findings discussed in this section are summarized in Table 1.

III. COUNTERMEASURES AND PERFORMANCE

Pharmacological or medical countermeasures to these CW agents can produce CNS sequelae, and these neurobehavioral effects will also be discussed briefly in this chapter. This section focuses primarily on currently available countermeasures, with one exception, that of scavenging enzymes. Of course, CW agents, which have high toxicity in CNS tissue, like the nerve agents and blood agents, require medical countermeasures that may be expected to produce significant CNS and performance effects, and those effects would need to be evaluated. In the case of choking agents (e.g., phosgene) and blister agents (e.g., sulfur mustard), current treatments are symptomatic and supportive, and have few performance impacts beyond those produced by the agents themselves. Two areas of interest regarding countermeasures are highlighted. First, the rapid action of CN and the need for current therapies to be administered intravenously (a difficult requirement on the battlefield or in a mass casualty situation) have led to programs to develop prophylactics or pretreatments for this CW agent. The most promising approach to this point has been pretreatment by methemoglobin-forming compounds. In this strategy, methemoglobin acts as a scavenger

TABLE 13.1
Morbidity of Four Classes of Chemical Warfare Agents and Their Principal Targets and Medical Countermeasures

Class of CW Agent	Historic Lethality/Morbidity in Warfare	Principal Target Tissue	Physiological/ Performance Effects
Choking (e.g., phosgene)	1%[a]	Deep lung compartment such as pulmonary capillary	Pulmonary edema, hypoxia
Blood (e.g., cyanide)	Unknown[b]	Cellular respiratory enzymes	Depression of cortical function, unconsciousness, convulsions
Blister (e.g., "mustard gas")	2–4%[c]	Skin, airway, eyes, GI tract, bone marrow	Loss of function due to skin, lung, ocular lesions, recovery over time
Nerve (e.g., sarin)	Unknown[d]	CNS, neuromuscular junction; cholinergic synapse	GI tract, miosis, nausea, weakness, loss of consciousness, convulsions

Note: Estimates derived from U.S. published sources.

[a]WWI figures for the U.S. are estimates because phosgene was often mixed with chlorine; however, a total of 6834 injured (average hospitalization = 49 days) have been directly attributed to phosgene with 66 fatalities.

[b]No data from wartime use; however, wartime experiences suggest difficulty in achieving militarily effective concentrations unless confined to closed spaces.

[c]WWI, 2% with 27,711 U.S. injured; Iran-Iraq War, 4% with 45,000 estimated injured.

[d]No data from wartime use; however, on 20 March 1995, using a primitive method of dispersal, sarin was released on Tokyo subways with 5,500 people seeking medical care; approximately 1500 had defined symptoms of exposure, and 12 casualties died. Less well known is the fact that on June 27, 1999, sarin was released in Matsumoto, Japan, with estimates of 471 subjects exposed to sarin and 7 deaths.

with a much higher affinity for CN than the terminal mitochondrial cytochrome oxidase a_3 protein. Displacement of CN from cytochrome a_3 permits the return to normal respiration.[39] Research studies in animals have led to an estimate that methemoglobin levels of 5–15% will be protective against up to 2 × the LD_{50} of cyanide.[40,41] Putting this in perspective, the level of methemoglobin in smokers' blood is 2%. The effects of a level of 5–15%-induced methemoglobin on performance need to be evaluated. However, chronic methemoglobinemia is seen by some as a toxic condition with potential for long-term hematotoxicity.[42] Thus, other pretreatment strategies have been explored as part of a drug discovery program. A strategy of providing sulfur-donating compounds to possibly speed the conversion of cyanide to thiocyanate

was one of the alternatives pursued. A number of promising compounds, some without any apparent disruptive effects on behavior (in mice), have been identified and the authors suggested that those newly synthesized compounds provide a rationale for a new class of anti-CN pretreatment compounds.[43] Although some limited data were reported by Baskin et al. concerning the ability of anti-CN compounds to reverse the motor (performance) impairment caused by a near-lethal dose of CN, a significant data gap exists in the area of recovery of function after mild to moderate CN intoxication.[43]

Second, medical protection from the effects of nerve agents may involve pretreatment with a reversible acetylcholinesterase inhibitor like pyridostigmine bromide or with biological scavengers targeted at these CW agent compounds. The drug pyridostigmine bromide (PB) has recently been given a considerable amount of scrutiny. This attention stems from its use as a pretreatment to protect U.S. Armed Forces against the potential use of nerve agents by the forces of Saddam Hussein during the Gulf War. Several studies of PB effects on military performance have been reviewed.[44] These studies include effects of PB upon a number of components of pilot performance such as tolerance to altitude changes or acceleration tolerance.[45,46] Additionally, Kolka and Stephenson examined the effects of PB on endurance and parameters of exercise physiology under several simulated environments.[47] In general, there were no significant effects of PB found on these performance parameters. Laboratory studies using more traditional psychological tests also support the lack of PB effects on performance.[48] Similarly, following chronic PB administration, soldiers of the Israeli Defense Force (IDF) reported infrequent and mild effects.[49] Additionally, PB's potential health consequences, when taken by otherwise healthy U.S. services members, were reviewed by Dunn et al.[43] These authors suggested that PB has a "good safety record over the years of its administration to patients with myasthenia gravis." Moreover, at the prescribed dose of 30 mg every 8 h, no significant decrements have been found in performance of a variety of military tasks. It is not within the scope of this paper to discuss the linkage, if any, between PB and Persian Gulf War Illness. A comprehensive review of the literature regarding PB with emphasis on how it might pertain to Persian Gulf War Illness can be found at http://www.gulflink.osd.mil/library/randrep/pb_paper.[50] However, the reader is again directed to http://www.va.gov/resdev/pgrpt97.htm.[30] This website provides summaries and abstract reports of more than a score of research projects examining the health effects of PB either alone or in combination with a variety of other compounds. In general, these studies explore the possible linkages and complex chemical interactions of PB and other compounds in relation to Persian Gulf War Illness.

Protection from nerve agent poisoning may also involve pretreatment with a biological scavenger. Lenz and Cerasoli suggest that the biological scavenger approach avoids the side effects associated with the current nerve agent antidotes and, from the limited amount of animal data available, appears to prevent or significantly alleviate the neurobehavioral effects of the nerve agents.[51–53] Moreover, the level of protection from the neurobehavioral effects of nerve agents is greater than that seen following the use of "conventional therapy" for nerve agents. Several approaches to the scavenger concept have been explored—antibodies, enzymes, and catalytic

bioscavengers. The latter, in general, have been developed by introducing amino acid changes into stoichiometric enzymes, such as human butyrylcholinesterase and human carboxylesterase. Promising results have been obtained, and this research program remains active.[5]

The demonstrations of bioscavenger protection from the behavioral deficits that normally follow exposure to nerve agents have been made in several animal species. For mice, there is a well-characterized deficit in ability to respond on the inverted screen test.[54,55] Mice pretreated with fetal bovine serum acetylcholinesterase (FBS-AChE), equine butyrylcholineserase (Eq-BuChE) or human BuChE were completely protected from these deficits.[52,53,56] An elegant study by Brandeis et al. characterized the effects of soman on naïve rats or rats pretreated with human BuChE.[57] The Morris Water Maze (MWM) was employed in these studies, as maze learning or spatial memory tests had previously been demonstrated to be sensitive to the effects of cholinergic drugs to include OP nerve agents such as soman.[24] In Brandeis' study, naïve rats given a toxic but sublethal dose of soman had significant impairments in MWM performance that persisted for several weeks. Pretreatment with human BuChE provided significant protection from those effects of nerve agent. In fact, performance of the BuChE-pretreated animals was indistinguishable from untreated controls. Furthermore, the BuChE enzyme itself was without effect on MWM performance.

In non-human primates, a series of studies using the Serial Probe Recognition (SPR) task have yielded similar results. The scavenger enzyme was without effect on performance in the SPR task.[58] The exposure of rhesus monkeys to soman produced pronounced deficits in this task, and the animals were protected by pretreatment with BuChE (even after exposure to 4–5 $\times$ LD_{50} of nerve agent).[25] Using the Primate Equilibrium Platform, investigators at the School of Aerospace Medicine demonstrated the effects of soman on performance.[59] They found complete protection of animal performance with either FBS-AChE or Eq-BuChE, even when up to a cumulative 5 $\times$ LD_{50} of nerve agent were administered.[59] When compared to similar studies employing conventional therapies such as atropine and 2-PAM, the scavenger enzymes approach provided a remarkable improvement. The findings on effects of current medical countermeasures to CW agents discussed in this section are summarized in Table 2.

One final point about the response to chemical agents on the battlefield or in the homeland concerns the possible presence of stress casualties. These have been variously labeled as cases of "gas hysteria," "gas mania," or "gas neurosis." In a recent review of this literature, Stokes and Banderet reported that the official U.S. Army Medical Department history of WWI notes that two such cases occurred for each actual chemical injury.[60] Their analysis suggested several origins for these cases: (a) conversion disorders, (b) mistaking normal physiological stress symptoms for exposure to CW agents (despite significant efforts to train soldiers in proper recognition of signs of poisoning), (c) mistaking or magnifying the symptoms of minor illnesses, and (d) deliberate faking or malingering. One might add the possibility of an additional type of "self-inflicted wound" to this list; by this, we mean the inadvertent or misguided use of antidotal compounds, e.g., atropine and diazepam.

TABLE 13.2
Potential Performance Effects of Current Countermeasures

Agent Type	Countermeasure	Potential Physiological/Performance Effects
Choking	Symptomatic	N/A
Blood	Sodium nitrate (i.v.)	Reduces blood oxygen capacity, hypotension[a]
	Sodium thiosulfate (i.v.)	
Blister	Symptomatic	N/A
Nerve	Atropine	Mydriasis, reduced sweating, dry mouth,[b] mild sedation, delirium, at 10 mg or higher
	2-PAM Cl	Minimal, except at high i.v. doses[2]
	Pyridostigmine	Mild GI and urinary discomfort in ~50%, severe in ~1% (see also http://www.gulflink.osd.mil/library/rand/rep/pb_paper)
	Diazepam	Sedation, muscle relaxation, drowsiness, ataxia

[a]Baskin, S.I. and Brewer, T., in *Textbook of Military Medicine—Medical Aspects of Chemical and Biological Warfare,* Zajtchuk, R. and Bellamy, R.F., eds., Office of the Surgeon General, Department of the Army, Washington, DC, 1997, chap. 10.

[b]Sidell, F.R., in *Textbook of Military Medicine—Medical Aspects of Chemical and Biological Warfare,* Zajtchuk, R. and Bellamy, R.F., eds., Office of the Surgeon General, Department of the Army, Washington, DC, 1997, chap. 2.

Self-administration of two nerve agent antidote autoinjectors can produce headache, restlessness, and fatigue, symptoms that can be aggravated in a tired, dehydrated, or stressed individual. The possibility of widespread mental health disorders that may result from fear or actual use of chemical weapons has also been recently reviewed by DiGiovanni.[61] He pointed to potential difficulties in sorting out the physical effects of CW agents from the psychological response of the exposed person. Confusion about these various phenomena may result in behaviors that are difficult to differentiate from a backdrop of generalized war syndromes. In their review of poorly understood war syndromes from the U.S. Civil War to the Persian Gulf War, Hyams et al. analyzed symptoms to identify possible unifying factors.[62] These authors concluded that there was little evidence of a single, unique war syndrome that is unrelated to psychological stress. It is also certainly true that rumors of CW agent use or of its actual use can contribute to high rates of acute combat stress reactions. Ursano suggests that CW agents stir fear in military personnel for several reasons: (1) the particular, personal psychological fears of CW agents, (2) a sense of the need to continue to operate after a CW agent attack, and (3) due to the indiscriminate nature of CW agents, a fear for the safety of family members.[63]

Insights into the likelihood and consequences of such reactions can be found in a series of reports describing effects of SCUD missile attacks on Israeli civilian populations during the Persian Gulf War. One such report described the use of "anti-chemical warfare kits," to include protective masks, during the Gulf War.[64] The authors reported that the unfortunate misuse of such equipment led to the death by suffocation of 13 individuals. These deaths occurred despite detailed instructions and demonstrations provided by civil defense personnel. It appears that even intensive education efforts may not completely prevent inappropriate actions under the stress of anticipated CW agent attacks. Bleich et al. interviewed 773 Israeli civilians who were treated at 12 hospital emergency departments after either a missile attack or a false alarm.[65] Their report was revealing: 43% suffered from a stress reaction, and 27% had mistakenly injected themselves with atropine, an antidote to nerve agents. The authors surmised that anxiety might also have caused the death of several citizens who panicked during the missile attacks. Furthermore, the authors made several interesting suggestions as to the staffing of emergency centers and the processing of stress casualties. These suggestions included establishment of "stress reaction centers" co-located with the receiving hospital, the types of interventions to be found at these centers, and the optimal time frames necessary to achieve the patient's return to his home or family. Finally, they pointed to potential increased difficulty in the differential diagnosis of stress reaction vis-à-vis "OP-induced organic brain syndromes."[65] The relationships between PTSD and structural changes in brain related to sarin exposure, and the clinical implications of that relationship as it pertains to the survivors of the Tokyo subway poisoning are described by Yokoyama et al.[66] These authors did extensive evaluations of the neurobehavioral, CNS, and PNS effects in 18 exposed, hospital-treated patients. In general, Yokoyama et al. supported Bleich's contention of confounding neurobehavioral and psychological symptoms. Incidents of this type will present an enduring challenge to emergency medicine and psychology.

IV. SUMMARY

Had this review been developed in the late 1980s, its application and focus would have generally been limited to the protection of deployed U.S. Armed Forces. We believe that the world has changed. The CW agents discussed in this review should be considered as threats to deployed and deploying forces, fixed military installations either overseas or in the continental U.S., and to the American homeland and its population. Moreover, in the last decade the unthinkable has happened—CW agents have been employed against unprotected civilians by terrorists. These events have challenged the civilian health care and emergency response systems charged with their protection. The magnitude and impact of this challenge to both the military and civilian health care systems are carefully delineated by Stokes and Banderet, Sidell et al., and Ohtomi.[60,67,68] These works provide a detailed look at the current approaches to management of CW agent casualties. Therefore, the current world situation requires that we properly prepare by ensuring that accurate, up-to-date information on the behavioral, functional, and

neurological impacts of CW agents, as well as their medical countermeasures, are available. A number of credible Internet sites provide general toxicologic and first-aid information and, on occasion, medical training. See http://www.nbc-med.org, http://www.cbiac.apgea.army.mil, and http://chemdef.apgea.army.mil as useful starting points.

Exposure to CW agents may produce immediate and/or long-lasting effects on behavior and psychology of exposed individuals. The greater the initial exposure, the greater the time for recovery of normal function. Medical countermeasures are available to mitigate, or even prevent, these effects. Occasionally exposure to the countermeasures may produce transient effects on behavior and/or psychological performance. Research promises to provide, at least for some agents, countermeasures that completely block these effects of CW agents, while being innocuous in their own right.

Nevertheless, these pharmacologic and toxicologic actions will occur in the broad context of the so-called "nuclear, biological, and chemical (NBC)" combat environment (and terrorist activity) with its attendant confounding variables. These phenomena will remain among the most challenging and enduring areas of military and emergency medicine and psychology.

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