

Chapter 1

OVERVIEW: DEFENSE AGAINST THE EFFECTS OF CHEMICAL AND BIOLOGICAL WARFARE AGENTS

FREDERICK R. SIDELL, M.D.^{*}; AND DAVID R. FRANZ, D.V.M., PH.D.[†]

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^{*}Formerly, Chief, Chemical Casualty Care Office, and Director, Medical Management of Chemical Casualties Course, U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, Maryland 21010-5425; currently, Chemical Casualty Consultant, 14 Brooks Road, Bel Air, Maryland 21014

[†]Colonel, Veterinary Corps, U.S. Army; Commander, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland 21702-5011

INTRODUCTION

"Gas! Gas!" This warning cry, so common in World War I, almost became real to U.S. forces again as they prepared to liberate Kuwait in late 1990. The threat of chemical, and even biological, warfare was foremost in the minds of U.S. military personnel during Operation Desert Shield, the preparation for the Persian Gulf War. Iraq was known to have a large stockpile of chemical weapons and had demonstrated during its conflict with Iran that it would use them. It was not until after the Persian Gulf War that the U.N. Special Commission on Iraq confirmed that Saddam Hussein also had biological agents loaded in weapons. The chemical and biological threats were major concerns to those in the military medical departments who would be called on to care for poisoned or infected casualties, possibly in a chemically contaminated environment. Fortunately the ground war of the Persian Gulf War (Operation Desert Storm) was brief, and even more fortunately, our adversary did not employ these weapons.

In the desert, during the fall and winter of 1990–1991, the threat of chemical warfare became very real to our military medical personnel. The threat of biological warfare was no less feared. The military medical departments realized that medical personnel were not prepared to provide care to chemical or biological casualties or to function in a contaminated environment. This textbook should help accelerate the assimilation of medical defense information in the next war; in the past, such information has not been readily accessible. Two handbooks have also been prepared: *Medical Management of Chemical Casualties Handbook*, Chemical Casualty Care Office, Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, Maryland (September 1994); and *Medical Management of Biological Casualties Handbook*, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Frederick, Maryland (March 1996).

Rapid and intense teaching programs helped prepare our medical healthcare providers, so that by the onset of Operation Desert Storm, they were as ready as any military medical personnel might be to go to war. Hundreds of thousands of troops were supplied with chemical pretreatment and therapeutic agents and thousands were immunized against anthrax and the botulinum toxins, the two most likely biological

battlefield threats.

Two lessons were learned from this conflict, lessons that should never be forgotten by those in the military. The first was that there are countries that have chemical and biological weapons, and there are other countries that might obtain or produce them. The second was that the U.S. military medical departments must be prepared at all times to treat both types of casualties. As long as potential adversaries exist, the U.S. military might face a chemical or biological battlefield.

Military medical personnel of the United States have not treated a chemical casualty on the battlefield for nearly 8 decades, and they have never treated a biological casualty. Chemical agents have not been used as weapons in a major war or in any military conflict in which the United States has been involved since World War I. Despite the recent dissolution of the Warsaw Pact, the breakup of the Soviet Union, and other events that have seemingly reduced the conventional military threat to the United States, a textbook for military medical personnel on the management of chemical and biological agent casualties is still urgently needed. The breakup of the Soviet Union, and the consequent glut of biowarfare experts on the world employment market, may have actually increased the threat of biological proliferation. In addition to the recent experience in the Persian Gulf, a review of other events of the past 2 decades bears out this conclusion (Exhibit 1-1).

EXHIBIT 1-1

RECENT TARGETS OF CHEMICAL OR BIOLOGICAL AGENTS

Laos (mid to late 1970s; alleged)

Kampuchea (late 1970s and early 1980s; alleged)

Afghanistan (1980s; alleged)

Iran (1980s; Iran–Iraq War; confirmed)

Iraqi Kurds (1988; confirmed)

HISTORICAL PRECEDENTS

During the Arab–Israeli War (also called the Yom Kippur War) of 1973, chemical weapons were not used. While processing captured soldiers, however, Israeli troops found that the Egyptians carried personal protective equipment, a decontamination kit containing items unfamiliar to U.S. personnel, and an antidote with which we were also unfamiliar. This evidence suggested that the Egyptians were prepared for a chemical battlefield, and the components of the antidote suggested that they were prepared for the use of the nerve agent soman. (The antidote was a mixture of three compounds: atropine, benactyzine, and the oxime, TMB4.) The U.S. military soon issued the antidote to U.S. troops, only to withdraw it about 5 years later.

In the mid to late 1970s, reports began to appear that chemicals were being used against Hmong tribesmen in Laos. The Hmong had been loyal to the United States and had served this country in many ways during the Vietnam War; it was suggested that chemicals were being used against the Hmong in retaliation. Investigations were conducted by U.S. State Department personnel, by a medical team sent by The U.S. Army Surgeon General, and by international groups. Little definitive evidence was discovered, primarily because the alleged attacks took place deep in Laos. The victims took weeks to travel to Thailand to be examined, and outsiders could not enter Laos to examine the attack sites. The Hmong who reached Thailand provided graphic accounts of attacks by sprays and bombs from airplanes and how these “smokes,” which were of all colors, killed many in their villages. One member of the medical team brought back a sample of a yellow substance on the outer (barklike) layers of a bamboo culm (ie, stalk); the sample had been given to him by a Hmong, who claimed that the material had killed many of his fellow villagers. This yellow substance, along with samples from many other locations, later became known as “yellow rain” (see Chapter 34, *Trichothecene Mycotoxins*, which discusses yellow rain in greater detail).

Moreover, in the late 1970s and early 1980s, allegations were made of chemical agent use against refugees fleeing the barbaric conditions that existed in Kampuchea at that time.¹ The clinical response of the exposed humans did not fit what we understood about the effects of classic chemical agents. Tearing and itching looked like the effects of tear gas. Convulsions suggested nerve agents. But the

occurrence of internal hemorrhage and skin lesions could not be explained. Analysis of a leaf sample collected in Kampuchea 24 hours after an attack implicated trichothecene mycotoxins, a family of toxins produced by fungi but having characteristics more like chemical than biological agents.

In August 1981, based on limited physical evidence, the U.S. government announced that trichothecene mycotoxins had been used—but the findings were less than convincing to some in the scientific community and the issue became extremely contentious. This controversy was never totally resolved, and the question of which, if any, agents were used against civilians was not answered. If mycotoxins were, in fact, used it was the first recorded use of biological agents since before World War II, when the Japanese used them against the Chinese in the early 1940s.²

In the 1980s, Soviet troops battled Afghan rebels protesting the communist Afghan regime. During this lengthy conflict, frequent allegations were made of the use of chemical agents against the Afghans. One of these chemicals, known as Blue-X, was said to cause instant immobilization, the victim remaining in place for a number of hours before recovering. The use of other, more lethal agents was also alleged, but again no definitive evidence was found.

The most widespread and most open use of chemical weapons on a battlefield in recent decades was by Iraq in its conflict with Iran. This time the evidence of chemical use was conclusive. Undetonated shells were sampled and their contents were analyzed by several laboratories in Europe. A vesicant or blister agent (mustard) and a nerve agent (tabun) were identified. About 100 Iranian soldiers with chemical wounds were sent to European hospitals for care; their wounds were consistent with vesicant (mustard) injury. A team appointed by the U.N. secretariat went to Iranian battlefields and hospitals and found chemical shells and patients with chemical injuries. The public outcry at the use of these weapons was less than overwhelming. Ignoring protests from the world community, Iraq continued to use these agents.

Evacuating wounded soldiers to Europe not only lessened the burden on the medical facilities in Iran (although the number sent was a small fraction of the total) and provided soldiers with good medical care, but it also provided the rest of the world with evidence that Iraq was using these weapons. In gen-

eral, the casualties were sent privately, not through governmental connections. Physicians in Europe accepted the patients and assumed responsibility for their care, usually in private hospitals (a situation that made a retrospective analysis of the care rendered and the effectiveness of different treatment regimens difficult).

A similar situation enabled three physicians from the U.S. Army medical community to examine several casualties from Iraq's use of chemical weapons. On March 19, 1988, Iraqi airplanes bombed the village of Halabja, in Iraq. The inhabitants were Kurdish Iraqi citizens, a tribespeople who live in the region where the borders of Turkey, Iran, and Iraq meet. The casualties from this raid received worldwide media attention. The chemical weapons allegedly used were nerve agents, cyanide, and mustard. The casualties were cared for by Iran, and five of them (a man, a woman, and three young children, all unrelated) were sent to the United States for care by an Iranian physician living here. On examination by three authors of chapters in this textbook, the casualties were found to have skin lesions and pulmonary pathological changes (as determined by radiograph) consistent with mustard exposure.

Other items in the news over the past decade have suggested that the proliferation of chemical and biological agents is greater than we might hope. For example, numerous accounts claimed that Libya had built a facility capable of chemical agent production at Rabta—Libya's protestation that this facility was a pharmaceutical plant notwithstanding. One report even noted that monthly production was about 30 tons of mustard.

In 1979, an accident at a previously undetected biological weapons plant in Sverdlovsk, Russia, surprised even the intelligence community.³ At least 66 humans living or working downwind of the plant died of pulmonary anthrax. Soviet troops quickly attempted to decontaminate the facility and the city following airborne release of anthrax spores, and medical teams instituted preventive therapy, but the message was clear. The Soviet biological warfare program was thriving, more than 6 years after the

Soviet Union had signed the Biological Weapons Convention.

In addition to their being used on the battlefield, chemical and biological agents might also be used in terrorist attacks. The nerve agent sarin was twice used in Japan. The first incident, in Matsumoto in June 1994, produced more than 200 casualties including 7 fatalities. In the second incident—in the Tokyo subway system on 20 March 1995—5,510 people were taken to medical facilities or sought medical assistance. About 20% of these were hospitalized, and 12 died. The cult that was accused of both attacks was found to have a large facility for manufacturing both chemical and biological agents.

In the face of overwhelming evidence, the Soviet Union continued to officially deny having an offensive biological weapons program until 1992, when Russian President Boris Yeltsin admitted publicly to having maintained a program until March of that year. Since then, visits by teams from the United States and the United Kingdom to former biological warfare facilities under the Joint United States/United Kingdom/Russia Trilateral Statement on Biological Weapons have clearly documented the capabilities to produce biological warfare agents in massive quantities.

Verification of compliance with agreements such as the Trilateral and with the chemical and biological weapons conventions are plagued by the "dual-use" nature of the facilities in which these agents are developed and produced. A legitimate chemical facility can be converted fairly easily for the manufacture of chemical agents. On threat of inspection by an international group, the facility can readily be converted back to a legitimate use. The dual-use nature of production facilities is even more applicable to the production of biological agents. Partly for this reason, chemical and biological weapons have been called "the poor man's atom bomb." It has also been said that agents can be made in a bathtub, which may be true to a limited extent for a skilled microbiologist or chemist. Production of even tactical quantities of these agents and their deployment on the battlefield, however, is not a trivial undertaking.

INTRODUCTION TO CHEMICAL AND BIOLOGICAL AGENTS

Chemical and biological agents differ in several important ways. Chemical agents are typically man-made through the use of industrial chemical processes. Biological agents are either replicating agents (bacteria or viruses) or nonreplicating materials (toxins or physiologically active proteins or

peptides) that can be produced by living organisms. Some of the nonreplicating biological agents can also be produced through either chemical synthesis, solid-phase protein synthesis, or recombinant expression methods. Almost none of the biological agents are dermally active (the mycotoxins are a

rare exception) and none are volatile. On the other hand, most of the chemical agents are dermally active, volatile, or both.

Therefore, while many of the dermally active or volatile chemical agents can be disseminated as liquids or aerosols, and the biological agents must be dispersed as respirable aerosols (particles approximately 1–10 μ m in diameter). Dispersing a respirable aerosol on a battlefield requires a high-energy generating system to produce the small particle size, appropriate weather conditions to assure that the aerosol cloud stays near the ground, and adequate infectivity or toxicity of the agent to produce the desired effect. Except for infectivity, these are all important practical requirements for the field use of chemical, as well as biological, warfare agents.

In World War I, the use of chemical agents began with the small-scale use of irritants (known today as riot control agents). Chlorine, the first agent used on a large scale, and phosgene caused large numbers of deaths. Cyanide was introduced in midwar, but the agent that caused the greatest number of casualties was the vesicant mustard, which was introduced late in the war. Cyanide, phosgene, and mustard are still potential chemical weapons today.

In the period before World War II, German scientists synthesized the first nerve agents; during the war, Germany had thousands of tons of nerve agents stockpiled in munitions. The United States and the Soviet Union captured the stockpiles and manufacturing facilities late in the war, and they began to manufacture and stockpile these agents. Nerve agents are 15- to 100-fold more potent than the chemical agents used in World War I. In the 1950s, the United States put the incapacitating compound BZ into munitions (which have been destroyed); late in that decade, the currently used riot control agent CS was introduced for military use.

Military chemical agents are classified as “persistent” and “nonpersistent.” Persistent agents are those with low volatility or which evaporate slowly. Since they do not readily evaporate, they stay on terrain, materiel, or equipment for days, weeks, or months, depending on the weather. Chief among the persistent agents are the vesicant mustard and the nerve agent VX. Nonpersistent agents are those that are volatile and hence evaporate quickly; they are not expected to be present for more than several hours. The nonpersistent agents are phosgene, cyanide, and the G series of nerve agents. Each type has military advantages. Advancing troops might disperse a nonpersistent agent ahead of their attack to have the advantage of its effects on the enemy and later to have uncontaminated terrain into which

to advance. A persistent agent might be used to contaminate terrain, supplies, and equipment, denying the enemy their use.

Biological weapons may contain either replicating or nonreplicating agents. Although hundreds of naturally occurring bacteria, viruses, and toxins, as well as “designer compounds,” could potentially be considered agents by an aggressor, a finite number of these are actually useful as area weapons on the battlefield. The agents’ utility is limited by ease of production, stability, and infectivity (bacteria and viruses), or toxicity/effectivity (toxins and other physiologically active materials). *Bacillus anthracis*, for example, is often touted as the best of bacterial agents. Stability of the spore form and ease of production are its greatest strengths as weapons material. Among viral agents, Venezuelan equine encephalitis virus is easily grown to extremely high titers, making it a potential incapacitating agent. The bacterial agents that cause tularemia, Q fever, and brucellosis are infective at extremely low doses (1–10 organisms per person). Finally, the extraordinary toxicity (1,000- to 10,000-fold more toxic than the classic nerve agents) of the staphylococcal enterotoxins as incapacitants and the botulinum toxins as lethal agents makes them candidates for weaponization.

Most of the chemical compounds noted above have characteristics that make them uniquely suited to warfare. Closely related chemical substances, however, and some of the threat agents, are found throughout the civilian community. Unlike the chemical warfare agents, which are not found in nature, essentially all of the biological agents described are found in nature and cause the same or very similar disease syndromes. Military medical personnel might encounter persons exposed to the organisms as endemic disease agents on remote battlefields.

Similarly, civilians as well as military personnel could be exposed during peacetime to commercial chemicals closely related to chemical warfare agents. Thousands of tons of cyanide, for example, are manufactured annually for industrial use and are shipped to users by truck and train throughout the country. Phosgene is also manufactured in large amounts and shipped cross-country. The nerve agents are not available outside the military, but they are closely related to most pesticides or insecticides that are sprayed on orchards or used by the backyard rose gardener. The effects of these agricultural compounds are nearly identical to those of nerve agents, and medical therapy is the same. The incapacitating agent BZ (3-quinuclidinyl benzilate)

is used in small amounts in research pharmacology (where it is known as QNB). Also, BZ is pharmacologically related to anticholinergic drugs, which are present in many over-the-counter preparations, such as sleeping medications.

Unlike the chemical warfare agents, essentially all of the biological agents described cause syndromes that mimic or are identical to naturally occurring diseases. Outbreaks of disease caused by bacteria or viruses or isolated intoxications caused by toxins may result in syndromes similar to those seen in biological warfare attacks. In the case of these agents, the route of exposure—universally via the airways on the battlefield—may cause slightly or significantly different clinical presentations. General principles of prophylaxis and therapy presented in this text, however, often apply. Although the reader may initially think that the information presented in this textbook is needed only in wartime, much of the contents will also be useful to the physician in a busy emergency room.

On the battlefield, knowledge of the chemical or biological agent threat and its medical and physical countermeasures can actually reduce the threat. In World War I, the death rate for chemical casualties was about 3%. Data are not available for the Iran–Iraq War, but informal reports indicate that the death rate for those chemical casualties who reached medical care was probably less than 5%, despite the use of the highly toxic nerve agents against rela-

tively unprotected troops. With well-trained troops and well-prepared medical personnel, these figures will be lower. For the chemical agents, real-time detectors allow exploitation of the excellent individual physical protective mask, effective pretreatment, and therapy.

These countermeasures, in conjunction with training of our forces, can make an enormous difference and actually serve as a deterrent to chemical agent use. A chemical attack on a battlefield will not be the devastating event that some military medical personnel fear. Soldiers will survive and return to duty. For the biological agents, field detectors are still not responsive enough to allow timely warning of a cloud moving across the battlefield. Although the mask is protective, adequate warning may still be a problem. Knowledge of the meteorological conditions necessary for effective deployment of biological and chemical agents can at least limit the time during which a force must be on highest alert. In addition, effective medical countermeasures (vaccines, drugs, and diagnostics) are available for many of the agents of greatest concern. An integrated system of countermeasures for the chemical and biological agents can significantly reduce the threat by raising the cost/benefit ratio for the would-be aggressor. If the agents are used, appropriate medical care from well-informed medical care providers that enables soldiers to survive could be the factor determining whether a battle is won or lost.

IMPLICATIONS FOR THE MILITARY MEDICAL DEPARTMENTS

From 18 January to 28 February 1991, 39 Iraqi-modified SCUD missiles reached Israel.⁴ Although many were off target or malfunctioned, some of them landed in and around Tel Aviv. Approximately 1,000 people were treated as a result of missile attacks, but only 2 died. Anxiety was listed as the reason for admitting 544 patients and atropine overdose for hospitalization of 230 patients. Clearly, these conventionally armed SCUDs were not effective mass casualty weapons, yet they caused significant disruption to the population of Tel Aviv. Approximately 75% of the casualties resulted from inappropriate actions or reactions on the part of the victims. Had one of the warheads contained a chemical or biological agent that killed or intoxicated a few people, the “terror effect” would have been even greater.

The likelihood of such a weapon causing panic among military personnel decreases, however, when the leaders and troops become better educated regarding these agents. As General John J. Pershing wrote after World War I: “Whether or not

gas will be employed in future wars is a matter of conjecture. But the effect is so deadly to the unprepared that we can never afford to neglect the question.”^{5(p623)}

The experience in the Persian Gulf War reinforced General Pershing’s warning. Despite the improvement in relations between the East and the West, potential adversaries still exist—and potential adversaries have chemical and biological agents. These agents have been used in recent years, and probably will be used again on the battlefield or in small, regional conflicts. They might also be used in acts of terrorism within the United States, in which case, by authority of Presidential Decision Directive 39 (1995), the military will assist civilian authorities and medical personnel.

Fortunately, U.S. troops and medical personnel have not been involved in these attacks; it is hoped that they never will be. We must be prepared, however. The purpose of this textbook is to assist in that preparation.

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