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Introduction

Purpose

Poisoning by (ie, exposure to) toxic chemicals, a process also called intoxication, has been an important medical issue for centuries. A particularly frightening type of poisoning is the generation of mass casualties on the battlefield by the use of either chemicals developed specifically for that purpose or chemicals produced for industry and coopted for battlefield use. These agents can also produce civilian casualties during warfare and, when used by terrorists, cause both military and civilian casualties in settings remote from a defined battlefield.

Military healthcare providers have a responsibility to recognize and manage chemical casualties whatever the setting. This is primarily because military healthcare providers will likely be the first medical personnel to receive exposed service members. Secondly, because of the preeminence of the US military medical establishment in research, response, and training in chemical warfare agents, military medical personnel must be able to respond to chemical exposures at US stockpile sites of chemical warfare agents and provide expert consultation to their civilian counterparts in the event of a terrorist attack involving these agents. Knowledge of the medical aspects of the prevention, preparedness, response, and recovery phases of any military or civilian event involving chemical exposure is expected of every military medical care provider.

This handbook has been produced to help address the need for first provider training. Its primary use is as an adjunct, together with a companion biological agent handbook, to the Medical Management of Chemical and Biological Casualties (MCBC) course offered jointly by the US Army Medical Research Institute of Chemical Defense (USAMRICD) and the US Army Medical Research Institute of Infectious Disease. It is intended not to replace the hands-on training afforded by this course, but to provide an additional resource for MCBC students both during the course and after its completion.

The treatment protocols and drug dosages described in this handbook are not to be construed as replacements for sound
clinical judgment. Please utilize the Internet site of USAMRICD’s Chemical Casualty Care Division for the latest available resources: http://ccc.apgea.army.mil.

Nine appendices at the end of this handbook illustrate and summarize the major concepts of the publication. Review cards for each type of agent presented can be found in the back of the handbook.

Chemical Agents: General Concepts and Terminology

To paraphrase Paracelsus, any substance delivered in excess can act as a poison; it is the dose that makes the poison. Even oxygen can be toxic to the central nervous system at high partial pressures. Nevertheless, the term poison traditionally refers to chemicals that are sufficiently potent to induce poisoning in relatively low doses. The terms toxic chemical, chemical agent, and chemical warfare agent are often defined in different ways, and their use in this handbook needs to be clarified at the outset, along with the use of related terms.

The Chemical Warfare Convention (CWC) is an arms control treaty that outlaws the production, stockpiling, and use of chemical weapons and their precursors. The CWC defines a toxic chemical as “any chemical which through its chemical action on life processes can cause death, temporary incapacitation or permanent harm to humans or animals”; specifies that this definition includes “all such chemicals, regardless of their origin or their method of production”; and specifically includes toxins such as ricin and saxitoxin. Toxic chemicals can also be produced from precursors that include binary or multicomponent chemical systems. Not all chemical warfare agent precursors are listed under the CWC.

The US Army defines chemical warfare agents (often called simply chemical agents) as toxic substances developed for military use to produce death, serious injury, or incapacitation through their toxicological effects on exposed humans or animals. The Army officially excludes from this definition three broad categories of chemicals: (1) riot-control agents, (2) herbicides, and (3) smoke and flame materials.

Toxic industrial materials, or TIMs, are industry-associated
materials with harmful effects on humans; they can be subdivided into toxic industrial biologicals, or TIBs; toxic industrial chemicals, or TICs; and toxic industrial radiologicals, or TIRs. The North Atlantic Treaty Organization (NATO) has a more restricted definition for toxic industrial chemical as a chemical that (1) is more toxic than ammonia and (2) is produced in quantities greater than 30 tons per year at a given production facility. However, TICs are also commonly defined as any industrially manufactured chemicals that could be used to produce mass casualties.

Toxicant is a general synonym for poison and can be used interchangeably with the latter term. Toxin is also commonly used as a synonym for poison, but in discussions of chemical and biological agents is best defined in its more restricted sense as a toxic chemical synthesized by a living organism. Toxins have characteristics of both chemical and biological agents and are increasingly being separately classified as mid-spectrum agents, which include not only toxins but also bioregulators (small molecules with regulatory functions in the body in physiological doses but with toxic effects in larger doses), synthetic viruses, and genocidal weapons.

Chemical, biological, and mid-spectrum agents are often referred to as weapons of mass destruction, or WMDs, and the official military definition of WMD includes these three kinds of agents. However, in the strict sense of the term, weapons of mass destruction are weapons capable of causing extensive damage to physical structures, such as buildings, and include high explosives and nuclear and thermonuclear bombs. Chemical agents, biological agents, toxins, and point sources of radiation may cause mass casualties while leaving structures intact; a better term for these kinds of weapons is mass-casualty weapons, or MCWs. Unconventional weapons is a term used to refer to chemical agents, biological agents, toxins, nuclear and thermonuclear bombs, radiological dispersal devices (or RDDs, also called “dirty bombs”), and point sources of radiation used as weapons.

The list of chemical warfare agents officially designated as such by the US military includes those chemicals that are intended to cause death or serious injury and also those intended to cause incapacitation, that is, temporary inability to perform one’s
military duties. The former are called toxic agents and include (1) lung-damaging agents (also called pulmonary or choking agents); (2) “blood” agents (specifically, cyanide compounds); (3) vesicants (blistering agents); and (4) nerve agents. Those designed to produce only temporary incapacitation are referred to as incapacitating agents. This handbook will address each of these groupings of “official” chemical warfare agents as well as riot-control agents, which are technically not chemical warfare agents according to the US military definition, but are widely used in law enforcement for mass incapacitation.

Chemical agents may have chemical names as well as common names. Chemical agents developed for military use may also have a NATO code. The NATO code is a one- to three-letter designation assigned after World War II to provide standard recognizable shorthand identification. For example, the chemical compound O-isopropyl methylphosphonofluoridate has the common name sarin and the NATO code GB. This handbook will use NATO codes as well as common names for chemical agents.

**Physical Forms of Chemical Agents**

Chemical agents, like all other substances, may exist as solids, liquids, or gases, depending on temperature and pressure. Except for riot-control agents and the incapacitating agent BZ, which are solids at usually encountered temperatures and pressures, chemical agents in munitions are liquids. Following detonation of the munitions container, the agent is primarily dispersed as liquid or as an aerosol, defined as a collection of very small solid particles or liquid droplets suspended in a gas (in this case, in the explosive gases and the atmosphere). Thus, “tear gas,” a riot-control agent, is not really a gas at all, but rather an aerosolized solid. Likewise, mustard “gas” and nerve “gas” do not become true gases even at the boiling point of water (212°F / 100°C at sea level).

Certain chemical agents, such as hydrogen cyanide, chlorine, and phosgene, may be gases when encountered during warm months of the year at sea level. The nerve agents and mustard are liquids under these conditions, but they are to a certain extent volatile as temperature rises; that is, they volatilize or evaporate,
just as water or gasoline does, to form an often invisible *vapor*. A vapor is the gaseous form of a substance that is normally a liquid at usual environmental temperatures. Another way to conceptualize a vapor is as the gaseous form of a substance at a temperature lower than the boiling point of that substance at a given pressure. Liquid water, for example, becomes a gas (steam) when heated to its boiling point at a given pressure, but below that temperature, it slowly evaporates to form water vapor, which is invisible. Visible water clouds (including “clouds of steam”) are composed neither of water vapor nor water gas (steam), but rather are suspensions of minute water droplets (i.e., an aerosol).

The tendency of a chemical agent to evaporate depends not only on its chemical composition and on the temperature and air pressure, but also on such variables as wind velocity and the nature of the underlying surface the agent is in contact with. Just as water evaporates less quickly than gasoline but more quickly than motor oil at a given temperature, pure mustard is less volatile than the nerve agent GB but more volatile than the nerve agent VX. However, all of these agents evaporate more readily when the temperature rises, when a strong wind is blowing, or when they are resting on glass rather than on, for example, porous fabric.

Volutility is thus inversely related to persistence, because the more volatile a substance is, the more quickly it evaporates and the less it tends to stay or persist as a liquid and contaminate terrain and materiel. The liquid hazard of a persistent agent is often more significant than the danger created by the relatively small amounts of vapor it may generate. The converse is true of nonpersistent agents, which may pose a serious vapor hazard but which also evaporate quickly enough not to create a liquid hazard for an extended time. The generally accepted division between persistent and nonpersistent agents is 24 hours, meaning that a persistent agent will constitute a liquid hazard and contaminate surfaces for 24 hours or longer. Such agents (mustard and VX) are thus suitable for contaminating and denying terrain and materiel to the enemy. Nonpersistent agents, such as GB and cyanide, find tactical employment in the direct line of assault into enemy territory since they will have evaporated within a day and will no longer contaminate
surfaces. These generalizations are obviously subject to the modifying factors of temperature, environmental factors such as wind, and surface characteristics.

**Exposure, Absorption, and Toxicity of Chemical Agents**

Toxicologically speaking, exposure means contact of a poison with an epithelial surface (such as the skin, respiratory epithelium, eyes, or gastrointestinal mucosa) and is an external dose. Penetration of an epithelial barrier is called absorption and results in an absorbed dose, or internal dose. An absorbed agent may exert local effects at or near the site of exposure and absorption or systemic effects following distribution in the circulation to sites remote from the exposure site (eg, as in liquid nerve agents absorbed through the skin). Biological effects occur following exposure to chemical agents dispersed as solids, liquids, gases, aerosols, or vapors. Eye or skin injury may follow direct exposure to the suspended solid particles of aerosolized riot-control agents, and inhalation of these agents brings the aerosolized solid in contact with the epithelium of the respiratory tree. Nevertheless, systemic effects from exposure to riot-control agents are rare. Contact of the eyes, or more likely the skin, with liquid nerve or vesicant agents may produce local effects or lead to absorption and systemic effects.

Liquid exposure is the most important hazard associated with persistent agents. Healthcare providers managing liquid exposure must properly wear chemical protective clothing. At low temperatures, hydrogen cyanide (AC), cyanogen chloride (CK), and phosgene (CG) exist as liquids. However, because of their high volatility (low persistence), they seldom present a significant liquid hazard unless the area of exposure is large or evaporation is impeded when liquid agent is trapped in saturated, porous clothing. Penetration of fragments or clothing contaminated with liquid chemical agent of any type may also lead to intramuscular or intravenous exposure and subsequent systemic effects.

Chemical agents in the form of aerosolized liquid droplets, vapor, or gas may come into direct contact with the eyes, skin, or (through inhalation) the pulmonary compartments. Local
damage is possible at any of these sites, but systemic absorption through dry, intact skin is usually less important than with the other routes. Vapor or gas exposure to the eyes, and especially the respiratory tree, is the most important hazard associated with nonpersistent agents; to prevent such exposure, a mask that provides both ocular and inhalation protection must be properly worn.

Specialized terms refer to the amount of chemical agent encountered during an exposure. The effective dose, denoted by $ED_{50}$, and the incapacitating dose, denoted by $ID_{50}$, refer to the quantities (usually measured as the weight in $\mu g$, mg, or g) of liquid agent that will predictably cause effects (E) or incapacitation (I) in 50% of a given group. Similarly, the lethal dose, denoted by $LD_{50}$, refers to the quantity (weight) of liquid agent that will kill 50% of a group. Note that the lower the $LD_{50}$, the less agent is required and thus the more potent the agent is. Because of differences in absorption, the $ED_{50}$ and $LD_{50}$ values for a given agent are site-specific; for example, the $LD_{50}$ for mustard absorbed through dry, unabraded skin is much higher than the $LD_{50}$ for mustard absorbed through the eye.

Comparison of the amounts of chemical agent encountered as aerosol, vapor, or gas requires use of the concentration-time product, or $Ct$, which refers to the agent concentration (usually in $mg/m^3$) multiplied by the time (usually in minutes) of exposure. For example, exposure to a concentration of 4 $mg/m^3$ of agent vapor for 10 minutes results in a $Ct$ of 40 $mg\cdot min/m^3$. Exposure to 8 $mg/m^3$ for 5 minutes results in the same $Ct$ (40 $mg\cdot min/m^3$). For almost any given agent (with the notable exception of cyanide, which will be discussed in a separate chapter), the $Ct$ associated with a biological effect is relatively constant even though the concentration and time components may vary within certain limits (Haber’s law). Therefore, a 10-minute exposure to 4 $mg/m^3$ of agent causes the same effects as a 5-minute exposure to 8 $mg/m^3$ or to a 1-minute exposure to 40 $mg/m^3$. The $ECt_{50}$, $ICt_{50}$, and $LCt_{50}$ correspond for vapor or gas exposures to the $ED_{50}$, $ID_{50}$, and $LD_{50}$ respectively, for liquid exposure and are likewise site-specific. However, the $Ct$ does not take into account variables such as respiratory rate and depth and is therefore not an exact measure of inhalation exposure.
General Principles of Chemical Casualty Care

Chemical casualties must be recognized and appropriately managed. Management includes triage, medical treatment, decontamination (if liquid contamination is present), and disposition, which may include evacuation and eventual return to duty.

Casualty Recognition

Recognition of a chemical casualty is heavily dependent upon recognition and differential diagnosis of toxidromes, that is, constellations of symptoms and signs that characterize exposure to a specific agent, as well as intelligence reports and detection equipment. This handbook will present distinct toxidromes characteristic of exposure to central-compartment lung-damaging agents, peripheral-compartment lung-damaging agents, cyanide compounds, sulfur mustard, lewisite, phosgene oxime, nerve agents, anticholinergic incapacitating agents, “traditional” riot-control agents, and vomiting agents (a subset of riot-control agents). It is important to recognize these toxidromes and also to recognize other conditions that could mimic them.

Chemical agent casualties may be exposed to more than one agent and may also have other diagnoses, such as concomitant exposure to other kinds of mass-casualty agents, preexisting medical or surgical conditions, or trauma. It is just as important to view the casualty, and the situation, as a whole as it is to identify chemical exposure. The best way to accomplish this is to consider the triad of agent, environment, and host. Specifically, the astute clinician will think of (1) the agent; (2) the forms or states of the agent in the environment; (3) the passage of agent from the environment to the host, that is, the route or routes of entry; (4) whether exposure and absorption by the host are producing only local effects (restricted to the site of exposure) or are also generating systemic effects (effects remote from the site of exposure); (5) the severity of exposure and of effects; (6) the time course of effects; (7) other possible differential diagnoses and concomitant diagnoses; and (8) any possible interaction or synergism among coexisting diagnoses. Healthcare providers
engaged in treatment have a tendency to focus on the chemical exposure, sometimes to the neglect of other life-threatening conditions.

**Casualty Management**

Once a chemical casualty has been recognized, appropriate management must begin. *Triage* is the process of sorting casualties for medical treatment when not all casualties can receive care simultaneously. It is in some ways both an assessment step and a management step and can act as a bridge between initial assessment and management. The triage categories used by the US military are (1) *immediate* (those who are in danger of losing their lives unless action is taken within a few minutes); (2) *delayed* (those who require significant medical intervention but who can tolerate a longer delay in treatment); (3) *minimal* (casualties who have minor injuries, illnesses, or intoxications, often amenable to self or buddy care); and (4) *expectant* (those who are gravely ill and who cannot be treated with available resources without causing the death, by misallocation of resources, of other casualties). In this handbook, triage for specific chemical agents will be addressed within the chapter devoted to that agent.

Initial management for severely affected chemical casualties (especially those who are triaged as immediate) can be summarized as an application of the ABCDDs: **Airway**, **Breathing**, **Circulation**, immediate **Decontamination**, and **Drugs** (ie, specific antidotes). These interventions will be described in specific agent chapters and also in the sections on decontamination and casualty management in a contaminated area. It is important to note that the ABCDDs might have to be applied nonsequentially, for example, during a nerve agent poisoning, atropine may have to be administered to ease airway restriction first. Immediate decontamination may mitigate the effects of the agent.