Common chemical agent threats

RANDALL R. MCCAFFERTY, M.D., AND PETER J. LENNARSON, M.D.

Neurosurgical Services, Wright-Patterson Air Force Base, Ohio

The events of September 11, 2001, highlight the fact that we live in precarious times. National and global awareness of the resolve and capabilities of terrorists has increased. The possibility that the civilian neurosurgeon may confront a scenario involving the use of chemical warfare agents has heightened. The information reported in this paper serves as a primer on the recognition, decontamination, and treatment of trauma patients exposed to chemical warfare agents.

KEY WORDS • chemical warfare • terrorism • casualties • war

Prior to World War I, chemical agents were considered but were infrequently used or ineffective products of warfare. The Chinese used arsenical smokes as early as 1000 B.C. The Spartans used noxious smokes during the Peloponnesian War. During the American Civil War, numerous proposals for the use of chlorine, sulfur, chloroform, and hydrochloric and sulfuric acids were developed; however, most proposals were likely never acted upon.

With the onset of World War I, few people believed that the proposals and research into chemical weapons would result in any significant battlefield operations. Initial attempts at chemical warfare were ineffective against opposition forces. In April and May of 1915, German forces successfully deployed large stores of chlorine gas by wind drift against Allied forces defending Ypres. Within the next 2 years, the chemical warfare techniques practiced by German and Allied forces evolved into the use of phosgene gas, cyanogens, and vesicants. In addition, both forces were supplied with chemical protective devices, including gas masks. By Armistice Day in 1918, 26 million casualties were recorded, approximately 1 million of which were attributable to gas warfare.

In the years between World War I and World War II, new chemical weapons and protective and deployment capabilities were developed. All of the major nations involved in World War I and several other countries developed chemical weapons programs. Participants involved in international conferences and treaties attempted to define, limit, and/or prohibit the storage, development, and training in the use and deployment of chemicals in warfare.

At the start of World War II, training in the use, storage, and deployment of, and protection from chemical warfare was high. Although there was no major event involving the use of chemical agents during World War II, the capabilities of participating countries were impressive. In addition to choking, blister, and blood agents, nerve agents were being produced in mass quantities. Despite significant efforts by all parties to garner intelligence on the capabilities of opposition forces, the magnitude of chemical weapons programs was not fully understood until after the war.

Throughout the remainder of the 20th century, chemical weaponry continued to be developed and used in major wars around the world. Those involved in international organizations and treaties continued to define and restrict various aspects of chemical weapons programs as well as in the more recently developing atomic and biological programs. As recently as the Persian Gulf War, the alleged use of nerve and mustard agents by Iraqi troops has been reported. Following that war, there have been reports of chemical agent use ordered by Saddam Hussein against Kurd and Shiite Muslims as well as proliferation of chemical weapons development in Libya.

Finally in 1993, the long awaited Chemical Weapons Convention was finalized. This treaty prohibited the development, production, stockpiling, and use of chemical weapons and provided for the verification and destruction of known stockpiles. Although 130 countries signed the treaty, notable exceptions included Iraq and North Korea. Despite diplomatic efforts, chemical weapons will remain a threat in warfare and more recently have become a potential weapon of the terrorist. In 1994, a religious cult, Aum Shinrikyo, released nerve gas in a residential area in Matsumoto, Japan, and in 1995 a sarin attack occurred in a Tokyo subway.

The ease with which chemical weapons can be obtained and manufactured increases the concern that nonmilitary people may be exposed to chemical agents. These agents are most effectively employed against individuals who lack knowledge of their properties as well as to protect against themselves and personnel against them. Cities, ports, and airfields are especially vulnerable civilian targets. Following terrorist activity against the Pentagon and World Trade Center on September 11, 2001, President Bush established a Homeland Defense program in the US.

Abbreviations used in this paper: CNS = central nervous system; US = United States.
In light of these recent events, there is a real possibility that civilian medical personnel may be exposed to patients and circumstances involving chemical weapons. The following is a brief synopsis of those chemicals and their effects that a neurosurgeon may need to recognize and be able to treat when managing victims in a mass-casualty scenario. Chemical weapons may be classified in a variety of different ways. For this discussion, the common nerve agents, vesicants, blood agents, choking agents, and riot control agents will be discussed. In addition, basic protective mechanisms and decontamination procedures will be addressed.

NERVE AGENTS

The biological primary effect of nerve agents is their inhibition of the enzyme acetylcholinesterase. Although these agents are commonly used as insecticides and may also be used in medicine, the chemicals of military importance tend to be more potent and longer lasting. Nerve agents can be divided into G and V agents. Tabun (GA), sarin (GB), soman (GD), and VX are examples of these agents. Nerve agents are frequently clear and colorless in a pure state and tend to liquify at moderate temperatures, although G agents much more likely than V agents can present a vapor hazard.

Nerve agents can be absorbed through any body surface area or through the gastrointestinal and respiratory tracts. The effects of nerve agents occur extremely rapidly when inhaled as a vapor, but cutaneous absorption of liquid nerve agents can take several minutes. Holding one's breath and donning an effective mask can prevent exposure to vaporized nerve agent. The liquid form of nerve agent can penetrate regular clothing extremely quickly. Rapid removal of permeable clothing and decontamination of exposed body surfaces can markedly reduce the amount of the compound that is absorbed cutaneously. These agents are rapidly inactivated by alkali and chlorinating compounds. Diluted chlorinating compounds may be used to decontaminate patients and healthcare personnel, and stronger solutions may be used to clean clothing and equipment.

Because the action of nerve agents is to inhibit acetylcholinesterase enzymes, symptoms are produced when acetylcholine accumulates at muscarinic and nicotinic receptors throughout the body. These symptoms can occur locally at a site of exposure or systemically. Following exposure to small amounts of vapor, miosis may result, secretions increase, and the patient may have slight bronchoconstriction. When exposed to a small dose of liquid, increased sweating and muscular fasciculation at the site of exposure may occur. As doses of the nerve agent increase, nausea, diarrhea, and generalized fatigue or weakness may begin. Vomiting, lacrimation, salivation, and dyspnea may become more intense. Exposure to large amounts of any form of nerve agent may quickly induce loss of conciousness, seizures, flaccid paralysis, and apnea.

To be able to recognize and thus diagnose cases involving exposure to nerve agents practioners must be aware of the aforementioned signs and symptoms. No other chemical agent can produce the characteristic muscular fasciculations, pinpoint pupils, and autonomic and CNS symptoms like the acetylcholinesterase inhibitors. In scenarios in which groups of patients experience symptoms such as runny nose, blurred vision, drooling, stomach cramps, and chest tightness, medical personnel must consider that mild exposures have occurred as well as the possibility of a contaminated working area, equipment, or clothing.

The first principle in treating patients exposed to a nerve agent is to protect the medical personnel from exposure. This may require the donning of a protective mask and hood, gloves, and impermeable clothing as the situation dictates. Second, the source of nerve agent exposure must be terminated. This may require that the patient be removed from a contaminated scene, as well as removal of clothing and personal items, cleansing of the patient, and/or placement of a protective mask. Ideally decontamination would involve the use of diluted household bleach or charcoal and resorative resins. If these are not available, large amounts of water may be used to wash skin surfaces and dilute the exposure, or tissue paper can be used to wipe away nerve agent resins. Care must be used to contain contaminated items to avoid exposure to other people.

Third, an airway should be established (or maintained). Suction of large secretions and supplemental oxygen may be all that is necessary. Endotracheal intubation or cricothyroidotomy may be required in more critically ill patients.

Chemical Agent Antidotes

The US military recognizes the following antidotes in the treatment of nerve agent exposure: atropine, pralidoxime chloride, and diazepam. Certain troops deployed in combat may be provided with antidote-containing autoinjectors for self- or buddy administration. In general medical treatment of the nerve agent–exposed patient should be directed at combating the physiological effects of the nerve agent, as well as those effects of the medications given to treat the patient.

Atropine blocks the effects of acetylcholine at muscarinic receptors. Thus, atropine decreases secretions and reverses the contraction of smooth muscle (that is, it relieves bronchoconstriction and gastrointestinal hypermotility). Except in very high doses, atropine does not resolve miosis. Field troops are given autoinjectors that supply a 2-mg dose of atropine. In a civilian healthcare setting, 2 mg of atropine should be given every 5 to 10 minutes until secretions and dyspnea are minimized. Pralidoxime chloride or 2-PAM CL is an oxime that is effective against some of the nerve agents. The drug can either block inhibition of cholinesterase and/or reactivate acetylcholine at muscarinic receptors. Oximes must be administered early in the course of treatment because it becomes ineffective over short periods of time that are different for each nerve agent. Initially, 1 to 1.5 g of oxime should be given over 20 to 30 minutes and, if effective, may be repeated one to two times over 60 to 90 minutes. In severe cases of nerve agent exposure, seizures may result. Diazepam has been shown to be effective against these seizures and can also be effective in sedating a patient during resuscitation. Ten-milligram doses may be administered until the desired effect is achieved. Transient arrhythmias can occur after exposure to either nerve agent or during administration of atropine. Beta adrenergic blocking agents may be effective at controlling the tachycardia and ST segment changes associated with atropine.
VESICANTS (BLISTER AGENTS)

The vesicants, also known as blister agents, can be lethal. Vesicants burn or blister any part of the body they contact. They have been used militarily to disable troops, contaminate equipment, and thus degrade fighting capability. The common blister agents include the mustards, lewisite, and phosgene oxime. Mustard and lewisite both induce fluid-filled blisters. Phosgene oxime, which is not a true blister agent, forms a solid wheal. The weapons-grade property of these compounds is typically an oily liquid, although phosgene oxime can be disseminated in a crystalline form. Protection from these agents requires both a mask and protective overgarments.

The pain, as well as the clinical tissue effects associated with mustard exposure will take hours to commence. The mildest and earliest sign of cutaneous mustard exposure is erythema, which may be accompanied by burning, itching, and stinging. If exposure is extensive enough, small blisters will begin to develop within the erythematous region and will eventually coalesce. If the eye is exposed to mustard vapor, pain, blepharospasm, conjunctivitis, corneal damage, and photophobia will result. In cases of mild exposure of the airways, rhinorrhea, sneezing, epistaxis, and a hacking cough begin. As the exposure increases, the cough may become productive and the patient may experience severe dyspnea. Immunosuppression may also occur. In addition to timing of symptoms, exposure to mustards may be diagnosed by measuring and noting a significant amount of thiodiglycol in the urine of an exposed patient.

The pain, erythema, and blister formation associated with lewisite exposure occurs much more rapidly than in cases of mustard exposure. Pain will often commence in seconds to minutes. Additionally the lesions that do occur tend to heal much faster, and secondary infection is much less common. Although eye-related vapor exposure may cause pain and irritation, the onset of blepharospasm is so rapid that severe eye injury is much less likely. Shock may ensue in cases of exposure to large amounts of lewisite because the resultant capillary-related protein and plasma leakage causes hemoconcentration and hypotension. The rapid onset of symptoms can help differentiate lewisite exposure from mustard exposure, but additional data will be needed to distinguish this from a phosgene exposure. Development of a blister compared with a wheal may be helpful in this differential diagnosis. Additionally arsenic may be present in the urine of a lewisite-exposed patient.

Phosgene causes immediate pain and irritation to exposed body parts. Within 5 to 30 minutes, skin edema may form around an erythematous wheal and the center of the lesion may become necrotic. Painful conjunctivitis and keratitis may ensue. The major lesion of phosgene exposure is pulmonary edema and thrombosis caused by pulmonary venules.

Decontamination is the mainstay of treatment of vesicant exposure. Patients should be thoroughly decontaminated before allowing contact with unexposed patients. Decontamination may be performed using either a dilute hypochlorite solution or water. Skin lesions should be kept clean to avoid secondary infection. Calamine or another soothing lotion may relieve burning or itching. Analgesic medication may be necessary for severe pain. Lesions of the eye should be liberally irrigated periodically. The use of topical analgesic and antibiotic agents may be necessary. Vaseline should be placed on edges of the eyelids to prevent the lids from adhering to each other and reduce scarring. A topical mydriatic can be administered to prevent synechia formation. Supplemental oxygen, obtaining and maintaining an airway, and/or mechanical ventilation may be necessary depending on the extent of exposure. For lewisite exposure, a specific antidote (BAL [dimecaprol]) that binds to the arsenic in lewisite and can reduce its systemic effects; BAL can cause hypertension and tachycardia.

BLOOD AGENTS

Blood agents are distributed by the blood and generally enter the body via inhalation. They inhibit the ability of blood cells to utilize and transfer oxygen. Thus, blood agents are poisons that effectively cause the body to suffocate. Examples of blood agents include hydrogen cyanide, cyanogen chloride, and arsine.

At room temperature, hydrogen cyanide is a colorless liquid. The most important route of poisoning is through inhalation. Both gaseous and liquid hydrogen cyanide, as well as cyanide salts in solution, can also be absorbed through the skin. Its high volatility makes hydrogen cyanide difficult to use outdoors. On the other hand, the concentration of it may rapidly reach lethal levels if it is released in confined spaces.

Cyanide poisoning-related effects are those of progressive tissue hypoxia. The symptoms, signs, and physical findings are directly related to the dose of cyanide, the route of exposure, and the type of cyanide compound. In addition to the effects we will describe, cyanogen chloride also produces irritation of the eyes and mucous membranes similar to that produced by agent used in riot control agents.

Within seconds of exposure to high concentrations of cyanide gas an initial hyperpnea is followed by a loss of consciousness (30 seconds postexposure). This progresses to apnea (3–5 minutes postexposure), cessation of cardiac activity (5–8 minutes postexposure), and death. After exposure to lower concentrations, or exposure to lethal amounts via the oral or percutaneous routes, the effects develop more slowly. For example, after ingestion of a lethal dose of a cyanide salt, the patient might survive 15 to 30 minutes during which an antidote could be administered. Prominent early signs and symptoms of cyanide poisoning include a transient hyperpnea, headache, dyspnea, and findings of general CNS excitement, including anxiety, personality changes, and agitation progressing to seizures. Diaphoresis, flushing, weakness, and vertigo may also be present. Late-appearing indications of CNS depression, such as coma and dilated, unresponsive pupils, are prominent signs of cyanide intoxication. The tell-tale odor of bitter almonds cannot be used as a guide because up to 60% of people are unable to detect the odor.

Relevant laboratory findings include an early decreased arteriovenous difference in the partial pressure of oxygen with progressive lactic acidosis. Although cyanide levels in blood, urine, and various tissues (for example lung and liver) can be measured, results are generally not available.
during the treatment phase. The first principle of treatment is to eliminate any source of continued poisoning by removing the victims from the offending environment, removing their clothing, and washing their skin with soap and water. For ingested sources, activated charcoal lavage is indicated. General supportive measures may be all that are required in the conscious patient. Specific therapies are based on encouraging and accelerating the body’s own ability to excrete cyanide and to bind cyanide in the blood. Antidotes include sodium thiocyanate, sodium nitrite, dimethylenophenol, and hydroxycobalamine.

The most likely arsenic-containing compound to be used in chemical warfare is Lewisite. Lewisite is a colorless liquid that causes injuries similar to the mustard agents, although the onset of its effects is much more rapid. Lewisite was more described in detail in the previous section (see Vesicants). A specific antidote, dimercaptopyrropanol, more commonly called British Anti Lewisite, protects against injuries to the skin and mucous membranes as well as systemic poisoning.

CHOKING AGENTS

Choking agents inflict injury mainly on the respiratory tract including the nose, throat, and especially the lungs. Victims typically inhale these agents, which can all lead to pulmonary edema and respiratory failure. Examples of choking agents include chlorine, phosgene, diphosgene, and chloropicrin.¹

Chlorine is a dense, pungent, greenish-yellow gas that is easily recognized by both color and odor. Because of its tendency to settle in low-lying areas, this gas is especially hazardous in closed spaces. Symptoms of chlorine exposure include ocular and nasal irritation, spasmodic coughing, and a feeling of suffocation. Signs of pulmonary edema develop with continued exposure. Treatment is symptomatic, because there is no specific antidote. Although not clinically proven, administration of corticosteroid agents, as soon as possible after exposure, has been recommended to lessen the severity of pulmonary edema.² Whereas the majority of chlorine exposure–induced deaths occur in the first 24 hours, victims who survive the initial insult may live with minimal pathological or physiological sequelae.¹

Phosgene, a gas heavier than air, generally appears as a white cloud, and at low concentrations has an odor of freshly mown hay. Symptoms of exposure range from mild cough, chest tightness, and dyspnea to those of severe, rapidly developing pulmonary edema. Treatment and prognosis are similar to those in cases of chlorine exposure.

RIOT CONTROL AGENTS

Riot control agents are defined as any chemicals not listed in a specific chemical warfare schedule that can rapidly produce sensory irritation or disabling physical effects that disappear within a short time following termination of exposure. The four compounds of most significance are o-chlorobenzylidene malononitrile, 1-chloroacetophenone also known as mace, dibenz (b,f)-1,4-oxazepine, and diphenylaminearsine.³ At room temperature all agents tend to be white powders that are most effectively disseminated in an aerosolized form. These compounds produce temporary disability because the extreme ocular irritation and blepharospasm cause the eyes to close temporarily, and the irritation of the airways causes coughing, shortness of breath, and sometimes retching or vomiting.³ These agents are also characterized by their rapid onset of effects (seconds to several minutes), a relatively brief duration (15–30 minutes) of effects once the victim has escaped the contaminated atmosphere and has been decontaminated (that is, removed the material from his clothing), and a high safety ratio (the ratio of the lethal dose to the effective dose).² In contrast to human beings, animals generally have low sensitivity to tear gases. Dogs and horses can therefore be used by police for riot control even when tear gas is used.

The mainstay of tear gas exposure–related treatment is removal from the contaminated environment and the use of soap and water to wash the skin and clothes. No long-term effects of tear gas exposure have been documented.

CONCLUSIONS

Recent national and international events have increased the possibility of civilian healthcare organizations having to care for an injured patient who has been exposed to a chemical agent. In this paper we briefly described chemical agents that civilian healthcare personnel may need to have knowledge to provide treatment to exposed patients. Basic principles of delivering care in an affected environment include the following. 1) Protect medical and supportive personnel from chemical exposure. 2) Decontaminate the patient and the surrounding environment to limit the effects of the exposure and avoid additional exposure. To treat the victim, this may require placement of a mask, removal of clothing, and washing of skin surfaces or surrounding surfaces. Care must be taken to prevent contamination of medical equipment transport vehicles, and rooms (for example, ambulances and hospital rooms). 3) Finally, a specific treatment must be provided based on the patient’s type of exposure and manifesting symptoms. The following references will serve as a more comprehensive resource for in-depth reading on the aforementioned topics.

References


Manuscript received January 18, 2002. Accepted in final form February 20, 2002

The views expressed in this article are those of the author(s) and do not reflect the official policy or position of the US Air Force, Department of Defense, or the US Government.

Address reprint requests to: Randall R. McCafferty, M.D., 74th Medical Group/SGOSN, 4881 Sugar Maple Drive, Wright-Patterson Air Force Base, Ohio 45433.