Chapter 83
The Role of the Anesthesia Provider in Natural and Human-Induced Disasters*

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83A The Role of the Anesthesia Provider in Natural Disasters

Key Points

- Disasters may be natural or human-made. Both types produce a surge of casualties that involve both anesthesia providers and intensivists.
- Of the range of natural disasters, earthquakes produce the most casualties requiring an emergency and anesthesiologic response.
- Natural disasters may affect anesthetic practice either directly, as a result of effects on hospital operation and resilience, or indirectly because of the workload from excessive casualties.

For more than 30 years, Miller’s Anesthesia has been recognized as the most complete single resource regarding modern anesthesia. During these years, the expanding role and responsibility of anesthesia care have required a scholarly analysis of many aspects of medical care overall. In the seventh edition, the potential role of anesthesia in rare major threats to society resulted in David J. Baker’s chapter, “Chemical and Biological Warfare Agents: The Role of the Anesthesiologist.” This editor’s memory is imprinted with radio accounts of the New York City and Washington, DC, September 11, 2001 terrorist attacks and wondering if San Francisco would be the next target. That morning, I was in charge of the operating rooms, and I and others deliberated on how to proceed and whether to leave some operating rooms open—just in case. Fortunately, San Francisco was not hit, and our decision to carry on as usual with our operating room schedules proved to be the right one. This personal experience convinced me that this chapter was and continues to be necessary. My overriding premise, shared by the associate editors, was that although most anesthesia providers will never be exposed to a terrorist attack, they should be familiar with the basic principles of anesthetic care for those “just in case” scenarios.

When planning for this eighth edition, the editors concluded that the chapter in the seventh edition was excellent, but one major component needed to be added—the role of anesthesia in natural disasters such as earthquakes and tsunamis. Some areas are known to be susceptible to natural disasters such as earthquakes and tsunamis. Some areas are known to be susceptible to natural disasters (e.g., Chile with earthquakes, the Philippines with typhoons, or the Gulf Coast of the United States with hurricanes) and, as we have experienced more recently, other locations are subject to unexpected severe weather, floods, or fires. Because of the unpredictability and magnitude of these events, anesthesia providers can be caught off guard, and for many, it may be the first time they have been called on to provide anesthesia under the strenuous conditions in a natural disaster.

The editors have concluded that this revised and updated chapter by the same author, David J. Baker, provides a global baseline of information for anesthesia providers who may be required to provide clinical emergency care in the face of these unexpected disasters and in locations with limited resources.

Ronald D. Miller

*The views expressed in this chapter are solely those of the author and do not necessarily represent those of Service d’Aide Médicale Urgente (SAMU) de Paris.
INTRODUCTION

The exact definition of disaster medicine is difficult and depends not only on the event but the nature and number of casualties. The working definition used by the World Health Organization (WHO) is “a sudden ecological phenomenon of sufficient magnitude to require external assistance.” Such events can exceed a given response system. A better medical approach more suited to the impact of disaster on anesthesia is a potential mass injury or event that causes illness. This definition is gradually gaining acceptance. Eric K. Noji, MD, Consulting Medical Epidemiologist, Centers for Disease Control and Prevention at Johns Hopkins University, has suggested an alternative definition of disaster as “any community emergency that seriously affects people’s lives and exceeds the capacity of the community to respond effectively to the emergency.”

Dr. Patrick Guérisse of the Emergency Department at CHU Brugmann-Brien, Brussels, has discussed several definitions of a medical disaster and suggests that the term should best be reserved for situations in which the social and medical infrastructure is so damaged by the event that it places extraordinary burdens on fundamental societal functions such as law and order, communication, transportation, and water and food supply.

CLASSIFICATION

Disasters can be classified as natural or human-induced. Both affect anesthesiology and intensive care in terms of the volume of casualties with both injuries and infection. Natural disasters occur regularly and involve mechanisms related to climate and seismic activity. Human-induced disasters, however, involve the accidental or deliberate release of toxic substances and pathogens, explosions, and fire. The anesthesiologic management of conventional trauma and burns is considered in other sections of this book (see also Chapter 81). This chapter deals with the implications for anesthesia in natural disasters and of chemical and biologic agent release as human-induced disasters.

Natural disasters are events produced by meteorologic and geologic causes. These events can sometimes happen with a certain degree of warning (e.g., hurricanes) or with little or no warning (e.g., earthquakes). Natural disasters occur in both developing and developed countries but the impact on poorer nations where the medical infrastructure is already fragile magnifies the effect.

Natural disasters include the following:
- Flooding
- Heat wave
- Fires
- Storms
- Tsunamis
- Earthquakes

Of these, earthquakes are the events that produce most casualties with mass physical trauma that requires an emergency surgical response.

RESPONDING TO NATURAL DISASTER

Natural disasters affect anesthetic practice either directly, because of effects on the local hospital service, or indirectly, as a result of the excess flow of casualties to the degraded hospital facility. The consequences of natural disaster may affect services and infrastructure in developed and developing nations alike, but the effects in developing nations are usually greater and provide the biggest challenge for mounting an emergency medical response.

For anesthesia providers involved with foreign medical teams (FMTs) in nations with limited resources, special understanding and preparation are necessary for an effective intervention. Lind and associates defined a framework necessary for FMTs to be regulated and organized. In the context of earthquakes, the authors define four phases of development.

- Phase 1 (approximately 72 hours): FMTs are not present; therefore, any aid has to be sourced locally during this acute phase.
- Phase 2 (4 to 21 days): FMTs arrive, establish services, and carry out operations for trauma. During the first weeks after an earthquake, trauma workload increases and nontrauma workload decreases.
- Phase 3 (4 to 12 weeks): A slow return to the usual burden of disease. FMTs are established by this phase, but the pressure of local health needs begins to predominate.
- Phase 4 (3 to 6 months): A gradual return occurs to normal functioning of the health services to predisaster levels. The length of time for return to normalcy depends on the magnitude and severity of the earthquake.

Within these phases of disaster, three levels of care are recognized:
- Basic (primary) and immediate emergency care
- Secondary (intermediate level of health care), which includes diagnosis and treatment in hospital
- Tertiary, which involves specialized highly technical care up to state-of-the-art standards

Note that individual countries have very different levels of care at the predisaster level. Within this framework a cycle of disaster onset, response, and recovery has been described.

THE IMPACT OF NATURAL DISASTER ON THE WORK OF THE ANESTHESIA PROVIDER

Within the phases of disaster, anesthesia providers are involved as part of the emergency surgical response teams. The overall stages in the deployment of such teams are as follows:

1. Planning and training: Establishing techniques for the use of unfamiliar equipment that is not used in everyday practice in developed nations
2. Response: The provision of anesthesia and high-dependency care at a field level
3. Recovery: Dealing with the chronic effects of trauma and reestablishing the normal local anesthetic practice

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In practical terms, natural disasters have considerable implications for the anesthesia provider, including the following:

- The impact on the normal social infrastructure: Natural disasters disrupt communications and essential services, such as water and power supplies. This disruption creates a challenging background through which emergency medical services, including anesthesia, must be mobilized before any organized medical response can be mounted. The 1995 Kobe, Japan earthquake effectively cut off access to the city’s main hospital by staff and casualties, because the hospital was located on a separate island from the city.6
- Effects on the prehospital response: After natural disasters, anesthesia providers may be involved in prehospital care as part of a standing emergency medical system (EMS), as in France, where the EMS is medicalized,7 or as part of an onsite surgical intervention to free entrapped patients.8 In addition, anesthesia providers may be required to provide high-quality anesthesia for the severely injured in a field hospital, where facilities may be basic and often very different from those available in the normal place of work.
- Effects within the hospital: At the hospital, mass casualties will occur requiring initial emergency care and often early surgical intervention. Time for resuscitation, investigation, and preparation of such casualties for surgery is often limited, and resources may be stretched.
- Further management of casualties in critical care: The problems caused by natural disasters are further complicated by the need for the provision of postoperative critical and high-dependency care in normal hospital surroundings, which have themselves been affected by the disaster. The complex equipment in such units depends on power and gas supplies, all of which may be disrupted by the effects of the disaster. Nevertheless, critical care must still be provided for victims of both physical and toxic trauma alike.9

It is essential that emergency medical response by national teams be part of a coordinated international response, preferably at the request of the nation affected by the disaster. A piecemeal, “disaster tourism” approach with a short stay and no postoperative patient follow-up presents problems that have been highlighted by van Horning and colleagues.10

**RESPONDING TO A NATURAL DISASTER: PRACTICAL CONSIDERATIONS**

**PREPARATION AND PLANNING**

Anesthesia providers, including nurse anesthetists, will be involved in phase 2 of disasters as members of the field surgical teams. Planning and preparation of necessary equipment is essential, preferably as part of an existing special response plan that was established before a disaster occurs. The Haiti earthquake of 2010 provided lessons for emergency responders, including that a coordinated effective field response can be created quickly from a major academic center with no special planning for a disaster response in another country.11 In addition to the preparation logistics, the anesthesia provider must be familiar with the manifesting pathophysiology of victims of natural disasters, which include crush injury, penetrating and blunt trauma, acute lung injury, burns management, drowning, and near drowning. These are characteristics of the specialty of disaster medicine.12

**TRAINING**

Apart from the need for disaster management planning, EMS teams require special training and experience on the available equipment used in disaster situations and the techniques involved in anesthetic care, which are very different from those used in everyday practice in developed countries. For those with military and humanitarian aid experience or who have worked in developing nations where facilities are often basic, the transition to emergency circumstances will be familiar. However, many anesthesia providers have never worked outside the setting of a sophisticated modern hospital with facilities and abilities to support complex high-technology equipment. This group will require training that familiarizes them with the relatively basic equipment and facilities of field anesthesia.

The practical aspects of field anesthesia are discussed later in this chapter.

**PREHOSPITAL ON-SITE EMERGENCY CARE**

Anesthesia providers may be involved in the onsite management of casualties. This may be as a result of entrapment (such as after earthquakes and collapsed buildings) in which anesthesia may be required for extraction (emergency amputation). Usually, specialist teams are deployed for this purpose. In France, special teams that are part of the prehospital emergency response system, the Service d’Aide Médicale Urgente, are deployed for disaster management as part of their national policy of bringing the hospital to the patient.13 The equivalent in a paramedical system is the United Kingdom’s Hazardous Area Response Team and Urban Search and Rescue Teams (USARs),14 which can be supplemented by medical teams as required.

Also, military medical teams are usually qualified. Such teams are able to provide immediate triage; assessment; and medical care, including surgery.

**EARTHQUAKES: A SPECIAL DISASTER SITUATION**

Earthquakes are a major cause of death and injury. Over 1 million deaths as a result of seismic activity have been recorded over the past 40 years.15 Earthquakes affect both developed and developing nations, and in both cases social and medical infrastructure are affected. The effects on developing nations with an often fragile infrastructure are potentially greater. Earthquakes are sudden-impact disasters that strike quickly and without warning. These
are caused by shifts in the plates that form the crust of the earth, known as tectonic plate shift. Where plates meet, fault lines occur that determine the sites of potential earthquakes.\(^\text{16}\)

The factors affecting the outcome of an earthquake are as follows:\(^\text{16}\):

- **Strength of the earthquake**
- **Degree of planning and preparation**
- **Local geologic conditions**
- **Building design**
- **Demographics:** Many densely populated areas exist along fault lines

The strength of an earthquake is measured using the Richter scale. This scale is logarithmic between 1 and 10. A change of one unit on the Richter scale is equivalent to a 10-fold change in ground motion and a 32-fold change in radiated energy. Earthquakes are measured using instrumentation, observation of human effects, or both. Earthquakes above 5 on the Richter scale cause damage. Those above 7 are regarded as major earthquakes. The 2011 northern Japan earthquake registered 8.9 on the Richter scale and triggered a massive tsunami with 30-foot waves that swept inland for 3 miles resulting in the loss of 15,000 people and creating a nuclear meltdown at Fukushima.

### THE PREHOSPITAL RESPONSE AFTER AN EARTHQUAKE

Earthquakes can cause injury from the direct effects of the release of energy leading to structural damage and secondary effects from sequela such as fires, landslides, floods, tsunamis, and the release of toxic substances. Also, health care facilities may be damaged. They must be inspected immediately, before care is given.

The key problems in prehospital casualty management are as follows:

- **Hospital autoreferral:** Earthquake casualties who are not trapped often take themselves to the nearest hospital, which can rapidly overwhelm the available medical facilities. At times, inappropriate referral (e.g., many patients without significant injury may autorefer to major trauma centers), leads to the inappropriate use of resources.\(^\text{17}\)
- **Communications:** Early breakdown or overload of standard communications systems such as mobile telephones and the internet may occur. Often an overreliance on these systems is seen, and they have not proved resilient under disaster conditions. A further identified problem is the lack of standardization of radiofrequencies among emergency responders.
- **Transportation and social infrastructure:** Earthquakes may cause direct effects on links to major regional hospitals as was the case in the 1995 Kobe earthquake.\(^\text{7}\) In addition, in poorer countries, airport and air traffic capacities may rapidly be overrun as in the 2010 Haiti earthquake.\(^\text{18}\) This had a major impact on teams trying to enter the country to provide emergency medical help.
- **Entrapment:** Most of the fatalities from earthquakes are a result of injury from collapsing buildings or entrapment in the ruins. Death rates rise 67-fold and injury rates rise 11-fold for trapped victims in contrast to those not trapped but injured. Ninety percent of deaths in earthquakes occur as a result of structural collapse.\(^\text{19}\) Survival rate decreases with entrapments longer than 24 to 48 hours after the earthquake. A study of more than 3000 earthquake survivors after the 1980 earthquake in Irpinia, Italy showed that 93% of those who were trapped and survived were extricated within the first 24 hours. In contrast, 95% of those who died did so before they could be extricated.\(^\text{20}\) The provision of advanced life support in airway, ventilation, and circulatory management is an essential part of the primary rescue response for casualties. In entrapment cases, the anesthesia provider not only administers anesthetics but also general anesthesia and sedation to aid extrication.
- **Triage:** Triage of earthquake casualties is essential, particularly in settings where medical care is limited. Several systems of triage have been developed, and the anesthesia provider should be familiar with these. Of these, the Simple Triage and Rapid Treatment (START) system is probably the most familiar and has been evaluated.\(^\text{21}\) This system emphasizes essential lifesaving measures, but rescuers are instructed not to provide any definitive care procedures at the scene.
- **Delays in the delivery of emergency care:** Many victims from earthquakes die because of delays in the delivery of lifesaving emergency medical care. Special urban search and rescue teams (USARs) have now been set up around the world and are ready for immediate response in their home country and for rapid deployment elsewhere. The problem still remains in the delays associated with dispatching the teams. Studies have shown that USAR teams require 24 hours for deployment within the United States and longer for international missions. As an example, the first U.S. team to deploy in Turkey after the 1999 earthquake required 48 hours to begin operations.\(^\text{16}\)

### HOSPITAL RESPONSES

Earthquakes have a direct impact on hospital services, aggravating an initial imbalance of demand for medical care and surge capacity, particularly evident in a developed country, Japan, with the 2009 Kobe earthquake.\(^\text{7}\) All operating services are disrupted, including anesthesia, with loss of power, water, piped gas supplies, and internet technology systems. Most major hospitals around the world now have a general disaster plan. For hospitals within earthquake zones, this plan should be specially modified. It is important that hospital sustainability be a part of any disaster plan.

Other major obstacles delaying the immediate response in hospital include being able to contact off-site staff and arranging their transportation to the facility.

### PATIENT MANAGEMENT

In both the developed and developing nation settings, a patient identification and tracking system should be started as soon as possible. In the early stages, identification numbers may have to be assigned until true identities...
can be established. Anesthesia providers and surgeons should be aware of the patient flow pattern to hospital, to plan the best use of operating facilities. The following pattern of patient flow to hospital is described by Schutz and Deynes.16

- Thirty to 60 minutes after the tremor: Walking wounded with minor injuries and lacerations. These patients should be quickly evacuated to an observation area. Treatment should be postponed until a more detailed appraisal is available.
- More than 60 minutes after the tremor: Victims with more serious injuries such as crush. These patients will be accompanied by paramedical staff or other emergency medical responders and may have received some treatment in the prehospital zone. This wave of casualties may rapidly overwhelm the available hospital resources, and further triage is essential at this stage. The START system mentioned previously will not discriminate between those injured who will consume large quantities of limited supplies and those whose prognosis will remain poor, despite aggressive treatment. To overcome this problem a modified system of triage, Secondary Assessment of Victim Endpoint (SAVE), has been introduced. The objectives of this system are to reduce victim mortality and ensure that resources will be allocated only to those who will benefit from them.22

SPECIFIC INJURIES AND ANESTHETIC IMPLICATIONS

Earthquakes will produce a wide range of traumatic injury. Major injuries include skull fractures and intracranial hemorrhage, spinal injuries, and intraabdominal and pelvic trauma. Studies of previous earthquakes have revealed the following major medical complications of trauma:

- Hypothermia
- Wound infection
- Gangrene
- Sepsis
- Acute respiratory distress syndrome (ARDS)
- Exacerbations of chronic pulmonary disease, such as asthma
- Myocardial infarction
- Multiple organ failure
- Crush syndrome

Crush injuries are a major cause of fatality after earthquakes. The mortality from crush syndrome among those requiring renal dialysis may reach 40% or more.23

The following life-threatening conditions may arise as a result of crush injury:

- Hypovolemic shock
- Lactic acidosis
- Rhabdomyolysis
- Acute renal failure
- Hypocalcemia
- Hyperkalemia
- ARDS
- Disseminated intravascular coagulation
- Fatal cardiac arrhythmias

The possibility of hyperkalemia is of particular importance given the need in some cases for rapid sequence intubations using suxamethonium (succinylcholine).

FIELD ANESTHESIA

Natural disasters can challenge anesthesia providers because of the need to manage large numbers of casualties over a short period. In essence, standard anesthetic practice has to be followed but in an abbreviated and simplified format in terms of assessment of the patient and the anesthetic techniques used.

RESUSCITATION AND TRIAGE

Disaster anesthesia providers must be familiar with systematic standardized trauma management systems (e.g., Advanced Trauma Life Support [ATLS]),24 which are used to provide a unified system of care to the victims. Box 83A-1 presents the conventional guidelines for resuscitation and triage of mass casualties (also see Chapters 81 and 108).

PREOPERATIVE ASSESSMENT

History

In the management of mass casualties in the field, a basic and consistent system of preoperative anesthetic management is required. If the patient is conscious, a rapid history can be taken following the AMPLE mnemonic, as follows11:

- Allergies/Airway problems
- Medications (either taken or given on site)
- Past medical history
- Last meal
- Environment/event

Every patient to undergo emergency anesthesia in the field must be considered to have a full stomach. Injury causes delayed gastric emptying, and normal gastric clearance times may not be appropriate.

BOX 83A-1 Primary Responses for Casualties of a Natural Disaster

<table>
<thead>
<tr>
<th>RESUSCITATION</th>
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<tbody>
<tr>
<td>Airway maintenance with cervical spine protection</td>
</tr>
<tr>
<td>Breathing and ventilation (including the management of chest injury)</td>
</tr>
<tr>
<td>Circulation with control of hemorrhage</td>
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<tr>
<td>Disability or neurologic status (AVPU scale)</td>
</tr>
<tr>
<td>Exposure (undress the patient for full examination of primary and secondary injuries)</td>
</tr>
<tr>
<td>Environment (avoidance of hypothermia and security of the working area)</td>
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<th>TRIAGE</th>
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<tbody>
<tr>
<td>P1 Requiring immediate lifesaving surgery</td>
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<tr>
<td>P2 Surgery can be delayed up to 2 hours</td>
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<tr>
<td>P3 Ambulant injured: Treatment can be delayed by several hours</td>
</tr>
<tr>
<td>P4 Expectant</td>
</tr>
</tbody>
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AVPU, Acronym for alert, voice, pain, unresponsive.
Part V: Adult Subspecialty Management

Physical Examination

Little time may be available for a complete physical examination of the patient before anesthesia. Instead, an abbreviated essential examination should be used as a basic response. This examination involves the following:

- Measurement of vital signs
- Airway evaluation
- Examination of the heart and lungs
- Evaluation of hemorrhage and hypovolemia
- Assessment of chest, abdominal, and other injuries

FIELD ANESTHETIC EQUIPMENT AND TECHNIQUES

Sophisticated anesthetic workstations typical in developed nations are unlikely to be available or usable at or near the disaster site because of damage to the infrastructure. Therefore, the need exists to be familiar with basic anesthetic equipment designed to work in extreme conditions and equally basic and safe anesthetic techniques. Resources such as bottled gases and power may be in very short supply or nonexistent, so equipment must be used that takes this into account. Anesthetic equipment to be used in natural disasters must meet the following standards:

- Simple to operate
- Rugged and reliable
- Easily transportable

Anesthesia providers in the nineteenth century used simple inhaled anesthetic techniques that could be used in the hospital or outside. Field anesthetic equipment has developed along the lines of simplicity and preservation of the approaches of the early anesthesia providers. Development has been driven by the military, which has a requirement to provide safe general anesthesia in battlefield surroundings. However, providing care in remote areas away from mainstream hospitals presents problems because many anesthetic providers do not have the experience with the equipment or techniques of field anesthesia; also, the equipment used is absent from standard hospital practice and thus, providers are not likely to have acquired necessary skills.

USING FIELD ANESTHETIC EQUIPMENT

Field anesthetic equipment sets should be assembled and used for training before disasters occur. This practice may raise complications with current hospital procedures and regulations where the daily practice is to use sophisticated modern equipment. However, it is necessary that anesthesia providers be completely familiar with the equipment and adept at field techniques before deploying to the site of a disaster.

Field anesthetic equipment sets should contain at minimum the following items:

- Torches and emergency lighting
- Airway management
  - Handheld wide-bore suction device
  - Laryngoscopes: Conventional and visualization devices (see also Chapter 55)

FIELD ANESTHESIA SYSTEMS

A number of field anesthetic systems have been developed (see also Chapter 29). Only two will be mentioned here as representative of the origins and development of field anesthesia. The British Triservice anaesthetic apparatus (TSA) was developed over 35 years ago (Fig. 83A-1). In its simplest form, the circuit relies on draw-over of air as a carrier gas. Originally two vaporizers containing trichloroethylene and halothane were placed in series. Oxygen from a compressed source was supplemented via a regulator and a T-piece. Later the circuit was modified to be used in a ventilatory mode with a self-inflating bag placed distal to the vaporizers. The discovery in 1992 that the vaporizers performed equally well in the draw-over and plenum modes allowed the circuit to be modified with a portable ventilator driving air across a single vaporizer containing isoflurane.

The TSA anaesthetic apparatus achieved great success, notably during the Falklands War and is still widely used around the world. However, it suffers from the disadvantage that the Oxford Miniature Vaporiser 50 (OMV 50, Penlon, Abingdon, United Kingdom) cannot be used with modern anesthetics such as sevoflurane because of the physical characteristics.

A more recent field anesthetic system that uses standard plenum vaporizers is the Magellan machine (Oceanic Medical Products, Atchison, Kan.) (Fig. 83A-2). The Magellan can supplement the level of O₂ in the anesthetic gas using a bottled source or an O₂ concentrator. In this way, precious gas resources are conserved. The main driving gas used in the system is again air, but there is a field anesthetic ventilator (ComPac,
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Pneupac, Smiths Medical International, Luton, United Kingdom) built-in that can run from a variety of power sources, including a 28-V vehicle supply (Fig. 83A-3). This turns the Magellan into a plenum system using standard vaporizers without the need for a compressed gas supply.

Figure 83A-2. The Magellan anesthesia machine. (Courtesy Pneupac Ventilation, Smiths Medical International, Luton, United Kingdom.)

ANESTHETIC TECHNIQUES FOR USE IN NATURAL DISASTERS

No set rules exist for which technique of general anesthesia should be used in disasters. The following factors are used in making the choice:

- Familiarity of anesthesia providers with basic equipment and the ability to train on it in their standard daily practice
- Circumstances and infrastructure
- Availability of anesthetics and equipment that are found in both the developed world and developing nations and, therefore, are familiar to anesthesia providers who may find themselves responding to disasters in developing countries
- Considering the potential workload and the requirement in mass casualty management to provide the greatest good for the greatest number

In general, in extreme disaster conditions only a limited role exists for local analgesic procedures and for epidural and spinal anesthesia given the collapsed preoperative condition of many of the patients and the nonsterile conditions that often apply. However, in some situations, regional anesthesia techniques have been used successfully before general anesthetic capability is established.27

All patients receiving field general anesthesia should be regarded as having a full stomach; therefore, a full rapid sequence induction of anesthetics is required followed by tracheal intubation. Thereafter, a balanced technique should be employed with muscle relaxant, opioid, and ventilation. The actual choice of anesthetics to be used will depend on circumstances and national availability. Drugs requiring refrigerated storage (e.g., suxamethonium chloride/succinylcholine) may not be usable, and

alternatives that are stable at room temperature should be sourced.

The anesthesia technique should be designed to minimize the time spent in postoperative recovery and should aim for awake extubation of the trachea at the end of the surgery. Sufficient analgesia should be given until this can be continued by nursing care.

Anesthesia providers working in developing nations may find that modern anesthetics with suitable rapid induction and emergency profiles may not be available, even in normal practice. Here basic inhaled anesthetics such as ether or halothane, often long since discarded in developed nation practice, may be in daily use. A revision of the properties of such anesthetics should therefore be part of disaster training for anesthesia providers.

INDUCTION OF GENERAL ANESTHESIA IN FIELD ANESTHESIA

The use of intravenous anesthetics depends on availability and experience. Propofol, which has achieved dominance over intravenous barbiturates such as thiopental in recent years, may not be the ideal drug of choice in disaster settings. It is dispensed in solutions that can easily become contaminated in the potentially nonsterile conditions that may prevail in disaster management. However, where circumstances of sterility and storage permit, propofol may be appropriate for rapid procedures such as wound dressing change and burn debridement. Because
of cost, propofol may not be readily available in certain developing nations.

Ketamine, a short-acting but potentially hallucinogenic anesthetic that has been in service for several decades, still remains one of the most useful and safe anesthetics for field anesthesia. Its properties and use are shown in Box 83A-2.

**VENTILATION IN THE FIELD AND WHERE HOSPITAL FACILITIES ARE DISRUPTED**

Ventilation in the austere conditions that surround disaster requires planning before entering the situation. Ventilation is required as part of emergency balanced anesthesia and for postoperative care in some cases. Consideration must be given to the use of ventilators that are suitable for disaster conditions where main power and compressed gas supplies may be absent. Most hospital ventilators, including those in anesthetic workstations, are not suitable for this setting.

Anesthesia providers should therefore be familiar with portable gas or battery-powered ventilators suitable for use in disaster conditions. A wide range are available, and the following factors are important to consider: (1) Familiarity. Is the device used or known in standard practice? (2) Simplicity of operation. Does the ventilator have the absolute essentials for field use? In disaster anesthesia, most ventilation is part of balanced anesthesia to ensure a rapid recovery and throughput of cases. Thus, complex ventilation modes used in hospital practice are not required. Pneumatic portable ventilators that offer flow generation, time cycling, and preset volume delivery have been tried and tested in field conditions and have been widely used by the military in recent battlefield operations. The Pneupac ComPac ventilator (Pneupac Ventilation, Smiths Medical International, Luton, UK) shown in Figure 83A-3 is a good example of a device that will function without the requirement for compressed O₂ and with a variety of field available power sources.²⁸

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**83B The Role of the Anesthesia Provider in Chemical and Biologic Warfare Injuries**

**Key Points**

- The management of chemical and biologic warfare (CBW) injury is a continuing process from the site of release to the hospital. The anesthesia provider may be involved at all stages from the provision of essential early life support through intensive care unit care.
- CBW management requires advanced life support and other specialized skills that are part of the anesthesia provider’s sphere of operation.
- CBW injury should not be approached in isolation from the many clinical lessons that already exist from accidental hazardous materials (HAZMAT) releases and natural epidemic infections. CBW release poses a risk to the medical responder, and he or she should be trained and equipped to operate safely in a contaminated or infected zone.
- Chemical and biologic hazards form part of a continuous hazard spectrum. Agents from different parts of the spectrum may have common effects on susceptible somatic systems. Because detection of a released agent may not be immediate, response should be passed on presenting signs and symptoms and may require the provision of life support.
**KEY POINTS—cont’d**

- Each hazard in the spectrum has four key properties: toxicity, latency, persistency, and transmissibility. The first two determine the management of the patient, and the second two determine the management of the incident.
- A wide range of suggested potential hazards (often loosely described as threats) have been suggested in a climate of apprehension because of the possibility of terrorist attack. On the basis of preexisting military and intelligence information, these potential hazards can be refined down to provide a framework of genuine hazards and management protocols that can be applied across the hazard spectrum.
- CBW agents should not be regarded medically as weapons of mass destruction; instead, they are agents that may cause mass injury. Early life support and specific therapy can break the link between mass injury and mass loss of life.
- Most of the toxic hazards likely in civil life are part of the U.N. HAZMAT classification. Planning for accidental industrial releases is relevant to the management of deliberated CBW release.
- Toxic agents have been used in both military and civil releases over the past 35 years and currently should be regarded as a potential terrorist threat.
- Management of exposed patients depends on the protection of medical responders, early provision of life support, and specific antidote and antimicrobial therapy. Decontamination of patients may cause delays in starting treatment and is not always necessary. Essential advanced life support for acute toxic injury (TOXALS) should be given during decontamination if required. Mass ventilation capability in the hospital is important in the management of respiratory failure from accidental and deliberate chemical and biologic causes.
- Military chemical warfare agents, such as nerve agents, vesicants, pulmonary edemagens, cyanides, and certain toxins, pose the greatest hazard in civil releases. Many industrial chemicals are equally hazardous.
- Classic biologic warfare agents, such as anthrax and plague, manifest as a deliberately induced epidemic with far longer latencies than chemical warfare attack. Anesthetic involvement is usually at the intensive care stage.
- Lessons learned from the current fears of deliberate toxic release will have value for the management of the increasing number of accidental individual and mass toxic exposures that form the greater risk for human life in the twenty-first century.

**INTRODUCTION**

Until recently, the effects of exposure to chemical and biologic warfare (CBW) agents was a remote area of clinical practice that concerned military specialists, microbiologists, and toxicologists. Since the World Trade Center attack in New York City in September 2001, the level of concern has increased about the possible impact of CBW agents released by terrorists on a civilian population. The attacks in London in July 2005 involved the use of high-explosive devices in a confined space. Toxic effects occurred, and the use of a chemical device by the terrorists was considered by the emergency responders. Anesthesia providers from the helicopter emergency service were among the first to treat the injured onsite. With the continuing real threat of the use of CBW agents by terrorists, anesthesia providers have become more involved in theprehospital and hospital management of CBW injuries. As a result, CBW casualty management, previously dominated by considerations of toxicity and pathogenicity, now includes considerations of modification of outcome by provision of early and continuing life support.

This section discusses the anesthesia aspects of management of casualties who may have been injured or infected after a deliberate exposure to CBW agents. Important lessons for management of CBW incidents can be taken from plans for accidental toxic releases. In some countries, anesthesia providers are part of the initial emergency medical response and are trained in the essentials of personal protection and decontamination. They also may be involved in the initial reception of contaminated casualties at the hospital itself, particularly when autoreferral occurs. Casualties with toxic injuries also may have conventional injuries requiring surgery, and this brings a whole new dimension to the management of operative anesthesia, modified by the effects of a toxic agent. Finally, many of the victims from a CBW attack require immediate and long-term ventilation and other intensive care, which is an area in which anesthesia providers and intensivists are actively involved.
In this chapter, the nature and management of chemical and biologic hazards will be approached first by considering their definition and classification and second by discussion of the properties of key representative agents in terms of pathophysiologic effects. A wide range of potential CBW hazards exist that have been the subject of exhaustive literature, and it is not the intention here to repeat specialized information. Instead, key features of representatives of various classes of hazard are discussed from the standpoint of anesthetic and intensive care practice. Finally, the practical aspects of the involvement of the anesthesia provider and intensivist in management of CBW agent release will be considered. This discussion covers the management of the patients and safe operation during the incident, including detection of release, protection of responding personnel, and decontamination.

**APPROACHES TO THE LITERATURE**

Many different specialties—both scientific and clinical—have been involved in the study of CBW for over a century. The literature is very extensive and covers a wide clinical range. Of the specialties involved, toxicology, microbiology, and occupational health have been the most dominant and have left their particular influences. Much of the literature relevant to CBW agents predates the Medline era and is not readily accessible from this source. Fortunately many reviews and books exist, particularly in the exhaustively studied area of cholinergic transmission, which makes the careful and relevant work of early researchers still easily accessible to modern anesthetists. The reader is advised to consult these resources to gain a working background of the nature of CBW agents.

**EVIDENCE-BASED STUDIES**

The study of CBW agents in humans has been less extensive than human studies in other areas of clinical medicine. This is understandable because prospective studies that involve exposure of human subjects either willingly or otherwise have been strictly controlled or proscribed by international convention. Despite this, a large amount of information exists in the literature from early clinical volunteer studies and from accidental exposures to chemical warfare agents and many unpublished or previously inaccessible reports are now openly published. In the biologic warfare field, recent reviews are available, along with valuable continuing clinical study in the parallel field of accidental (rather than deliberate) infection together with literature on the development of antimicrobial and antiviral agents, which is of immediate relevance to biologic warfare release.

**SECRECY**

Although considerable information about the pathophysiology and management of CBW cases exists in the open literature, it is highly likely that far more information is still classified by governments involved in the subject and is not easily accessible. Nevertheless, much historical information is available from time-declassified government sources and from searching the sources provided by the Freedom of Information Act in the United States. Other nongovernmental organizations, such as the Stockholm International Peace Research Institute, have published extensive information, although this information may have a political bias. By far the most research on CBW agents was carried out by the Soviet Union (Union of Soviet Socialist Republics [USSR]) during the Cold War, and large amounts of this remain unpublished. However, Soviet scientists involved in programs such as Mikrobioprom and the application of genetic engineering to CBW openly published many articles on techniques; these can be accessed through the databases because the major part of the Soviet program started after the signing of the 1972 biologic warfare Treaty, which led to the discontinuation of biologic warfare research by the West.

**DEFINITIONS**

**CLASSIC DEFINITIONS OF CHEMICAL AND BIOLOGIC AGENTS**

The accepted classic definition of a chemical warfare agent is a chemical substance that is intended for use in military operations to kill, seriously injure, or otherwise incapacitate people through pathophysiologic effects. Traditionally, riot control agents and herbicides were excluded from this definition, although they have frequently been used in a way that would be compatible with the definition of a chemical warfare agent. Biologic agents were defined by the 1972 biologic warfare treaty as living organisms, whatever their nature, or infective material derived from them, intended to cause disease or death in humans, animals, or plants. Toxins, which are essential part of the pathophysiologic process in bacterial infection, were excluded from the biologic warfare treaty and are regarded essentially as chemical agents.

**THE CHEMICAL-BIOLOGIC HAZARD SPECTRUM**

Although chemical and biologic agents have traditionally been separated, it is appropriate medically to regard them as part of a continuous spectrum of hazards; this is shown diagrammatically in Figure 83B-1. Agents in Figure 83B-4 are arranged in ascending order of molecular weight through chemical toxic agents through to self-replicating agents such as bacteria and viruses, on the right. The spectral approach to hazards is useful in emphasizing that agents from different parts of the line act in a similar way on the body. The failure of the neuromuscular junction caused by nerve agent anticholinesterases and botulinum toxin is a good example. Bacteria exert their toxic effects through toxins that may affect various somatic systems. The spectral approach serves as a reminder that medical management of CBW injury should respond primarily to system dysfunction rather than to specific etiologic factors.
The four essential properties of hazards within the CBW spectrum are toxicity, latency, persistency, and transmissibility. These four characteristics are common to both chemical and biologic agents and determine the degree of risk and the appropriate response. Toxic effects of CBW agents appear to have a specific latent period. In general, chemical agents and toxins have short periods of latency before the appearance of specific signs and symptoms. In contrast, classic biologic warfare agents have extended latency periods (usually familiar as incubation periods) before the effects of the induced disease begin to appear. Persistency relates to the ability of a toxic agent to remain in the environment into which it was released and is a function of the physicochemical properties of the agent. For chemical agents, the persistency may vary, but for most biologic warfare agents, with the exception of spore-forming agents such as anthrax, persistency is usually very short. Finally, transmission of a hazard may take place as a result of the physical contamination of the victim from a persistent chemical agent or as a result of infection in the case of an airborne agent. Chemical transmission can be contained by decontamination, but biologic warfare agent transmissibility is more difficult to control because of continuing activity.

In summary, toxicity and latency determine the management of the casualty, and persistency and transmissibility determine the management of an incident involving the release of a CBW agent.

**TOXICITY AND ITS MODIFICATIONS**

Toxicity is usually expressed in terms of median lethal dose (LD$_{50}$) or LC$_{50}$, where $C$ is the concentration of agent inhaled for time $t$ required to produce lethality in 50% of the exposed population. LD$_{50}$ usually relates to toxicity via injected routes. In the case of most chemical agents, the inhaled route is usual, so expressions of concentration and time are used.

Haber defined a *lethality coefficient* as follows:

$$W = C \times t$$

where $C$ is the inhaled concentration of toxic agent and $t$ is the time of exposure. In practice, the absorbed amount of agent depends on the respiratory minute volume of the exposed person. This is just one factor modifying the expression of toxicity. Others include life support responses in the case of respiratory failure and the effects of antidotes. The reader is referred to specialized texts for a more detailed discussion.

**THE NUCLEAR, BIOLOGIC, AND CHEMICAL WEAPONS CLASSIFICATION**

Since the end of World War II, nuclear, biologic, and chemical weapons have by convention been classified together as “NBC” agents, giving rise to a new subsection of warfare, which was developed by both sides during the Cold War. Although all three components are “toxic,” the classification ignored the very intense level of physical damage caused by nuclear explosions. Over the years, the term *weapons of mass destruction* (WMDs) has been applied to NBC agents, although the term was originally used by the United Kingdom at the end of World War II. Recently, the term NBC has been altered to reflect the threat perception from the use of explosive devices that can spread radioisotopes (rather than create them as in a fission process) into chemical, biologic, radiologic, and nuclear (CBRN) hazards. CBW agents are defined by their effects after mass release on large populations. The term is not usually applied to the use of such agents for individual or small group poisonings.

**MYTH AND REALITY OF CHEMICAL AND BIOLOGIC WARFARE AGENTS AS WEAPONS OF MASS DESTRUCTION**

At the end of World War II, the Tizard report appeared, which looked at the future potential of nuclear and biologic weapons, both of which had been used during that conflict. The term *weapons of mass destruction* appears to have been used for the first time in this report because it was thought that both agents would cause mass loss of life. Chemical weapons were added to this group during the 1950s, when the equilibrium of international power depended on analysis of the possession of the three WMD agents. In retrospect, however, the WMD classification is (at least medically) inappropriate. Consideration of the events of World War II showed that nuclear weapons should be classified with conventional weapons systems that cause mass loss of life and destruction to material and the environment, such as the conventional high explosive and firebombing of Germany in the latter part of the war.
CIVIL TOXIC HAZARDS (HAZMAT)

Parallel to the definitions of CBW agents is a classification of hazardous materials used in everyday industrial life. These are usually released by accident. Many of these are as toxic as chemical warfare agents. Such toxic substances are classified as hazardous materials (HAZMAT) and are covered by the U.N. convention controlling the use and transportation of such materials (Box 83B-1). A HAZMAT material is defined as that which causes mass injury and death if released from a confined state. The civil equivalent of biologic warfare agent release is natural infection expressed as an epidemic. Another term for HAZMAT is toxic industrial chemicals (TICs). TICs are substances that could be used as improvised chemical agents in a terrorist attack.

**BOX 83B-1 HAZMAT System of Classification**

The U.N. hazardous materials classification for toxic substances (HAZMAT) defines nine classes of hazard. These are identified during production and transportation by a class number and a hazard identification number. Vehicles carrying compounds controlled by HAZMAT must display a plate (the Kemler plate) that carries this essential information for the use of emergency responders. The form of the Kemler plate varies internationally.

<table>
<thead>
<tr>
<th>Class</th>
<th>Subclass</th>
<th>Hazard Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.1-1.5</td>
<td>Mass explosion hazard</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very sensitive substances</td>
</tr>
<tr>
<td>2</td>
<td>2.1</td>
<td>Flammable gases</td>
</tr>
<tr>
<td></td>
<td>2.2</td>
<td>Nonflammable nontoxic gases</td>
</tr>
<tr>
<td></td>
<td>2.3</td>
<td>Toxic gases</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Flammable liquids</td>
</tr>
<tr>
<td>4</td>
<td>4.1</td>
<td>Flammable solids</td>
</tr>
<tr>
<td></td>
<td>4.2</td>
<td>Spontaneous combustion</td>
</tr>
<tr>
<td></td>
<td>4.3</td>
<td>Dangerous substances when wet</td>
</tr>
<tr>
<td>5</td>
<td>5.1</td>
<td>Oxidizing substances other than</td>
</tr>
<tr>
<td></td>
<td></td>
<td>organic peroxides</td>
</tr>
<tr>
<td></td>
<td>5.2</td>
<td>Organic peroxide</td>
</tr>
<tr>
<td>6</td>
<td>6.1</td>
<td>Poisons</td>
</tr>
<tr>
<td></td>
<td>6.2</td>
<td>Infectious substances</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>Radioactive substances</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>Corrosive substances</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>Other dangerous substances</td>
</tr>
</tbody>
</table>


WORLD WAR I

Chemical agents were used from 1915 to 1918 in World War I. Their use was catalyzed by the battlefield stalemate of trench warfare. They do not fit well with the tactics of a mobile war, which was the case in World War II. Large-scale releases of chlorine and phosgene in 1915 had considerable effects against unprotected troops and caused large numbers of casualties and deaths. It was these early attacks that probably gave rise to the notion of CBW agents being weapons of mass destruction. In fact, chemical weapon injury produced the lowest ratio of dead to wounded of all the arms used during the war at less than 4%, whereas explosive shells had the highest ratio at over 15%. Artillery caused 59% of the overall mortality on all sides. Many different chemical agents were tried during the war, delivered usually by shell fills, but the difficulty was in building sufficiently high concentrations of agent to be lethal and the continuing countermeasures meant that better trained troops with masks were less affected. Although phosgene easily could be regarded as the most lethal of the agents used, causing untreatable toxic pulmonary edema, mustard gas, a vesicant disabling agent, caused the most injuries and removed many from the field of battle (usually temporarily). One overlooked feature of the casualties from World War I is the possibility of mixed toxic and physical trauma. The exact figures are not available, but of 546 American soldiers who died after exposure to chemical warfare agents during the period March to November 1918, 6% also had ballistic injuries. The figures for dead and wounded do not reveal the true extent of the disability caused by exposure to toxic agents, and it is likely that the long-term pathology was high, particularly given the limited postwar medical facilities at that time.

DEVELOPMENT AND USE OF CHEMICAL AND BIOLOGIC WARFARE AGENTS DURING WORLD WAR II

Organophosphate pesticide research by Gerhard Schrader in 1936 led to the development of anticholinesterase “nerve agents” by Germany under conditions of the strictest secrecy during World War II. Although never used in action during that time, nerve agents became the major toxic hazard faced by armies during the Cold War and beyond. A major nerve agent plant was captured by the Russians and rebuilt in the Soviet Union in 1945, giving the USSR a “mass destructive” capability long before it possessed nuclear weapons. A lesson for both military and civil anesthesia providers is that mixed casualties can be expected after the
use of toxic agents, because Soviet commanders saw the use of chemical weapons as part of a normal armamentarium, rather than being exceptional weapons.51

Some evidence exists of the use of biologic warfare agents in China by the Japanese, who had a secret unit devoted to the subject since the early 1930s.42 Plague and clostridia were used in tests on prisoners and against civilian populations. The considerable knowledge gathered was passed on to the United States by the head of the section after his capture and formed the basis of an offensive biologic warfare development program that was terminated in 1972 with the signing of the biologic warfare treaty.

COLD WAR DEVELOPMENT

It is now known that a major Soviet biologic warfare program began in the early 1970s that used genetic engineering and other techniques to develop a whole new range of possible agents, including toxins and “agents of biologic origin,” which are probably deployed at the present time.49 Development of nerve and other agents also continued during the Cold War, along with extensive research into an antidote-based approach to the management of the wounded.

With the end of the Cold War, much of the expertise in USSR laboratories may have moved to other countries, increasing the risk that developed CBW agents and delivery technology may be more easily available to terrorist groups.

THE IRAN-IRAQ WAR

The Iran-Iraq War during the 1980s saw the sustained use of chemical agents and the first application of modern medical techniques to chemical warfare injuries (Box 83B-2). Extensive U.N. investigations established that sulfur mustard and lewisite, both vesicant agents, had been used together with the nerve agent tabun and a toxin agent, mycotoxin.52,53 Casualties were almost exclusively on the Iranian side and numbered approximately 27,000, with a mortality rate less than 1%. This continued the trend noted during World War I of the low mortality rate for chemical warfare compared with other weapons, and almost certainly reflects the impact of organized medical care for the casualties and techniques of protection. In comparison, the Iraqi attack in 1989 against civilians in the unprotected Kurdish village of Halabja, which had few or no medical facilities, produced 5000 dead.

TERRORIST CHEMICAL AND BIOLOGIC WARFARE RELEASES DURING THE LAST PART OF THE TWENTIETH CENTURY

In 1995, the first recorded terrorist use of a chemical warfare agent against a civilian population occurred with the use of the nerve agent sarin in attacks in Matsumoto and Tokyo, Japan, and for the first time, hospital medical teams were brought into direct contact with a chemical injury. The treatment must be adjusted to the degree of injury. Humidified air or oxygen helps prevent airway obstruction. Bronchodilators, mucolytics, and expectorants are useful. In cases of serious injury, mechanical ventilation with positive end-expiratory pressure and acid-base balance control are used to support the patient until the injuries resolve.

Injury to the eyes was treated with irrigation and antibiotic cream. Pain is treated with systemic medications. Because of weight loss, often in excess of 10 kg (22 lb), nutritional support is instituted to help reduce the significant mortality associated with negative nitrogen balance. Once the patient reaches a setting for definitive care, therapy is divided into two parts: a general supportive treatment for sepsis and dehydration and treatment to eliminate toxins from the body.3

Significant observations from the Iran–Iraq War include the following:

- Decontamination, using soap and water and shaving body hair, was done early. This protected medical personnel and simplified further treatment.
- Comatose casualties of nerve agents who did not have cardiovascular problems were treated with large doses of atropine 50 to 200 mg administered intravenously. Most casualties received 2 mg every 8 hours. Comatose casualties with significant cardiovascular deterioration (such as bradycardia after 2 mg of intravenous atropine) were most often found not to survive.
- Mustard, although it dates from World War I, continues to be an important chemical agent. It is a vesicant but also has effects on multiple organ systems.

**BOX 83B-2 Iran-Iraq War Experience With Chemical Warfare Agents**

During the Iran-Iraq War, modern medicine was applied to the treatment of injuries caused by sulfur mustard, tabun, lewisite, and the biologic agent mycotoxin.7 Although data are limited, there are lessons that should be noted. The most unexpected was the surprisingly low mortality: fewer than 1% of the estimated 27,000 Iranian chemical casualties.3

Troops with organophosphate exposure fell into four categories. Those with the greatest exposure died in the field. The number appears to have been very small, even though most of the Iraqi attacks were made against unprotected Iranian troops. Those most severely injured who reached medical aid were unconscious, unresponsive, and often in respiratory arrest. The seriously intoxicated had symptoms of dizziness, disorientation, anxiety, salivation, and respiratory difficulty. Those with relatively mild symptoms were often physically difficult to manage because of their disorientation. By far the largest number of casualties required no treatment other than decontamination.

Treatment of mustard exposure during the Iran-Iraq War reflects the experience gained in the management of burn wounds during the 80 years since World War I. Treatment begins with early and thorough decontamination. Early in the course of injury, blistering may not be present. Still, removal of contaminated clothing is important to limit contact time with the agent. Shaving of the affected areas followed by washing mechanically removes and dilutes the agent. Aspiration of blisters, removal of necrotic tissue, and treatment of the skin lesions with silver sulfadiazine cream forms the basis for treatment of skin injury. Respiratory exposure to mustard creates its own set of problems. Depending on the degree of injury, the treatment must be adjusted to the degree of injury. Humidified air or oxygen helps prevent airway obstruction. Bronchodilators, mucolytics, and expectorants are useful. In cases of serious injury, mechanical ventilation with positive end-expiratory pressure and acid-base balance control are used to support the patient until the injuries resolve.

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- Mustard, although it dates from World War I, continues to be an important chemical agent. It is a vesicant but also has effects on multiple organ systems.


HAZARDS AND THREATS

Confusion between the concept of a hazard and a threat is common. CBW agents are, by definition, hazardous. The term threat is usually used in the military context if a hazard has been weaponized and the assailant has the capability and the intention to use the weapon. The relationship may be expressed by the simple equation:

\[ \text{Threat} = \text{Hazard} + \text{Capability} + \text{Intention} \]

For a balanced medical response to CBW attack, the reality is that many of the CBW hazards causing public concern are very difficult to weaponize and deliver. This understanding is important for the medical responder because it reduces the likelihood of encountering casualties from CBW attack to a restricted number of agents, the properties and pathophysiology of which can be considered before casualties present.

MODES OF RELEASE OF CHEMICAL AND BIOLOGICAL WARFARE AGENTS

CHEMICAL AGENT RELEASE

Military Release

In warfare, the release of CBW agents is a deliberate action achieved through the use of shells or missiles or through spraying. Aerosol release is the essential technique that allows attack through the respiratory route, but for more persistent agents designed to deny terrain, the use of spray devices is more common. By the end of World War I, delivery of chemical warfare agents was almost exclusively through explosive shells, and at that time nearly 40% of the fills were chemical, indicating the effectiveness of chemical warfare agents on the battlefield. The rise of aerial bombardment before World War II brought great fears that cities would be wiped out by gas attacks, but these fears were never substantiated and it is now realized that dissemination of chemical warfare agents over a wide area (rather than a limited tactical area) by explosion is not easy.

During the Cold War, the Russians developed considerable expertise in the use of BM21/24 multiple rocket launchers (Stalin organs) that could rapidly deliver a high concentration of nonpersistent agents, such as hydrogen cyanide, and then allow their dispersal and the entry of unprotected troops. Missiles such as the Scud were also developed for chemical warfare release at this time, and it was feared that they had been developed for chemical warfare use by Iraq before the Gulf War of 1991.

In the military context, release of toxic agents may be revealed or concealed. Attack, by whatever means, is usually predicted and detectable with the considerable resources that the military can bring to bear in this area, for both chemical and biologic agents. Tuned detection systems are employed wherever there is perceived to be a threat, and the threat itself is usually supported by intelligence information about the hazards concerned, which means that the systems can be tuned. Broad detection systems such as mass spectrography are also employed by CBW reconnaissance units in the field (Box 83B-3).

Release on a Civilian Population

In civil life, toxic agent release is usually accidental and is usually revealed by the circumstances. Road and other transportation accidents, particularly when vehicles carrying HAZMAT identification plates are involved, give an immediate warning about the nature of the problem. Accidental releases, particularly in nations with poor emergency response resources, can be catastrophic, as in the case of the mass release of methyl isocyanate in the Indian city of Bhopal in 1984, which caused over 5000 deaths and 50,000 casualties. Civil populations, unlike their military counterparts, are usually untrained and unprotected against toxic agent release. In addition, the panic induced by the fear of the actions of CBW agents compounds the flexibility of the emergency medical response.

BIOLOGIC WARFARE AGENT RELEASE

The deliberate release of classic biologic warfare agents, such as bacteria or viruses, may not be as easy as the

<table>
<thead>
<tr>
<th>BOX 83B-3 Detection Techniques</th>
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<tbody>
<tr>
<td><strong>Detection:</strong> Detecting the presence of a chemical or biologic weapon agent in a contaminated environment. Specific detection techniques include the following:</td>
</tr>
<tr>
<td>Agent-specific chemistry</td>
</tr>
<tr>
<td>Generic chemical detection techniques</td>
</tr>
<tr>
<td>Mass spectrography</td>
</tr>
<tr>
<td>Ion current devices</td>
</tr>
<tr>
<td>Bioluminescence</td>
</tr>
<tr>
<td>Microbial techniques</td>
</tr>
<tr>
<td>Chemical and pathologic studies on an affected patient after the attack</td>
</tr>
<tr>
<td>Internal versus external detection</td>
</tr>
<tr>
<td><strong>Monitoring:</strong> Detecting contamination on an exposed patient. Monitoring is important to determine the risk for transmission and the effectiveness of decontamination.</td>
</tr>
</tbody>
</table>
media have led the public to believe. Effective mass release implies aerosol release, and very few of the biologic warfare agents are capable of withstanding the environmental stresses involved. Some, such as anthrax spores, have long been recognized as being sufficiently robust and have therefore attracted the most research attention. The only other bacteria that have probably been used as biologic warfare agents are Francisella tularensis, which is spread through infected fodder and causes tularemia, and Yersinia pestis, which causes plague and was said to have been used by the Japanese during the World War II campaign against China, and where the vector used was the traditional one of the rat-borne flea.42

Considerable research work was carried out by the USSR during the Cold War to try to find new ways of delivering biologic agents and for their modification using genetic engineering.44 This work also developed agents of biologic origin that lie in the middle of the CBW spectrum and produce subtle pathophysiologic effects and are difficult to detect postmortem in the body. In military terms, biologic warfare has always been seen as a debilitating weapon, self-propagating, and of long latency, that could be used to degrade the capability of static enemy formations or key formations operating behind front lines, such as airfields. In the civil context, biologic warfare agents have yet to be used in a terrorist attack, evidence of continued interest exists.57

Numerous reviews34-39,41,45 are available giving details of agents that are regarded as CBW hazards. This section concentrates on selected hazards that can be regarded as being potential threats and that are likely to be encountered by the responding anesthesia provider.

**AGENT-SPECIFIC CLINICAL APPROACH: WHAT IS IMPORTANT TO THE ANESTHESIA PROVIDER**

In the management of CBW casualties, the anesthesia provider acts as part of a clinical team. To provide a safe and effective response, the following are required:

- Physical, pharmacologic, and immunologic methods of individual protection
- Immediate measures for life support
- Specific antidote therapy
- Consideration of latent effects

In the following section, specific agents have been selected that are representative of classes of hazards and in some cases have been used as weapons of warfare. They are hazards that either can be synthesized relatively easily or are potentially available from stockpiles or reference laboratories.

**NERVE AGENTS**

Nerve agents are members of a very large group of chemical compounds called organophosphates (OPs), known since the nineteenth century but first examined in detail in the 1930s.35,36,58 More than 50,000 OP compounds have been synthesized, and several are in regular use as insecticides around the world, including parathion, malathion, and fenthion.59 Although OPs were originally developed as insecticides, certain highly toxic members of the class—known as nerve agents—have been developed since before World War II specifically for military use. As a result of development by Germany, and later by Russia, the United States, and Great Britain, at least five nerve agents have been produced. The formulae of the more common nerve agents are shown in Figure 83B-2. Tabun (military designation GA) was the first nerve agent to be produced, followed during World War II by sarin (GB) and soman (GD). 2-(Diisopropylamino)ethyl-O-ethyl methylphosphonothioate (VX), N,N-diethyl-2-(methyl-(2-methylpropoxy) phosphoryl) sulfanylethanamine (VR), and cyclosarin (GF) were developed during the Cold War. Cyclosarin (in which the isopropyl group in sarin is replaced by a cyclopropyl group) was found stockpiled in Iraq during the First Gulf War in 1992. Currently the most important nerve agent hazard likely to face the anesthesia provider is soman (isopropyl methyl phosphonofluoridate), which has been widely produced, stockpiled, and also synthesized and used by terrorists.31,55

In terms of physical properties, tabun, VX, and VR are persistent and sarin, soman, and cyclosarin are not. However, soman may be made in a thickened form that is persistent. The relevance of the physicochemical data to the clinical situation is that the nonpersistent agents generally pose a respiratory risk and the persistent agents...
are a danger because of absorption through the skin. This means that different agents pose specific risks both to victims and medical attendants.

Nerve agents were originally termed nerve gases, but are in fact liquids with volatilities varying between those of petrol and heavy lubricating oil. None freezes until −40 °C (−40 °F). They are pale yellow to colorless, odorless, and soluble in water, in which they undergo slow hydrolysis. However, in the presence of strong alkalis and hypochlorite solution, the hydrolysis is rapid and this is the basis of the decontamination of the G agents. Decontamination of V agents with hypochlorite can produce toxic products and is not recommended. Nerve agents can penetrate clothing, skin, and leather. Rubber and synthetic materials, such as polyethylene and butyl rubber, are more resistant. The physical properties of the nerve agents are shown in Table 83B-1.

### Actions of Nerve Agents

The main effect of nerve agents is inhibition of acetylcholinesterase (AChE) and butyryl cholinesterase in the cholinergic nervous system (see also Chapter 18). These enzyme systems include the carbamate anticholinesterase and neostigmine, to reverse the action of nondepolarizing neuromuscular blocking drugs. OPs also inhibit other enzymes, notably neurotoxic esterase (NTE). This inhibition causes long-term neurologic effects unrelated to cholinergic changes (organophosphate-induced delayed neuropathy [OPIDN]). The interaction of OPs with AChE is complex and is analogous to the interaction of the enzyme with the natural substrate acetylcholine (Fig. 83B-3). Inhibition of AChE causes a buildup of acetylcholine at muscarinic and nicotinic synapses of the cholinergic nervous system. Thus, central and peripheral signs and symptoms occur that can be directly explained from the classic pharmacologic knowledge of how the cholinergic system operates.

Although the classic effects of OPs are essentially cholinergic, important effects on other receptor systems occur, notably γ-aminobutyric acid (GABA) and N-methyl-D-aspartate, which gives rise to central excitation, causing the initial seizures seen in acute OP poisoning.

The interaction of OPs with AChE is nonreversible after a certain time depending on the nerve agent. The formation of an irreversible complex is known as aging. Each nerve agent has an aging half-life. For sarin, this is about 5 hours, whereas for soman it is only 2 minutes. Tabun and VX both have aging half-lives of 40 hours. After five half-lives, more than 95% of the enzyme AChE has aged and cannot be reactivated. This has important consequences on the window of clinical opportunity for treatment to try to reverse the AChE inhibition (see later section on Oximes).
TABLE 83B-2 SYMPTOMS AND SIGNS OF NERVE AGENT POISONING BY TYPE OF CHOLINERGIC RECEPTOR

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Target Organ</th>
<th>Symptoms and Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscarinic</td>
<td>Iris muscle ciliary muscle</td>
<td>Miosis; spasm leading to failure of accomodation and pain in the eyes; nausea and vomiting; headache</td>
</tr>
<tr>
<td></td>
<td>Conjunctival vessels</td>
<td>Vasodilation and hyperemia</td>
</tr>
<tr>
<td></td>
<td>Nasal glands</td>
<td>Rhinorrhea and hyperemia</td>
</tr>
<tr>
<td></td>
<td>Bronchial glands</td>
<td>Increased secretion</td>
</tr>
<tr>
<td></td>
<td>Bronchial muscle</td>
<td>Bronchoconstriction; tightness in the chest; expiratory wheezing; dyspnea</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal tract</td>
<td>Anorexia; nausea; vomiting; abdominal cramps; diarrhea; tenesmus; involuntary defecation</td>
</tr>
<tr>
<td></td>
<td>Sweat glands</td>
<td>Increased activity</td>
</tr>
<tr>
<td></td>
<td>Salivary glands</td>
<td>Increased activity</td>
</tr>
<tr>
<td></td>
<td>Lacrimal glands</td>
<td>Lachromiation (not usually marked)</td>
</tr>
<tr>
<td></td>
<td>Heart</td>
<td>Bradycardia; occasionally tachycardia</td>
</tr>
<tr>
<td></td>
<td>Bladder</td>
<td>Frequency; involuntary micturition</td>
</tr>
<tr>
<td>Nicotinic</td>
<td>Skeletal muscle</td>
<td>Weakness; fatigue; fasciculations; cramps; flacid paralysis (early effects on respiratory muscles may produce dyspnea)</td>
</tr>
<tr>
<td>Muscarinic and nicotinic</td>
<td>Autonomic ganglia</td>
<td>Pallor; occasional elevation of blood pressure</td>
</tr>
<tr>
<td></td>
<td>Central nervous system</td>
<td>Anxiety; giddiness; restlessness; headache; withdrawal and depression; memory failure; impaired concentration; slurred speech; depression of respiratory and cardiovascular centers; Cheyne-Stokes respiration</td>
</tr>
</tbody>
</table>


Signs and Symptoms of Nerve Agent Poisoning

The classic signs and symptoms of nerve agent poisoning are shown in Table 83B-2. Poisoning is caused by the accumulation of acetylcholine and not by the OP itself. As a result of stimulation of muscarinic synapses, miosis; ciliary body spasm causing pain; glandular hypersecretion; increased salivary, bronchial, and lachrymal; sweating; cardiac effects, including bradycardia (or tachycardia due to the effects on the anomalous sympathetic system), atrioventricular block, and Q-T prolongation; bronchoconstriction; vomiting; severe diarrhea; and fecal incontinence also occur. The nicotinic effects are manifested by fasciculation and paralysis at the skeletal neuromuscular junction. Central effects give rise to apprehension, dizziness, amnesia, seizures, coma, and respiratory depression. Lower chronic doses of OPs lead to irritability, fatigue, loss of concentration, and memory loss.

Clinical Experience With Organophosphate Intoxication

Much of the information about actions of OPs in humans has been gathered from animal studies and management of pesticide poisoning. It should be noted that animal studies do not necessarily represent human reactions, and pesticide studies may not accurately represent the development of the cholinergic syndrome after nerve agent exposure. Although some evidence exists from accidental exposure to sarin and from some human volunteer studies conducted early in the Cold War, the clinical evidence base is smaller than that for pesticide poisoning. During the early stages of the Cold War a number of experimental studies were done on human volunteers exposed to nerve agent, and these have been reviewed by Sidell. The attacks in Japan in 1994 and 1995 also have provided important information concerning the signs and symptoms after sarin release.

Clinical Evidence From Recent Military Experience

The Iran-Iraq War produced first-hand clinical information about the effects and management of nerve agent poisoning. Iranian casualties from nerve agents apparently fell into four broad categories. Individuals who suffered the greatest exposure died in the field; filtration mask protection by Iranian troops was severely compromised by their beards, which they had for religious reasons. Despite the fact that Iraqi attacks were made against troops having compromised or poor protection, the number of deaths appears to have been low. The most severely injured who reached medical care were unconscious and unresponsive and often in respiratory arrest. The next group who were seriously poisoned had symptoms of dizziness, disorientation, anxiety, salivation, and respiratory difficulty. Disorientation was a problem, and often cases with only mild symptoms were difficult to manage because of this (this parallels experience gained with the management of OP pesticides). Finally, most of those exposed required only decontamination. Treatment of nerve agent poisoning relied on giving large doses of atropine, usually 50 to 200 mg intravenously. These cases were usually comatose, and the degree of advanced life support given was limited. Most patients received only atropine 2 mg every 8 hours. Comatose patients with significant cardiovascular deterioration usually did not survive.

Clinical Evidence From Pesticide Poisoning

Considerable clinical evidence exists about the effects of OP pesticides from the many thousands of cases that occur in agricultural areas of the world each year. Although these give an overall picture that corresponds to the signs and symptoms described previously, considerable differences exist with nerve agents. It is also likely...
that the various nerve agents have relatively different effects on the central and nervous systems.

Cardiovascular Effects of Nerve Agents

Critical care management of OP pesticide poisoning has indicated short-term and medium-term cardiac changes.\textsuperscript{63,64} After an initial tachycardia (mediated through the anomalous sympathetic nervous system) and a vagally induced bradycardia, ventricular dysrhythmias, including torsade des pointes and prolongation of the Q-T interval may occur. Dysrhythmias have been reported as a poor prognostic sign.

The Treatment of Nerve Agent Poisoning: Antidotes and Life Support

Atropine. Atropine has long been a mainstay in the management of OP poisoning.\textsuperscript{56,62} Its antagonistic action against acetylcholine at the muscarinic synapses allows control of the muscarinic effects, the most severe of which is bradycardia. Atropine also has been used for many years in the management of OP pesticide poisoning. However, the relevance of the experience with pesticides to poisoning with nerve agents is not clear.\textsuperscript{36} The traditional military response to confirmed or suspected attack with nerve agents is to use a self-administered autoinjector containing atropine 2 mg, a benzodiazepine, and an oxime. An example is shown in Figure 83B-4. During the Cold War, NATO troops were provided with three such devices to be used sequentially. Useful treatment indications have been gained from the Iran-Iraq War\textsuperscript{65} and the Japanese terrorist experience.\textsuperscript{55} Atropine 2 mg is given intravenously (pediatric dose 0.02 to 0.05 mg/kg) with repeat doses every 5 to 10 minutes until pupillary dilatation occurs and the heart rate increases above 80 beats/minute.\textsuperscript{36,66} Atropine infusions may be used for persistent bradycardia in pesticide poisoning.\textsuperscript{67}

Oximes. Oximes are compounds capable of reactivating, in some cases, the complex formed by the OP and AChE. Clinically this means that oximes can reverse the actions of OP at the nicotinic receptor and reduce the degree of paralysis.\textsuperscript{68,69} Oximes are widely used in the clinical management of both OP pesticide and nerve agent poisonings. Chemically they are monopyridinium or bispyridinium compounds that can bind to the complex and cause the nerve agent molecule to separate from the enzyme. Oximes are a mainstay of the standard military response to nerve agent attacks and are widely used in the management of pesticide poisoning. However, their effectiveness depends on (1) the exact nature of the nerve agent involved and (2) the length of time after the attack before they are given. This is because aging chemical changes take place in the nerve agent–enzyme complex. Aging occurs very rapidly in humans after soman exposure, but less so after exposure to other nerve agents. One of the major problems related to oxime research is the selection of a suitable animal model. Originally monkeys and guinea pigs were both thought to be good models for human OP intoxication, and human treatment protocols were developed from such studies. However, major differences are known to exist between enzyme complex aging rates for primates and those for rodents.\textsuperscript{70} The rate of formation of aged enzyme in different species increases in the following order: mouse < rat < guinea pig < rabbit < dog < cow < monkey = human. From erythrocyte studies in humans, the rate of aging is known to be very rapid (half-life 1.3 minutes), indicating that the guinea pig would not be a good model for the use of oximes in humans.

Several oximes are available, and recent years have seen the development of new compounds.\textsuperscript{68,69} The most commonly used is pralidoxime (as either the chloride or methane sulphonate [mesylate]). Obidoxime is used in some countries for OP pesticide poisoning and may be effective against tabun. Recent research has concentrated on the rational use of a range of oximes both in terms of the type of oxime used and dose and timing.\textsuperscript{68,69,71} HI-6, a Hagadorn oxime, reactivates the soman-enzyme complex, the most difficult clinical situation to treat. However, HI-6 may be useful because of other pharmacologic properties and may be advantageous in the treatment of cyclosarin poisoning and other cases in which obidoxime was previously used.

For most anesthesia providers treating a patient with the symptoms of nerve agent poisoning, a civilian setting is the most likely. Exposure to sarin is the most probable situation, and treatment schedules logically should be based on this premise. Military anesthesia providers may face other hazards, but they would be provided with specialized detection equipment and treatment modalities based on a threat assessment. All nerve agent casualties should receive pralidoxime mesylate initially, in addition to atropine and ventilatory life support.

Practical Treatment Regimen. Oxime therapy should be given simultaneously with atropine.\textsuperscript{66,68} A slow intravenous injection of pralidoxime is recommended to prevent laryngospasm, muscle rigidity, and hypertension. Pralidoxime 15 to 30 mg/kg intravenously or intramuscularly is given over 20 minutes for adults and children. This dose may be repeated after 4 hours (or 1 hour if paralysis is worsening). The target therapeutic blood concentration should be 4 μg/mL. However, studies by Worek and colleagues\textsuperscript{71} show that the full therapeutic effects of pralidoxime may be achieved at higher concentrations. The same group demonstrated that reactivation of AChE is a possibility after pralidoxime treatment in human erythrocytes, but the relevance to the whole body is unclear. Sarin is broken down rapidly in the blood by hydrolysis. Oxime treatment in the hospital should continue for as long as atropine is required.

Benzodiazepines. The central actions of OPs give rise to spike discharges and seizures. Benzodiazepines have long...
been used to counter this action. Given the known action of OPs at the GABA receptor and the antagonistic action of benzodiazepines at this site, the action may be non-cholinergic.\textsuperscript{72,73}

Seizures may be an early sign of severe nerve agent poisoning and must be controlled quickly to avoid long-term cerebral damage.

**Pyridostigmine Pretreatment.** The problem of aging of the OP AChE complex, particularly with soman and the ineffectiveness of oxime therapy, gave rise to a novel military approach to prophylaxis against nerve agent poisoning.\textsuperscript{37} Pyridostigmine is a dimethyl carbamate compound with a quaternary nitrogen atom. As a result, it does not penetrate the blood-brain barrier to any extent. In common with other carbamates such as neostigmine and physostigmine, pyridostigmine is an anticholinesterase and has essentially the same action as OPs. In the case of carbamates, the complex formed with the enzyme is readily reversible. The normal treatment dose of pyridostigmine is 30 mg every 8 hours. No plasma protein binding occurs and no drug interactions involving competition for binding sites. Of the absorbed dose, 79% to 90% is excreted unchanged in the urine. The reversibility of the complex formed with AChE is such that the enzyme returns to 90% of normal within 12 hours after the last dose. In addition, at steady state, only 40% of the available AChE is complexed. Given the considerable safety margin that exists in the level of enzyme at cholinergic synapses, treatment with pyridostigmine does not produce any more than mild parasympathetic signs.\textsuperscript{74}

The protective action of pyridostigmine against OPs is based on the fact that the carbamylate-complexed AChE is resistant to attack after subsequent exposure to OPs. If a person taking pyridostigmine is exposed to a subsequent potentially lethal dose of OP, a reserve of enzyme is effectively autotransfused into the patient during the subsequent period. This process does not require the presence of an oxime. OP is rapidly hydrolyzed in the bloodstream after exposure and has no further action on the released AChE. The amount of enzyme released from the carbamylate complex is sufficient to restore neuromuscular transmission because of the safety margin that exists at the synapse. However, in severe cases of OP poisoning, life support measures are necessary to bridge the gap between OP attack on the synapse and restoration of the AChE level through the autotransfusion.

**Anesthetic Implications of Pyridostigmine Pretreatment.** The anticholinergic actions of pyridostigmine have considerable relevance to normal anesthetic practice. Butaryl cholinesterase, a determinant of the metabolism of succinylcholine, is also inhibited, and prolonged action of this drug may be expected in patients taking pyridostigmine.\textsuperscript{75} The carbamate neostigmine is usually given at the end of an operation to reverse the action of nondepolarizing neuromuscular blocking drugs. Pretreatment with a carbamate in a patient who is not subsequently exposed to OP may be expected to produce some resistance to the action of the neuromuscular blocker. Experimental studies indicate that pyridostigmine does not alter the overall characteristics of neuromuscular block in an isolated human forearm, and the neuromuscular effects may be minimal, particularly because more central muscles of respiration such as the diaphragm have a higher safety margin of neuromuscular transmission and are less affected by the pyridostigmine pretreatment.\textsuperscript{76}

Estimations of the degree of neuromuscular block using fade relationships such as the train-of-four\textsuperscript{77} theoretically may be affected by pyridostigmine pretreatment because the determinant of fade is feedback to the prejunctional cholinergic receptor\textsuperscript{78} (see also Chapter 18). The hysteresis loops for the onset and offset of fade and paralysis relationships in the isolated forearm are not affected by pyridostigmine pretreatment.\textsuperscript{76} The civilian anesthesia provider is referred to more specialized military texts\textsuperscript{36,41} for a more complete discussion of pyridostigmine and its clinical actions.

**Vesicant Agents**

Vesicant agents were first used as chemical weapons during World War I.\textsuperscript{42} The most well known is sulfur mustard (1917, commonly known as mustard gas). It was used as a disabling agent and has a long latency of 2 to 4 hours. Its successor, lewisite (1919), an arsenic-based compound (2-chlorovinyl dichloroarsine), is more volatile, has a short latency, and causes immediate eye pain in addition to its vesicant properties.\textsuperscript{46} Sulfur mustard is the most commonly encountered vesicant. Although an early chemical warfare agent, it is still widely distributed around the world and its easy synthesis makes it a possible agent for use by terrorists. It has a number of pathologic properties that make it of concern to anesthesia providers. The overall management of mustard gas injury is the domain equally of the surgeon and specialized pulmonary physician.\textsuperscript{36,79,80} Intensive care unit (ICU) management presents longer term problems that are mainly respiratory. Eye and skin injuries fall within the aegis of other specialties.

**Properties**

Sulfur mustard (bis-2-chloroethyl sulfide) is a colorless or pale yellow, oily liquid that smells faintly of mustard. Its odor threshold is 1.3 mg/m\textsuperscript{3}, which is below the concentrations usually reached in a battlefield, and several minutes of detection are possible before incapacitating doses are reached. The LC\textsubscript{50} is approximately 1500 mg/min/m\textsuperscript{3}. Although the latency of action in cooler climates is approximately 4 hours, information from the Iran-Iraq War, the scene of its most recent use,\textsuperscript{81,82} indicates that at higher ambient temperatures, the agent has a far shorter latency and causes significant respiratory damage apart from its classic action as a skin vesicant.

**Signs and Symptoms**

After exposure to mustard gas, a latent period of 4 to 12 hours occurs, after which ocular symptoms comprising eye pain, blurred vision, and lachrymation are experienced, accompanied by a diffuse erythema of exposed skin with edema and first-degree burns. The groin and genital areas are particularly susceptible. Exposure to high doses produces severe cutaneous injury with necrosis. The burns bear some resemblance to thermal burns, but are very slow to heal and prone to secondary infection.
The bullae characteristic of exposure to mustard agent are filled with a fluid that is not corrosive (Fig. 83B-5). A feature of exposure is that fluid-filled bullae appear for several days afterward in an apparently random way (i.e., not cropped). The eyes are particularly vulnerable to mustard gas, causing a usually temporary blindness (Fig. 83B-6). The fluid in the bullae has itself no vesicant effect.

Respiratory Effects
The respiratory effects of mustard gas exposure are potentially serious, particularly when the ambient temperature is high. After exposure, an early tracheobronchitis with dry cough and hoarseness occurs. Heavy exposure will produce severe damage to the tracheal and main bronchial architecture with necrosis, sloughing, and blockage (Fig. 83B-7). A chemical bronchiolitis occurs at lower doses in high ambient temperatures and causes severe bronchospasm, requiring ventilation and intensive care. Lung damage after mustard gas exposure can be severe and permanent, with chronic obstructive pulmonary disease, bronchiectasis, and reactive airways dysfunction syndrome.

Cellular Action of Mustard Agent
Sulfur mustard agent acts at a cellular level forming highly reactive sulfonium ions, which attack DNA by alkylation of sulfhydryl and amino groups. This causes the epithelial manifestations of exposure and also long-term carcinogenesis, particularly of the skin, pharynx, and respiratory tract.

Treatment
Mustard gas exposure has no specific treatment, but experimental studies in animals have shown a combination of sodium thiosulfate, vitamin E, and dexamethasone...
can improve survival and reduce organ damage. The key points of treatment are (1) the need for decontamination, (2) the latent period of action, and (3) respiratory support for exposure affecting the respiratory tract. Willems reviewed information concerning the clinical management of mustard gas casualties and found that a proactive approach to airway management and ventilation was evident with endotracheal intubation done early to allow adequate ventilation and assess for debridement of the large airways. Willems reported that the onset of severe respiratory symptoms is a serious development, with a loss of 87% of patients who required ventilation. Another point of concern for longer term management is the leukopenia that follows exposure to mustard gas. This becomes evident 3 to 5 days after exposure and usually reaches its lowest point 7 to 9 days after exposure. Cellular replacement, either peripherally or as marrow, could be considered here because mustard is bound very quickly in the body after exposure and will not cause destruction of new cells.

**Recent Clinical Evidence**

The Iran-Iraq war during the 1980s saw the extensive use of sulfur mustard and produced a significant amount of clinical information about casualties with both cutaneous and respiratory injuries. The treatment given reflects the experience gained in the treatment of burn injuries since its first use. Decontamination was achieved early to limit the contact time with the agent. Because of the long latency of mustard gas, vesicle formation was often not present at this time. Shaving of the affected areas was done and dilution of the agent by irrigation. The management of the vesicles followed the pattern of aspiration, removal of necrotic tissue, and the use of silver sulfadiazine cream. From the anesthetic standpoint, the respiratory effects found in the casualties were important and unprecedented from the use of mustard in the lower temperature conditions of World War I. Chemical bronchiolitis giving rise to increased airway resistance was reported, together with soiling of the larger airways due to sloughing. Intermittent positive-pressure ventilation with positive end-expiratory pressure was required with ICU support for the more seriously injured cases. Many of these were managed in hospitals around Europe, introducing chemical warfare injury to many anesthesia providers and intensivists for the first time. For the casualties who reached definitive hospital care, the recovery period was often a long one, and patients had cachexia with significant negative nitrogen balance.

**LUNG-DAMAGING AGENTS**

Lung-damaging agents were formally known as choking agents, a term that does not adequately describe the many levels of the lung at which they act. Lung-damaging agents act at both the upper and lower respiratory tract levels, but their main lethal action is to cause toxic pulmonary edema. Lung-damaging agents were the first to be used as chemical weapons during World War I, with the use initially of chlorine, followed by phosgene. These agents are a universal hazard in military and civilian populations because they are also used widely as industrial feed stocks in many chemical engineering processes. The isocyanates are widely used in this respect, and the accidental release of methyl isocyanate at Bhopal, India in 1984 caused the largest number of casualties ever recorded after toxic release in either war or peace, with over 5000 deaths from toxic pulmonary edema. Chemical warfare and HAZMAT sources list many lung-damaging agents.

**Phosgene**

Phosgene has been used as a chemical warfare agent, is an established worldwide industrial hazard, and may be regarded as a potential terrorist threat. It is a model for consideration of other hazards in its class. Phosgene is carbonyl chloride, familiar to earlier anesthesia providers as the product of the reaction of trichloroethylene with soda lime used in circle absorbers. First synthesized in the nineteenth century, phosgene has been in industrial use for over a century but achieved notoriety during World War I, when it was used extensively by both sides from 1915 onward. It caused more than 85% of all deaths from chemical warfare agents. Phosgene is a gas at normal temperatures and is nonpersistent. It is less water-soluble than chlorine, its immediate chemical warfare predecessor in 1915, a feature that results in the gas being taken further down the respiratory tree and into the alveoli. Phosgene has been known since World War I to have a dual latency of action, which underlies its essentially dangerous character. The stages after exposure are as follows:

- **Stage 1**: Immediately after exposure, intense upper respiratory irritation occurs, with coughing, retching, choking, and chest tightness. These symptoms are accompanied by eye irritation and lacrimation. In some cases, death followed exposure to high concentrations of phosgene without development of toxic pulmonary edema. The reason for this is obscure, but it may be related to hypoxia as a result of intense laryngeal or bronchospasm.
- **Stage 2**: The immediate choking symptoms are followed by a latent period of 2 to 24 hours before the onset of more serious symptoms and signs, including dyspnea,
painful cough, and cyanosis, with increasing signs of pulmonary edema leading to circulatory collapse and cardiac arrest.

**Pathophysiology of Toxic Pulmonary Edema.** The lung is a delicately balanced system in which the entire cardiac output passes through the pulmonary circulation arranged as a fine capillary mesh in the interstitial space (a loose organization of collagen, elastin, and various cell types). Because of its fragile organizational nature, the lung commonly reacts to toxic challenge by producing pulmonary edema, in which fluid flows from the capillaries to the interstitial space and then to the interalveolar space. Phosgene reacts through covalent attack on many substrate groups, including, NH₂ and SH.⁸⁸ Potential cell targets are type I and II pneumocytes and alveolar macrophages. Covalent binding can be seen as the primary attack leading to free radical release. This stage is followed by a secondary attack involving released inflammatory mediators, including prostaglandins (causing vasoconstriction, vasodilatation, and platelet aggregation), bradykinin (causing increased capillary permeability), S-hydroxytryptamine (causing constriction of postcapillary vessels), thromboxane A₂ (causing vasoconstriction), and the release of complement activating enzymes (leading to attraction of leukocytes and leukotriene release).

**Management of Phosgene Exposure.** Patients who have been exposed to phosgene should be removed from the site of exposure as quickly as possible by protected emergency responders. There is usually no requirement for decontamination unless liquid contamination has occurred. Phosgene has no specific antidote, and treatment is based around use of supportive measures and pharmacologic modification of the effects of the inflammatory mediator cascade.⁸⁷ One of the firm rules for the management of phosgene exposure dating from World War I was complete bed rest after exposure and observation for 24 hours, and this still applies. No patient who has had a risk for significant exposure should be discharged from the hospital in less than 24 hours unless accompanied by a responsible observer. Provision of specialized respiratory care both at the prehospital and hospital level is necessary. Some cases may require early intubation and ventilation, and more will require O₂ and supported ventilation at the prehospital and hospital level. Some cases may require early intubation and respiratory care both at the prehospital and hospital level, and the release of complement activating enzymes (leading to attraction of leukocytes and leukotriene release).

**Use of Steroids.** The use of inhaled and systemic steroids in the treatment of toxic phosgene exposure has been controversial.⁹² Recently, however, chlorine has produced some encouraging results in both pig and rat studies. Gunnarsson and associates⁹³ found that in a study of 18 pigs subjected to 140 ppm chlorine for 10 minutes of inhaled beclomethasone dipropionate produced higher PaO₂ and ventilation-perfusion ratios, with less histologic damage, than the control group. In another study, Wang and colleagues⁹⁴ exposed 24 pigs to a higher concentration of 400 ppm for 10 minutes and found that the inhaled steroid budesonide 0.1 mg/kg given within 30 minutes of exposure was associated with more favorable cardiorespiratory symptoms and lower wet lung weights at autopsy. Demnati and co-workers⁹⁵ studied the effects of dexamethasone in rats exposed to a high concentration of chlorine (1500 ppm for 5 minutes). They found that the dexamethasone group had significantly reduced pulmonary airway resistance and methacholine-induced bronchoconstriction than the controls. However, species differences in challenges to chemical warfare agents dictate caution when applied to humans. In a clinical area in which few therapeutic options are available, the results provide encouragement for further research and for clinical intervention if the need arises. Borak and Dille⁹⁶ reviewed the available evidence for treatment regimens in human phosgene exposure.

**Role of Cyclic Adenosine Monophosphate Diesterase Inhibitors.** Kennedy and colleagues⁹⁷ suggested that amiphylline may protect against phosgene-induced phosgene exposure as a result of its ability to increase cyclic adenosine monophosphate levels. Other compounds, including β-adrenergic agonists, also have this effect and may indicate a new therapeutic direction.

**Phosgene and Glutathione Modification.** Another promising therapeutic approach is provided by compounds that can increase intracellular reduced glutathione levels as a means of preventing lipid peroxidation-induced phosgene exposure. The rationale behind this approach is that phosgene reacts with cellular SH groups, reduces reduced glutathione redox state, and increases arachidonic acid mediator production and lipid peroxidation. Sciuto and co-workers⁹⁸ studied the effects of N-acetylcysteine on anesthetized rabbits exposed to 1500 ppm phosgene. The N-acetylcysteine–treated group had smaller increases in pulmonary wet weight, lower leukotriene levels, and higher glutathione levels. This work suggests that N-acetylcysteine may protect against phosgene exposure by maintaining reduced glutathione levels and inhibiting production of inflammatory leukotrienes.
CELLULAR TOXIC AGENTS (BLOOD AGENTS): HYDROGEN CYANIDE

Hydrogen cyanide (HCN) is one of several agents known originally as blood agents, although the term is a misnomer because the agent acts at the cellular mitochondrial level.99 HCN is a highly volatile liquid used widely in industry and potentially available to terrorists. It has been used since World War I as a chemical warfare agent. Its very short persistence means that decontamination is usually not required after release. It is not absorbed by the activated charcoal of level C respirators (see the section on Involvement of the Anesthesia Provider in the Management of Casualties From Exposure to Chemical and Biologic Warfare Agents), but is removed by impregnating the charcoal with silver salts, with which HCN reacts. HCN in high concentrations is rapidly fatal. The LC₅₀ has been estimated at 200 mg/m⁻³ for 10 minutes. HCN acts by binding to the iron atom in cytochrome oxidase enzymes inhibiting the catalytic function that allows O₂ to act as an electron receptor and produce adenosine triphosphate. Because of this mitochondrial uncoupling, the resulting lactic acidosis theoretically cannot be reversed by restoring oxygenation of the blood by resuscitation measures to improve tissue oxygenation.

Signs and Symptoms

After exposure in humans, the first sign is hyperventilation, which has the effect of increasing the absorbed dose. This is followed by dizziness, rapid loss of consciousness, and seizures, followed by respiratory arrest. At levels that are not fatal, patients report a smell of almonds, a feeling of apprehension, and a metallic taste in the mouth; dyspnea also may occur. Because of the rapid action of HCN, patients with acute intoxication are unlikely to be encountered in hospital. Long-term management of the consequences of HCN poisoning is unlikely, although survivors of near fatal doses can suffer long-term effects, such as intellectual deterioration, mental confusion, and parkinsonism.

Treatment

In the body, HCN is broken down by rhodanese, which detoxifies cyanide to thiocyanate.100,101 This process can be accelerated by provision of sodium thiosulfate, which provides a store of sulfane sulfur for the enzyme.102 The usual dose of sodium thiosulfate is 50 mL of 25% solution (pediatric dose 1.65 mL/kg of 50% solution). It is usually administered in conjunction with sodium nitrite (300 mg given intravenously over 10 minutes [pediatric dose 0.15 to 0.33 mL/kg of a 3% solution]), which causes the formation of methemoglobin. This acts as a scavenger for HCN and reduces its plasma levels. Sympathomimetic support may be required for hypotension produced by sodium nitrite. HCN also reacts with heavy metals, and this is the basis of the use of dicobalt edetate and hydroxyco- balamin as cobalt providers for this reaction. Cobalt ions themselves are toxic, but the toxicity can be countered by giving glucose, which is part of standard therapy. Dicobalt edetate is thought to be more effective in the binding of cyanide ions than methemoglobin despite its secondary effects of hypertension and nausea. It has long been thought that O₂ therapy and ventilation have no role in the treatment of cyanide intoxication because the blood is fully oxygenated in this condition. However, this view has recently been challenged because some studies have shown that O₂ enhances the antidotal effects of the classical cyanide antidotes.103 Table 83B-3 details current antidote treatment approaches.

TOXINS

Toxins are high molecular weight compounds that are in the middle of the CBW spectrum.47 They do not reproduce and have characteristics of chemical warfare agents, although they have been considered with biologic agents by international convention. They are produced naturally by bacteria and by organisms ranging from protozoans up to reptiles such as snakes and scorpions.104 Toxins are hazardous to humans from natural and deliberate exposure, and this has fueled much research into their actions and treatment.105 Scientifically, they are of considerable interest and are used as research tools to probe natural processes such as nerve conduction and neuromuscular transmission. In the context of toxic warfare, toxins have often been cited as doomsday weapons, and considerable public fear exists about their actions. More than 500 toxins have been described, but only a few are suitable for battlefield and terrorist attack because of difficulties in production and their lack of stability in a released aerosol. The characteristics of some common toxins are shown in Table 83B-4.

In the chemical warfare context, the anesthesia provider may encounter toxins as either short latency (neurotoxins, such as botulinum toxin), requiring immediate life support and treatment, or long latency (the DNA toxins, such as ricin), which cause major organ dysfunction and present intensive care problems.

Botulinum Toxin

Botulinum toxin is produced by the anerobe Clostridium botulinum and has the reputation of being the most toxic substance by weight, being at least 5000 times more toxic than sarin.106 Botulism, the natural occurrence of the toxin in food poisoning, is a disease of both humans and animals. Seven different functionally related neurotoxins (A through G) are produced by the parent organism. Botulism is essentially an intoxication, brought on by ingestion of the toxin produced by clostridial infection of food, usually incorrectly canned meats. Primary botulism, a direct infection, is rare and affects only infants in the human species. The interest of botulinum toxin as a toxic agent is that it can be relatively easily produced by fermentation processes (which have been developed to produce antitoxins) and that it is stable as an aerosol, making mass delivery a theoretic possibility. Calculations that 1 kg of the toxin would be sufficient to destroy every human on the planet have rested on this fact. However, botulinum intoxication can be treated, and this modifies the toxicity considerably. It is estimated that less than 10% of natural cases receiving ventilatory and antitoxin support are fatal. A consensus document examines the risks to civilian populations exposed to botulinum toxin.107 Botulinum toxin acts at the nerve terminal of cholinergic synapses and blocks the release of acetylcholine by being taken up into the vesicles and translocated to the
### Table 83B-3: Antidotes Used in the Treatment of Cyanide Poisoning

<table>
<thead>
<tr>
<th>Antidote</th>
<th>Action</th>
<th>Route</th>
<th>Dose</th>
<th>Concurrent Drugs</th>
<th>Duration of Administration</th>
<th>Possible Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>Increases arterial O₂ content, potentiates activity of other antidotes</td>
<td>Inhalation via mask or ETT</td>
<td>High flow via mask or 100% via ETT</td>
<td>O₂ used as primary antidote in all cases</td>
<td>≤24 hr</td>
<td>Unlikely—possible in patients with COPD</td>
</tr>
<tr>
<td>Amyl nitrite</td>
<td>Methemoglobin formation</td>
<td>Inhalation</td>
<td>Adult: 0.2 mL</td>
<td>O₂ (not simultaneously)</td>
<td>30 sec/min</td>
<td>Difficult to achieve effective antidotal levels without cardiovascular collapse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pediatric: 0.2 mL/kg; may need repeating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium nitrite</td>
<td>Methemoglobin formation</td>
<td>Intravenous injection</td>
<td>Adult: 300 mg (10 mL of 30 mg/mL (3%))</td>
<td>Adult: Sodium thiosulfate 25 mL of 500 mg/mL, (50%) solution and O₂</td>
<td>≥5 min, ≤20 min</td>
<td>Methemoglobinemia, vasodilation, and cardiovascular collapse</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pediatric: 0.13-0.33 mL/kg of 30 mg/mL, (3%) solution (i.e., 4-10 mg/kg body weight)</td>
<td>Pediatric: Sodium thiosulfate 1.65 mL/kg body weight of 250 mg/mL (25%) solution (~400 mg/kg body weight) and O₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dicobalt edetate</td>
<td>Binding of cyanide ions by dicobalt edetate and by free cyanide ions</td>
<td>Intravenous injection</td>
<td>Adult: 300 mg (20 mL of 15 mg/mL (15%))</td>
<td>50 mL dextrose (500 g/L) intravenously immediately after each dose and O₂</td>
<td>1 min</td>
<td>Urticaria, edema of face and neck, chest pains, dyspnea, hypotension, seizures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pediatric: 4-7.5 mg/kg (0.3-0.5 mL/kg of 15 mg/mL (15%))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-DMAP</td>
<td>Methemoglobin formation</td>
<td>Intravenous injection</td>
<td>Adult: 3.25 mg/kg</td>
<td>O₂ and sodium thiosulfate</td>
<td>1 min</td>
<td>Methemoglobinemia, vasodilation, and cardiovascular collapse; hemolysis; elevated bilirubin and iron (this is unlikely to be relevant to single-dose exposure)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pediatric: 3.25 mg/kg/ kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydroxycobalamin</td>
<td>Binds cyanide ions</td>
<td>Intravenous injection</td>
<td>Adult: 5-10 g</td>
<td>5 g reconstituted in 100 mL 0.9% saline; O₂</td>
<td>20 min</td>
<td>Reddish discoloration to skin and mucous membranes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pediatric: 70 mg/kg/ kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium thiosulfate</td>
<td>Sulfur donor for endogenous enzymatic conversion of cyanide to thiocyanate</td>
<td>Intravenous injection</td>
<td>Adult: Sodium thiosulfate 25 mL of 500 mg/mL (50%) solution and O₂</td>
<td>O₂ and sodium nitrite or O₂ and DMAP</td>
<td>10 min</td>
<td>Excess administration may cause hematremia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pediatric: Sodium thiosulfate 1.65 mL/kg body weight of 250 mg/mL (25%) solution (~400 mg/kg body weight) and O₂</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

COPD, Chronic obstructive pulmonary disease; ETT, endotracheal tube.

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cytoplasm, where it catalyzes the proteolysis of components involved in the calcium-mediated exocytosis of acetylcholine. The inhibition is permanent, and recovery occurs only after the creation of new terminal boutons. The toxin thus blocks neurotransmission, parasympathetic synapses, and peripheral ganglia. The signs and symptoms of botulism can be explained on this basis.

Conventionally, after ingestion of the toxin (the usual route), a latent period of several hours occurs, after which the parasympathetic action produces a dry mouth, followed by signs of a progressive bulbar palsy (dysarthria, dysphagia, and dysphagia) and ocular signs (diplopia and ptosis). These signs are followed by a progressive symmetric descending muscular weakness, leading to respiratory failure requiring prolonged ventilatory support. Neuromuscular testing shows a classic presynaptic decremental pattern to repeated stimuli with posttetanic facilitation. Single-fiber electromyography detects the neuromuscular changes before conventional nerve stimulation; increased jitter and blocking occur, which are reduced by increasing the nerve firing rate. The pattern of signs and symptoms after a deliberate mass inhalation release is not known, but botulinum toxin must be considered along with the nerve agents in any cases manifesting with sudden disturbances of cholinergic transmission.

Conventional level C protection (see section on Personal Protection) and decontamination procedures are effective against the toxin, and several antiserum agents are available. A heptavalent antitoxin exists for all the serotypes, but the human efficacy is not known with certainty. Established cases require supportive treatment with antitoxin and positive-pressure ventilation. The latter may be required for some time.

**Saxitoxin**

Saxitoxin has been suggested as a possible terrorist toxic agent, but no record exists of its production or use in a military context. In nature, it is produced by dinoflagellate sea organisms (causing the “red tide”) including *Alexandrium tamarense, Gymnodinium catenatum, and Pryridinium bahamense*. The toxin is concentrated in shellfish and is the cause of paralytic shellfish poisoning. The toxin is approximately 20 times more toxic than sarin, having an LD50 in mice of 8 μg/kg. Saxitoxin is active by the inhalation route and causes bulbar palsy, respiratory failure, and cardiovascular failure. The toxin acts by blocking voltage-gated sodium channels. Treatment is based on ventilatory and organ support. An antitoxin has been developed in guinea pigs.

**Ricin**

Ricin is considered a serious terrorist threat because it can be extracted relatively easily from the seeds of the castor bean plant, *Ricinus communis*. Waste from the production of castor oil contains approximately 5% ricin, making it a potential source for terrorists. Ricin has been used in assassinations, and high inhaled concentrations are thought to be fatal. A substantial latent period occurs before generalized signs and symptoms of the inhibition of protein synthesis, which include fever, abdominal pain, diarrhea, weakness, drowsiness, confusion, seizures, coma, cardiovascular collapse, and respiratory failure, all progressing to multiple organ failure and death within 36 to 72 hours. Ricin poses a considerable ICU problem. Treatment is supportive, but an antitoxin has been developed for use in animals.

**PHARMACOLOGIC AGENTS AND AGENTS OF BIOLOGIC ORIGIN**

The events in the Moscow theater siege in 2002 highlighted the possible use of substances that were originally developed as anesthetic agents or adjuncts used as “knock down” weapons. In the siege, a substance was released into the air-conditioning system by special forces entering the theater, which led to the deaths from respiratory failure of 127 of 800 of the hostages. The event emphasized the need for immediate life support after toxic attack with short-latency agents. The Russian government, after challenge, declared that the agent used was “fentanyl.” Many fentanyl agents have been synthesized.

---

**TABLE 83B-4 CHARACTERISTICS OF COMMON TOXINS**

<table>
<thead>
<tr>
<th>Source</th>
<th>Toxin</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Bacillus anthracis</em></td>
<td>Anthrax toxin</td>
<td>DNA toxin</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Staphylococcal enterotoxin B</td>
<td>Enterotoxin</td>
</tr>
<tr>
<td><em>Vibrio cholera</em></td>
<td>Cholera toxin</td>
<td>Enterotoxin</td>
</tr>
<tr>
<td><em>Clostridium botulinum</em></td>
<td>Botulinum toxins</td>
<td>Prejunctional decrease in acetylcholine release</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>Perfringens toxin</td>
<td>Necrosis through phospholipase C</td>
</tr>
<tr>
<td><em>Clostridium tetani</em></td>
<td>Tetanus toxin</td>
<td>Neurotoxin increase in excitability of motor neurons</td>
</tr>
<tr>
<td><strong>Protozoa</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Gonyaulax catenella</em></td>
<td>Saxitoxin</td>
<td>Depolarization block</td>
</tr>
<tr>
<td><strong>Fungi</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Fusarium spp.</em></td>
<td>Tricothecenes</td>
<td>DNA toxin; hemorrhagic syndrome</td>
</tr>
<tr>
<td><strong>Plants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Ricinus communis</em> (castor bean)</td>
<td>Ricin</td>
<td>DNA toxin; hepatorenal Na+ channel blockade failure</td>
</tr>
<tr>
<td><strong>Amphibia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colombian frog</td>
<td>Batrachotoxin</td>
<td>Irreversible; Na+ channel blockade</td>
</tr>
<tr>
<td><strong>Reptilia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian cobra <em>(Naja naja oxiana)</em></td>
<td>Cobra toxin</td>
<td>Postsynaptic neurotoxin via phospholipase A2</td>
</tr>
<tr>
<td>Taiwan banded krait <em>(Bungarus multicinctus)</em></td>
<td>α-Bungarotoxin</td>
<td>Acetylcholine receptor blocker</td>
</tr>
<tr>
<td><strong>Fish</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deadly pufferfish</td>
<td>Tetrodotoxin</td>
<td>Na+ channel blockade</td>
</tr>
</tbody>
</table>


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apart from those familiar in clinical practice and some are too toxic for general use. Another possibility is the use of a short-chain neuropeptide. Considerable research effort went into investigating such compounds during the last days of the USSR. Agents such as 3-quinuclidinyl benzilate (BZ or agent-15) (also initially considered as a possible cause of the theater casualties) have been used for many years and are centrally acting anticholinergic agents. Phencyclidine compounds (related to ketamine) and other hallucinogens were tested during the early days of chemical warfare research during the Cold War and should be considered as part of the differential diagnosis of patients presenting with central nervous system symptoms after a possible toxic attack.

CLASSIC BIOLOGIC WARFARE AGENTS

General Considerations

Although many organisms have been suggested as being capable of use as biologic warfare agents, only a few have been studied to the point of being a threat rather than a hazard. Management of deliberate epidemics is the role of specialist physicians, and anesthesia providers are likely to encounter only agents that have serious pulmonary effects and are likely to require ICU care. Many analogies from normal epidemic outbreaks are relevant to deliberate biologic warfare attacks, particularly by terrorists. The severe acute respiratory syndrome (SARS) epidemic in 2004 was a valuable lesson about the spread of a new infectious pathogen in a world linked by fast air travel connections. Although previous slower forms of travel allowed the incubation of symptoms before arrival at the destination, air travel does not, and patients may be asymptomatic at the time of their arrival. All hospital practitioners must now be aware of the possibility of transmission of infection from distant locations. Recent travel history should be an essential part of the initial patient interrogation process.

Anthrax

*Bacillus anthracis*, an aerobic gram-positive, spore-forming, rod-shaped organism, is one of the few listed “standard” biologic warfare agents that has been proved to be a hazard and a weaponized threat. The natural reservoir of the disease is spores in the soil, and it is these highly resilient spores than form the basis for its use as a biologic agent. During tests in World War II, a whole Scottish island was experimentally contaminated and remained in this condition for over 40 years. Evidence for weaponization of the bacillus by several other countries has been presented. An accidental release from a military installation in the USSR in 1979 claimed more than 100 lives. The Iraq War in 2003 was fought under the shadow of a possible anthrax attack, although no such weapons were found. Although the standard biologic warfare release is by aerosolization of the spores, the agent was distributed in the United States by mail as a powder in 2001 and claimed several lives, demonstrating its terrorist use.

Anthrax exists in cutaneous, gastrointestinal, and pulmonary forms, but the pulmonary form is the major concern of the anesthesiology provider and intensivist. In its natural state, pulmonary anthrax is rare, but deliberate release of spores in an aerosol would make the presentation more common.

**Physical Findings.** The physical findings in pulmonary anthrax are nonspecific, but chest radiography may show signs of effusion or pulmonary edema and mediastinal widening. An immunoassay is available that can detect circulating toxin. The infective dose of anthrax when inhaled is 8000 to 15,000 spores. Spores between 2 and 5 μm reach the alveoli; spores greater than this size are trapped in the upper airways. After trapping, the spores are removed to the mediastinal and hilar lymph nodes by pulmonary macrophagocytes. After a germination period of 1 to 3 days, large amounts of anthrax toxin are released into the circulation, causing the clinical manifestations of the pulmonary form of the disease. An initial insidious phase lasting 1 to 4 days consists of general malaise, fatigue, myalgia, nonproductive cough, and fever. During the next phase of the pulmonary disease, a necrotizing hemorrhagic mediastinitis occurs causing chest discomfort, dyspnea, and stridor. In untreated cases, multiple organ failure follows, which is very refractory to treatment and causes death within 24 to 36 hours. In 50% of cases, hemorrhagic meningitis with coma occurs.

**Pathogenesis.** Considerable work has been done on the mechanism of the pathogenesis of anthrax infection and the effects of the toxin. This consists of three proteins with a central protective component binding the other two, known as the edema and lethal factors. After transfer to the cytoplasm edema factor, a calmodulin-dependent adenyl cyclase converts adenosine triphosphate to cyclic adenosine monophosphate, which in turn causes tissue edema and suppression of the oxidative burst associated with polymorphonuclear phagocytosis. Lethal factor is thought to be associated with macrophage expression of tumor necrosis factor and interleukin-1, cytokines that are a fundamental part of the systemic inflammatory response.

**Treatment.** Treatment of anthrax infection has classically been founded on the use of benzylpenicillin, but evidence of resistance has been reported. The current antibiotic recommendation is to use ciprofloxacin 400 mg every 8 hours, and this was widely used as prophylaxis during the 2001 anthrax attacks in the United States. Other approaches may be more appropriate, including doxycycline 200 mg intravenously followed by 100 mg intravenously every 8 hours, gentamycin, erythromycin, or chloramphenicol (Table 83B-5).

The recommended antibiotic prophylaxis is ciprofloxacin 500 mg every 12 hours or doxycycline 100 mg every 12 hours orally. This should be started as soon as possible after exposure. Vaccines have been studied, and the standard Michigan vaccine should be given at 0, 2, and 4 weeks and then at 6, 12, and 18 months, followed by annual boosters. If vaccines are unavailable, antibiotic prophylaxis should be continued for 60 days. For anesthesia providers, intensivists, and other staff working on the longer term care of patients with anthrax, prophylaxis is important, together with careful filter protection of ventilation and disinfection. Wherever possible, disposables should be used.
<table>
<thead>
<tr>
<th>Agent</th>
<th>Infective Dose</th>
<th>Incubation Period</th>
<th>Effects (After Inhalation)</th>
<th>Staff Protection</th>
<th>Specific Treatment</th>
<th>Chemoprophylaxis</th>
<th>Vaccine</th>
<th>Mortality if Untreated</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bacillus anthracis</em></td>
<td>8000-15,000 spores</td>
<td>1-5 days</td>
<td>Mediastinitis, meningitis, MOF</td>
<td>Isolation, vaccination, universal precautions</td>
<td>Ciprofloxacin 400 mg IV tid; doxycycline 200 mg IV once, then 100 mg IV tid; penicillin 2 million units IV 2 hourly plus streptomycin 30 mg/kg IM daily</td>
<td>Ciprofloxacin 500 mg PO bid × 4 wk + vaccine; doxycycline 100 mg PO bid × 4 wk + vaccine</td>
<td>Michigan at 0, 2, 4 wk, 6, 12, 18 mo, then annually</td>
<td>Pneumonic, 100%</td>
</tr>
<tr>
<td><em>Yersinia pestis</em></td>
<td>100-500 organisms</td>
<td>2-3 days</td>
<td>Pneumonia, septicemia, MOF</td>
<td>Isolation, universal precautions</td>
<td>Streptomycin 30 mg/kg IM daily × 10 days; doxycycline 200 mg IV, then 100 mg IV tid × 14 days</td>
<td>Doxycycline 100 mg PO bid × 7 days; tetracycline 500 mg PO daily × 7 days</td>
<td>Greer at 1-3 mo plus 3-6 mo</td>
<td>Pneumonic, 100%</td>
</tr>
<tr>
<td>Viral hemorrhagic fevers</td>
<td>1-10 organisms</td>
<td>4-21 days</td>
<td>Coagulopathy, edema, MOF</td>
<td>Isolation, HEPA masks, universal precautions</td>
<td>Ribavirin 30 mg/kg IV once, then 15 mg/kg IV daily × 4 days, then 7.5 mg/kg IV tid × 6 days (chloramphenicol)</td>
<td>NA</td>
<td>None</td>
<td>90% (Ebola-Zaire)</td>
</tr>
<tr>
<td>Viral encephalitides</td>
<td>10-100 organisms</td>
<td>2-6 days (VEE)</td>
<td>Encephalitis, seizures, coma, CNS damage</td>
<td>Universal precautions</td>
<td>Supportive, anticonvulsants</td>
<td>NA</td>
<td>Available for VEE, EEE, and WEE</td>
<td>75% (EEE)</td>
</tr>
<tr>
<td><em>Francisella tularensis</em></td>
<td>10-50 organisms</td>
<td>2-10 days</td>
<td>Pneumonia, pleural effusions</td>
<td>Universal precautions</td>
<td>Streptomycin 30 mg/kg IV daily × 10-14 days; gentamicin 3-5 mg/kg IV od</td>
<td>Doxycycline 100 mg PO bid × 14 days</td>
<td>Live attenuated</td>
<td>35%</td>
</tr>
<tr>
<td><em>Varicella</em></td>
<td>10-100</td>
<td>7-10 days</td>
<td>Rash, secondary pneumonia</td>
<td>Isolation, universal precautions</td>
<td>Cidofovir 5 mg/kg IV once every 2 wk</td>
<td>Vaccinia immunoglobulin</td>
<td>Wyeth</td>
<td>Unvaccinated 30%, vaccinated 3%</td>
</tr>
<tr>
<td><em>Burkholderia mallei</em></td>
<td>1-10 organisms</td>
<td>10-14 days</td>
<td>Septicemia, pneumonia, lymphadenopathy, fever</td>
<td>Universal precautions</td>
<td>Co-amoxiclav 20 mg/kg IV tid</td>
<td>Tetracycline 500 mg PO daily × 14 days</td>
<td>None</td>
<td>Uncertain: &gt;30% if septicemic &lt;1%</td>
</tr>
<tr>
<td><em>Coxiella burnetii</em></td>
<td>1-10 organisms</td>
<td>10-14 days</td>
<td>Myalgia, malaise, fever</td>
<td>Barrier nursing</td>
<td>Doxycycline 100 mg PO bid × 5-7 days after exposure × 5 days</td>
<td>Doxycycline 100 mg PO bid for 8-12 days</td>
<td>Q vax</td>
<td>5%</td>
</tr>
<tr>
<td><em>Brucella</em> spp.</td>
<td>1-100 organisms</td>
<td>5-60 days</td>
<td>Malaise + cough, sacroiliitis, pancytopenia</td>
<td>Barrier nursing</td>
<td>Doxycycline 100 mg PO bid plus rifampicin 900 mg tid PO for 6 wk</td>
<td>Doxycycline and rifampicin for 3 wk</td>
<td>None</td>
<td>&lt;5%</td>
</tr>
<tr>
<td><em>Escherichia</em></td>
<td>1-100 organisms</td>
<td>1-5 days</td>
<td>Vomiting and diarrhea, renal failure</td>
<td>Barrier nursing</td>
<td>Antibiotics not required</td>
<td>NA</td>
<td>None</td>
<td>&lt;5% E. coli O157:H2</td>
</tr>
</tbody>
</table>


CNS, Central nervous system; EEE, eastern equine encephalitis; HEPA, high-efficiency particulate air filter; IM, intramuscularly; IV, intravenously; MOF, multiple organ failure; NA, not applicable; PO, orally; VEE, Venezuelan equine encephalitis; WEE, western equine encephalitis.
PART V: Adult Subspecialty Management

Plague

Plague was the scourge of the medieval world, and natural outbreaks continued well into the twentieth century. Plague has long been considered a potential biologic warfare agent and was researched extensively by the USSR.44 The pulmonary form is very serious and requires ICU support. The causative organism, *Y. pestis*, is an anaerobic, gram-negative coccobacillus transmitted to humans by fleas carried by rodents or by animal-human or human-human droplet infection.117,118 Bubonic, pneumatic, and septicemic forms of plague exist; the latter two are fatal without treatment. Only approximately 100 to 500 organisms constitute an infective dose. The incubation period is 2 to 3 days, after which a pneumonia develops with malaise, high fever, myalgia, hemoptysis, and finally septicemia. There is dyspnea, stridor, and cyanosis. With the worsening condition, intermittent positive-pressure ventilation is required with aggressive antibiotic treatment. Confirmation of the diagnosis comes from the causative organism in blood, lymph nodes, or sputum cultures. An enzyme-linked immunosorbent assay is available. Pneumonic plague has long been recognized as being fatal, but antibiotic treatment reduces the mortality to at least 60%. The first line of treatment is streptomycin 30 mg/kg every 12 hours for 10 days. Alternatives are gentamycin or chloramphenicol. An inactivated vaccine (Greer vaccine) is available, but its effectiveness is not thought to be high.

Cholera

Cholera is a widespread natural infection originating from the Far East, which caused several epidemics in Europe throughout the nineteenth century. Although cholera is in the domain of the specialized physician, the profound fluid imbalances caused by the disease make admission of patients to the ICU likely in severe cases. Cholera has been suspected of being weaponized, but it can be spread effectively only by causing mass poisoning through the water supply. Outbreaks occurring in China during World War II were thought to be caused in this way.42

Pathogenesis. The infection is localized to the small bowel and causes a major outpouring of fluid and electrolytes. Paradoxically, fluid can still be absorbed, and this is the basis of the use of oral rehydration solutions in mass outbreaks in developing countries.

Treatment. The management of cholera is essentially fluid and electrolyte replacement. Traditionally, the intravenous route was used, but modern practice is to use oral rehydration solutions containing electrolytes and glucose.119 Early rehydration in this way avoids the need for admission to the ICU. In the case of a deliberate cholera epidemic, early rehydration would be a high priority for treatment of mass casualties. Tetracyclines have traditionally been the antibiotic treatment of choice but resistance has been reported.119

Glanders

Glanders is an equine disease caused by the gram-negative bacillus *Burkholderia mallei*. It has long been considered a potential biologic warfare agent in a modified form because the organism is known to be highly infectious in the aerosolized form. Acute and chronic forms occur in humans.120 The septicemic form appears 10 to 14 days after exposure, making the agent one of long latency. It is characterized by a sudden onset of high fever, rigors, and myalgia, with cervical lymphadenopathy, splenomegaly, leukopenia, or leukocytosis. In this form, septic shock and multiple organ failure occur, and the fatality rate without treatment is high. After inhalation of the organism, the acute pulmonary form is seen, with septicemia, bilateral pneumonia, and pulmonary nodular necrosis. The chest radiograph shows miliary shadowing. The severe acute forms of the disease are most likely to concern intensivists, but an oropharyngeal form also occurs with ulceration of the septum and turbinate and a blood-stained mucopurulent discharge and macropapular or pustular rash similar to smallpox. In the chronic form, glanders can produce chronic lymphadenopathy, multiple musculocutaneous abscess formation, and oropharyngeal nodules. The first-line treatment of glanders is an antibiotic combination (co-amoxiclav and sulfadiazine 30 mg/kg−1 every 8 hours for 3 weeks). Doxycycline, rifampicin, and ciprofloxacin are second-line drugs. No vaccine against glanders exists.

Viral Diseases Regarded as Potential Biologic Warfare Hazards

A number of viral illnesses are considered to be potential biologic warfare agents. They are the province of the specialized infectious disease physician, and the anesthesia provider is referred to the specialized texts for a broader discussion.

Smallpox. Of the potential biologic warfare viral disease agents, smallpox is placed high on the potential terrorist hazard list because of the continuing presence of laboratory stocks of virus, which is normally promulgated only through human hosts. The success of the worldwide vaccination campaign led the WHO to declare smallpox an extinct disease, and mass vaccination programs were stopped. However, laboratory studies continued, and there is a fear at present that strains could be stolen and used to create a deliberate widespread epidemic in a largely unprotected population. Intensive care may be required for cases contracting overwhelming secondary infection. Although treatment is based on isolation and supportive therapy, there is current interest in the use of the antivirals cidofovir and ribavirin.121

IN VolvEME OF THE ANESTHESIA PROVIDER IN THE MANAGEMENT OF CASUALTIES FROM EXPOSURE TO CHEMICAL AND BIOLOGIC WARF ARE AGENTS

APPROACHES TO MANAGEMENT OF CHEMICAL AND BIOLOGIC WARF ARE INCIDENTS

Anesthesia providers may be confronted with the management of victims from the deliberate or accidental release of CBW hazards inside and outside the hospital.
A system of management of such cases is essential that provides for the safety of the medical responders and the correct treatment for the patient. Management should be considered in terms of (1) management of the incident and (2) management of the patient’s condition. In terms of the four properties of agents in the CBW spectrum (see the section on Agents of Chemical and Biologic Warfare: Background and Development), management of the incident is determined by persistency and transmissibility, and management of the patient’s condition by toxicity and latency.

Many chemical hazards have very limited persistency, and decontamination is not required. Limited persistency means reduced risk for contact transmission to other persons. However, certain chemical agents have long persistency and thus high transmissibility. Many such agents do not pose a significant threat by inhalation, but may be absorbed through the epithelia (e.g., nerve agent VX). For such agents, careful decontamination is essential.

Most classic biologic warfare agents have low persistency, being rapidly degraded by the environment, and depend on host transmission via an incubation period. In such cases, transmissibility is high. Anthrax is a notable exception; its spores have very long persistency, but no infective transmissibility. At the other extreme, the viral hemorrhagic fevers have very short persistency but high infective transmissibility.

MANAGEMENT OF THE INCIDENT

Disaster planning is a process familiar to many anesthesia providers and provides a good model of how to approach toxic releases. A toxic release is a special case of disaster and may be either accidental or deliberate. Plans put in place for a terrorist release of a CBW agent are equally valuable for the more likely case of accidental release. Moles summarized the essential points of disaster planning as follows:

1. The importance of risk assessment: Not all listed hazards are identifiable risks
2. The essential stage of preplanning: Should bring together all the different emergency agencies, such as fire, civil defense, and police, who would be involved in CBW incident management
3. A phased response: Importance of, based on exercises and assessment

PERSONAL PROTECTION

Protection is a key feature of incident management, and anesthesia providers should be familiar with personal protection levels (Box 83B-5), protective suits and masks, and techniques of decontamination. As Box 83-7 shows, several levels of protection are used in the management of toxic releases, but the appropriate level for medical intervention is level C, which allows reasonable tactile dexterity and contact with the patient to provide essential life support and antidote therapy onsite. Level C protection (Fig. 83B-8) is equivalent to that used by the military to provide protection against the most toxic chemical warfare agents and virulent biologic warfare organisms.

DETECTION AND IDENTIFICATION OF THE HAZARD

Unlike military CBW releases, civil incidents may not provide early information about the nature of the hazard (Box 83B-6). Patterns of signs and symptoms manifesting in victims may be the first indication of the nature of the causative agent. Detection and

BOX 83B-5 Levels of Personal Protection in HAZMAT Incidents

| LEVEL A |
| Positive-pressure SCBA |
| Fully encapsulating chemical-resistant suit |
| Double layer of chemical-resistant gloves |
| Chemical-resistant boots |
| Airtight seal between suit and gloves and boots |

| LEVEL B |
| Positive-pressure SCBA |
| Chemical-resistant, long-sleeved suit |
| Double layer of chemical-resistant gloves |
| Chemical-resistant boots |

| LEVEL C |
| Full-face air-purification device (respirator) |
| Chemical-resistant suit |
| Chemical-resistant outer gloves |
| Chemical-resistant boots |

| LEVEL D |
| Equipment does not provide specific respiratory or skin protection and usually consists of regular work clothes |

SCBA, Self-contained breathing apparatus.

Figure 83B-8. Civil (A) and military (B) level C protective respirators and suits. (Courtesy Service d’Aide Médicale Urgente [SAMU] de Paris, France.)
monitoring devices for established military chemical warfare hazards exist but are not widely available in the civil context. Intelligence information may be available for terrorist attacks. In the case of accidental toxic agent release, information would be available from the HAZMAT system and the appropriate classification codes (see Box 83-3).

**EARLY PATIENT MANAGEMENT AFTER CHEMICAL AND BIOLOGIC WARFARE RELEASE**

If the released hazard is persistent and transmissible, decontamination is essential in the decontamination zone. In some countries, level C–protected medical staff or paramedics can now operate in this area and work alongside fire personnel in providing (1) triage, in terms of whether the patient requires decontamination and the patient’s medical status; (2) immediate life support measures (TOXALS); and (3) immediate antidote and other pharmacologic support.

Figure 83B-9 shows a medically operated chemical warfare casualty reception facility in a Parisian hospital. Early life support measures in the decontamination zone are very important (see also Chapter 107). The concept of TOXALS, introduced in 1996, expands the familiar ABCs of life support to relate to toxic releases as follows:

- **Airway** (see also Chapter 55) of the casualty patient must be obviously maintained at all times. In the unconscious casualty, this may involve simple basic airway maneuvers plus suction of the copious secretions associated with chemical poisoning. Occasionally, advanced airway management, such as tracheal intubation, may be required to protect the airway from the excessive secretions and to prevent aspiration of regurgitated stomach contents.
- **Breathing** must be carefully observed until full decontamination and recovery have occurred. Supplemental O2 will speed the recovery from volatile chemical poisoning. If breathing becomes compromised, artificial ventilation with supplemental O2 must be administered using a self-inflating resuscitation bag-valve-mask or automatic ventilator. Entrained air must be filtered when ventilating casualties in a contaminated environment.
- **Circulation** must be carefully observed and monitored. Noninvasive blood pressure, pulse oximetry, and electrocardiogram monitoring are all useful indicators of circulatory function. The early establishment of intravenous access aids the administration of fluids and drugs.
- **Disability** (conscious level) should be assessed using the simple AVPU scale (Alert, responds to Voice, responds to Pain, Unresponsive). This assessment should be repeated at frequent intervals to assess the progress of the casualty.
- **Drugs**, especially the specific antidotes, should be administered when a specific agent has been identified.
- **Exposure of the casualty** is essential not only to assess physical damage, but also to remove all clothes that have been contaminated by the chemical. Approximately 80% of surface contamination is removed by undressing.
- **Environment.** The primary management as described may be severely limited by the need for the rescuer to wear protective clothing. Only those skilled in these techniques and trained in protective clothing should enter and treat casualties in a contaminated area. All others should await the casualties’ arrival in the cold or clean zone after decontamination.

Identification of the chemical and its specific antidote might take some time. However, this must not delay the basic medical management of the casualty.

**Somatic Systems Affected by Toxic Hazards**

Early patient management is based on (1) identification information and (2) the manifesting signs and symptoms.
symptoms. Usually information will be available to help with identification of the agent used. On the basis of manifesting signs and symptoms, it is useful to consider attacks on the various clinical systems as guide to the agent used (Table 83B-6). A wide range of chemical agents affect the respiratory system. These are summarized in Table 83B-7.

### EFFECTS OF CHEMICAL AND BIOLOGIC WARFARE AGENTS ON SOMATIC SYSTEMS

<table>
<thead>
<tr>
<th>System Affected</th>
<th>Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial</td>
<td>Vesicants (e.g., sulfur mustard), smallpox, ricin</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Vesicants, phosgene</td>
</tr>
<tr>
<td>Upper, lower airway</td>
<td>Nerve agents, ABO</td>
</tr>
<tr>
<td>Respiratory control system</td>
<td>Pulmonary edemagens</td>
</tr>
<tr>
<td>Gaseous exchange</td>
<td>Nerve agents, neurotoxins</td>
</tr>
<tr>
<td>Mechanisms of breathing</td>
<td>Nerve agents, cyanide, neuropeptides, agents of anesthetic origin</td>
</tr>
<tr>
<td></td>
<td>(phencyclidines, BZ)</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>Nerve agents, cyanide, neuropeptides, agents of anesthetic origin</td>
</tr>
<tr>
<td></td>
<td>(phencyclidines, BZ)</td>
</tr>
<tr>
<td>Peripheral nervous system</td>
<td>Nerve agents, neurotoxins (e.g., botulinum, saxitoxin)</td>
</tr>
<tr>
<td>Immune system</td>
<td>Vesicants, ABO (provocation of immune responses, inflammatory responses, organ failure)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Nerve agents, ABO</td>
</tr>
<tr>
<td>Alimentary, renal</td>
<td>Nerve agents, toxins, infectious agents</td>
</tr>
</tbody>
</table>

**ABO,** Agents of biologic origin; **BZ,** quinuclidinyl benzilate.

### EFFECTS OF CHEMICAL AND BIOLOGIC WARFARE AGENTS ON RESPIRATION

<table>
<thead>
<tr>
<th>Respiratory Component</th>
<th>Effect</th>
<th>Toxic Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>Depression of respiratory drive and seizures leading to apnea</td>
<td>Nerve agents, cyanide, neuropeptides</td>
</tr>
<tr>
<td>Peripheral nervous system</td>
<td>Neuromuscular paralysis of respiratory muscles</td>
<td>Nerve agents, neurotoxins</td>
</tr>
<tr>
<td>Nasopharynx</td>
<td>May become blocked by excess secretions</td>
<td>Lung-damaging agents, nerve agents</td>
</tr>
<tr>
<td></td>
<td>Prodrmal rhinitis and rhinorrhea</td>
<td>Vesicants</td>
</tr>
<tr>
<td></td>
<td>Sneezing</td>
<td>Early symptom of mustard agent</td>
</tr>
<tr>
<td>Larynx</td>
<td>Irritation, laryngeal spasm</td>
<td>Upper respiratory irritant, lung-damaging agents</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Riot-control agents, particularly CS and CR (tear gas)</td>
</tr>
<tr>
<td>Large airways</td>
<td>Blocked by secretions</td>
<td>Nerve agents (theoretic)</td>
</tr>
<tr>
<td></td>
<td>Blocked by inhaled vomitus</td>
<td>Various agents</td>
</tr>
<tr>
<td></td>
<td>Sloughing of walls of trachea and main bronchi, produces “pseudophirtheric” membrane, serious cause of large airway obstruction, leading to bronchopneumonia and death</td>
<td>Viscant agents</td>
</tr>
<tr>
<td>Small airways</td>
<td>Blocked by secretions</td>
<td>Nerve agents</td>
</tr>
<tr>
<td></td>
<td>Cholinergic innervation affected; bronchospasm (relieved by atropine)</td>
<td>Viscant agents</td>
</tr>
<tr>
<td></td>
<td>Chemical bronchiolitis, followed by bronchospasm</td>
<td>Viscant agents</td>
</tr>
<tr>
<td>Alveoli</td>
<td>Toxic pulmonary edema</td>
<td>Various agents, especially lung-damaging agents (latency 6-24 hr)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Viscant agents, particularly if inhaled at high ambient temperature</td>
</tr>
</tbody>
</table>


CR, Dibenzoxazepine; CS, 2-chlorobenzalmononitrile (tear gas).

agent on the subsequent conduct of general anesthesia are important. Many of the agents described earlier affect the condition of the patient and the action of anesthetic agents.

EFFECTS ON THE CONDITION OF THE PATIENT

Shock and toxic airway injury can produce ventilation-perfusion inequality, which affects preoxygenation for emergency induction of anesthesia (see also Chapter 55). The respiratory uptake of anesthetic vapors and alveolar ventilation itself are affected by degrees of shunt and pulmonary edema. Above all, the action of toxic agents may be expected to alter the balance and flow of general anesthesia and may cause delays in recovery, which would be labor-intensive in management. In terms of postoperative intensive care, patients who have been exposed to pulmonary edemagen and to OPs may pose the greatest problem (Box 83B-7).

Intensive Care Implications

Chemical warfare agent exposure may cause several syndromes that require medium-term or even long-term ICU treatment. These include pulmonary edema and ARDS. In the case of OP exposure, it is possible intermediate syndrome may develop \(^{125,126}\) with a re paralysis of the patient requiring several days of ventilation. Experience with OP anticholinesterases in this area is lacking, although considerable evidence has been reported from pesticide poisoning.

Many of the infectious agents considered biologic warfare agents can cause infections and even an overwhelming inflammatory response and organ dysfunction. Intensive care is required for cases of systemic inflammatory response syndrome and multiple organ dysfunction syndrome cases (see also Chapter 100). The continued possibility of an avian flu pandemic highlights the need to provide simple mass ventilation systems in high-dependency units. Many patients infected with biologic warfare agents can receive ventilation using simpler machines than those found in the ICU and that can be operated by non-ICU personnel. Mass procurement of devices and training is necessary. The ability of hospitals to provide intermittent positive-pressure ventilation for large numbers of casualties is a necessary step in managing not only epidemics of respiratory disease but also the consequences of a number of the CBW agents in which respiratory failure is the end stage of the pathologic condition.

Complete references available online at expertconsult.com

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