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# Pharmacy Preparedness for Incidents Involving Nuclear, Biological, or Chemical Weapons

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*Recent worldwide terrorist attacks and hoaxes have heightened awareness that more incidents involving weapons of mass destruction (WMD) may occur in the United States. With federal funding assistance, local domestic preparedness programs have been initiated to train and equip emergency services and emergency department personnel in the management of large numbers of casualties exposed to nu-*

*clear, biological, or chemical (NBC) agents. Hospital pharmacies will be required to provide antidotes, antibiotics, antitoxins, and other pharmaceuticals in large amounts and/or have the capability for prompt procurement. Pharmacists should become knowledgeable in drug therapy of NBC threats with respect to nerve agents, cyanide, pulmonary irritants, radionucleotides, anthrax, botulism, and other possible WMD.*

**KEY WORDS:** Antidotes, WMD preparedness, disaster preparedness, chemical warfare, biological warfare.

**E**VENTS SUCH AS the sarin gas attack in a Tokyo subway station in March 1995; the September 11, 2001, attacks; several anthrax hoaxes; and the actual anthrax letters in the United States have heightened concern among public health and law enforcement agencies that a real nuclear, biological, or chemical (NBC) attack may occur in this nation. The potential for a terrorist attack using a chemical or biological agent has many individuals involved in public health and safety equipping themselves with information, contingency plans, and procedures to cope with such threats. Information concerning preparedness for a terrorist attack involving NBC weapons is available from various governmental agencies and other organizations.<sup>1-5</sup> Instruction in this area is available via journal articles, Web sites, on-site and Internet training programs, seminars, and conferences. Most references will provide practical discussion on issues such as local and statewide planning, on-site and hospital decontamination procedures, recognition and detection of NBC agents, diagnosis and pathophysiology of disease states, protocols for first responders, and a variety of other public health issues.<sup>6-10</sup>

The objective of this article is to provide the practitioner a concise summary and description of the types of pharmaceutical products that a health care facility pharmacy may be asked to provide as part of an overall response to an incident involving weapons of mass destruction (WMD). These products include antidotes, antibiotics, antitoxins, and other agents used in the symptomatic and supportive care of the poisoned pa-

tient. Pharmacy managers are urged to check inventory for these products and to know where the nearest supplier (eg, wholesaler, pharmaceutical manufacturer, etc) is located for each agent. It is important to know how supplies can be obtained quickly in emergencies; many health care facilities are unprepared for poisoning emergencies. Small nonurban hospitals are more likely to have fewer antidotes in stock than are larger urban, tertiary care facilities.<sup>11-16</sup> In addition to monitoring inventory, pharmacy managers and pharmacy and therapeutics committee members should be aware of their local or state governmental agencies that may support a depot of some pharmaceuticals. Often, this information is classified and not readily available to individuals not serving on WMD readiness task forces or committees.

The Nunn-Lugar-Domenici Domestic Preparedness Act of 1996 established a \$250,000,000 program to

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train 120 cities in the United States in the preparedness of emergency and medical response to chemical and biological agents.<sup>17</sup> Headed by the Department of Homeland Security, federal agencies involved with domestic preparedness programs include the Department of Energy, Federal Bureau of Investigation, Federal Emergency Management Agency, Environmental Protection Agency, and Centers for Disease Control and Prevention (CDC). Local government bodies created metropolitan medical response systems (MMRS), whose mission is to create a multiple-level, technically diverse, professional response to any deliberate or accidental act involving an NBC agent within that jurisdiction. Antidote caches funded by federal grants to MMRS will be intended for use by emergency medical system (EMS) first responders for self-administration, to treat a number of casualties at the site of the NBC incident, and to provide pharmaceuticals to treat large numbers of hospitalized patients and asymptomatic outpatients. The first 4 to 12 hours of emergency response will need to be managed by local resources prior to the arrival of the Department of Homeland Security and other federal assistance, such as delivery and distribution of the strategic national stockpile (SNS), formerly known as the national pharmaceutical stockpile. Two primary missions of the Homeland Security Act of 2002 are to reduce the vulnerability of the United States to terrorism and to minimize the damage and assist in the recovery from terrorist attacks that occur within the United States.

### THE STRATEGIC NATIONAL STOCKPILE

The CDC, in consultation with other partners in chem/bio preparedness, has developed a stockpile to respond to biological or chemical terrorism emergencies. To determine and review the composition of the SNS, CDC considers many factors, such as current biological and/or chemical threats, the availability of medical materiel, and the ease of dissemination of pharmaceuticals. One of the most significant factors in determining SNS composition, however, is the medical vulnerability of the U.S. civilian population.

SNS depots are stored at strategic locations throughout the United States to assure the most rapid response possible. CDC ensures that the medical material in these SNS storage facilities is rotated and kept within potency shelf life limits.<sup>18</sup>

More information about the SNS program is available at [www.bt.cdc.gov/stockpile](http://www.bt.cdc.gov/stockpile) or by calling the CDC at (404) 639-0459.

The Veteran's Administration (VA) is a part of the National Disaster Medical System and can be asked to

aid local civilian responders. The VA has a role in maintaining the SNS. The VA procures pharmaceuticals for the CDC and manages contracts for the storage, rotation, security, and transportation of these items. It is also responsible for the deployment of up to 5 "push packages" of pharmaceuticals in an emergency. The VA has stockpiled 4 packages of pharmaceuticals and medical surgical supplies for the National Disaster Medical System and has a fifth package that is placed on-site at high-risk national events such as a presidential inauguration.

### Chempack Project

In 2003, the Department of Homeland Security/CDC Strategic National Stockpile Program began pilot testing a project that forward-positions nerve agent antidote and symptomatic treatments at the local hospital and EMS level. The Chempack Project is a sustainable resource that would enhance local response to nerve agent attacks. As a cost-avoiding measure, the Chempack pharmaceuticals are kept fresh with respect to expiration dating via participation in the Food and Drug Administration (FDA) Shelf-Life Extension Program (FDA SLE). It is projected that FDA SLE participation will deliver \$97 million of cost-avoidance savings to taxpayers over 10 years, with the alternative being outright replacement of product when it reaches expiration dating. Hospitals and EMS participation in this project is voluntary. The pilot test was successful, demonstrating project implementation and maintenance procedures to be feasible. The project will expand throughout 2004, with SNS selecting more localities nationwide to position Chempacks. Where Chempacks have been positioned, hospital pharmacists play a lead role, working with SNS and the local health department to receive, secure, and maintain these assets.

Every hospital should have a WMD plan as part of their disaster readiness. The US Army Edgewood Chemical Biological Center and the Army Corps Department of Justice Office of Domestic Preparedness offers training and technical assistance to jurisdictions to help them respond to and mitigate the consequences of domestic terrorism.<sup>19</sup>

### CHEMICAL AGENTS

As defined by the US Army, a chemical warfare agent is a "chemical substance intended for use in military operations to kill or seriously injure or incapacitate humans or animals through its toxicologic effects."<sup>20</sup> Terrorists would find chemical agents

attractive to use for several reasons, such as their being extremely toxic and readily available or easily synthesized.

In many respects, emergency response systems and health care facilities need to respond to a WMD chemical attack in the same fashion as a hazardous materials incident. The same principles regarding triage, decontamination, and allocation of resources that shape disaster plans related to hazardous materials go into action during a WMD chemical attack.

Chemical agents are generally classified into several groups: blood agents, nerve agents, choking agents, and blistering agents. Each agent has been designated its own North Atlantic Treaty Organization (NATO) designation symbol (a military symbol), which is not its chemical formula. This may be confusing at times. For instance, the NATO designation symbol for cyanide is AC, while its chemical formula is CN; the NATO designation symbol for Mace is CN.

An important principle to recognize concerning chemical agents is that the onset of symptoms is very rapid, typically within minutes. Therefore, prompt initiation of rescue, decontamination, medical attention, and antidotal therapy is critical in minimizing casualties. The Chemical and Biological Hotline (1-800-424-8802), based in Aberdeen, Maryland, serves as an emergency resource to all health care providers for technical assistance. Much of the following information has been adapted from the US Army handbook, *USAMRIID's Medical Management of Chemical Casualties Handbook*.<sup>20</sup> This reference is located online at [www.vnh.org/Providers.html#NBC](http://www.vnh.org/Providers.html#NBC).

## CYANIDE

In the form of an NBC agent, cyanide would most likely be encountered as hydrogen cyanide (AC), cyanogen chloride (CK), cyanogen bromide, or cyanogen iodide gases. An explosion of an industrial storage tank containing acetonitrile or acrylonitrile would pose a high risk of delayed cyanide toxicity. Cyanide toxicity is characterized by a rapid onset of dizziness, confusion, dyspnea, tachycardia, and hypertension followed by coma, convulsions, bradycardia, hypotension, arrhythmias, and metabolic acidosis. Death may occur within minutes following significant exposures. Cyanide is classified as a blood agent by some WMD references.<sup>20</sup> A cyanide antidote kit is available containing amyl nitrite pearls, injectable sodium nitrite, and sodium thiosulfate. Nitrites in this kit convert red blood cell hemoglobin into

methemoglobin. Methemoglobin combines with cyanide to form cyanomethemoglobin, which theoretically decreases the amount of free cyanide available. In synergism with 100% oxygen, thiosulfate combines with cyanide via the rhodenese enzyme to form less toxic thiocyanate, which is eliminated in the urine. Two other pharmaceuticals, which serve as adjunctive therapy for cyanide poisoning, are injectable sodium bicarbonate to correct metabolic acidosis and benzodiazepines (eg, diazepam or lorazepam) as anti-convulsants. Their availability is discussed later in the article.<sup>21</sup> Hydroxocobalamin (vitamin B<sub>12</sub>A) is a promising cyanide antidote; however, it is not currently available in the United States unless in conjunction with some ongoing phase III trials. This chemical binds with cyanide in vivo to form nontoxic cyanocobalamin (vitamin B<sub>12</sub>). Another antidote, cobalt edentate (Kelocyanor), is used in Great Britain and France. A more rapid methemoglobin inducer, 4-dimethylaminophenol, is used in some European countries. Stroma-free methemoglobin has been studied in animals and is not available for human use.

Eli Lilly & Company no longer manufactures the cyanide antidote package. It is now available from Akorn Inc. Each package contains 12 amyl nitrite pearls, two 10-mL vials of 3% sodium nitrite for injection, and two 50-mL vials of 25% sodium thiosulfate for injection.

Akorn Inc is located at 2500 Millbrook Drive, Buffalo Grove, IL 60089. The phone number to the company is (800) 535-7155. Its Web site address is [www.taylorpharm.com](http://www.taylorpharm.com). The price of the kit is \$274.56, and its shelf life is 24 months.

Three percent sodium nitrite for injection (300 mg/10 mL vials) is available from Hope Pharmaceuticals, located at 8260 East Gelding, Suite 104, Scottsdale, AZ 85260. The phone number to the company is (800) 755-9595. Its Web site address is [www.hopepharm.com](http://www.hopepharm.com). This product costs \$42.48 and has a shelf life of 24 months.

Packages of 12 amyl nitrite pearls (0.18 mL or 0.3 mL) are available from James Alexander Corporation, located at 845 Route 94, Blairstown, NJ 07825. The phone number to the company is (908) 362-9266. Its Web site address is [www.james-alexander.com](http://www.james-alexander.com). The product costs \$3.96 and has a shelf life of 4 years (refrigerated).

This product is also available from Pharma-Tek Inc, P.O. Box 1920, Huntington, NY 11743-0568. The phone number to the company is (800) 645-6655. Its Web site address is [www.pharma-tek.com](http://www.pharma-tek.com). Please note that for maximum product stability, amyl nitrite inhalant

should be packaged in unit-dose containers wrapped loosely in gauze or other suitable material and stored at 2°C to 15°C.<sup>22</sup>

Sodium nitrite powder USP can be used to extemporaneously prepare 3% sodium nitrite solution for injection, although no referenced source could be found for compounding instructions. Suppliers will add additional charges for special packaging and shipping. Sodium nitrite powder USP is available from Spectrum Chemicals and Laboratory Products, located at 14422 South San Pedro Street, Gardena, CA 90248. The phone number to the company is (800) 772-8786. Its Web site address is [www.spectrumchemical.com](http://www.spectrumchemical.com). The product costs \$21.90/50 g or \$88.00/2500 g. The product's shelf life is 3 to 5 years.

The product also is available from Integra Chemical Company, located at 710 Thomas Avenue SW, Renton, WA 98055. The phone number to the company is (800) 474-8993. Its Web site address is [www.integrachemical.com](http://www.integrachemical.com). The product costs \$40.64/500 g or \$120.40/2500 g.

The product also is available from Ruger Chemical Company Inc, P.O. Box 806, Hillside, NJ 07205. The phone number to the company is (800) 274-7843. Its Web site address is [www.rugerchemical.com](http://www.rugerchemical.com). The cost of the product is \$3.50 to \$7.00/lb in bulk.

Fifty milliliter vials of 25% sodium thiosulfate solution for injection are available from American Regent Laboratories Inc, a subsidiary of Luitpold Pharmaceuticals Inc. The company is located at One Luitpold Drive, Shirley, NY 11967. The phone number to the company is (800) 645-1706. Its Web site address is [www.luitpold.com](http://www.luitpold.com). The cost of the product is \$22.50/vial and has a shelf life of 36 months.

## NERVE AGENTS

Nerve agents are organophosphates, which are potent inhibitors of acetylcholinesterase enzymes. Some examples of this group are sarin (GB), soman (GD), tabun (GA), GF, and VX. Signs and symptoms of nerve agent or organophosphate poisonings include muscarinic, nicotinic, and central nervous system (CNS) findings. Muscarinic symptoms include "SLUDGE BAM": salivation, lacrimation, urination, defecation, gastric secretions, emesis, bronchospasm, bronchorrhea, bradycardia, abdominal cramping, and miosis. Nicotinic symptoms may include tachycardia, mydriasis, hypertension, muscle weakness, fasciculations, and respiratory paralysis. CNS symptoms range from blurred vision, restlessness, anxiety, and headaches to seizures and coma. Serious poison-

ings are managed with 3 antidotal agents.<sup>20</sup> Atropine sulfate blocks muscarinic receptor sites, thus reversing all SLUDGE BAM complications. Glycopyrrolate (Robinul), a quaternary ammonium anticholinergic medication, has been proposed as an adjunctive agent in the management of organophosphate insecticide poisoning; however, it is not routinely administered. Pralidoxime chloride (Protopam), also known as 2-PAM, regenerates cholinesterase enzyme activity. Administration of 2-PAM reverses nicotinic complications and works synergistically with atropine sulfate to correct muscarinic and CNS symptomatology. Obidoxime dichloride (Toxogonin, LUH6) is an alternative agent to pralidoxime chloride, which is available in some European countries but is not FDA approved for use in the United States. It is important to note that both atropine sulfate and pralidoxime chloride must be stocked for adequate antidote preparedness; atropine sulfate alone will correct muscarinic signs and symptoms, but 2-PAM is necessary to correct nicotinic signs and symptoms. Diazepam, lorazepam, or other benzodiazepines as anticonvulsants are adjunctive measures to treat nerve agent-induced seizures. Barbiturates (eg, phenobarbital) may be considered for seizures refractory to benzodiazepines. Topical ocular homatropine or atropine can relieve miosis, pain, dim vision, and nausea. Pyridostigmine bromide (Mestinon) dosed at 30 mg orally every 8 hours serves as a prophylactic antidote or antidote enhancement. Based on animal studies, pretreatment provides some protection against nerve agents, especially soman, which demonstrates rapid aging of the cholinesterase enzyme.

On February 5, 2003, the FDA approved the use of pyridostigmine bromide to increase survival after exposure to soman nerve agent poisoning. Pyridostigmine bromide binds reversibly to 30% of the cholinesterase enzymes, thus temporally protecting the enzyme from the nerve agent. Tablets are provided to military personnel in combat zones; pyridostigmine stockpiling in civilian hospitals is unnecessary and not recommended.

Pralidoxime chloride (2-PAM, Protopam) was previously available from Wyeth, but as of August 2003, this product was sold to Baxter Inc. The cost of the product is \$108.38/1 g vial and has a shelf life of 5 years. Baxter Inc is located at 95 Spring Street, New Providence, NJ 07974. The phone number to the company is (908) 286-7000. Its Web site address is [www.baxter.com](http://www.baxter.com).

Atropine sulfate for injection is available as a generic product from a variety of manufacturers. Some common forms are 0.4 mg/mL, 20 mL multidose vials

(8 mg/vial) with a shelf life of 24 to 36 months; syringe sizes (0.1 mg/mL, 5 mL, or 10 mL syringes); and 1 mg/mL, 1 mL single-dose vials.

Stability of expired injectable atropine sulfate solutions was addressed in one study. The authors tested several samples ranging from in date to 12 years beyond expiration. They noted high concentrations of atropine sulfate in clear colorless solutions along with an absence of breakdown products in the test samples.<sup>23</sup> These findings suggest their potential utility in times of emergency. Readers are advised to refer to the *Drug Topics Red Book*<sup>21</sup> or nearest pharmacy wholesaler for a complete list of drugs.

Atropine sulfate USP powder is available from several suppliers. This pharmaceutical-grade powder may be used to prepare atropine sulfate for injection extemporaneously in large amounts. Two references were identified that give instructions for preparing intravenous solutions extemporaneously.<sup>24,25</sup> The manufacturers of this pharmaceutical-grade chemical have provided no shelf-life guidelines. One study of extemporaneously prepared atropine sulfate 1 mg/1 mL, in 100 mL multidose bags, demonstrated stability of more than 95% at controlled temperatures of 22.2°C (72°F) and 37.8°C (100°F) for periods of up to 72 hours.<sup>26</sup> When ordering product, additional charges are added for special packaging and shipping. The product is available from Ruger Chemical Company, located at 83 Cordier Street, Irvington, NJ 07111. The phone number to the company is (800) 274-2636; fax (973) 926-4921. Its Web site address is [www.rugerchemical.com](http://www.rugerchemical.com). The cost of the product is \$11.20/5 g or \$44.80/125 g.

The product also is available from Spectrum Chemicals and Laboratory Products, located at 14422 South San Pedro Street, Gardena, CA 90248. The phone number to the company is (800) 772-8786. Its Web site address is [www.spectrumchemical.com](http://www.spectrumchemical.com). The cost of the product is \$20.45/5 g or \$80.60/25 g.

The Letco Companies also has the product available. The company is located at 1316 Commerce Drive NW, Decatur, AL 35601. The phone number to the company is (800) 239-5288; fax (256) 353-7237. Its Web site address is [www.letcoinc.com](http://www.letcoinc.com). The cost of the product is \$16.00/25 g or \$415/1 kg.

Diazepam for injection is available as a generic product from a variety of manufacturers. Some common forms are 5 mg/mL, 2 mL prefilled syringes (10 mg/syringe) with a shelf life of 24 months; 5 mg/mL, 2 mL ampoules (10 mg/amp); and 5 mg/mL, 10 mL multidose vial (50 mg/vial).

Lorazepam for injection is available as a generic product from a variety of manufacturers. Some com-

mon forms are 2 mg/mL, 1 mL single-dose vial (2 mg/vial) with a shelf life of 18 to 24 months; 2 mg/mL, 10 mL multidose vial (20 mg/vial); 4 mg/mL, 1 mL single-dose vial (4 mg/vial); and 4 mg/mL, 10 mL multidose vial (40 mg/vial).

Military-style autoinjectors containing atropine sulfate, pralidoxime chloride, and diazepam are available from Meridian Medical Technologies Inc, the only FDA-approved manufacturer in the United States.<sup>27</sup> These autoinjectors are manufactured in large quantities of 25,000 and 40,000. Small orders may be filled if the product is in company inventory; however, the shelf life may be shorter. On June 20, 2003, the FDA approved the marketing of pediatric-strength Atropen autoinjectors (atropine sulfate 1 mg/0.7 mL and 0.5 mg/0.7 mL). The doses approved for use in children and adolescents with mild symptoms of nerve agent poisoning include 0.5 mg for children weighing between 15 and 40 lbs (generally 6 months to 4 years), 1 mg for children weighing between 40 and 90 lbs (generally 4 to 10 years of age), and 2 mg doses for adults and children weighing more than 90 lbs (generally older than 10 years). For children with symptoms of severe nerve agent poisoning, doses up to 3 times these doses may be given.

Each Mark I Kit (nerve agent antidote kit) contains 1 AtroPen (atropine sulfate, 2 mg/0.7 mL) and 1 ComboPen (pralidoxime chloride, 600 mg/2 mL).

The diazepam autoinjector contains 10 mg diazepam in 2 mL. Both the Mark I Kit and the diazepam autoinjector are available from Meridian Medical Technology Inc, located at 10240 Old Columbia Road, Columbia, MD 21046. The phone number to the company is (800) 638-8093; fax (443) 259-7801. Its Web site address is [www.meridianmeds.com](http://www.meridianmeds.com) (Table 1). Per Meridian Medical Technologies, "Please note that, MMT requires the following information to accompany a Purchase Order (excluding the training kits which do not contain drug): a physician's prescription for all items; a copy of the DEA Registration Certificate is required if the Purchase Order includes the diazepam auto-injector; the Purchase Order must include the following wording: 'We certify that the items purchased under P.O.# [ . . . ] will be used only by [ . . . ]. The material will not be sold to a third party, distributed or used for any other purpose.'"

As of February 2004, Bound Tree Medical Inc became the exclusive distributor of all Meridian autoinjector products to hospital pharmacies. Bound Tree Medical Inc is located at 6106 Bausch Road, Gallo-way, OH 43119, and can be reached at (800) 533-0523 or by fax at (800) 257-5713. Its Web site address is

**Table 1**  
Nerve Agent Autoinjectors by Meridian Medical Technologies

Autoinjector	Item Number	Shelf Life	Units per Box	Price per Box	Unit Price
Mark I Kit (NAAK)	NSN 6505-01-174-9919	5 years	30	\$605.00	\$21.00
Atropen 2 mg	NDC 11704-106-01	3 years	12	\$117.00	\$9.75
Atropen 1 mg	NDC 11704-105-01	3 years	12	\$114.00	\$9.50
Atropen 0.5 mg	NDC 11704-104-01	3 years	12	\$111.00	\$9.25
ComboPen (2 Pam Cl)	NSN 6505-01-125-3248	5 years	100	\$1480.00	\$14.80
Diazepam (CANAs) C-IV	NSN 6505-01-274-0951	4 years	15	\$225.00	\$15.00

www.boundtree.com. The cost of a 2 mg Atropen is \$13.93, a 600 mg pralidoxime chloride Combopen is \$18.40, a 10 mg diazepam autoinjector is \$294.45, and a Mark I Kit is \$28.80.

Diomed in Istanbul, Turkey, manufactures DIO-ATRO, an autoinjector containing atropine sulfate 2 mg and pralidoxime chloride 600 mg and has a NATO stock #6515-27-013-3995.<sup>28</sup>

### PULMONARY OR CHOKING AGENTS

Chlorine (Cl), phosgene (CG), diphosgene (DP), and chloropicrin act primarily as pulmonary irritants causing cough, shortness of breath, and dyspnea. However, it may be several hours before serious complications become evident (eg, pulmonary edema). No specific antidote is available for treatment of these exposures. Symptomatic and supportive care may include administration of oxygen, ventilatory support, and bronchodilators such as albuterol sulfate. Nebulized 3.75% sodium bicarbonate has provided dramatic symptomatic improvement in chlorine exposures, as noted in several anecdotal case reports.<sup>29-31</sup> This may be prepared by mixing 2 mL of 7.5% sodium bicarbonate for injection with 2 mL of sterile 0.9% sodium chloride. Antibiotics should be reserved for those patients with an infectious process documented by sputum gram staining and culture. Parenteral steroids may be indicated in those patients demonstrating latent or overt reactive airway disease. Ipratropium bromide (Atrovent) may be used adjunctively following chloropicrin exposure.

Albuterol sulfate is available as a generic product in a variety of forms such as a solution for actuation, 0.09 mg/inhalation (17 g) with a shelf life of 18 to 36 months; a solution for inhalation, 0.083% 3 mL vials; and a solution for inhalation, 0.5% 20 mL multidose vial.

Sodium bicarbonate for injection is available in concentrations of 4.2%, 7.5%, and 8.4% in syringes and vials in sizes of 10 mL or 50 mL and has a shelf life of 18 months.

Methylprednisolone acetate for injection is available as a generic product in several concentrations, including 20 mg/mL, 10 mL vials (200 mg/vial) with a shelf life of 24 to 36 months; 40 mg/mL, 5 mL vials (200 mg/vial); and 80 mg/mL, 5 mL vials (400 mg/vial).

### BLISTER AGENTS

A number of potent alkylating agents may be used as chemical warfare agents. Examples include nitrogen mustard (HS), distilled mustard (HD), mustard gas, phosgene oxime (CX), and lewisite (L). Toxicity produced by these agents includes blisters, vesications, eye injury, airway damage, vomiting and diarrhea, and bone marrow stem cell suppression. Blisters may form several hours after contact with the skin. Erythema may be treated with calamine or other soothing lotion or cream. Denuded skin areas should be treated with topical antibiotics such as silver sulfadiazine or mafenide acetate.<sup>20</sup> Systemic analgesics should be used liberally. For eye exposures, 2.5% sodium thiosulfate irrigations, homatropine ophthalmic ointment (or other mydriatics), topical antibiotics, and topical steroids may be indicated depending on the severity of injury. Atropine or other anticholinergic agent or antiemetics should control the early nausea and vomiting. Antibiotics are necessary to treat infections, which are usually the cause of death. Colony-stimulating factors (eg, filgrastim [Neupogen], sargramostin [Leukine]) may be considered for patients demonstrating serious cytopenia. Lewisite is the only blistering agent for which an antidote may be useful since it is an arsenic derivative. The antidote dimercaprol (British anti-lewisite [BAL]) is a chelating agent for arsenicals and other heavy metals.<sup>32</sup> BAL administration may reduce systemic toxicity of lewisite. Although not commercially available, 5% BAL skin and eye ointments may reduce severity of lesions when applied soon after decontamination. Since BAL is formulated in peanut oil, it must be given intramuscularly. BAL is available

as 300 mg/3 mL vials in quantities of 10 from Akorn Inc, located at 2500 Millbrook Drive, Buffalo Grove, IL 60089. The phone number to the company is (800) 535-7155. Its Web site address is [www.taylorpharm.com](http://www.taylorpharm.com). The cost of the product is \$623.00 and has a shelf life of 5 years.

Dimercaptosuccinic acid (succimer, Chemet) has been used experimentally in animals for the treatment of lewisite exposures.<sup>33-37</sup> It may be preferred in the treatment of multiple exposures because it is administered orally and exhibits fewer adverse reactions. Chemet is supplied in 100-mg capsules and is available in quantities of 100 from Sanofi Pharmaceuticals Inc, located at 90 Park Avenue, New York, NY 10016. The phone number to the company is (800) 223-1062. Its Web site address is [www.sanofi-synthelabous.com](http://www.sanofi-synthelabous.com). The cost of the product is \$477.88 and has a shelf life of 24 months.

DMPS, which is the sodium salt of 2,3-Dimercapto-1-propanesulfonic acid, is a chelating agent available in Europe demonstrating some efficacy in treating lewisite-exposed experimental animals.<sup>38</sup>

The colony-stimulating factors are available as Leukine in 250 mcg/mL, 1 mL, multidose vial (\$152.95) and 500 mcg/mL, 1 mL, multidose vial (\$305.90). This product is available from Berlex Laboratories Inc, located at 1191 Second Avenue, Seattle, WA 98101-2120. The phone number to the company is (888) 237-5394. Its Web site address is [www.berlex.com](http://www.berlex.com). The shelf life is 18 months for the liquid product and 36 months for the powder product. Neupogen in 300 mcg/0.5 mL, which costs \$227.60; 480 mcg/0.8 mL, which costs \$362.60; and 480 mcg/1.6 mL, which costs \$330.60. These products are available from Amgen Inc, located at One Amgen Center Drive, Thousand Oaks, CA 91320. The phone number to the company is (805) 447-1000. Its Web site address is [www.amgen.com](http://www.amgen.com). The product has a shelf life of 24 months.

Based on experimental studies, it has been proposed that administration of sodium thiosulfate 12.5 g may act as a "mustard scavenger" following exposure to mustard agents. Potential benefits of sodium thiosulfate therapy following mustard agent exposure are not known.<sup>39</sup> See the Cyanide section for suppliers of sodium thiosulfate.

### INCAPACITATING AGENTS

BZ, also known as QNB, (3-quinuclidinyl benzilate) and Agent 15 (the Iraqi equivalent of BZ) are anticholinergic agents that incapacitate victims by causing delirium and hallucinations. BZ and related

anticholinergic compounds can be synthesized in clandestine laboratories. Patients demonstrate anticholinergic signs and symptoms (eg, mydriasis, tachycardia, dry flushed skin, urinary retention).<sup>20</sup> Symptoms of agitation and hallucinations may be managed with benzodiazepines. Serious symptoms may be reversed by intravenous physostigmine salicylate (Antilirium), a reversible carbamate cholinesterase inhibitor. Neostigmine methylsulfate (Prostigmin) and pyridostigmine bromide (Mestinon) are quaternary amines that do not cross the blood-brain barrier and therefore will not reverse CNS symptomatology caused by these agents. Antilirium is available in 2-mL vials (1 mg/mL) in quantities of 10 vials from Akorn Inc, located at 2500 Millbrook Drive, Buffalo Grove, IL 60089. The phone number to the company is (800) 535-7155. Its Web site address is [www.taylorpharm.com](http://www.taylorpharm.com). The cost of the product is \$48.60 and has a shelf life of 24 months.

On October 26, 2002, the Russian government used aerosolized fentanyl as an incapacitating agent during a terrorist attack in a Moscow theater.<sup>40</sup> This incident resulted in the death of more than 100 hostages and terrorists and critically injured many more. Fentanyl is a very potent opiate narcotic with significant exposures causing sedation, miosis, bradycardia, hypotension, and respiratory depression leading to coma and respiratory arrest. Fentanyl toxicity may be completely reversed by adequate doses of the opiate antagonists naloxone (Narcan) or nalmefene (Revex). Injectable naloxone is available generically in 0.4 mg/1 mL ampoules; 0.4 mg/1 mL syringes; 1, 2, and 10 mg vials; and 1 mg/1 mL in 2 and 10 mL ampoules.<sup>21</sup> Nalmefene is available in ampoules of 1 mg/2 mL and 0.1 mg/1 mL from Baxter Inc.

### RIOT CONTROL AGENTS

These agents are commonly known as CN (alpha-chloroacetophenone, Mace), CS (ortho-chlorobenzylidene malononitrile), or CR (dibenzoxazepine) tear gas. Diphenylaminochloroarsine (adamsite) and diphenylchloroarsine are riot control/vomiting agents that are organic arsenicals; however, they do not cause systemic arsenic poisoning. Some pepper spray products contain hot pepper extracts such as oleoresin capsicum. Usually, the exposure effects of these agents are self-limiting. They include burning, itching, and watering of the eyes; burning and tingling of the skin; and respiratory discomfort. In most cases, no specific therapy is indicated other than basic measures such as movement of the patient to fresh air, eye irrigation with water, and skin

washing. More pronounced symptoms such as bronchospasm and pulmonary edema are possible with significant exposures (ie, in enclosed spaces). Symptomatic patients may require supplemental oxygen, ventilatory support, and inhaled  $\beta$  agonist with or without systemic steroids.

## NUCLEAR AGENTS

Although the detonation of a nuclear weapon is a concern with respect to global and international conflicts, it is considered to be very difficult for a terrorist group to obtain, build, conceal, or deliver such a weapon. It is believed that a "dirty bomb" is more likely to be deployed. Dirty bombs are conventional explosives combined with radioactive material and are designed to frighten the populace and cause a major hazardous material cleanup rather than many injuries.

Radiation emitted by radioactive materials can be characterized into 3 types:  $\alpha$  particles,  $\beta$  particles, and  $\gamma$  rays. The health hazards of radiation are divided into acute or chronic exposure risks. Chronic exposures (ie, a low dose over a long period of time) increase the risk of cancers and cataracts, while acute exposures produce nausea, vomiting, blood dyscrasias, and death. Since  $\alpha$  and  $\beta$  particles do not travel great distances, materials such as protective clothing easily block them. Inhalation or ingestion exposures pose the greatest potential for harm.  $\gamma$  rays are the most harmful because they travel great distances and require dense materials such as lead to block penetration of tissues.<sup>41</sup>

After exposure to a radiologic agent, patients may require treatment with either a chelator or a radionuclide blocker.<sup>42</sup> Chelating agents for radionuclides are available through Radiation Emergency Assistance Center/Training Site (REAC/TS). Insoluble Prussian Blue (ferric hexacyanoferrate) is indicated for cesium and thallium chelation therapy.<sup>43</sup> This Prussian Blue is a pharmaceutical-grade product obtained from Germany under the brand name Radiogardase. It is available in 500-mg capsules, manufactured by Heyl GmbH, located in Berlin, Germany. On October 2, 2003, the FDA approved a new drug application for Radiogardase, to treat patients exposed to harmful levels of cesium-137 or thallium. Prussian Blue is now a component of the national strategic stockpile.

Zinc-diethylenetriamine pentaacetic acid (Zn-DTPA), also known as pentetate zinc trisodium, and calcium-DTPA (Ca-DTPA), also known as pentetate calcium trisodium, are chelators for radioactive transuranic elements (see Table 2).<sup>42,44,45</sup> Both of these drugs are supplied in 1-g ampules, also manufactured by Heyl GmbH, but must be obtained through REAC/TS.

**Table 2**  
Chelating Agents for Radionucleotides<sup>41</sup>

Chelating Agent	Radionucleotide
Calcium and zinc-DTPA	Americium ( <sup>243</sup> Am), californium, cesium, curium, lanthanum, lutetium, plutonium, promethium, scandium, uranium, yttrium, zinc, and rare earth metals
Calcium disodium EDTA	Copper, lead, and uranium
D-penicillamine	Copper, lead, and mercury ( <sup>203</sup> Hg)
Deferoxamine mesylate	Iron
Dimercaprol	Copper, mercury, and polonium
Succimer/DMSA	Lead and mercury

REAC/TS trains, consults, and assists in the response to all types of radiation accidents or incidents. The center uses physicians, nurses, health physicists, radiologists, and emergency coordinators to provide 24-hour assistance at the local, national, or international level.

Other pharmaceutical chelators may be used for a variety of radionucleotide exposures and would be found in any well-stocked hospital pharmacy. These include d-penicillamine (Cuprimine), calcium disodium EDTA (Versenate), dimercaprol (BAL), succimer (Chemet), and deferoxamine (Desferal).<sup>46</sup>

Colony-stimulating factors, filgrastim (Neupogen) and sargramostin (Leukine), may be considered in patients experiencing significant bone marrow suppression. See the Blister Agents section for suppliers of colony-stimulating factors.

Radionuclide-blocking agents saturate tissues with a nonradioactive element, which reduces the uptake of radioactive iodine. The most commonly used agents are potassium iodide (KI) tablets (130 mg and 65 mg), saturated solution of potassium iodide (300 mg/0.3 mL), and Lugol's solution (10% potassium iodide, 5% iodine), which reduce uptake of <sup>131</sup>I into the thyroid tissue.<sup>41</sup> Most states with Departments of Nuclear Safety will stock enough quantity of potassium iodide tablets to protect workers and emergency personnel involved in a nuclear reactor incident. Some states offer supplies of KI to the general public residing in areas close to nuclear reactors. Sodium iodide (NaI) can theoretically be used instead of potassium iodide; however, no such pharmaceutical product is available in the United States. Sodium iodide USP powder is available from several sources listed in the *Drug Topics Red Book*.<sup>21</sup>

Several other examples of substances employed as radionuclide blockers include sodium alginate for

**Table 3**  
**Threshold Thyroid Radioactive Exposures and Recommended Doses of Potassium Iodide (KI) for Different Risk Groups**

	Predicted Thyroid Exposure (cGy)	KI Dose (mg)	Number of 130 mg Tablets	Number of 65 mg Tablets
Adults older than 40 years	≥ 500	130	1	2
Adults 18-40 years	≥ 10			
Pregnant or lactating women	≥ 5			
Adolescents 12-18 years <sup>a</sup>		65	1/2	1
Children 3-12 years				
1 month to 3 years		32	1/4	1/2
Birth through 1 month		16	1/8	1/4

Note: KI from tablets (either whole or fractions) or a fresh saturated KI solution may be diluted in milk, formula, or water and the appropriate volume administered to babies. A home preparation procedure for emergency administration of KI tablets to infants and small children using water, milk, juice, syrup, or soda pop can be found at [www.fda.gov/cder/drugprepare/kiprep.htm](http://www.fda.gov/cder/drugprepare/kiprep.htm).<sup>47,48</sup> The KI prepared in these liquids will keep for up to 7 days in the refrigerator. The Food and Drug Administration recommends that the potassium iodide drink mixtures be prepared weekly; unused portions should be discarded.

a. Adolescents approaching adult size (≥ 70 kg) should receive the full adult dose (130 mg).

strontium, chlorthalidone for rubidium, and Lugol's for technetium.<sup>41</sup>

Table 3 is provided by the US FDA, Center for Drug Evaluation and Research ([www.fda.gov/cder/guidance/4825fnl.htm](http://www.fda.gov/cder/guidance/4825fnl.htm)). It gives the recommended doses of KI for various age and risk groups.

FDA-approved manufacturers of KI tablets are Iosat, Anbex Inc, located at 15 West 75th Street, New York, NY 10023. The phone number to the company is (212) 580-2810. Its Web site address is [www.anbex.com](http://www.anbex.com). The product is available as 130 mg tablets with 14 tablets to a package. The cost of the product is \$10.00/package and has a shelf life of 4 to 5 years. Thyro-Block, distributed by Nitro-Pak Inc, manufactured by Medpointe Inc ([www.nitro-pak.com](http://www.nitro-pak.com) or [www.medpointeinc.com](http://www.medpointeinc.com)), is available as 130 mg tablets with 14 tablets to a bottle; a case is 100 bottles. The cost of a single bottle is \$9.95; a case of 100 bottles costs \$799. Medpointe Inc markets potassium iodide tablets directly to nuclear power plants and utility companies. The phone number to the company is (732) 564-2200. Thyrosafe, manufactured and distributed by Reciep AB ([www.thyrosafe.com](http://www.thyrosafe.com)). The phone number to the company is (866) 894-7672. The product is available as 65 mg tablets with 20 tablets per package. The cost of the product is \$9.95 per package.

For immediate assistance regarding a nuclear or radiological agent incident, contact REAC/TS, located at P.O. Box 117, MS-39, Oak Ridge, TN 37831-0117. The phone number is (865) 576-3131 (business hours) or (865) 576-1005 (24-hour emergency line) or [www.orau.gov/reacts](http://www.orau.gov/reacts). Also contact the Department of Nuclear Safety—for the state in which the incident occurred—and the health physicists affiliated with hos-

pital nuclear medicine departments, who can serve as expert consultants for radiation incidents.

## BIOLOGICAL AGENTS

As NBC terrorist weapons, biological agents may be encountered as bacteria (eg, anthrax), viruses (eg, smallpox), or toxins (eg, botulinum or ricin). This fact will explain the striking difference in the manner in which victims will present to health care facilities. A catastrophe caused by detonation of a chemical weapon (eg, nerve agent or cyanide) would be characterized by immediate death or severe disablement of individuals at the site of the attack. First responders to such an incident would be paramedics, police, and other emergency personnel.

In contrast, with respect to biologicals, there is a delayed onset of signs and symptoms since incubation may take days. Emergency department clinicians and primary care practitioners would be the first to recognize and manage exposed patients. Knowledge of what medical and pharmaceutical interventions may be requested in a mass casualty event is crucial. It is beyond the scope of this article to delineate all the diagnostic clues, pathophysiology, laboratory monitoring, infectious disease control, guidelines for patient isolation, epidemiologic procedures, and public health ramifications of a bioterrorism event. Clinicians, however, should take note of this extensive list of pharmaceuticals (both oral and parenteral) that may be required in extraordinarily large amounts during an outbreak involving a biological weapon. In addition, the duration of illness may be weeks to months, thus creating an additional stress on the health care infrastruc-

ture. Once the cause of illness in a large number of patients has been identified as a biological agent, prompt availability and distribution of appropriate medication can greatly mitigate the destructive impact of the act of terrorism. It should be noted that special products, uncommonly used vaccines and antitoxins, would be provided via federal government storage and distribution programs. Pharmacist and public health personnel in the drug-delivery system must be aware that it may require 24 to 48 hours or more for material in the strategic national stockpile to be transported, broken down, and delivered to local distribution centers. See the discussion of the SNS in the introduction section. Adjunctive medications such as analgesics and antipyretics should be readily available to manage symptoms such as headache, fever, and myalgias. New therapies are under development. Detailed information on diagnosis, patient management, vaccines, and so forth may be obtained through COMMANDER US Army Medical Research Institute of Infectious Diseases<sup>49</sup> (USAMRIID) at (301) 619-2833 during business hours or at (888) USA-RIID, 24 hours/day. In the event of an emergency, contact the US Army response center at (800) 424-8802. Also contact the CDC bioterrorism response unit at (770) 488-7100.

The following information is a very brief synopsis of 14 possible threats as biological agents. Much of this information has been adapted from an article in the *Journal of the American Medical Association*<sup>1</sup> and *USAMRIID's Medical Management of Biological Casualties Handbook*.<sup>49</sup>

## Bacteria

**Anthrax.** The etiologic agent causing anthrax is *Bacillus anthracis*, a gram-positive spore-forming bacillus. As a biological weapon, the spores of these bacteria would be aerosolized, with inhalation being the primary route of exposure. The clinical course is characterized by a necrotizing hemorrhagic mediastinitis. Initially, symptoms may resemble a flu-like illness with fever, fatigue, malaise, vague chest pain, and nonproductive cough. Initial symptoms are followed by abrupt progression to dyspnea, stridor, diaphoresis, and cyanosis. Systemic complications of sepsis, shock, and meningitis may occur in up to half of cases. Unfortunately, once symptoms occur, treatment is usually ineffective. Intravenous ciprofloxacin should be initiated at the earliest sign of anthrax. Other fluoroquinolones may be substituted; however, no animal studies exist for quinolones other than ciprofloxacin.<sup>50</sup> All natural strains of anthrax have been found to be sensitive to erythromycin, chloramphenicol, and gentamicin. His-

torically, penicillin G has been the drug of choice for anthrax. An alternative regimen is doxycycline and 1 or 2 other antibiotics with in vitro activity against *B anthracis*, such as rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin. Ampicillin and penicillin should not be used alone because of possible  $\beta$ -lactamase production.<sup>51</sup> Chemoprophylaxis with oral ciprofloxacin, doxycycline, or amoxicillin if the strain of *B anthracis* is proven susceptible in exposed individuals should be initiated and continued for at least 60 days or until 3 doses of anthrax vaccine are administered.<sup>50</sup> A licensed attenuated vaccine, anthrax vaccine adsorbed (BioThrax) in 5 mL multidose vials, is available for prophylaxis. This vaccine stock is owned by the Department of Defense. To obtain it, contact USAMRIID at (301) 619-2833. It is manufactured by BioPort Corporation, located at 3500 North Martin Luther King Jr. Boulevard, Lansing, MI 48906. The phone number to the company is (517) 327-1500. Its Web site address is [www.bioport.com](http://www.bioport.com). The cost of 5 mL (10 doses) of the product is \$1331.19, and it has a shelf life of 18 months. The product must be stored between 2°C to 8°C. Per BioPort Corporation, as of June 2003, the only way one could obtain BioThrax was by writing a letter describing the reason for the request, the number of people to be vaccinated, and contact information. Once this letter is received, it would go through an approval process at the Department of Defense. Depending on the level of risk, they would either accept or reject the request.

BioPort Corporation currently has vaccine available for civilian personnel and is very close to signing a domestic distributor for the management of the sale of BioThrax. Once this becomes official, a physician will be able to contact the distributor to find out if he or she is eligible to receive the vaccine. The supply of the vaccine is still low in comparison to the very high demand, but BioPort will be selling the vaccine to those civilian markets that are most at risk and most vital to our country.

**Brucellosis.** Human infection may be caused by 4 species of *Brucella*, which is a nonspore-forming gram-negative aerobic coccobacillus. Clinical manifestations include fever, chills, and malaise, which may lead to cough and pleuritic chest pain. Other complications may include osteomyelitis, genitourinary infection, hepatitis, endocarditis, and CNS infections. To prevent the possibility of relapse, combination therapy is advised. Various antibiotic regimens have been proposed from the following list of antimicrobials: doxycycline, gentamicin, streptomycin, rifamin, ofloxacin, and sulfamethoxazole/trimethoprim (SMZ/TMP). There

are no approved vaccines or chemoprophylaxis treatments.

**Cholera.** This infection is caused by *Vibrio cholerae*, a gram-negative nonspore-forming bacillus. Clinical manifestations include vomiting, abdominal distention and pain, with little or no fever, followed rapidly by diarrhea. Fluid losses may be excessive, with death caused by dehydration and shock. Antibiotic treatment may include tetracycline, ampicillin, and SMZ/TMP. Intravenous fluid/electrolyte solutions are necessary to treat dehydration. At the present time, the manufacture and sale of the only licensed cholera vaccine in the United States (Wyeth-Ayerst) has been discontinued. Two recently developed vaccines for cholera are licensed and available in other countries (Dukoral, Biotec Ab, and Mutacol, Berna); however, neither of these 2 vaccines are available in the United States.<sup>52</sup>

**Glanders.** Glanders and melioidosis are caused by *Burkholderia mallei* and *Burkholderia pseudomallei*, respectively. Both are gram-negative bacilli with a safety pin appearance on microscopic examination.<sup>49</sup> Both pathogens affect animals (eg, horses, mules, donkeys) and human beings. Symptoms of inhalation exposure include high fever, rigors, sweating, myalgias, headache, pleuritic chest pain, cervical adenopathy, hepatosplenomegaly, and generalized papular/pustular eruptions. Pulmonary disease may progress to potentially fatal bacteremia and septicemia. Oral antibiotic regimens include amoxicillin/clavulanate, tetracycline, or sulfamethoxazole/trimethoprim given for 60 to 150 days. For serious systemic disease, administer parental ceftazidime and SMZ/TMP for 2 weeks followed by oral therapy for 6 months. There are currently no available vaccines for human use. Chemoprophylaxis may be considered using SMZ/TMP.

**Pneumonic plague.** The gram-negative, nonspore-forming bacillus *Yersinia pestis* is responsible for both pneumonic and bubonic plague. Patients exposed to pneumonic plague as a biological weapon will present with high fever, chills, malaise, cough with bloody sputum, headache, myalgia, and sepsis. Late in the course of illness, dyspnea, cyanosis, and respiratory failure may be noted. Effective antibiotic therapy includes streptomycin or gentamicin. Alternative drugs are ciprofloxacin, chloramphenicol, and doxycycline. In the United States, a licensed, killed, whole bacilli vaccine was discontinued by its manufacturer in 1999 and is no longer available. Exposed individuals may be treated with doxycycline, ciprofloxacin, or chloramphenicol for 7 days for chemoprophylaxis.

**Q-fever.** Q-fever is a rickettsial disease caused by *Coxiella burnetii*. The most common symptoms of Q-

fever are fever, chills, headache, fatigue, diaphoresis, malaise, anorexia, and myalgias. In some cases, cough with chest pain may be noted. Rare complications include hepatomegaly, splenomegaly, and jaundice. Effective therapies for Q-fever include tetracycline or doxycycline for 5 to 7 days. Alternatives are ofloxacin or pefloxacin. Hydroxychloroquine added to antibiotic therapy has increased the effectiveness of therapy. There is currently no commercially available Q-fever vaccine in the United States. One product, Q-VAX, is available in Australia. Tetracycline or doxycycline may be given as chemoprophylaxis to exposed patients.

**Tularemia.** Tularemia is caused by *Francisella tularensis*, a gram-negative aerobic coccobacillus. It is known as "rabbit fever" or "deer fly fever." Inhalation of tularemia organisms produces a typhoidal tularemia. Patients present with fever, weight loss, substernal discomfort, and nonproductive cough. The drug of choice is streptomycin. Other treatment options include gentamicin, fluoroquinolones (ciprofloxacin, norfloxacin), tetracycline, and chloramphenicol; however, high relapse rates are associated with these treatment options. Although not commercially available, a live attenuated vaccine is available under investigational new drug (IND) status for prophylaxis (available through USAMRIID). Doxycycline or tetracycline may be used for chemoprophylaxis.

## Viruses

**Smallpox.** The etiologic agent that causes smallpox is the variola major virus. Smallpox was declared eradicated by the World Health Organization in 1980. Much concern exists regarding the stockpiling of this infectious agent as a weapon of bioterrorism due to its high morbidity and mortality. Patients infected with variola present with fever, malaise, rigors, vomiting, headache, and backache. Dermal manifestations include appearance of a rash followed by lesions, which appear as macules, then papules, then eventually form pustular vesicles. By the second week, scabs form, which leave depigmented scars upon healing. Patients are contagious until all scabs are healed. All patients exposed to variola virus must be immediately vaccinated. Those US citizens who were vaccinated against smallpox in the 1950s and the 1960s are no longer protected against the virus.<sup>53</sup> The only smallpox vaccines available in the United States are Dryvax (Wyeth Laboratories Inc; Wet Vax, Aventis Pharmaceuticals Inc), available by calling the CDC at (404) 639-3670. Both smallpox vaccine products are components of the SNS. The CDC has con-

tracted with Acambis to develop a new smallpox vaccine (ACAM 2000), which may have a more acceptable safety profile.<sup>54</sup> In early 2003, the CDC made the smallpox vaccine available through state health departments to civilian health care workers on a voluntary basis. Dryvax is available as 1 vial of dried smallpox vaccine and 1 container of diluent (0.25 mL) with 100 sterile bifurcated needles. The manufacture of Dryvax was discontinued in 1981. The US Army and the CDC maintain a supply of vaccinia immune globulin (VIG), which is used for the treatment of complications due to the vaccinia vaccination.<sup>55</sup> Limited data suggest that VIG may be of value in postexposure prophylaxis of smallpox when given within the first week following exposure and concurrently with vaccination.<sup>49</sup> Contact the CDC at (888) 246-2675 or USAMRIID at (301) 619-2833 to obtain VIG. There is currently no chemotherapeutic agent proven effective against smallpox. Cidofovir (Vistide) is not a licensed treatment for smallpox; however, it is being studied under an FDA investigational protocol. Cidofovir is a nucleoside analog DNA polymerase inhibitor that has been demonstrated in *in vitro* studies to inhibit poxvirus replication and cell lysis.<sup>56</sup> Cidofovir is currently licensed for the treatment of CMV retinitis and has demonstrated antiviral activity against poxviruses *in vitro* and against cowpox and vaccinia viruses in mice. However, its use for the treatment of vaccinia adverse reactions is restricted under an IND protocol. Under the IND, cidofovir would be used only when VIG was not efficacious. Renal toxicity is a known adverse reaction of cidofovir. Although the CDC makes no recommendations for the use of antivirals at this time, it is recommended that health care providers continue to consult the CDC at (877) 554-4625 to obtain updated information regarding treatment options for serious vaccine complications.<sup>55</sup> Many states have surveyed hospital pharmacies to identify local sources of this product if a smallpox outbreak is suspected.<sup>57,58</sup>

Cidofovir (Vistide) is available from Gilead Sciences, located at 333 Lakeside Drive, Foster City, CA 94404. The phone number to the company is (800) 445-3235. Its Web site address is [www.gilead.com](http://www.gilead.com). The product is available as 75 mg/mL, 5 mg vial for \$888.00. It has a shelf life of 3 years.

*Venezuelan equine encephalitis (VEE)*. Members of the  $\alpha$  virus genus of the Togaviridae family produce this encephalopathic syndrome. The usual mode of transmission is mosquitoes; however, aerosolization makes those pathogens a very effective WMD.  $\alpha$  virus will produce neurologic syndromes noted by fever, headaches, confusion, drowsiness, seizures, dysphasia, ataxia, myoclonus, cranial nerve palsies,

photophobia, myalgia, and vomiting. No specific chemotherapeutic agents are indicated. Treatment is symptomatic and supportive care. Antipyretics and anticonvulsants may be used in severe cases. A live attenuated vaccine for VEE TC-83 is available for prophylaxis, while inactivated vaccines are under IND status. A monoclonal antibody has been developed and is in the animal test phase for protection against infection and disease when given before or up to 24 hours after an airborne challenge with virulent virus.

*Viral hemorrhagic fevers (VHF)*. The most widely known examples of this group are the Ebola and Marburg viruses; these belong to the family Filoviridae, which are enveloped, nonsegmented, negative-stranded RNA viruses. Common features of VHF are myalgias, fever, and prostration. Mild symptoms include conjunctival injection, mild hypotension, flushing, and petechial hemorrhaging that may progress to shock. More severe symptoms include mucous membrane hemorrhage with maculopapular rashes and disseminated intravascular coagulation. Other VHF agents include Crimean Congo hemorrhagic fever (Bunyaviridae family), Hanta virus (Bunyaviridae family), and Lassa fever (Arenaviridae family). No specific antiviral agents are effective against Ebola or Marburg viruses. Other related strains (eg, Crimean Congo, Lassa) may respond to ribavirin. Postexposure prophylaxis may be considered with oral ribavirin.<sup>49</sup> Many different pharmaceutical agents may need to be employed in the supportive management of hypotension, shock, and disseminated intravascular coagulation. No vaccines or medicinal exists to protect against these viral illnesses.

Ribavirin (Virazole) is available from ICN Pharmaceuticals Inc, located at 3300 Hyland Avenue, Costa Mesa, CA 92626. The phone number to the company is (800) 548-5100. Its Web site address is [www.icnpharm.com](http://www.icnpharm.com). The product is available as 6-g vial of lyophilized powder for \$1416.09. It has a shelf life of 5 years.

Ribavirin (Rebetol) is available from Schering Plough Corporation, located at 2000 Galloping Hill Road, Kenilworth, NJ 07033. The phone number to the company is (800) 222-7579. Its Web site address is [www.schering-plough.com](http://www.schering-plough.com). It markets 200-mg capsules, available in bottles of 42, 56, 70, and 84, which cost \$10.60/tab. Its shelf life is "proprietary information."

## Toxins

*Botulinum*. Botulinum toxin is a protein exotoxin produced by *Clostridium botulinum*, an anaerobic

gram-positive bacillus. There are 7 types of botulism neurotoxins known as types A-G. Botulism poisonings are more commonly associated with improperly processed or canned foods. As a WMD, botulinum toxin may be inhaled from an aerosol or ingested in the form of sabotaged food. These toxins are the most toxic of all the NBC weapons. Clinical manifestations include blurred vision, mydriasis, diplopia, ptosis, photophobia, dysarthria, dysphonia, and dysphasia. Skeletal muscle paralysis follows, which presents as a symmetrical and descending progressive weakness resulting in respiratory failure. Patients are typically awake, alert, and afebrile. A trivalent equine antitoxin (types A, B, and E) for food-borne botulism is available from the CDC at 8 urban quarantine sites: Atlanta, Chicago, Honolulu, Los Angeles, Miami, New York City, San Francisco, and Seattle. To obtain these antitoxins, contact the CDC 24 hours a day at (404) 639-2888 or during business hours at (404) 639-2206. Connaught Laboratories Ltd, 1 of only 3 suppliers in the world, manufactures this antitoxin for the CDC. A despeciated equine heptavalent antitoxin against all 7 types was prepared and is under IND status. It should be noted that all horse serum-based antitoxins pose the risk of anaphylaxis and serum sickness; therefore, skin testing is advised. A pentavalent (types A-E) toxoid also is available under IND status.<sup>49</sup>

*Ricin/abrin.* Ricin is a biological toxin that is derived from the plant *Ricinus communis*, commonly known as the castor bean. After inhalation exposure, victims may experience fever, weakness, cough, necrosis of upper and lower airway, and pulmonary edema followed by hypotension and cardiovascular collapse. Ingestion of castor beans or ricin may cause esophagitis, abdominal pain, nausea, vomiting, profuse bloody diarrhea, shock, and delayed cytotoxic effects to the liver, kidney, CNS, and adrenal glands. Abrin is a similar biotoxin that is found in the seeds of the *Abrus precatorius*, commonly known as the jequirity bean or rosary pea. There are no available antitoxins for either ricin or abrin. Treatment is supportive care only. Also, there are no commercially available vaccines or other chemoprophylactic agents; however, candidate vaccines for ricin are under development that are immunogenic and confer protection against lethal aerosol exposures in animals.<sup>49</sup>

*Staphylococcus enterotoxin B (SEB).* SEB is an exotoxin produced by *Staphylococcus aureus*, a gram-positive cocci. SEB is most commonly recognized as a cause of food poisoning, as it is produced by bacterial growth in improperly handled foods. Inhalation of SEB in a biological warfare scenario may rapidly incapacitate its victims. Signs of exposure may include fever, chills, headache, myalgias, and nonproductive cough with severe problems including dyspnea, retrosternal chest pain, vomiting, and diarrhea. No specific antitoxin is available. Supportive therapies are directed toward adequate oxygenation and hydration. Antipyretics and antitussives may provide symptomatic relief. The value of steroids is unknown. No vaccines for SEB are currently available; however, several vaccine candidates are in development.<sup>49</sup>

*Trichothecene (T-2) mycotoxins.* Fungi of the genera *Fusarium*, *Myrothecium*, *Trichoderma* and *Stachybotrys* produce these compounds. Clinical manifestations of exposure include skin irritation, pruritus, redness, vesicles, necrosis, sloughing of the epidermis, nose and throat pain, nasal discharge, fever, cough, dyspnea, chest pain, and hemoptysis. Serious cases are associated with prostration, weakness, shock, and death. There is no antidote or antitoxin. Treatment is supportive care. No vaccine or chemoprophylactic agent exists for T-2 mycotoxins.

The following are some of the aforementioned pharmaceutical products available for the treatment of patients exposed to biological warfare agents. If a variety of sizes and formulations are available for a particular pharmaceutical product, only the largest dose forms are listed. (Readers are advised to refer to the *Drug Topics Red Book*<sup>21</sup> or nearest pharmacy wholesaler for a complete list of companies that manufacture or distribute the following products.)

- Ciprofloxacin is available in several different oral and parenteral dosage forms.
- Doxycycline hyclate is available from a number of generic suppliers in 100-mg tablets or capsules.
- Erythromycin is available in a large variety of salt forms and strengths: 500-mg tablets or capsules.
- Penicillin V and G are available in a variety of formulations, both oral and parenteral: 500-mg tablets, 10 million unit vials.
- Gentamicin sulfate is a powerful aminoglycoside antibiotic that is only used for systemic infections. It is available in a variety of formulations: 40 mg/mL, 20 mL multidose vials (800 mg/vial), 40 mg/mL, 2 mL single-use vials (80 mg/vial).
- Streptomycin is a rarely used antibiotic; however, it has efficacy against several of the biological warfare agents. It is supplied in 1-g vials for injection. Streptomycin is available from Pharma-Tek Inc, P.O. Box 1920, Huntington, NY 11743-0568. The phone number to the company is (800) 645-6655; its Web site address is [www.pharma-tek.com](http://www.pharma-tek.com). The cost of the product is \$6.90/vial. It has a shelf life of 24 months.

- Chloramphenicol is another rarely used antibiotic. It can be obtained in vials, or large quantities may be obtained in powdered form. This may be required to treat a large number of casualties: 1000-mg vial, 25 g USP powder.
- SMZ/TMP is another antibiotic that has efficacy against several of the biological warfare agents. The most commonly used formulation contains 800 mg of sulfamethoxazole and 160 mg of trimethoprim (Bactrim DS): SMZ/TMP (800/160 tablets).
- Rifampin is available in 300-mg capsules or in large quantities in powdered form: 300-mg capsules, 500 g USP powder.
- Tetracycline is available in 500-mg capsules or also in powdered form: 500-mg capsules, 100 g USP powder.

## CONCLUSION

With the increasing probability of an incident involving a WMD agent, many local, state, and federal agencies have initiated plans for appropriate and effective emergency medical response. Experts in the area of EMS, emergency medicine, infectious disease, and public health are becoming trained in the medical management of exposure to NBC agents.

Any large mass casualty scenario will demand the expertise and professional services of a hospital pharmacy. Therefore, clinicians should equip themselves with knowledge of antidotes, antibiotics, antitoxins, and other supportive agents used to treat casualties and how they may be obtained quickly in the event of an act of terrorism. Currently, there are no guidelines mandating minimum hospital inventory of the pharmaceutical products that may be needed. Pharmacy managers, poison center personnel, and pharmacy and therapeutics committee members are urged to participate in, or at least be familiar with, plans coordinated through local domestic preparedness programs.

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## REFERENCES

1. Franz DR, Jahrling PB, Friedlander AM, et al. Clinical recognition and management of patients exposed to biological warfare agents. *JAMA*. 1997;278:399-411.
2. Danzig R, Berkosky PB. Why should we be concerned about biological warfare? *JAMA*. 1997;278:431-432.
3. Sharp TW, Brennan RJ, Keim M, et al. Medical preparedness for a terrorist incident involving chemical or biological agents during the 1996 Atlanta Olympic games. *Ann Emerg Med*. 1998;32:214-223.
4. Tucker JB. National health and medical services response to incidents of chemical and biological terrorism. *JAMA*. 1997;278:362-368.
5. Anteau CM, Williams LA. The Oklahoma bombing: Lessons learned. *Crit Care Nurs Clin North Am*. 1997;9:231-236.
6. Richards CF, Burstein JL, Waeckerle JF, et al. Emergency physicians and biological terrorism. *Ann Emerg Med*. 1999;34:183-190.
7. Pesik N, Keim M, Sampson TR. Do U.S. emergency medicine residency programs provide adequate training for bioterrorism? *Ann Emerg Med*. 1999;34:173-176.
8. Forrow L, Sidel VW. Medicine and nuclear war: from Hiroshima to mutual assured destruction to abolition 2000. *JAMA*. 1998;280:456-461.
9. Zilinskas RA. Iraq's biological weapons: the past as future? *JAMA*. 1997;278:418-424.
10. Lebeda FJ. Deterrence of biological and chemical warfare: a review of policy options. *Mil Med*. 1997;162:156-161.
11. Dart RC, Stark Y, Fulton B, et al. Insufficient stocking of poisoning antidotes in hospital pharmacies. *JAMA*. 1996;276:1508-1510.
12. Woolf AD, Chrisanthus K. On-site availability of selected antidotes: results of a survey of Massachusetts hospitals. *Am J Emerg Med*. 1997;15:62-66.
13. Chyka PA, Conner HG. Availability of antidotes in rural and urban hospitals in Tennessee. *Am J Hosp Pharm*. 1994;51:1346-1348.
14. Santucci KA, Shah BR, Linakis JG. Acute isoniazid exposures and antidote availability. *Pediatr Emerg Care*. 1999;15:99-101.
15. Antidotes dangerously understocked in Colorado, Montana, and Nevada. *Am J Health Syst Pharm*. 1997;54:16, 19.
16. Webster KS, Burda AM, Sigg T, et al. Antidote preparedness of Illinois hospitals. *Pharmacotherapy*. 1999;19:1229-1230.
17. Preparedness and Response for Terrorist Incidents Amendment (Nunn-Lugar-Domenici Act) of 1996. Public Law Number G250-12, Federal Emergency Management Agency; 1996:1-24.
18. The Centers for Disease Control and Prevention. Strategic national stockpile; December 2002. Available at: <http://www.bt.cdc.gov/stockpile>.
19. US Department of Justice Office of Justice Programs. April 2003. Available at: <http://ojp.usdoj.gov/terrorism/conferences.htm>.
20. US Army Medical Research Institute of Infectious Diseases. *USAMRIID's Medical Management of Chemical Casualties Handbook*. 4th ed. Fort Detrick, Md: Chemical Casualty Care Division, USAMRIID; 2000.
21. *2004 Drug Topics® Red Book*. 108th ed. Montvale, NJ: Medical Economics Company, Inc; 2003.
22. *AHFS Drug Information 2003*. Bethesda, Md: American Society of Health-System Pharmacists; 2003.
23. Schier JG, Mehta R, Mercurio-Zappala M, Nelson LS, Howland MA, Hoffman RS. Preparing for chemical terrorism: stability of expired atropine. *J Toxicol Clin Toxicol*. 2002;40:625-626.
24. Kozak RJ, Siegel S, Kuzma J. Rapid atropine synthesis for the treatment of massive nerve agent exposure. *Ann Emerg Med*. 2003;41:685-688.
25. Geller RJ, Lopez GP, Cutler S, Lin D, Bachman GF, Gorman SE. Atropine availability as an antidote for nerve agent casualties: validated rapid reformulation of high-concentration atropine from bulk powder. *Ann Emerg Med*. 2003;41:453-456.
26. Dix J, Freeman B, Hess M, et al. Atropine stability for use in mass chemical terrorism events. *J Toxicol Clin Toxicol*. 2002;40:696.
27. *Field Manual: Treatment of Chemical Agent Casualties and Conventional Military Chemical Injuries*. Departments of the

- Army, the Navy, and the Air Force, and Commandant, Marine Corps. Available at: [http://nbc-med.org/SiteContent/MedRef/OnlineRef/FieldManuals/fm8\\_285/toc.htm](http://nbc-med.org/SiteContent/MedRef/OnlineRef/FieldManuals/fm8_285/toc.htm).
28. Diomed<sup>®</sup> Pharmaceutical Company. May 2003. <http://www.diomed.com.tr/default.asp>.
  29. Doudar SM. Nebulized sodium bicarbonate in acute chlorine inhalation. *Pediatr Emerg Care*. 1997;13:406-407.
  30. Bosse GM. Nebulized sodium bicarbonate in the treatment of chlorine gas inhalation. *J Toxicol Clin Toxicol*. 1994;32:233-241.
  31. Vinsel PJ. Treatment of acute chlorine gas inhalation with nebulized sodium bicarbonate. *J Emerg Med*. 1990;8:327-329.
  32. Delgado J, Hurlbut KM, Bogdan GM, et al. *Poisindex<sup>®</sup>, Arsenic* [monograph on CD-ROM]. Vol 116. Englewood, Colo: Micromedex<sup>®</sup> Healthcare Series; 2002.
  33. Aposhian HV, Carter DE, Hoover TD, et al. DMSA, DMPS, and DMPA as arsenic antidotes. *Fundam Appl Toxicol*. 1984;2(2 pt 2):S58-S70.
  34. Aposhian HV, Mershon MM, Brinkley FB, et al. Anti-lewisite activity and stability of meso-dimercaptosuccinic acid and 2,3-dimercapto-1-propanesulfonic acid. *Life Sci*. 1982;31:2149-2156.
  35. Aposhian HV. Biological chelation: 2,3-dimercapto-propanesulfonic acid and meso-dimercaptosuccinic acid. *Adv Enzyme Regul*. 1982;20:301-319.
  36. Inns RH, Rice P. Efficacy of dimercapto chelating agents for the treatment of poisoning by percutaneously applied dichloro(2-chlorovinyl)arsine in rabbits. *Hum Exp Toxicol*. 1993;12:241-246.
  37. Inns RH, Rice P, Bright JE, et al. Evaluation of the efficacy of dimercapto chelating agents for the treatment of systemic arsenic poisoning in rabbits. *Hum Exp Toxicol*. 1990;9:215-220.
  38. Radabaugh TR, Sampayo-Reyes A, Zakharyan RA, et al. Arsenate reductase II: purine nucleoside phosphorylase in the presence of dihydrolipoic acid is a route for reduction of arsenate to arsenite in mammalian systems. *Chem Res Toxicol*. 2002;15:692-698.
  39. Coppock R, Hurlbut KM. *Poisindex<sup>®</sup>, Mustard Gas* [monograph on CD-ROM]. Vol 116. Englewood, Colo: Micromedex<sup>®</sup> Healthcare Series; 2001.
  40. Chemical weapons: shifting the goal posts [editorial]. *Lancet Neurol*. 2002;1:254-255.
  41. Hendee W, Palmer R, Hall AH, et al. *Poisindex<sup>®</sup>, Radiation* [monograph on CD-ROM]. Vol 116. Englewood, Colo: Micromedex<sup>®</sup> Healthcare Series; 2001.
  42. Lincoln TA. Importance of initial management of persons internally contaminated with radionuclides. *Am Ind Hyg Assoc J*. 1976;37:16-21.
  43. Ricks RC, Lowry PC, Townsend RD. *Radiogardase-Cs insoluble Prussian Blue (ferric hexacyanoferrate, Fe<sub>4</sub>[Fe(CN)<sub>6</sub>]<sub>3</sub>)*. Oak Ridge, Tenn: Radiation Emergency Assistance Center/Training Site; November 2002.
  44. Ricks RC, Lowry PC, Townsend RD. *Ca-DTPA (trisodium calcium diethylenetriaminepentaacetate)*. Oak Ridge, Tenn: Radiation Emergency Assistance Center/Training Site; November 2002.
  45. Ricks RC, Lowry PC, Townsend RD. *Zn-DTPA (trisodium zinc diethylenetriaminepentaacetate)*. Oak Ridge, Tenn: Radiation Emergency Assistance Center/Training Site; November 2002.
  46. *Physicians' Desk Reference*. 57th ed. Montvale, NJ: Medical Economics Company; 2003:3243.
  47. CDER KI Taskforce. Guidance potassium iodide as a thyroid blocking agent in radiation emergencies. US Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research. 2001. Available at: <http://www.fda.gov/cder/guidance/index.htm>.
  48. CDER KI Taskforce. Home preparation procedure for emergency administration of potassium iodide tablets to infants and small children. US Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research. 2002. Available at: <http://fda.gov/cder/drugprepare/kiprep.htm>.
  49. US Army Medical Research Institute of Infectious Diseases. *USAMRIID's Medical Management of Biological Casualties Handbook*. 4th ed. Fort Detrick, Md: Operational Medicine Department, USAMRIID; 2001. Available at: <http://www.usamriid.army.mil/education/bluebook.html>.
  50. Inglesby TB, Henderson DA, Bartlett JG, et al. Anthrax as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. *JAMA*. 1999;281:1735-1745.
  51. Hurlbut KM. *Poisindex<sup>®</sup>, Anthrax* [monograph on CD-ROM]. Vol 116. Englewood, Colo: Micromedex<sup>®</sup> Healthcare Series; 2002.
  52. Centers for Disease Control and Prevention. Update on cholera vaccine, August 2000. Available at: <http://cdc.gov/travel/other/cholera-vaccine.htm>.
  53. Henderson DA, Inglesby TV, Bartlett JG, et al. Smallpox as a biological weapon: medical and public health management. Working Group on Civilian Biodefense. *JAMA*. 1999;281:2127-2137.
  54. Weltzin R, Liu J, Pugachev KV, et al. Clonal vaccinia virus grown in cell culture as a new smallpox vaccine. *Nat Med*. 2003;9:1125-1130. Available at: <http://www.acambis.com/default.asp?id=591>.
  55. Centers for Disease Control and Prevention. Guide B: vaccination guidelines for state & local health agencies. November 2002. Available at: <http://www.bt.cdc.gov/agent/smallpox/response-plan/index.asp>.
  56. Hogan CJ, Harchelroad F. Smallpox. *Emedicine*. March 2003. Available at: <http://www.emedicine.com/emerg/topic885.htm>.
  57. Thorne CD, Hirshon JM, Himes CD, McDiarmid MA. Emergency medicine tools to manage smallpox (vaccinia) vaccination complications: clinical practice guidelines and policies and procedures. *Ann Emerg Med*. 2003;42:665-680.
  58. Centers for Disease Control and Prevention. Smallpox fact sheet: medical management of smallpox (vaccinia) vaccine adverse reactions—vaccina immune globulin and cidofovir. February 2003. Available at: <http://www.bt.cdc.gov/agent/smallpox/vaccination/mgmt-adv-reactions.asp>.